

# European Food Safety Authority



## Peer Review Report on Flupyradifurone

- Comments on the assessment report
  - Reporting table
- Pesticides peer review meeting reports
  - Evaluation table
- Comments on the additional information assessment
  - Comments on the draft EFSA conclusion

12 February 2015

## TABLE OF CONTENTS

	<b>Document</b>
00	Cover page
<b>01</b>	<b>Comments on the assessment report</b>
02	Reporting table
03	Pesticides peer review meeting reports
04	Evaluation table
05	Comments on the additional information assessment
06	Comments on the draft EFSA conclusion

Comments on the Draft Assessment Report on Flupyradifurone (NAS)

RMS NL

End of commenting period: 07.04.2014 (MS, EFSA, Applicant)

Date	Supplier	File
10.03.2014	Denmark	<a href="#">01 Flupyradifurone comments DK 2014-03-10.doc</a>
01.04.2014	Applicant	<a href="#">02 Flupyradifurone comments APPL 2014-04-01.docx</a>
07.04.2014	Austria	<a href="#">03 Flupyradifurone comments AT 2014-04-07.doc</a>
07.04.2014	France	<a href="#">04 Flupyradifurone comments FR 2014-04-07.doc</a>
07.04.2014	Sweden	<a href="#">05 Flupyradifurone comments SE 2014-04-07.doc</a>
07.04.2014	EFSA	<a href="#">06 Flupyradifurone comments EFSA 2014-04-07.doc</a>
07.04.2014	Germany	<a href="#">07 Flupyradifurone comment DE 2014-04-07.doc</a>
10.04.2014	Public	<a href="#">08 Flupyradifurone comment public - Nature et Progrès Be 2014-04-10.doc</a>
14.04.2014	Public	<a href="#">09 Flupyradifurone comment public - Igor Kondzielski IEP-NRI 2014-04-14.doc</a>

## Section 2 - Mammalian toxicology (B.6)

## 2. Mammalian toxicology (B.6)

<b>Short-term toxicity (B.6.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3.B.6.3.1, 28-day oral studies, study 3	DK: There is a statistically significant decrease in absolute and/or relative epididymis weights in all 3 dose groups	Rapporteur considers this effect not relevant because no relevant histological findings were observed. However, this effect seems to be dose related.
(2)	Vol. 3. B.6.3.4 Semichronic oral studies, study 1	DK: relative thyroid weight was also statistically significantly increased in the 500 ppm group but without histopathological findings which were observed at the higher dose of 2500 ppm. However, there seems to be dose response, supporting an effect at 500 ppm, making NOAEL 100 ppm.	

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B6.5.1, Chronic toxicity and carcinogenicity, study 1	DK: the increased incidence of colloid alteration in the thyroid was not considered adverse in the 400 ppm group because it was argued that it occurs with age in rats and was not associated with relevant follicular hypertrophy. The incidence of colloid alteration was 38 and 40 in the 400 ppm and 2000 ppm groups, respectively, taken together with an incidence of follicular cell hypertrophy of 1 and 3 in the 400 ppm and 2000 ppm groups, respectively.	The effect in the two highest doses is very similar. It should be considered if the effect observed in both dose groups is adverse or not adverse.

## Section 2 - Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol.3, B.6.6.1 Reproductive toxicity, study 2	DK: A statistically significantly decreased body weight PND 14-21 and a reduced weight gain in F2 generation in the mid- and high dose group was observed. In the F1 generation a significant decreased body weight week 10 of premating and during gestation and lactation in the mid – and high dose group was reported. The NOAEL should therefore be 100 ppm instead of 500 ppm.	The argument for not using this effect at 100 ppm is that the decrease is < 10 % but there seems to be dose- response and the effect in the F1 generation is persistent.

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol 3.B.6.9.5 Summary of toxicity studies with the metabolites	DK: Table 6.9.5-1 Summary of toxicity studies with the metabolites: 90-day dietary study Nukui T., Ikeyama S.; 1993 amended in 1997: it should be NOAEL instead of NOEL	

## Section 2 - Mammalian toxicology (B.6)

<b>Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol.3, B.6.11.1 Toxicokinetics	DK: in the summary of 90-day dietary study by Nukui T., Ikeyama S.; 1993. NOEL should be corrected to NOAEL	

## Section 4 - Environmental fate and behaviour (B.8)

## 4. Environmental fate and behaviour (B.8)

<b>PEC in soil (B.8.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.8.3, Estimation of PECsoil, Parent	DK: RMS accept PECsoil calculation for a.s. We are not sure if the calculation is correct, as we get a different result. It would be easier to check to check the calculation, if the formula and the parameters were all present in the DAR. We agree that DFOP from worst case field study (UK) should be used, but in accordance with FOCUS kinetics report, it is the slow phase DT50 that should be used (this can't be checked as it is not mentioned in the DAR).	

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.8.1.2.2, Field studies, Kinetic analysis	DK: We acknowledge that drafting the DAR is a balance between giving important information and not to provide too bulky DAR's. However, we would like to get more details on kinetic fitting of the field degradation studies (e.g. k1, k2, g), as the results are used later in the fate section.	

## Section 4 - Environmental fate and behaviour (B.8)

<b>PEC in surface water and ground water (B.8.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.8.6.3, PECgw, conversion of SFo to DFOP, pp 259	DK: Is it reasonable to estimate that 'g' by default is 0.5 for all soils were no 'g' value has been calculated.	
	Vol. 3, B.8.6.3, PECgw, Tier 2b, Time dependent sorption, hops and lettuce	DK: We have difficulties with this the use of time dependent sorption (tda) as a mean of refinement before harmonised guidelines for the derivation, use and assessment of tda has been agreed by EFSA (which to our knowledge is not the case). This is in line with the decision at the fate expert meeting at EFSA in September 2013. The gw assessment should be changed accordingly.	
	Vol. 3, B.8.6.3, PECgw, metabolites	DK: We are of the opinion, that all metabolites are relevant and refined gw-modelling should be pursued until the concentration for all soils (at least in one zone for zonal approach or majority for inter-zonal approach) are under 0.1 ug/L. The gw assessment should be changed accordingly.	

## Section 5 - Ecotoxicology (B.9)

## 5. Ecotoxicology (B.9)

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.9.2.5.5, Refined RA aquatic invertebrates	DK: For the acute RA to invertebrates from use in lettuce, not enough scenarios show TER values above the trigger. In our view, furthered refinements are required in order to address the risk to aquatic invertebrates, e.g. mesocosm study	

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol 3, B.9.4.1.3.1 Chronic toxicity on adult honeybees, B.9.4.1.3.1 Chronic toxicity on adult honeybees, STUDY IIA, 8.16.1/01	DK: We agree with RMS conclusion regarding control mortality. We would have liked at reference substance (toxic standard) in the study, but as this is not the case, we would like a statement in the study summary regarding previous exposure of bees to other pesticides.	
	Vol 3, B.9.4.1.3.1 Chronic toxicity on adult honeybees, B.9.4.1.3.1 Chronic toxicity on adult honeybees, Study IIA 8.16.1/09, Study IIA 8.16.1 /02, Study IIA 8.16.1/03, Study IIA 8.16.1 /04, Study IIA	DK: We would have liked at reference substance (toxic standard) in the study, but as this is not the case, we would like a statement in the study summary regarding previous exposure of bees to other pesticides.	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	8.16.1 /05 and Study IIA 8.16.1 /06		

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 1/56

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

### 1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

Identity (B.1, Annex C)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)			

Physical and chemical properties of the active substance (B.2.1)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

Physical, chemical and technical properties of the formulation (B.2.2)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

Further information (B.3)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

# Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 2/56

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Methods of analysis (B.5)																																																																																																																																																												
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations																																																																																																																																																									
(1)	Vol. 3, B.5.2, analytical methods for plants, plant products...	<p><u>BCS</u> (page 70): Recovery results of method 01330/<b>M001</b> (modification of method for commodities with high oil content = rape, seed), submitted in November 2012 in the updated version of the Annex II dossier, are not included, neither for the method (KIIA 4.3/10) nor the ILV (KIIA 4.3/11). The modification of the method showed improved recoveries for DFA in rape, seed.</p>	<p>In order to improve the recoveries for rape, seed, a modification of method 01330 was submitted in the updated version of the Annex II dossier (November 2012):</p> <p><b>Method 01330/M001: Recoveries for BYI 02960</b></p> <table border="1"> <thead> <tr> <th>Sample material</th> <th>FL* [mg/kg]</th> <th colspan="4">Individual values [%]</th> <th>Mean value [%]</th> <th>RS D [%]</th> <th>LOQ [mg/kg]</th> </tr> </thead> <tbody> <tr> <td colspan="2"><i>QUANTIFICATION MRM (289/126)</i></td><td>0.01</td><td>104</td><td>106</td><td>100</td><td>97</td><td>99</td><td>101</td><td>3.7</td></tr> <tr> <td rowspan="2">rape / seed</td><td>0.10</td><td>95</td><td>99</td><td>91</td><td>99</td><td>99</td><td>97</td><td>3.7</td><td>0.01</td></tr> <tr> <td></td><td colspan="4"><i>Overall recovery (n = 10)</i></td><td>99</td><td>4.2</td><td></td><td></td></tr> <tr> <td colspan="2"><i>CONFIRMATORY MRM (289/90)</i></td><td>0.01</td><td>107</td><td>105</td><td>107</td><td>104</td><td>103</td><td>105</td><td>1.7</td></tr> <tr> <td rowspan="2">rape / seed</td><td>0.10</td><td>99</td><td>102</td><td>95</td><td>102</td><td>101</td><td>100</td><td>3.0</td><td>0.01</td></tr> <tr> <td></td><td colspan="4" rowspan="2"><i>Overall recovery (n = 10)</i></td><td>103</td><td>3.6</td><td></td><td></td></tr> <tr> <td colspan="7"><b>Method 01330/M001: Recoveries for DFA</b></td></tr> <tr> <td colspan="2"></td><td>Sample material</td><td>FL* [mg/kg]</td><td colspan="4">Individual values [%]</td><td>Mean value [%]</td><td>RS D [%]</td></tr> <tr> <td colspan="2"></td><td colspan="2"><i>HILIC COLUMN (PRIMARY)</i></td><td>0.02</td><td>84</td><td>84</td><td>80</td><td>85</td><td>85</td></tr> <tr> <td rowspan="2">rape / seed</td><td>0.20</td><td>71</td><td>74</td><td>77</td><td>71</td><td>74</td><td>73</td><td>2.5</td><td>0.02</td></tr> <tr> <td></td><td colspan="4"><i>Overall recovery (n = 10)</i></td><td>79</td><td>3.4</td><td></td><td></td></tr> <tr> <td colspan="2"></td><td colspan="2"><i>HYPERCARB COLUMN (CONFIRMATORY)</i></td><td>0.02</td><td>73</td><td>78</td><td>80</td><td>82</td><td>82</td></tr> <tr> <td rowspan="2">rape / seed</td><td>0.20</td><td>94</td><td>80</td><td>89</td><td>81</td><td>90</td><td>88</td><td>4.7</td><td>0.02</td></tr> <tr> <td></td><td colspan="4" rowspan="2"><i>Overall recovery (n = 10)</i></td><td>83</td><td>8.8</td><td></td><td></td></tr> <tr> <td colspan="7"><b>ILV of method 01330/M001: Recoveries for BYI 02960</b></td></tr> </tbody> </table>	Sample material	FL* [mg/kg]	Individual values [%]				Mean value [%]	RS D [%]	LOQ [mg/kg]	<i>QUANTIFICATION MRM (289/126)</i>		0.01	104	106	100	97	99	101	3.7	rape / seed	0.10	95	99	91	99	99	97	3.7	0.01		<i>Overall recovery (n = 10)</i>				99	4.2			<i>CONFIRMATORY MRM (289/90)</i>		0.01	107	105	107	104	103	105	1.7	rape / seed	0.10	99	102	95	102	101	100	3.0	0.01		<i>Overall recovery (n = 10)</i>				103	3.6			<b>Method 01330/M001: Recoveries for DFA</b>									Sample material	FL* [mg/kg]	Individual values [%]				Mean value [%]	RS D [%]			<i>HILIC COLUMN (PRIMARY)</i>		0.02	84	84	80	85	85	rape / seed	0.20	71	74	77	71	74	73	2.5	0.02		<i>Overall recovery (n = 10)</i>				79	3.4					<i>HYPERCARB COLUMN (CONFIRMATORY)</i>		0.02	73	78	80	82	82	rape / seed	0.20	94	80	89	81	90	88	4.7	0.02		<i>Overall recovery (n = 10)</i>				83	8.8			<b>ILV of method 01330/M001: Recoveries for BYI 02960</b>										
Sample material	FL* [mg/kg]	Individual values [%]				Mean value [%]	RS D [%]	LOQ [mg/kg]																																																																																																																																																				
<i>QUANTIFICATION MRM (289/126)</i>		0.01	104	106	100	97	99	101	3.7																																																																																																																																																			
rape / seed	0.10	95	99	91	99	99	97	3.7	0.01																																																																																																																																																			
		<i>Overall recovery (n = 10)</i>				99	4.2																																																																																																																																																					
<i>CONFIRMATORY MRM (289/90)</i>		0.01	107	105	107	104	103	105	1.7																																																																																																																																																			
rape / seed	0.10	99	102	95	102	101	100	3.0	0.01																																																																																																																																																			
		<i>Overall recovery (n = 10)</i>				103	3.6																																																																																																																																																					
<b>Method 01330/M001: Recoveries for DFA</b>																																																																																																																																																												
		Sample material	FL* [mg/kg]	Individual values [%]				Mean value [%]	RS D [%]																																																																																																																																																			
		<i>HILIC COLUMN (PRIMARY)</i>		0.02	84	84	80	85	85																																																																																																																																																			
rape / seed	0.20	71	74	77	71	74	73	2.5	0.02																																																																																																																																																			
		<i>Overall recovery (n = 10)</i>				79	3.4																																																																																																																																																					
		<i>HYPERCARB COLUMN (CONFIRMATORY)</i>		0.02	73	78	80	82	82																																																																																																																																																			
rape / seed	0.20	94	80	89	81	90	88	4.7	0.02																																																																																																																																																			
		<i>Overall recovery (n = 10)</i>				83	8.8																																																																																																																																																					
<b>ILV of method 01330/M001: Recoveries for BYI 02960</b>																																																																																																																																																												

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 3/56

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Methods of analysis (B.5)													
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations										
			Sample material	FL [mg/kg]	Individual values [%]	Mean value [%]	RS D [%]						
<i>QUANTIFICATION MRM (289/126)</i>													
			rape / seed	0.01	76 85 83 83 78	81	4.7						
				0.10	93 94 94 89 93	93	2.4						
					<i>Overall recovery (n = 10)</i>	87	7.7						
<i>CONFIRMATORY MRM (289/90)</i>													
			rape / seed	0.01	77 84 85 82 81	82	3.9						
				0.10	94 93 92 88 95	92	2.8						
					<i>Overall recovery (n = 10)</i>	87	7.2						
ILV of method 01330/M001: Recoveries for DFA													
<table border="1"> <thead> <tr> <th>Sample material</th><th>FL [mg/kg]</th><th>Individual values [%]</th><th>Mean value [%]</th><th>RS D [%]</th><th>LOQ [mg/kg]</th></tr> </thead> </table>								Sample material	FL [mg/kg]	Individual values [%]	Mean value [%]	RS D [%]	LOQ [mg/kg]
Sample material	FL [mg/kg]	Individual values [%]	Mean value [%]	RS D [%]	LOQ [mg/kg]								
<i>HILIC COLUMN (PRIMARY)</i>													
			rape / seed	0.02	96 103 107 108 98	103	5.1						
				0.20	95 102 102 97 100	99	3.0						
					<i>Overall recovery (n = 10)</i>	101	4.3						
<i>HYPERCARB COLUMN (CONFIRMATORY)</i>													
			rape / seed	0.02	90 102 94 110 92	97	8.6						
				0.20	86 92 93 87 92	90	3.3						
					<i>Overall recovery (n = 10)</i>	94	7.6						

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(2)	Vol. 3, B.5.2, analytical methods for plants, plant	BCS (page 71): Please include method 01330/M001	Matrix: Plant Analyte: BYI 02960, DFA

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 4/56

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	products...		Method: 01330/M001 Method principle: HPLC-MS/MS LOQ: BYI 02960: 0.01 mg/kg; DFA: 0.02 mg/kg Reference: IIA 4.3/10 & IIA 4.3/10
(3)	Vol. 3, B.5.2, analytical methods for plants, plant products...	<u>BCS (page 71):</u> Please include the reference to method RARVP013 (= method 01304) and the respective extraction efficiency study	Reference: IIA 4.3/3 & IIA 4.3/4
(4)	Vol. 3, B.5.2, analytical methods for plants, plant products...	<u>BCS (page 71):</u> Please indicate that methods RARVP013 & 01212 (plant) and method RV-004-AII-04 (animal) are data collection methods	

## Section 2 - Mammalian toxicology (B.6)

**2. Mammalian toxicology (B.6)**

<b>Toxicokinetics (B.6.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Acute toxicity (B.6.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Short-term toxicity (B.6.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Genotoxicity (B.6.4)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 6/56

### Section 2 - Mammalian toxicology (B.6)

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Reproductive toxicity (B.6.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Neurotoxicity (B.6.7)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 7/56

### Section 2 - Mammalian toxicology (B.6)

<b>Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Toxicity of the product(s) (B.6.11)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Dermal absorption (B.6.12)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Toxicity of non-active substances (B.6.13)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 8/56

### Section 2 - Mammalian toxicology (B.6)

<b>Exposure data (B.6.14)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

## Section 3 - Residues (B.7)

## 3. Residues (B.7)

<b>Storage Stability (B.7.0)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Metabolism in plants (B.7.1)</b>																																										
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations																																							
(1)	Vol. 3, B.7.1.1, Metabolism study in apple	<u>BCS</u> (page 26; Table 7.1.1-8): DFEAF was not detected in the conventional extract of apple fruits; residue values are not correctly assigned to metabolites	Table 7.1.1-8: Distribution of radioactivity in apple fruit and leaves after a single foliar application of [furanone-4- <sup>14</sup> C]flupyradifurone <table border="1"> <thead> <tr> <th></th> <th colspan="2">apple fruits</th> </tr> <tr> <th>TRR [mg a.s. equiv/kg] =</th> <th colspan="2">0.28</th> </tr> <tr> <th>BYI 02960-</th> <th>% TRR</th> <th>mg/kg</th> </tr> </thead> <tbody> <tr> <td align="center" colspan="3"><i>Conventional extraction</i></td></tr> <tr> <td>parent compound</td><td>7.4</td><td>0.021</td></tr> <tr> <td>glucose/carbohydrates (M45)</td><td>50.3</td><td>0.141</td></tr> <tr> <td>DFEAF (M34)</td><td>---</td><td>---</td></tr> <tr> <td>acetic acid-glyc (M16)</td><td>0.3</td><td>0.001</td></tr> <tr> <td>OH-glyc (M8)</td><td>0.4</td><td>0.001</td></tr> <tr> <td>acetic acid (M15)</td><td>0.2</td><td>0.001</td></tr> <tr> <td>difluoroethyl-OH-glyc (M11)</td><td>---</td><td>---</td></tr> <tr> <td>OH (M3)</td><td>---</td><td>---</td></tr> <tr> <td align="center"><b>Subtotal identified</b></td><td><b>58.7</b></td><td><b>0.164</b></td></tr> </tbody> </table>		apple fruits		TRR [mg a.s. equiv/kg] =	0.28		BYI 02960-	% TRR	mg/kg	<i>Conventional extraction</i>			parent compound	7.4	0.021	glucose/carbohydrates (M45)	50.3	0.141	DFEAF (M34)	---	---	acetic acid-glyc (M16)	0.3	0.001	OH-glyc (M8)	0.4	0.001	acetic acid (M15)	0.2	0.001	difluoroethyl-OH-glyc (M11)	---	---	OH (M3)	---	---	<b>Subtotal identified</b>	<b>58.7</b>	<b>0.164</b>
	apple fruits																																									
TRR [mg a.s. equiv/kg] =	0.28																																									
BYI 02960-	% TRR	mg/kg																																								
<i>Conventional extraction</i>																																										
parent compound	7.4	0.021																																								
glucose/carbohydrates (M45)	50.3	0.141																																								
DFEAF (M34)	---	---																																								
acetic acid-glyc (M16)	0.3	0.001																																								
OH-glyc (M8)	0.4	0.001																																								
acetic acid (M15)	0.2	0.001																																								
difluoroethyl-OH-glyc (M11)	---	---																																								
OH (M3)	---	---																																								
<b>Subtotal identified</b>	<b>58.7</b>	<b>0.164</b>																																								
(2)	Vol. 3, B.7.1.2, Confined rotational crop study	<u>BCS</u> (page 99; Table 7.1.2-35): Table 7.1.2-35 has to be re-named into Table 7.1.2-15																																								

## Section 3 - Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>																																																						
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations																																																			
(1)	Vol. 3; B.7.2, Dietary burden of livestock	<p><u>BCS</u> (page 115 ff; Table 7.2-1 &amp; 7.2-2):            It's more conclusive to calculate the dietary burden based on (1) the <u>total BYI 02960 residues</u> (BYI 02960, DFA and DFEAF) detected in the field trials and (2) <u>separate</u> the residues into <u>BYI 02960</u> and <u>DFA</u> residues in the worst-case diet to estimate the different transfer of the two compounds in animal matrices on the basis of the different transfer factors determined in the feeding studies.</p>	<p>Input data to calculate dietary burdens for poultry and ruminants</p> <table border="1"> <thead> <tr> <th>Commodity</th> <th>Total residue* [mg/kg]</th> <th>Comment</th> </tr> </thead> <tbody> <tr> <td><i>Primary crops</i></td> <td></td> <td></td> </tr> <tr> <td>apple, pomace wet</td> <td>0.17 (0.125 x 1.34)</td> <td>STMR-p; STMR (fruit) PF = 1.34</td> </tr> <tr> <td><i>Rotational crops</i></td> <td></td> <td></td> </tr> <tr> <td>grass</td> <td>0.41</td> <td>HR (barley forage)</td> </tr> <tr> <td>rape forage</td> <td>0.41</td> <td>HR (barley forage)</td> </tr> <tr> <td>silage</td> <td>0.41</td> <td>HR (barley forage)</td> </tr> <tr> <td>cereal grain</td> <td>0.35</td> <td>STMR (barley grain)</td> </tr> <tr> <td>cereal grain, bran</td> <td>2.24 (0.35 x 6.4)</td> <td>STMR-p STMR (barley grain); PF (wheat white flour bran) = 6.4<sup>1</sup></td> </tr> <tr> <td>cereal straw</td> <td>0.39</td> <td>HR (barley straw)</td> </tr> <tr> <td>cereal hay</td> <td>0.39</td> <td>HR (barley straw)</td> </tr> <tr> <td>cabbage, kale</td> <td>0.21</td> <td>HR (lettuce at commercial harvest)</td> </tr> <tr> <td>root vegetables, roots</td> <td>0.14</td> <td>HR (turnip, roots)</td> </tr> <tr> <td>root vegetables, tops</td> <td>0.24</td> <td>HR (turnip, tops)</td> </tr> <tr> <td>potato, tuber</td> <td>0.27</td> <td>HR</td> </tr> <tr> <td>oilseed rape, meal</td> <td>0.10</td> <td>STMR of RAC; PF &lt;1</td> </tr> <tr> <td>pulses</td> <td>1.55</td> <td>STMR (field pea)</td> </tr> </tbody> </table> <p>* total residue (calc.) = sum of parent BYI 0296, DFA and DFEAF</p>	Commodity	Total residue* [mg/kg]	Comment	<i>Primary crops</i>			apple, pomace wet	0.17 (0.125 x 1.34)	STMR-p; STMR (fruit) PF = 1.34	<i>Rotational crops</i>			grass	0.41	HR (barley forage)	rape forage	0.41	HR (barley forage)	silage	0.41	HR (barley forage)	cereal grain	0.35	STMR (barley grain)	cereal grain, bran	2.24 (0.35 x 6.4)	STMR-p STMR (barley grain); PF (wheat white flour bran) = 6.4 <sup>1</sup>	cereal straw	0.39	HR (barley straw)	cereal hay	0.39	HR (barley straw)	cabbage, kale	0.21	HR (lettuce at commercial harvest)	root vegetables, roots	0.14	HR (turnip, roots)	root vegetables, tops	0.24	HR (turnip, tops)	potato, tuber	0.27	HR	oilseed rape, meal	0.10	STMR of RAC; PF <1	pulses	1.55	STMR (field pea)
Commodity	Total residue* [mg/kg]	Comment																																																				
<i>Primary crops</i>																																																						
apple, pomace wet	0.17 (0.125 x 1.34)	STMR-p; STMR (fruit) PF = 1.34																																																				
<i>Rotational crops</i>																																																						
grass	0.41	HR (barley forage)																																																				
rape forage	0.41	HR (barley forage)																																																				
silage	0.41	HR (barley forage)																																																				
cereal grain	0.35	STMR (barley grain)																																																				
cereal grain, bran	2.24 (0.35 x 6.4)	STMR-p STMR (barley grain); PF (wheat white flour bran) = 6.4 <sup>1</sup>																																																				
cereal straw	0.39	HR (barley straw)																																																				
cereal hay	0.39	HR (barley straw)																																																				
cabbage, kale	0.21	HR (lettuce at commercial harvest)																																																				
root vegetables, roots	0.14	HR (turnip, roots)																																																				
root vegetables, tops	0.24	HR (turnip, tops)																																																				
potato, tuber	0.27	HR																																																				
oilseed rape, meal	0.10	STMR of RAC; PF <1																																																				
pulses	1.55	STMR (field pea)																																																				

## Section 3 - Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>																																												
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations																																									
			<p><sup>†</sup> below LOQ</p> <p><sup>1</sup> average EU processing factor of 6.4 for wheat was used as worst-case scenario, NAFTA processing factor accounted for 1.6</p> <p>=&gt; processing factors for <u>total residue</u> can be used when estimating the worst-case diet</p> <p><b>Poultry</b></p> <p>(1) Worst-case diet for poultry</p> <table border="1"> <thead> <tr> <th>Commodity</th><th>DM intake (%)</th><th>Residue intake over DM intake</th><th>Actual contribution to total DM intake (%)</th><th>Actual contribution to total residue intake (mg/kg bw/d)</th></tr> </thead> <tbody> <tr> <td>Wheat bran</td><td>15</td><td>0.001590</td><td>15</td><td>0.023844</td></tr> <tr> <td><b>Peas (dry)</b></td><td><b>30</b></td><td><b>0.001138</b></td><td><b>30</b></td><td><b>0.034149</b></td></tr> <tr> <td>Potatoes</td><td>20</td><td>0.001137</td><td>20</td><td>0.022737</td></tr> <tr> <td>Cabbage</td><td>5</td><td>0.000947</td><td>5</td><td>0.004737</td></tr> <tr> <td>Rape seed</td><td>10</td><td>0.000073</td><td>10</td><td>0.000734</td></tr> <tr> <td><b>Sum</b></td><td></td><td></td><td><b>80</b></td><td><b>0.086201</b></td></tr> </tbody> </table> <p>⇒ Maximum dietary burden: 0.0862013 mg/kg bw/d = 1.364854 mg/kg dry feed</p> <p>⇒ Highest contributor: pea (dry)</p> <p>(2) Calculation of the proportion of the individual components (BYI 02960 and DFA) in the relevant residue in poultry worst-case diet</p> <table border="1"> <thead> <tr> <th>Crop</th><th>Residue levels (mg/kg)</th><th>Levels in dry matter</th><th>DM intake (%)</th><th>Dietary burden</th></tr> </thead> </table>		Commodity	DM intake (%)	Residue intake over DM intake	Actual contribution to total DM intake (%)	Actual contribution to total residue intake (mg/kg bw/d)	Wheat bran	15	0.001590	15	0.023844	<b>Peas (dry)</b>	<b>30</b>	<b>0.001138</b>	<b>30</b>	<b>0.034149</b>	Potatoes	20	0.001137	20	0.022737	Cabbage	5	0.000947	5	0.004737	Rape seed	10	0.000073	10	0.000734	<b>Sum</b>			<b>80</b>	<b>0.086201</b>	Crop	Residue levels (mg/kg)	Levels in dry matter	DM intake (%)	Dietary burden
Commodity	DM intake (%)	Residue intake over DM intake	Actual contribution to total DM intake (%)	Actual contribution to total residue intake (mg/kg bw/d)																																								
Wheat bran	15	0.001590	15	0.023844																																								
<b>Peas (dry)</b>	<b>30</b>	<b>0.001138</b>	<b>30</b>	<b>0.034149</b>																																								
Potatoes	20	0.001137	20	0.022737																																								
Cabbage	5	0.000947	5	0.004737																																								
Rape seed	10	0.000073	10	0.000734																																								
<b>Sum</b>			<b>80</b>	<b>0.086201</b>																																								
Crop	Residue levels (mg/kg)	Levels in dry matter	DM intake (%)	Dietary burden																																								

# Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 12/56

## Section 3 - Residues (B.7)

Metabolism in livestock (B.7.2)										
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations							
			total res.*	BYI 02960	DFA	% in crop	residue (mg/kg)	mg/kg bw/d (mg/kg feed)		
<b>Poultry</b>										
		Wheat bran	2.24	0.06		89	0.067	15 0.001 0.010		
		Peas (dry)	1.55	<0.01		86	0.012	5 <0.001 0.001		
		Potatoes	0.27	<0.01		15	0.067	20 0.001 0.013		
		Cabbage	0.21	0.08		14	0.571	30 0.011 0.171		
		Rape seed	0.10	<0.01		86	0.012	10 <0.001 0.001		
		<i>Subtotal BYI 02960:</i>		0.17				0.012 0.197		
		Wheat bran	2.24		2.11	89	2.371	15 0.022 0.356		
		Peas (dry)	1.55		1.55	86	1.802	5 0.006 0.090		
		Potatoes	0.27		0.25	15	1.667	20 0.021 0.333		
		Cabbage	0.21		0.12	14	0.857	30 0.016 0.257		
		Rape seed	1.10		0.08	86	0.093	10 0.001 0.009		
		<i>Subtotal DFA:</i>			4.11			0.066 1.046		
		<i>Totals:</i>					80	0.078 1.242		
<b>Ruminants</b>										
(1) Worst-case diet for dairy ruminants										
Commodity	DM intake (%)	Residue intake over DM intake		Actual contribution to total DM intake (%)	Actual contribution to total residue intake (mg/kg bw/d)					
Wheat bran	20	0.000915		20	0.018304					

## **Comments of Applicant on the draft assessment report on flupyradifurone**

(01.04.2014) 13/56

### Section 3 - Residues (B.7)

## Section 3 - Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>							
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations				
			the actual residues expected in feed commodities:				
			Dietary burden (mg/kg feed)	Matrix	Transfer factor	Resulting residue (mg/kg)	
<i>BYI 02960</i>							
0.093					milk	0.009 <sup>1</sup>	0.001
					muscle	0.013 <sup>1</sup>	0.001
					fat	0.009 <sup>1</sup>	0.001
					liver	0.036 <sup>1</sup>	0.003
					kidney	0.037 <sup>1</sup>	0.003
<i>DFA</i>							
1.954					milk	0.030 <sup>2</sup>	0.059
					muscle	0.097 <sup>2</sup>	0.190
					fat	0.086 <sup>2</sup>	0.168
					liver	0.097 <sup>2</sup>	0.190
					kidney	0.131 <sup>2</sup>	0.256
<sup>1</sup> TF for total residue for enforcement/risk assessment = parent BYI 02960 plus DFA; determined for 1X dose level in cattle feeding study							
<sup>2</sup> TF for DFA, only; determined for 49X dose level in cattle feeding study							
(2)	Vol. 3; B.7.2, Dietary burden of livestock	<u>BCS</u> (page 117; Table 7.2-2): Table 7.2-2 has to be re-named into Table 7.2-3 Proposal: Use the worst-case dietary burden calculated above.	<b>Table 7.2-3</b> Theoretical dietary intake calculations for livestock for total flupyradifurone residues				
			Maximum dietary burden mg/kg bw/d (mg/kg dry feed)	Median dietary burden mg/kg bw/d (mg/kg dry feed)	Highest contributing commodity	Dietary burden triggered?	
<i>Total BYI 02960 residue (BYI 02960, DFA and DFEAF)</i>							

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 15/56

### Section 3 - Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>					
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations		
			Dairy ruminant	0.077941 (2.143371)	0.035329 0.971546
			Meat ruminant	0.091859 (2.143371)	0.047880 (1.117198)
			Pig	0.084543 (2.113587)	0.049902 (1.247557)
			Poultry	0.086201 (1.364854)	0.058728 (0.929854)

<b>Residue definition (B.7.3)</b>				
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations	
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>		

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations	
(1)	Vol. 3, B.7.4, Use pattern	BCS (page 146, Table 7.4-1): Add frames in line 3 of table		

## Section 3 - Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(2)	Vol. 3, B.7.5, Critical GAPs	<u>BCS</u> (page 148, Table 7.5-1): Add frames in line 3 of table Add "home and garden use" as critical GAP	The "home and garden field use" represents the critical <u>field use</u> for lettuce. It was agreed with the RMS to conduct the field residue trials according to this cGAP since this GAP is more critical in respect to possible residues compared to the "agricultural field use". Thus it could be the driver for the MRL.  Therefore this field use (2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; max. 1 use per <b>12 months</b> ) should be added in the table.
(3)	Vol. 3, B.7.6, Residue trials	<u>BCS</u> (page 164, Table 7.6.2-1): Header is not in line with outdoor results shown => residue values of "home and garden use" (2 x 0.125 g a.s./ha, interval = 10 days, PHI = 3 days) should be shown instead of values of "agricultural use" (1 x 0.125 g a.s./ha, PHI = 10 days)	<b>2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; SEU:</b> Risk assessment: 0.39; 0.43; 0.53; 0.78; 1.2; 1.6; 2.2; 2.7; 3.2 mg/kg Enforcement: 0.38; 0.42; 0.53; 0.76; 1.1; 1.6; 2.2; 2.7; 3.2 mg/kg  <b>2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; NEU:</b> Risk assessment: 0.14; 0.40; 0.47; 0.61; 0.71; 0.87; 1.0; 1.6; 3.0 mg/kg Enforcement: 0.13; 0.39; 0.46; 0.60; 0.70; 0.85; 1.0; 1.5; 3.0 mg/kg
(4)	Vol. 3, B.7.6, Residue trials	<u>BCS</u> (page 165, Table 7.6.2-2): Add results of trials conducted according to the "home and garden" use pattern	<b>2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; SEU:</b> Risk assessment: 0.39; 0.43; 0.53; 0.78; 1.2; 1.6; 2.2; 2.7; 3.2 mg/kg Enforcement: 0.38; 0.42; 0.53; 0.76; 1.1; 1.6; 2.2; 2.7; 3.2 mg/kg  <b>2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; NEU:</b> Risk assessment: 0.14; 0.40; 0.47; 0.61; 0.71; 0.87; 1.0; 1.6; 3.0 mg/kg Enforcement: 0.13; 0.39; 0.46; 0.60; 0.70; 0.85; 1.0; 1.5; 3.0 mg/kg

<b>Processing (B.7.7)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.7.7, Processing	<u>BCS</u> (page 190, Table 7.7.2-1):	

## Section 3 - Residues (B.7)

<b>Processing (B.7.7)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		Add frame lines in table	

<b>Livestock feeding (B.7.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 199, Table 7.8.1-2): Add frame lines in table	
(2)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 204, wrong dose level mentioned) The estimation of the dose of DFA [...] was conducted on the basis of the data collected for the highest dose group ( <b>49N</b> in EU), ...	
(3)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 211, wrong dose level mentioned) Additional 25-day milk was collected [...] from one control cow and three of the <b>49N</b> dose group cows.	
(4)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 216, wrong range of RSD) As the relative standard deviations [...] in the range of <b>1-13%</b> - all...	
(5)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 216, please correct residue value for kidney in the 3 <sup>rd</sup> paragraph): [...] were as follows: 0.063 mg/kg in muscle, 0.041 mg/kg in fat, 0.165 mg/kg in liver, and <b>0.176 mg/kg in kidney</b> , respectively. In milk taken on day 28, total residues in the 2N group were 0.043 mg/kg.	

## Section 3 - Residues (B.7)

<b>Livestock feeding (B.7.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(6)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 216, wrong dose level mentioned in 4 <sup>th</sup> paragraph) In addition to the general testing [...] samples from the <b>49N</b> dose group...	
(7)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 219, wrong Table No.) Please change: Table 7.8.1-12 has to be <b>Table 7.8.1-14</b> ; the numbering of all succeeding tables has to be changed as well.	
(8)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 219, wrong dose level mentioned in 1st paragraph) [...] at average <i>actual</i> dose rates of 4.8 mg/kg feed (2N dose), 23 mg/kg feed (8N, which approximated a nominal NAFTA 1N dose), 50 mg/kg feed (18N), and 135 mg/kg feed ( <b>49N</b> ).	
(9)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 219, wrong dose level mentioned in 3 <sup>rd</sup> paragraph): Highest residue were determined at day 17 in the <b>49N</b> milk samples,...	
(10)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 223, Table 7.8.1-14 or Table 7.8.1-16 after correction of numbering): Add frame lines in table for 2N dose	

<b>Succeeding/Rotational crops (B.7.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.7.9.1, Field	<u>BCS</u> (page 245, plant-back interval for potato):	

## Section 3 - Residues (B.7)

<b>Succeeding/Rotational crops (B.7.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	rotational crops	Specify range of plant-back interval in 1 <sup>st</sup> paragraph: Potatoes were planted <b>25-33 DAT</b> and harvested 98-137 DAT.	
(2)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 246, harvest interval for leek): Please correct harvest interval: Leek was planted 26-33 DAT and harvested <b>97-130 DAT</b> (BBCH 49)	
(3)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 247, plant-back interval for cucumber and growth stage at harvest): Please correct: Cucumbers were planted <b>25-30 DAT</b> and harvested 69-83 DAT (BBCH 71-79)	
(4)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 248, plant-back interval for onion): Please correct: Onion was [...] sown directly on the plot (northern trials) <b>25-33 DAT</b> ...	
(5)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 256-261, trial numbers, plant-back interval and interval between treatment and harvest): Please correct the following trial numbers and the plant-back intervals 11-2250 => <b>11-2550</b> (PBI = <b>31</b> ; 33; <b>25</b> ; 30 days) 11-2251 => <b>11-2551</b> 11-2252 => <b>11-2552</b> 11-2253 => <b>11-2553</b> (PBI = 30; 33; 25; <b>28</b> days) 11-2255 => <b>11-2555</b>	

## Section 3 - Residues (B.7)

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>																											
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations																								
(1)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	<u>BCS</u> (page 266, proposed import tolerances): dry bean and dry pea seeds should be summarized as “ <u>pulses</u> ”. Proposed IT (pulses): <b>10 mg/kg</b> => estimated based on EU rotational data and AUS seasonal rate of 450 g a.s./ha and applying a soil accumulation factor	Residue data from EU limited rotational crop study with field peas ( $2 \times 0.125 \text{ g a.s./ha} = 250 \text{ g a.s./ha}$ ): 2.3; 1.0; 0.67; 2.1 mg/kg => extrapolation to AUS rate ( $3 \times 150 \text{ g a.s./ha} = 450 \text{ g a.s./ha}$ ) => multiplication with factor 1.8: 4.14; 1.8; 1.21; 3.78 mg/kg => considering a soil accumulation factor of 1.2 (probably requested by AUS): 4.97; 2.16; 1.45; 4.54 mg/kg => MRL proposal according OECD: 10 mg/kg																								
(2)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	<u>BCS</u> (page 266, proposed import tolerances): field corn grain => in accordance with sweet corn an EC MRL of 1.5 mg/kg should be proposed (based on rotational data for cereals)																									
(3)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	<u>BCS</u> (page 266, proposed import tolerances): legume vegetables => no import tolerance is needed for legume vegetables since there is no significant trade => EC MRL of 2 should apply																									
(4)	Vol. 3, B.7.12, proposed MRLs (animal matrices)	<u>BCS</u> (page 267, dietary burden according to notifier): The text refers to the dietary burden calculated by BCS in the Annex II dossier. This calculation considers also future uses. Either include this dietary burden calculation or refer to the dietary burden calculated in B.7.2.	<p><b>Poultry:</b>  Calculation of the proportion of the individual components (BYI 02960 and DFA) in the relevant residue in poultry worst-case diet</p> <table border="1"> <thead> <tr> <th rowspan="2">Crop</th> <th colspan="3">Residue levels (mg/kg)</th> <th colspan="2">Levels in dry matter</th> <th rowspan="2">DM intake (%)</th> <th colspan="2">Dietary burden</th> </tr> <tr> <th>total res.*</th> <th>BYI 02960</th> <th>DFA</th> <th>% in crop</th> <th>residue (mg/kg)</th> <th>mg/kg bw/d</th> <th>(mg/kg feed)</th> </tr> </thead> <tbody> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table>	Crop	Residue levels (mg/kg)			Levels in dry matter		DM intake (%)	Dietary burden		total res.*	BYI 02960	DFA	% in crop	residue (mg/kg)	mg/kg bw/d	(mg/kg feed)								
Crop	Residue levels (mg/kg)				Levels in dry matter		DM intake (%)	Dietary burden																			
	total res.*	BYI 02960	DFA	% in crop	residue (mg/kg)	mg/kg bw/d		(mg/kg feed)																			

# Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 21/56

## Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)										
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations							
		Proposal: Use dietary burden calculation and the estimated ratio of BYI 02960 and DFA in the worst-case diet as proposed in this commenting table.	Poultry							
			Wheat bran	2.24	0.06	89	0.067	15		
			Peas (dry)	1.55	<0.01	86	0.012	5		
			Potatoes	0.27	<0.01	15	0.067	20		
			Cabbage	0.21	0.08	14	0.571	30		
			Rape seed	0.10	<0.01	86	0.012	10		
			<i>Subtotal BYI 02960:</i>		0.17			0.012		
								0.197		
			Wheat bran	2.24		2.11	89	2.371		
			Peas (dry)	1.55		1.55	86	1.802		
			Potatoes	0.27		0.25	15	1.667		
			Cabbage	0.21		0.12	14	0.857		
			Rape seed	1.10		0.08	86	0.093		
			<i>Subtotal DFA:</i>		4.11			0.066		
								1.046		
			<i>Totals:</i>							
							80	0.078		
								1.242		
			Estimation of theoretical residues resulting from feeding grown BYI 02960 residues (comprising BYI 02960 and DFA) to poultry in a ratio relevant to the actual residues expected in feed commodities => corresponds to <b>Table 7.12.1-3 (chicken):</b>							
			Dietary burden (mg/ kg feed)	Matrix	Transfer factor*	Resulting residue (mg/kg)				
			<i>BYI 02960</i>							
			0.197	egg	0.038 <sup>#</sup>	0.007				
				muscle	0.062 <sup>#</sup>	0.012				

# Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 22/56

## Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																																	
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations																																														
			<table border="1"> <tr> <td></td><td>fat</td><td>0.026<sup>#</sup></td><td>0.005</td></tr> <tr> <td></td><td>offal</td><td>0.076<sup>#</sup></td><td>0.015</td></tr> <tr> <td colspan="4"><i>DFA</i></td></tr> <tr> <td rowspan="4">1.046</td><td>egg</td><td>0.097</td><td>0.101</td></tr> <tr> <td>muscle</td><td>0.172</td><td>0.180</td></tr> <tr> <td>fat</td><td>0.060</td><td>0.063</td></tr> <tr> <td>offal</td><td>0.216</td><td>0.226</td></tr> </table> <p>* Transfer factor determined for 1x dose level in poultry feeding study  <sup>#</sup> TF for total residue for enforcement/risk assessment = parent BYI 02960 plus DFA</p> <p>Levels of the relevant residue of BYI 02960 (comprising BYI 02960 and DFA) in poultry tissues and eggs expected after feeding a worst-case diet containing residues due to treatment of crops with BYI 02960  =&gt; corresponds to <b>Table 7.12.1-4 (chicken):</b></p> <table border="1"> <thead> <tr> <th>Dietary burden (mg/ kg feed)</th><th>Matrix</th><th>Resulting residue (sum of a.s. &amp; DFA) [mg a.s. equiv./kg]</th><th>MRL proposal EU / global [mg/kg]</th></tr> </thead> <tbody> <tr> <td colspan="4"><i>Total residue (BYI 02960 plus DFA)</i></td></tr> <tr> <td rowspan="4">1.242 <i>(0.197 + 1.046)</i></td><td>egg</td><td>0.109</td><td>0.15 / <b>0.50</b></td></tr> <tr> <td>muscle</td><td>0.192</td><td>0.20 / <b>0.80</b></td></tr> <tr> <td>fat</td><td>0.068</td><td>0.07 / <b>0.30</b></td></tr> <tr> <td>offal</td><td>0.241</td><td>0.30 / <b>1.00</b></td></tr> </tbody> </table> <p><b>Ruminants</b>  (1) Worst-case diet for dairy ruminants</p>		fat	0.026 <sup>#</sup>	0.005		offal	0.076 <sup>#</sup>	0.015	<i>DFA</i>				1.046	egg	0.097	0.101	muscle	0.172	0.180	fat	0.060	0.063	offal	0.216	0.226	Dietary burden (mg/ kg feed)	Matrix	Resulting residue (sum of a.s. & DFA) [mg a.s. equiv./kg]	MRL proposal EU / global [mg/kg]	<i>Total residue (BYI 02960 plus DFA)</i>				1.242 <i>(0.197 + 1.046)</i>	egg	0.109	0.15 / <b>0.50</b>	muscle	0.192	0.20 / <b>0.80</b>	fat	0.068	0.07 / <b>0.30</b>	offal	0.241	0.30 / <b>1.00</b>
	fat	0.026 <sup>#</sup>	0.005																																														
	offal	0.076 <sup>#</sup>	0.015																																														
<i>DFA</i>																																																	
1.046	egg	0.097	0.101																																														
	muscle	0.172	0.180																																														
	fat	0.060	0.063																																														
	offal	0.216	0.226																																														
Dietary burden (mg/ kg feed)	Matrix	Resulting residue (sum of a.s. & DFA) [mg a.s. equiv./kg]	MRL proposal EU / global [mg/kg]																																														
<i>Total residue (BYI 02960 plus DFA)</i>																																																	
1.242 <i>(0.197 + 1.046)</i>	egg	0.109	0.15 / <b>0.50</b>																																														
	muscle	0.192	0.20 / <b>0.80</b>																																														
	fat	0.068	0.07 / <b>0.30</b>																																														
	offal	0.241	0.30 / <b>1.00</b>																																														

## **Comments of Applicant on the draft assessment report on flupyradifurone**

(01.04.2014) 23/56

Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)											
No.	Column 1	Column 2	Column 3								
	Reference to assessment report	Comment (restricted to 500 characters, ca.10 lines)	Further explanations								
			Commodity	DM intake (%)	Residue intake over DM intake	Actual contribution to total DM intake (%)	Actual contribution to total residue intake (mg/kg bw/d)				
			Wheat bran	20	0.000915	20	0.018304				
			Grass (fresh)	100	0.000745	80	0.059636				
			<b>Sum</b>			<b>100</b>	<b>0.077941</b>				
			⇒ Maximum dietary burden: 0.077941 mg/kg bw/d = 2.143371 mg/kg dry feed ⇒ Highest contributor: grass (fresh)								
			(2) Calculation of the proportion of the individual components (BYI 02960 and DFA) in the relevant residue in ruminant worst-case diet								
			Crop	Residue levels (mg/kg)		Levels in dry matter	DM intake (%)	Dietary burden			
				total res.*	BYI 029 60	DFA	% in crop	residue (mg/kg)	mg/kg bw/d	(mg/kg feed)	
			<b>Dairy cattle</b>								
			Wheat bran	2.24	0.06		89	0.067	20	<0.001	0.013
			Grass (fresh)	0.41	0.02		20	0.100	80	0.003	0.080
			<i>Subtotal BYI 02960:</i>						0.003	0.093	
			Wheat bran	2.24		2.11	89	2.371	20	0.017	0.474
			Grass (fresh)	0.41		0.37	20	1.850	80	0.054	1.480

# Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 24/56

## Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																															
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations																																												
			<i>Subtotal DFA:</i>																																												
						0.071 <span style="color: green;">1.954</span>																																									
			<i>Totals:</i>		100	0.074 <span style="color: green;">2.048</span>																																									
			Estimation of theoretical residues resulting from feeding grown BYI 02960 residues (comprising BYI 02960 and DFA) to poultry in a ratio relevant to the actual residues expected in feed commodities => corresponds to <b>Table 7.12.1-3 (cattle):</b>																																												
			<table border="1"> <thead> <tr> <th>Dietary burden (mg/kg feed)</th> <th>Matrix</th> <th>Transfer factor</th> <th>Resulting residue (mg/kg)</th> </tr> </thead> <tbody> <tr> <td colspan="4"><i>BYI 02960</i></td></tr> <tr> <td rowspan="5">0.093</td><td>milk</td><td>0.009<sup>1</sup></td><td>0.001</td></tr> <tr> <td>muscle</td><td>0.013<sup>1</sup></td><td>0.001</td></tr> <tr> <td>fat</td><td>0.009<sup>1</sup></td><td>0.001</td></tr> <tr> <td>liver</td><td>0.036<sup>1</sup></td><td>0.003</td></tr> <tr> <td>kidney</td><td>0.037<sup>1</sup></td><td>0.003</td></tr> <tr> <td colspan="4"><i>DFA</i></td></tr> <tr> <td rowspan="5">1.954</td><td>milk</td><td>0.030<sup>2</sup></td><td>0.059</td></tr> <tr> <td>muscle</td><td>0.097<sup>2</sup></td><td>0.190</td></tr> <tr> <td>fat</td><td>0.086<sup>2</sup></td><td>0.168</td></tr> <tr> <td>liver</td><td>0.097<sup>2</sup></td><td>0.190</td></tr> <tr> <td>kidney</td><td>0.131<sup>2</sup></td><td>0.256</td></tr> </tbody> </table>	Dietary burden (mg/kg feed)	Matrix	Transfer factor	Resulting residue (mg/kg)	<i>BYI 02960</i>				0.093	milk	0.009 <sup>1</sup>	0.001	muscle	0.013 <sup>1</sup>	0.001	fat	0.009 <sup>1</sup>	0.001	liver	0.036 <sup>1</sup>	0.003	kidney	0.037 <sup>1</sup>	0.003	<i>DFA</i>				1.954	milk	0.030 <sup>2</sup>	0.059	muscle	0.097 <sup>2</sup>	0.190	fat	0.086 <sup>2</sup>	0.168	liver	0.097 <sup>2</sup>	0.190	kidney	0.131 <sup>2</sup>	0.256
Dietary burden (mg/kg feed)	Matrix	Transfer factor	Resulting residue (mg/kg)																																												
<i>BYI 02960</i>																																															
0.093	milk	0.009 <sup>1</sup>	0.001																																												
	muscle	0.013 <sup>1</sup>	0.001																																												
	fat	0.009 <sup>1</sup>	0.001																																												
	liver	0.036 <sup>1</sup>	0.003																																												
	kidney	0.037 <sup>1</sup>	0.003																																												
<i>DFA</i>																																															
1.954	milk	0.030 <sup>2</sup>	0.059																																												
	muscle	0.097 <sup>2</sup>	0.190																																												
	fat	0.086 <sup>2</sup>	0.168																																												
	liver	0.097 <sup>2</sup>	0.190																																												
	kidney	0.131 <sup>2</sup>	0.256																																												
			<sup>1</sup> TF for total residue for enforcement/risk assessment = parent BYI 02960 plus DFA; determined for 1X dose level in cattle feeding study																																												
			<sup>2</sup> TF for DFA, only; determined for 49X dose level in cattle feeding study																																												

## Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																											
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations																								
			<p>Levels of the relevant residue of BYI 02960 (comprising BYI 02960 and DFA) in ruminant tissues and milk expected after feeding a worst-case diet containing residues due to treatment of crops with BYI 02960  =&gt; corresponds to <b>Table 7.12.1-4 (cattle):</b></p> <table border="1"> <thead> <tr> <th>Dietary burden (mg/ kg feed)</th><th>Matrix</th><th>Resulting residue (sum of a.s. &amp; DFA) [mg a.s. equiv./kg]</th><th>MRL proposal EU / global [mg/kg]</th></tr> </thead> <tbody> <tr> <td align="center" colspan="4"><i>Total residue (BYI 02960 plus DFA)</i></td></tr> <tr> <td align="center" rowspan="5" style="text-align: right;">2.048 (0.093 + 1.954)</td><td>milk</td><td>0.059</td><td>0.08 / <b>0.3</b></td></tr> <tr> <td>muscle</td><td>0.191</td><td>0.30 / <b>1.0</b></td></tr> <tr> <td>fat</td><td>0.169</td><td>0.30 / <b>0.5</b></td></tr> <tr> <td>liver</td><td>0.193</td><td>0.30 / <b>2.0</b></td></tr> <tr> <td>kidney</td><td>0.259</td><td>0.40 / <b>2.0</b></td></tr> </tbody> </table>	Dietary burden (mg/ kg feed)	Matrix	Resulting residue (sum of a.s. & DFA) [mg a.s. equiv./kg]	MRL proposal EU / global [mg/kg]	<i>Total residue (BYI 02960 plus DFA)</i>				2.048 (0.093 + 1.954)	milk	0.059	0.08 / <b>0.3</b>	muscle	0.191	0.30 / <b>1.0</b>	fat	0.169	0.30 / <b>0.5</b>	liver	0.193	0.30 / <b>2.0</b>	kidney	0.259	0.40 / <b>2.0</b>
Dietary burden (mg/ kg feed)	Matrix	Resulting residue (sum of a.s. & DFA) [mg a.s. equiv./kg]	MRL proposal EU / global [mg/kg]																								
<i>Total residue (BYI 02960 plus DFA)</i>																											
2.048 (0.093 + 1.954)	milk	0.059	0.08 / <b>0.3</b>																								
	muscle	0.191	0.30 / <b>1.0</b>																								
	fat	0.169	0.30 / <b>0.5</b>																								
	liver	0.193	0.30 / <b>2.0</b>																								
	kidney	0.259	0.40 / <b>2.0</b>																								
(5)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	BCS (page 269, plant MRLs): STMR, HR and MRL should be taken from the same data set (either using the residue definition for RA or monitoring for calculation) – otherwise the data is not comprehensible																									
(6)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	BCS (page 269, plant MRLs): Rotational root vegetables => MRL proposal of 0.6 mg/kg is based on succeeding trials with potatoes, thus the MRL should refer to Rotational root <b>and tuber</b> vegetables => or separate into <b>Rotational root vegetables</b> (turnips and carrots):	<p>Total BYI 02960 residues</p> <ul style="list-style-type: none"> <li>• Carrots &amp; turnips (PBI = 25-30 days): 0.05, 0.07; 0.08; 0.14 mg/kg  =&gt; MRL proposal: 0.3 mg/kg</li> <li>• Potatoes (PBI = 25-33 days): 0.048; 0.056; 0.21; 0.27 mg/kg  =&gt; MRL proposal: 0.6 mg/kg</li> </ul>																								

## Section 3 - Residues (B.7)

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>																																																																																		
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations																																																																															
		MRL = 0.3 mg/kg <b>Rotational tuber vegetables</b> (potatoes): MRL = 0.6 mg/kg																																																																																
(7)	Vol. 3, B.7.12, proposed MRLs (animal matrices)	BCS (page 269, animal MRLs): Residues detected in the animal matrices in the livestock feeding study cannot be used to estimate the MRLs (even after normalizing to 1N dose) since animals were fed with BYI 02960 only and a realistic diet will consist of BYI 02960 and DFA => transfer factors for the two compounds – estimated in the feeding studies – have to be applied to the calculate residues in animal matrices	Residue data from field rotational crop study with a leafy crop (lettuce), a root crop (turnip and carrot) and cereals (wheat and barley): Carrot (1 <sup>st</sup> rotation):																																																																															
(8)	Vol. 3, B.7.12, proposed MRLs (animal matrices)	BCS (page 271, Table 7.12.2-4, estimation of animal MRLs according to RMS): <ul style="list-style-type: none"> <li>- for wheat grain and pea (dry) the STMR values and not the HR values should be used;</li> <li>- the DM content of cabbage is 14%</li> <li>- the residues taken for turnips are the residues detected for potatoes (was this intended?)</li> <li>- Rape forage is not a diet for dairy ruminants, should be replaced by grass</li> <li>- The contribution of turnips can account for 30% in maximum in the diet of cattle (60% was assumed in the DAR)</li> <li>- the maximum contribution of grass and other forages can account up to 100%</li> </ul> Please correct table accordingly (see values in	<p><b>Poultry</b></p> <table border="1"> <thead> <tr> <th>Crop</th> <th>TR</th> <th>a.s.</th> <th>DFA</th> <th>% DM</th> <th>mg/kg</th> <th>DM intake</th> <th>mg/kg bw/day</th> <th>mg/kg dry feed</th> </tr> </thead> <tbody> <tr> <td>Turnips</td> <td>0.27</td> <td>0.01</td> <td rowspan="4" style="background-color: #cccccc;"></td> <td>10</td> <td>0.10</td> <td>20</td> <td>0.001</td> <td>0.020</td> </tr> <tr> <td>Wheat grain</td> <td>0.65</td> <td>0.01</td> <td>86</td> <td>0.01</td> <td>45</td> <td>&lt;0.001</td> <td><b>0.005</b></td> </tr> <tr> <td>Peas (dry)</td> <td>2.3</td> <td>0.01</td> <td></td> <td>86</td> <td>0.01</td> <td>30</td> <td>&lt;0.001</td> <td>0.003</td> </tr> <tr> <td>Cabbage</td> <td>0.2</td> <td>0.08</td> <td></td> <td><b>14</b></td> <td>0.57</td> <td>5</td> <td>0.002</td> <td>0.029</td> </tr> <tr> <td colspan="2" style="text-align: right;"><i>Subtotal</i> BYI 02960:</td><td>0.12</td> <td></td> <td></td> <td></td> <td></td> <td><b>0.003</b></td> <td><b>0.057</b></td> </tr> <tr> <td>Turnips</td> <td>0.27</td> <td rowspan="3" style="background-color: #cccccc;"></td> <td>0.25</td> <td>10</td> <td>2.50</td> <td>20</td> <td>0.032</td> <td>0.500</td> </tr> <tr> <td>Wheat grain</td> <td>0.65</td> <td><b>0.33</b></td> <td>86</td> <td>0.38</td> <td>45</td> <td>0.011</td> <td>0.173</td> </tr> <tr> <td>Peas</td> <td>2.3</td> <td></td> <td><b>1.6</b></td> <td>86</td> <td>0.19</td> <td>30</td> <td>0.035</td> <td>0.558</td> </tr> </tbody> </table>	Crop	TR	a.s.	DFA	% DM	mg/kg	DM intake	mg/kg bw/day	mg/kg dry feed	Turnips	0.27	0.01		10	0.10	20	0.001	0.020	Wheat grain	0.65	0.01	86	0.01	45	<0.001	<b>0.005</b>	Peas (dry)	2.3	0.01		86	0.01	30	<0.001	0.003	Cabbage	0.2	0.08		<b>14</b>	0.57	5	0.002	0.029	<i>Subtotal</i> BYI 02960:		0.12					<b>0.003</b>	<b>0.057</b>	Turnips	0.27		0.25	10	2.50	20	0.032	0.500	Wheat grain	0.65	<b>0.33</b>	86	0.38	45	0.011	0.173	Peas	2.3		<b>1.6</b>	86	0.19	30	0.035	0.558
Crop	TR	a.s.	DFA	% DM	mg/kg	DM intake	mg/kg bw/day	mg/kg dry feed																																																																										
Turnips	0.27	0.01		10	0.10	20	0.001	0.020																																																																										
Wheat grain	0.65	0.01		86	0.01	45	<0.001	<b>0.005</b>																																																																										
Peas (dry)	2.3	0.01			86	0.01	30	<0.001	0.003																																																																									
Cabbage	0.2	0.08			<b>14</b>	0.57	5	0.002	0.029																																																																									
<i>Subtotal</i> BYI 02960:		0.12					<b>0.003</b>	<b>0.057</b>																																																																										
Turnips	0.27		0.25	10	2.50	20	0.032	0.500																																																																										
Wheat grain	0.65		<b>0.33</b>	86	0.38	45	0.011	0.173																																																																										
Peas	2.3			<b>1.6</b>	86	0.19	30	0.035	0.558																																																																									

## **Comments of Applicant on the draft assessment report on flupyradifurone**

(01.04.2014) 27/56

### Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)											
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations								
			(dry)								
		<b>bold and italics).</b>  BCS would favour the calculation as described under (4).	Cabbage	0.2		0.12	<b>14</b>	0.86	5	0.003	0.043
			<i>Subtotal DFA:</i>		2.38					<b>0.081</b>	<b>1.274</b>
			<i>Totals:</i>					100	<b>0.084</b>	<b>1.331</b>	
			<b>Cattle</b>								
			Turnip	0.27	0.01		10	0.10	<b>30</b>	<b>0.001</b>	<b>0.030</b>
			Grass (fresh)	0.41	0.02		20	0.10	<b>50</b>	<b>0.002</b>	<b>0.050</b>
			Pea (dry)	2.3	0.01		86	0.01	<b>20</b>	<0.001	<b>0.002</b>
			<i>Subtotal BYI 02960:</i>	0.03						<b>0.003</b>	<b>0.082</b>
			Turnip	0.27		0.25	10	2.50	<b>30</b>	<b>0.027</b>	<b>0.750</b>
			Grass (fresh)	0.41		0.37	20	1.85	<b>50</b>	<b>0.034</b>	<b>0.925</b>
			Pea (dry)	2.3		1.6	86	1.86	<b>20</b>	<b>0.014</b>	<b>0.372</b>
			<i>Subtotal DFA:</i>		2.80					<b>0.075</b>	<b>2.047</b>
			<i>Totals:</i>	0.03	2.80			100	<b>0.078</b>	<b>2.129</b>	
			<b>Pigs</b>								
			Rape forage	0.41	0.02		14	<b>0.14</b>	15	0.001	0.021
			Turnips	0.27	0.01		10	0.10	60	0.002	0.060
			Peas (dry)	2.3	0.01		86	0.01	25	<0.001	0.003
			<i>Subtotal BYI 02960:</i>	0.04						<b>0.003</b>	<b>0.084</b>
			Rape forage	0.41		0.37	14	2.64	15	0.016	0.396

## **Comments of Applicant on the draft assessment report on flupyradifurone**

(01.04.2014) 28/56

### Section 3 - Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)											
No.	Column 1	Column 2	Column 3								
	Reference to assessment report	Comment (restricted to 500 characters, ca.10 lines)	Further explanations								
			Turnips	0.27		0.25	10	2.5	60	0.060	1.500
			Peas (dry)	1.6		1.6	86	1.86	25	0.019	0.465
			<i>Subtotal DFA:</i>			5.10				<b>0.095</b>	<b>2.361</b>
			<i>Totals:</i>		0.04	5.10			100	<b>0.098</b>	<b>2.445</b>

## Section 3 - Residues (B.7)

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>																																																																																																																																																				
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations																																																																																																																																																	
(9)	Vol. 3, B.7.12, proposed MRLs (animal matrices)	BCS (page 272, Table 7.12.2-5, estimation of residues in animal matrices according to RMS): Due to the different proposed contribution of the crops in the diet, the MRL proposals could be adapted.	<p><b>Table 7.12.2-5:</b> Theoretical residues resulting from feeding BYI 02960 and DFA to poultry and to dairy cows in a ratio relevant to the actual residues expected in feed commodities</p> <table border="1"> <thead> <tr> <th>Dietary burden (mg/kg bw/d)</th> <th>Matrix</th> <th>TF*</th> <th>Resulting residue (mg/kg)</th> <th>Dietary burden (mg/kg bw/d)</th> <th>TF*</th> <th>Resulting residue (mg/kg)</th> <th>Sum of BYI 02960 and DFA (mg/kg)</th> </tr> </thead> <tbody> <tr> <td align="center" colspan="8"><b>chicken</b></td></tr> <tr> <td align="center" colspan="4"><i>BYI 02960</i></td><td align="center" colspan="4"><i>DFA</i></td></tr> <tr> <td align="center" rowspan="4">0.003†</td><td>egg</td><td>0.57</td><td>&lt;0.01</td><td align="center" rowspan="5">0.081</td><td>1.47</td><td>0.12</td><td><b>0.13</b></td></tr> <tr> <td>muscle</td><td>0.93</td><td>&lt;0.01</td><td>2.59</td><td>0.21</td><td><b>0.22</b></td></tr> <tr> <td>fat</td><td>0.39</td><td>&lt;0.01</td><td>0.91</td><td>0.07</td><td><b>0.08</b></td></tr> <tr> <td>liver</td><td>1.14</td><td>&lt;0.01</td><td>3.25</td><td>0.26</td><td><b>0.27</b></td></tr> <tr> <td align="center" colspan="8"><b>cattle</b></td></tr> <tr> <td align="center" colspan="4"><i>BYI 02960</i></td><td align="center" colspan="4"><i>DFA</i></td></tr> <tr> <td align="center" rowspan="5">0.003†</td><td>milk</td><td>0.24</td><td>&lt;0.01</td><td align="center" rowspan="6">0.075</td><td>0.77</td><td>0.06</td><td><b>0.07</b></td></tr> <tr> <td>muscle</td><td>0.35</td><td>&lt;0.01</td><td>2.49</td><td>0.19</td><td><b>0.20</b></td></tr> <tr> <td>fat</td><td>0.23</td><td>&lt;0.01</td><td>2.11</td><td>0.16</td><td><b>0.17</b></td></tr> <tr> <td>liver</td><td>0.92</td><td>&lt;0.01</td><td>2.30</td><td>0.17</td><td><b>0.18</b></td></tr> <tr> <td>kidney</td><td>0.98</td><td>&lt;0.01</td><td>3.26</td><td>0.24</td><td><b>0.25</b></td></tr> <tr> <td align="center" colspan="8"><b>pigs</b></td></tr> <tr> <td align="center" colspan="4"><i>BYI 02960</i></td><td align="center" colspan="4"><i>DFA</i></td></tr> <tr> <td align="center" rowspan="4">0.003†</td><td>muscle</td><td>0.35</td><td>&lt;0.01</td><td align="center" rowspan="4">0.095</td><td>2.49</td><td>0.24</td><td><b>0.25</b></td></tr> <tr> <td>fat</td><td>0.23</td><td>&lt;0.01</td><td>2.11</td><td>0.20</td><td><b>0.21</b></td></tr> <tr> <td>liver</td><td>0.92</td><td>&lt;0.01</td><td>2.30</td><td>0.22</td><td><b>0.23</b></td></tr> <tr> <td>kidney</td><td>0.98</td><td>&lt;0.01</td><td>3.26</td><td>0.31</td><td><b>0.32</b></td></tr> </tbody> </table>	Dietary burden (mg/kg bw/d)	Matrix	TF*	Resulting residue (mg/kg)	Dietary burden (mg/kg bw/d)	TF*	Resulting residue (mg/kg)	Sum of BYI 02960 and DFA (mg/kg)	<b>chicken</b>								<i>BYI 02960</i>				<i>DFA</i>				0.003†	egg	0.57	<0.01	0.081	1.47	0.12	<b>0.13</b>	muscle	0.93	<0.01	2.59	0.21	<b>0.22</b>	fat	0.39	<0.01	0.91	0.07	<b>0.08</b>	liver	1.14	<0.01	3.25	0.26	<b>0.27</b>	<b>cattle</b>								<i>BYI 02960</i>				<i>DFA</i>				0.003†	milk	0.24	<0.01	0.075	0.77	0.06	<b>0.07</b>	muscle	0.35	<0.01	2.49	0.19	<b>0.20</b>	fat	0.23	<0.01	2.11	0.16	<b>0.17</b>	liver	0.92	<0.01	2.30	0.17	<b>0.18</b>	kidney	0.98	<0.01	3.26	0.24	<b>0.25</b>	<b>pigs</b>								<i>BYI 02960</i>				<i>DFA</i>				0.003†	muscle	0.35	<0.01	0.095	2.49	0.24	<b>0.25</b>	fat	0.23	<0.01	2.11	0.20	<b>0.21</b>	liver	0.92	<0.01	2.30	0.22	<b>0.23</b>	kidney	0.98	<0.01	3.26	0.31	<b>0.32</b>	⇒ The estimated residues in all animal matrices are all covered by the				
Dietary burden (mg/kg bw/d)	Matrix	TF*	Resulting residue (mg/kg)	Dietary burden (mg/kg bw/d)	TF*	Resulting residue (mg/kg)	Sum of BYI 02960 and DFA (mg/kg)																																																																																																																																													
<b>chicken</b>																																																																																																																																																				
<i>BYI 02960</i>				<i>DFA</i>																																																																																																																																																
0.003†	egg	0.57	<0.01	0.081	1.47	0.12	<b>0.13</b>																																																																																																																																													
	muscle	0.93	<0.01		2.59	0.21	<b>0.22</b>																																																																																																																																													
	fat	0.39	<0.01		0.91	0.07	<b>0.08</b>																																																																																																																																													
	liver	1.14	<0.01		3.25	0.26	<b>0.27</b>																																																																																																																																													
<b>cattle</b>																																																																																																																																																				
<i>BYI 02960</i>				<i>DFA</i>																																																																																																																																																
0.003†	milk	0.24	<0.01	0.075	0.77	0.06	<b>0.07</b>																																																																																																																																													
	muscle	0.35	<0.01		2.49	0.19	<b>0.20</b>																																																																																																																																													
	fat	0.23	<0.01		2.11	0.16	<b>0.17</b>																																																																																																																																													
	liver	0.92	<0.01		2.30	0.17	<b>0.18</b>																																																																																																																																													
	kidney	0.98	<0.01		3.26	0.24	<b>0.25</b>																																																																																																																																													
<b>pigs</b>																																																																																																																																																				
<i>BYI 02960</i>				<i>DFA</i>																																																																																																																																																
0.003†	muscle	0.35	<0.01	0.095	2.49	0.24	<b>0.25</b>																																																																																																																																													
	fat	0.23	<0.01		2.11	0.20	<b>0.21</b>																																																																																																																																													
	liver	0.92	<0.01		2.30	0.22	<b>0.23</b>																																																																																																																																													
	kidney	0.98	<0.01		3.26	0.31	<b>0.32</b>																																																																																																																																													

## Section 3 - Residues (B.7)

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
			MRLs proposed by the RMS
(10)	Vol. 3, B.7.15, consumer risk assessment	<p>BCS (page 277, Table 7.15.2-1, input values for the consumer risk assessment:</p> <p><u>Chronic risk assessment:</u></p> <ul style="list-style-type: none"> <li>- the proposed IT-MTLs for poultry liver and milk were mixed up</li> <li><u>poultry liver:</u> <b>1.0 mg/kg</b> (instead of 0.3 mg/kg)</li> <li><u>cattle milk:</u> <b>0.3 mg/kg</b> (instead of 1.0 mg/kg)</li> <li>- the MRL for <u>goat and sheep milk</u> should be the <b>0.08 mg/kg</b> (instead of 0.15 mg/kg)</li> </ul> <p><u>Acute risk assessment:</u></p> <ul style="list-style-type: none"> <li>- proposed MRLs for milk has to be corrected</li> <li><u>cattle milk:</u> <b>0.08 mg/kg</b> (instead of 0.15 mg/kg)</li> <li><u>goat and sheep milk:</u> <b>0.08 mg/kg</b> (instead of 0.15 mg/kg)</li> <li>- MRLs used for cattle muscle, fat liver kidney should be in line with the values proposed in Table 7.12.2-6</li> <li>cattle muscle: <b>0.3 mg/kg</b> (instead of 0.5 mg/kg)</li> <li>cattle fat: <b>0.3 mg/kg</b> (instead of 0.4 mg/kg)</li> <li>cattle liver: <b>0.3 mg/kg</b> (instead of 0.4 mg/kg)</li> <li>cattle kidney: <b>0.4 mg/kg</b> (instead of 0.6 mg/kg)</li> <li>- what is the reason to use MRL values instead of IT-MRLs?</li> </ul>	
(11)	Vol. 3, B.7.15, consumer	BCS (page 277, Table 7.15.2-2, TMDI calculation:	Table 7.15.2-02 Worst-case results of the TMDI calculation in PRIMo

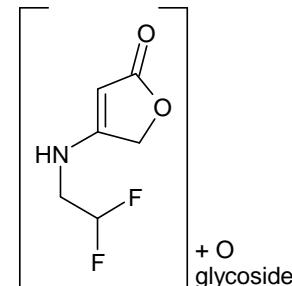
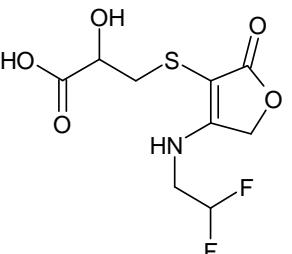
## Section 3 - Residues (B.7)

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>															
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations												
	risk assessment (chronic)	Using the corrected input values the TMDI values will slightly change (decrease)	model rev. 2 <table border="1"> <thead> <tr> <th>Highest calculated TMDI values in % of ADI</th> <th>MS Diet</th> </tr> </thead> <tbody> <tr> <td>76.3</td> <td>WHO Cluster diet B</td> </tr> <tr> <td>62.8</td> <td>NL child</td> </tr> <tr> <td>61.7</td> <td>DE child</td> </tr> <tr> <td>55.9</td> <td>UK Toddler</td> </tr> <tr> <td>50.4</td> <td>IE adult</td> </tr> </tbody> </table>	Highest calculated TMDI values in % of ADI	MS Diet	76.3	WHO Cluster diet B	62.8	NL child	61.7	DE child	55.9	UK Toddler	50.4	IE adult
Highest calculated TMDI values in % of ADI	MS Diet														
76.3	WHO Cluster diet B														
62.8	NL child														
61.7	DE child														
55.9	UK Toddler														
50.4	IE adult														
(12)	Vol. 3, B.7.15, consumer risk assessment (chronic)	BCS (page 278, typo in 1 <sup>st</sup> sentence): Two groundwater metabolites were identified, DFA and <b>6-CNA...</b>													
(13)	Vol. 3, B.7.15, consumer risk assessment (acute)	BCS (page 280, acute consumer intake calculations; NESTI of imported crops citrus and celery use more of the ARfD compared with lettuce): The NESTI uses maximally 69.2% of the ARfD for the German child for lettuce. <b>Only the imported crops citrus and celery use more of the ARfD (83.4 and 80.0% of the ARfD, respectively).</b>													
(14)	Vol. 3, B.7.15, consumer risk assessment	BCS (page 279 and 281, chronic and acute consumer intake calculations): Please replace figure if different input values are used													

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.7.16, Summary and Evaluation	BCS (page 291, summary livestock feeding): Please add an explaining sentence at the end of the 2 <sup>nd</sup> paragraph that the special study design allowed to calculate a transfer factor of DFA despite feeding BYI 02960, only.	Example: The feeding studies were designed to allow "material balancing" in order to evaluate levels and calculate transfer factors for both the total residue (parent BYI 02960 and DFA) and DFA, despite feeding parent compound only.
(2)	Vol. 3, B.7.16, Summary and Evaluation	BCS (page 291, consumer risk assessment): Please explain that the listed MRLs are based on EU data only.	Example: Based on the supervised residue trials, [...] the following <b>EU MRLs</b> are proposed (using EU data only).
(3)	Vol. 3, B.7.16, Summary and Evaluation	BCS (page 291, consumer risk assessment): The MRL for rotational root vegetables is identical with the MRL for rotational tuber vegetables indicating that the residue results from potatoes were used for the calculation. Why not using the residues detected in rotational carrots and turnips for rotational root vegetables as done in the MRL Evaluation Report?	Total BYI 02960 residues <ul style="list-style-type: none"> <li>• Carrots &amp; turnips (PBI = 25-30 days): 0.05, 0.07; 0.08; 0.14 mg/kg =&gt; MRL proposal: 0.3 mg/kg</li> <li>• Potatoes (PBI = 25-33 days): 0.048; 0.056; 0.21; 0.27 mg/kg =&gt; MRL proposal: 0.6 mg/kg</li> </ul>
(4)	Vol. 3, B.7.16, Summary and Evaluation	BCS (page 292, consumer risk assessment): The last paragraph is a bit misleading – only for citrus and celery, the HR instead of the MRL was used.	

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(5)	Vol. 3, B.7, Annex I, List of metabolites	BCS (page 312, name of metabolite 35): Please add the name DFEAF-OH-glyc as additional name as it was used by the RMS in the DAR	M35 <b>BYI 02960-difluoroethyl-amino-furanone-OH-glyc</b>  C <sub>12</sub> H <sub>17</sub> F <sub>2</sub> N O <sub>8</sub> 341.27 g/mol  <b>DFEAF-OH-glyc</b>
(6)	Vol. 3, B.7, Annex I, List of metabolites	BCS (page 313, name of metabolite 41): Please add the name DFEAF-mercaptopo-lactic acid as additional name as it was used by the RMS in the DAR	M41 <b>BYI 02960-mercaptopo-lactic acid</b>  C <sub>9</sub> H <sub>11</sub> F <sub>2</sub> N O <sub>5</sub> S 283.25 g/mol  <b>DFEAF-mercaptopo-lactic acid</b>
(1)	MRL Evaluation Report, proposed MRLs	BCS (page 3, proposed MRLs): Peanut should be mentioned under oilseeds (not under nuts)	

# Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 34/56

## Section 3 - Residues (B.7)

Other comments						
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations			
		Commodity	Existing EC MRL (mg/kg)	Proposed EC MRL (mg/kg)	Proposed import tolerance (mg/kg)	
(2)	MRL Evaluation Report, proposed MRLs	BCS (page 3, proposed MRLs): Since root and tuber vegetables as well as bulb vegetables are exported from North America to Europe, an IT-MRL should be set based on rotational crop data	0210000 Root & tuber vegetables, except potatoes	0.01	0.6	<b>1.5</b>
			0220000 Bulb vegetables	0.01	0.4	<b>0.8</b>
(3)	MRL Evaluation Report, proposed MRLs	BCS (page 3, proposed MRLs): - The IT-MRL of tomato (3 mg/kg) should also apply for eggplant. The proposed EC MRL should be based on the more critical rotational use (determined for the fruiting crop cucumber). - The IT-MRL for chili pepper should also apply for pepper	Tomato	0.01	<b>0.9</b>	3
			Egg plant	0.01	<b>0.9</b>	<b>3</b>
			pepper	0.01	1.0	<b>3</b>
			Chili pepper	<b>0.01</b>	<b>1.0</b>	3
(4)	MRL Evaluation Report, proposed MRLs	BCS (page 4, proposed MRLs): - According to the DAR is the proposed EC MRL for brassicaceae and other leaf vegetables & fresh herbs is 0.04 mg/kg - MRL for stem vegetables (0270000) does not	Commodity	Existing EC MRL (mg/kg)	Proposed EC MRL (mg/kg)	Proposed import tolerance (mg/kg)

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 35/56

### Section 3 - Residues (B.7)

Other comments					
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations		
		apply for celery - MRL for oilseeds does not apply for peanuts and soybean seeds - cereals include field corn	024000 Brassicacea	0.01	<b>0.4</b>
			All others of group 0250000 Leaf vegetables & fresh herbs	0.01	<b>0.4</b>
			0270000 Stem vegetables, <b>except celery</b>	0.01	0.5
			Peanut	0.01	0.15
			Soy bean seed	0.01	4
			Oilseeds, <b>except for peanuts and soybean seeds</b>	0.01	0.4
			Barley, sorghum and wheat grain	0.01	<b>1.5</b>
			Cereals ( <b>including field corn</b> ), <b>except barley, sorghum and wheat grain</b>	0.01	1.5
(5)	MRL Evaluation Report, 1.1. Enforcement methods	BCS (page 7, Enforcement methods for residues in food of plant origin): => Enforcement methods used are method 01330 and <b>its modification M001 for oilseeds</b> (see also C.1.1.1)			
(6)	MRL Evaluation Report, 1.1 Enforcement methods	BCS (page 7, Enforcement methods for residues in food of plant): - The LOQ in the box refers only to BYI 02960, the LOQ for DFA is 0.10 mg/kg for hops and 0.02			

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		mg/kg for all other crops as stated in the text	
(7)	MRL Evaluation Report, 1.2 Enforcement methods	BCS (page 7, Enforcement methods for residues in food of animal origin): - The LOQ in the box refers only to DFA, the LOQ for parent BYI 02960 is 0.01 mg/kg	
(8)	MRL Evaluation Report, 3. Residues	BCS (page 10, Header of Figure 3.1.1.1-01): The header could be misleading => New proposal: Overview on analytical targets analysed for in the supervised residue trials. 6-CNA was determined for information only since it is a known metabolite of other insecticides bearing this moiety.	
(9)	MRL Evaluation Report, 3. Residues	BCS (page 11, Supervised Residue trials): The text concerning 6-CNA is a bit misleading; 6-CNA was not included in the residue definition since - only small residues were detected in most field crops - there is no toxicological concern	<ol style="list-style-type: none"> <li>1.) 6-CNA was included in the <u>data collection method</u> to determine the residue of this metabolite under realistic conditions in field residues (other insecticides bearing the 6-CNA moiety can lead to rather high residues of 6-CNA in crops).</li> <li>2.) The residue trials showed that 6-CNA represents only a minor part of the residue, if at all.</li> <li>3.) 6-CNA was detected in the ADME studies, thus the metabolite constitute substantially to the tox effects of the parent and is therefore covered by the tox studies conducted with the parent compound. ⇒ 6-CNA should <b>not</b> be included in the residue definition</li> </ol>
(10)	MRL Evaluation Report, 3. Residues	BCS ( <b>general remark</b> ): - Calculation of MRL could be based on <b>total residue (BYI 02960, DFA and DFEAF)</b> as done	

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 37/56

### Section 3 - Residues (B.7)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		<p>in the Annex II dossier (DFEAF residues were always not significant and have thus no influence on the MRL)</p> <ul style="list-style-type: none"> <li>- Re-calculation of the combined residues of BYI 02960 and DFA can result in mistakes and will not result in different MRLs.</li> <li>- in the DAR STMR and HR were based on the residue definition for RA, whereas the MRL was based on the residue definition for monitoring. In the MRL Evaluation Report STMR, HR and MRL are based on the residue definition for monitoring. This is not conclusive - however the values are nearly identical.</li> <li>- Ranges of residues (BYI 0296, DFA or total residue) should be given for the <b>peak residue</b></li> <li>- several trials show increasing residues after the PHI, however due to prolonged sampling intervals it was shown that at least a residue plateau was reached and thus that the trials are valid for MRL setting – this information is no longer given in the MRL Evaluation Report</li> </ul>	
(11)	MRL Evaluation Report, 3. Residues	<p>BCS (page 14, Residue trials in grapes):</p> <ul style="list-style-type: none"> <li>- For MRL calculation, residues in bunch of grapes should be used since residue peak was often detected <b>after</b> the PHI. Berries were only collected at the PHI. Although the berries showed slightly higher residues, the residues were</li> </ul>	<p><b>N-EU (peak residues in grapes):</b></p> <p>BYI 02960: 0.42; 0.38; 0.15; 0.11; 0.16; 0.22; 0.42; 0.18; 0.21</p> <p>DFA: 0.06; 0.07; 0.11; 0.06; 0.03; 0.15; 0.08; 0.05; 0.03</p> <p>DFEAF: always &lt;0.01</p> <p>Total (a.s.+ DFA): 0.17; 0.19; 0.23; 0.24; 0.26; 0.37; 0.45; 0.48; 0.50</p> <p>STMR: 0.26 mg/kg</p>

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 38/56

### Section 3 - Residues (B.7)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		<p>comparable with those of bunch of grapes (same data set).</p> <p>- Calculation of MRL <b>could</b> be based on <b>total residue (BYI 02960, DFA and DFEAF)</b> as done in the Annex II dossier (DFEAF residues were always not significant and have thus no influence on the MRL)</p> <p>- Re-calculation of the combined residues of BYI 02960 and DFA results often in mistakes and will not result in different MRLs.</p>	<p>HR: 0.50 mg/kg  <math>\Rightarrow</math> MRL = 1.0 mg/kg</p> <p><b>S-EU (peak residues in grapes):</b>          BYI 02960: 0.22; 0.11; 0.09; 0.05; 0.08; 0.05; 0.07; 0.10          DFA: 0.05; 0.08; 0.06; &lt;0.02; 0.25; .05; 0.11; 0.06          DFEAF: always &lt;0.01          Total (a.s.+DFA): 0.07; 0.10; 0.15; 0.16; 0.18; 0.19; 0.27; 0.33          STMR: 0.17 mg/kg          HR: 0.33 mg/kg  <math>\Rightarrow</math> MRL = 0.6 mg/kg</p>
(12)	MRL Evaluation Report, 3. Residues	BCS (page 14, Residue trials in grapes): Please correct text in 2 <sup>nd</sup> and 3 <sup>rd</sup> paragraph.	<p><b>Peak residues</b> ranged from <b>0.05-0.42 mg/kg</b> for BYI 02960, from <b>&lt;0.02-0.25 mg/kg</b> for DFA and were <b>&lt;0.01 mg/kg</b> for DFEAF in all samples.</p> <p>Residue data from Northern European trials were <b>more critical</b> (STMR = <b>0.26 mg/kg</b>, HR = <b>0.50 mg/kg</b>) compared to Southern European trials (STMR = <b>0.17 mg/kg</b>, HR = <b>0.33 mg/kg</b>).</p>
(13)	MRL Evaluation Report, 3. Residues	BCS (page 14, Residue trials in pepper): Please correct text in paragraph 5, and paragraphs 10-12.	<p>Eight residue decline trials have been performed in Southern Europe in the seasons 2010 and 2011 and 8 residue decline trials indoor in the season 2011. A 200 g/L SL formulation was applied two times. The dose <b>rate (per application)</b> in the outdoor trials was 113-133 g a.i./ha (15.1-25 g a.i./hL), interval 14-15d and PHI 3d which is in line with the intended cGAP (<b>2 x 112.5 g a.i./ha</b>). The dose rate in the indoor trials <b>was adapted to the crop height</b> and accounted for 135-215 g a.i./ha (13.4-15.5 g a.i./hL, first application up to 22.5 g a.i./hL), interval 10-13d and PHI 3d which is in line with the critical GAP (<b>2 x 112.5 g a.i./ha</b>).</p> <p><b>Peak residues</b> ranged from <b>0.02-0.22 mg/kg</b> for BYI 02960, from <b>&lt;0.02-0.12 mg/kg</b> for DFA and were <b>&lt;0.01-0.015 mg/kg</b> for DFEAF in outdoor</p>

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
			<p>sweet pepper.</p> <p><b>Peak residues</b> ranged from <b>0.09-0.55 mg/kg</b> for BYI 02960, from &lt;0.02-<b>0.16 mg/kg</b> for DFA and were &lt;0.01-0.022 mg/kg for DFEAF in indoor sweet pepper.</p> <p>Selected residue data for monitoring from the indoor trials were worst case (STMR = 0.26 mg/kg, HR = 0.60 mg/kg) compared to Southern European outdoor trials (STMR = <b>0.16 mg/kg</b>, HR = 0.24 mg/kg).</p>
(14)	MRL Evaluation Report, 3. Residues	BCS (page 15, Residue trials in cucumber/gherkins): Please correct text in paragraphs 6-8.	<p>Four residue decline trials have been performed in Southern Europe in the season 2010 in cucumber. A 200 g/L SL formulation was applied two times. The dose rate <b>per application</b> was 125 g a.i./ha (15.6-25 g a.i./hL) and the interval was 14d and PHI 3d which is in line with the cGAP (2 x 112.5 g a.i./ha).</p> <p><b>Peak residues</b> ranged from &lt;0.01-0.06 mg/kg for BYI 02960, from <b>0.07-0.20 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in outdoor cucumber.</p> <p><u>Gherkin outdoor</u></p> <p>Four residue decline trials have been performed in Southern Europe in the season 2011 in gherkin outdoor. A 200 g/L SL formulation was applied two times at <b>112.5 g a.i./ha</b> (18.8-22.6 g a.i./hL) with interval 14-15d and PHI 3d which is in line with the cGAP (2 x 112.5 g a.i./ha).</p> <p><b>Peak residues</b> ranged from &lt;0.01-<b>0.27 mg/kg</b> for BYI 02960, from <b>0.09-0.66 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in outdoor gherkin.</p> <p><u>Cucumber indoor</u></p> <p>Eight residue decline trials have been performed in cucumber in greenhouses in Northern and Southern Europe in the seasons 2010. A 200</p>

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 40/56

### Section 3 - Residues (B.7)

Other comments			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			<p>g/L SL formulation was applied two times. The dose rate in the trials was adopted to the crop height and accounted for 113-250 g ai./ha per application (15.1-16.7 g a.i./hL), interval 9-14d and PHI 3d which is in line with the cGAP (2 x 112.5 g a.i./ha×m)).</p> <p><b>Peak residues</b> ranged from <b>0.04-0.19 mg/kg</b> for BYI 02960, from <b>0.08-0.47 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in indoor cucumber.</p>
(15)	MRL Evaluation Report, 3. Residues	BCS (page 15, Residue trials in cucumber/gherkins): Please delete the first paragraph under " <i>Selected worst case residue data for MRL setting</i> ") – this paragraph is misleading	
(16)	MRL Evaluation Report, 3. Residues	BCS (page 17, Residue trials in melon): - Please correct the sentences in the paragraph 1,3 and 6	<p>Residues of 6-chloronicotinic acid have also been determined in melon. <b>No residues were detected in 13 of 18 trials (&lt;0.005 mg/kg); in 5 trials residues were detected ranging from 0.008 – 0.02 mg/kg (in pulp).</b></p> <p><u>Watermelon outdoor</u></p> <p><b>Peak residues</b> ranged from &lt;0.01-<b>0.05 mg/kg</b> for BYI 02960, from <b>0.03-0.21 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in whole fruits.</p> <p><u>Watermelon indoor</u></p> <p><b>Peak residues</b> ranged from &lt;0.01-<b>0.12 mg/kg</b> for BYI 02960, from <b>0.06-0.28 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in whole fruits.</p>
(17)	MRL Evaluation Report, 3. Residues	BCS (page 17, Residue trials in melon): The P-factor increased from day 3 to day 7, but <u>decreased thereafter</u> . This indicates that the residue peak was approx. 7 days after application. Thus, DFA residues increased with time, but at least a residue plateau was reached at the end of the trials.	

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(18)	MRL Evaluation Report, 3. Residues	BCS (page 17, selected data for watermelon MRL ): BCS proposes to define the greenhouse as the "critical region" and an <b>MRL of 0.6 mg/kg</b> based on the greenhouse trials	MRL proposal outdoor (S-EU): Total residue (a.s. + DFA): 0.04; 0.05; 0.09; 0.10; 0.12; 0.14; 0.15; 0.18; 0.25 mg/kg ⇒ MRL = 0.4 mg/kg MRL proposal indoor: Total residue (a.s. + DFA): 0.09; 0.12; 0.13; 0.15; 0.16; 0.18; 0.26; 0.29; 0.30 mg/kg ⇒ MRL = 0.6 mg/kg
(19)	MRL Evaluation Report, 3. Residues	BCS (page 18, Residue trials in tomato): - Please correct the sentences in the paragraph <i>Tomato outdoor, Tomato indoor and Selected data for MRL setting</i>	<i>Tomato outdoor</i> <b>Peak residues</b> ranged from <0.01- <b>0.08</b> mg/kg for BYI 02960, from <0.02- <b>0.029</b> mg/kg for DFA and were <0.01 mg/kg for DFEAF in whole fruits.  <i>Tomato indoor</i> <b>Peak residues</b> ranged from <b>0.06</b> -0.36 mg/kg for BYI 02960, from <0.02-0.11 mg/kg for DFA and from <0.01-0.029 mg/kg for DFEAF in whole fruits.  <i>Selected data for MRL setting</i> Selected residue data for monitoring from the indoor Northern European trials were worst case ( <b>STMR = 0.13 mg/kg, HR = 0.47 mg/kg</b> )
(20)	MRL Evaluation Report, 3. Residues	BCS (page 19, Residue trials in apple): - Please correct the sentences in the paragraph <i>Apple NEU and Apple SEU</i>	<i>Apple NEU</i> <b>Peak residues</b> ranged from <b>0.05-0.32</b> mg/kg for BYI 02960, from <0.02- <b>0.03</b> mg/kg for DFA and were <0.01 mg/kg for DFEAF in whole fruits.

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
			<p><i>Apple SEU</i></p> <p><b>Peak residues</b> ranged from <b>0.01-0.09</b> mg/kg for BYI 02960, from &lt;0.02-<b>0.036</b> mg/kg for DFA and from &lt;0.01 mg/kg for DFEAF in whole fruits.</p>
(21)	MRL Evaluation Report, 3. Residues	<p>BCS (page 21, Table 3-1, Overview of available supervised residue trials):</p> <p>Please note that the residue values mentioned for <u>orange</u> are the values calculated according to the residue definition for risk assessment and not for enforcement.</p> <p>The conversion factor for censoring (CF) has to be <b>multiplied</b> with 3 mean</p>	<p><b>Enforcement:</b></p> <p>NAFTA region  Dilute spray  0.07; 0.087; 0.12; 0.14; 0.14; 0.16; 0.17; 0.2; 0.21; 0.27; 0.29; 0.29; 0.31; 0.53;  0.72; 1.5  STMR = 0.21  HR = 1.5  <b>OECD</b>  Mean + 4xSD = 1.738  <b>CF x 3xmean = 0.974</b></p> <p>Concentrated spray:  0.05; 0.10; 0.22; 0.24; 0.26; 0.26; 0.26; 0.37; 0.66; 0.92; 1.3; 2.2  STMR = 0.25  HR = 2.2  <b>OECD</b>  Mean + 4xSD = 3.082  <b>CF x 3xmean = 1.680</b></p> <p>Brazil:  1 soil drench + 2 foliar  0.20; 0.35; 0.40; 0.48; 0.52  STMR = 0.40  HR = 0.52  <b>OECD</b>  Mean + 4xSD = 0.901  <b>CF x 3xmean = 1.200</b></p>

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
			<p>2 foliar            0.15; 0.22; 0.27; 0.28; 0.39            STMR = 0.27            HR = 0.39  <u>OECD</u>            Mean + 4xSD = 0.891  <b>CF x 3xmean = 1.170</b></p>
(22)	MRL Evaluation Report, 3. Residues	<p>BCS (page 21 ff, Table 3-1, Overview of available supervised residue trials):            Please note that the non-EU residue values (including STMR and HR) mentioned for <u>grapefruit, lemon, mandarin, tree nuts, grape, blueberry, prickly pear, apple, pear, celery, tomato, pepper, chili pepper, sweet corn, pulses, soybean, hops, coffee, barley, sorghum, wheat, corn, cotton and peanuts</u> are the values calculated according to the residue definition <b>for risk assessment</b> and not for enforcement.</p> <p>The conversion factor for censoring (CF) has to be <b>multiplied</b> with 3 mean</p>	Corrected Table can be sent on request.
(23)	MRL Evaluation Report, 3. Residues	<p>BCS (page 22-23, Table 3-1, Overview of available supervised residue trials):            Please note that the re-calculated values for grapes (according to residue definition for enforcement) are not always correct</p>	<p><b>Enforcement:</b>  <b>Grape (N-EU)</b>            0.17; 0.19; 0.23; 0.24; 0.26; 0.37; 0.45; 0.48; 0.50            STMR: 0.26 mg/kg            HR: 0.50 mg/kg  <u>OECD</u>            Mean + 4xSD = 0.841</p>

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			<p>CF x 3xmean = 0.963  MRL = 1 mg/kg  <b>Grape (S-EU)</b>  0.07; 0.10; 0.15; 0.16; 0.18; 0.19; 0.27; 0.33  STMR: 0.17 mg/kg  HR: 0.33 mg/kg  <u>OECD</u>  Mean + 4xSD = 0.521  CF x 3xmean = 0.544  MRL = 0.5 mg/kg</p>
(24)	MRL Evaluation Report, 3. Residues	<p>BCS (page 24 ff, Table 3-1, Overview of available supervised residue trials):  Please note that the re-calculated values (EU trials) for <u>pepper, cucumber, tomato, lettuce</u> (according to residue definition for enforcement and the residue definition for RA) are not always correct</p>	Corrected Table can be sent on request.
(25)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	<p>BCS (page 32-33, processing):  The last sentence on page 32 and the first sentence of page 33 are a bit confusing:  For new proposals, see column 3</p>	<p>The respective LOQs for BYI 02960 and its metabolites DFA and DFEAF were 0.01, 0.02, and 0.01 mg/kg (all in parent equivalents) yielding a calculated LOQ of 0.03* mg/kg for monitoring (<b>since only BYI 02960 and DFA are considered</b>).  Only for one barley processing fraction higher LOQs were <b>needed</b>: LOQs were 0.1 mg/kg for BYI 02960 and DFEAF in hops draff and 0.2 mg/kg for DFA in hops draff (see study C.3.2.2.1).</p>
(26)	MRL Evaluation Report, 3.1.1.3 Effect of	BCS (page 32-33, processing factors and correction factors for barley):	Example calculation (rounding to two significant numbers):

## Section 3 - Residues (B.7)

<b>Other comments</b>																																																			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations																																																
	industrial processing...	<p>The residue for risk assessment was calculated by summing up the residues of BYI 02960, DFA and DFEAF. After summation the value was rounded to two <u>significant numbers</u> – this value was reported in the report</p> <p>When re-calculating the residue for monitoring by the RMS, the residues of BYI 02960 and DFA were added and rounded to <u>two decimal places</u>.</p> <p>When calculating the CF the same rounding rules should be applied.</p> <p>However, the rounding differences are minimal and considering that the conversion factor will be set to 1, no re-calculation is needed.</p>	<p><b>Table 3-2. Overview of the available processing studies with barley</b></p> <table border="1"> <thead> <tr> <th>Processed commodity</th> <th>Number of studies</th> <th>Median PF<sup>(a)</sup> Monitoring</th> <th>Median PF<sup>(b)</sup> Risk assessment</th> <th>Median CF<sup>(c)</sup></th> </tr> </thead> <tbody> <tr> <td>Malt sprouts</td> <td>2</td> <td>0.77</td> <td>0.91</td> <td><b>1.18</b></td> </tr> <tr> <td>Brewer's malt</td> <td>2</td> <td>0.49</td> <td>0.52</td> <td><b>1.05</b></td> </tr> <tr> <td>Brewer's grain</td> <td>2</td> <td>0.07</td> <td>0.08</td> <td><b>1.10</b></td> </tr> <tr> <td>Hops draff</td> <td>2</td> <td><b>0.35</b></td> <td>0.44</td> <td><b>1.23</b></td> </tr> <tr> <td>Brewer's yeast</td> <td>2</td> <td>0.10</td> <td>0.11</td> <td><b>1.08</b></td> </tr> <tr> <td>Beer</td> <td>2</td> <td>0.08</td> <td>0.08</td> <td><b>1.10</b></td> </tr> <tr> <td>Pearl barley rub off</td> <td>2</td> <td><b>2.93</b></td> <td>2.87</td> <td><b>0.99</b></td> </tr> <tr> <td>Pearl barley</td> <td>2</td> <td><b>0.12</b></td> <td>0.13</td> <td><b>1.10</b></td> </tr> </tbody> </table> <p>(a): The median processing factor is obtained by calculating the median of the individual processing factors of each processing study. The processing factor has to be applied to the sum of BYI 02960 and DFA (i.e. to be applied to the measured residue according to the residue definition for monitoring corrected with the correction factor CF to include DFEAF).</p> <p>(b): The median processing factor is obtained by calculating the median of the individual processing factors of each processing study. The processing factor has to be applied to the sum of BYI 02960, DFA and DFEAF (residue definition for risk assessment).</p> <p>(c): CF = correction factor to convert the residue for monitoring into the residue for risk assessment. The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.</p>	Processed commodity	Number of studies	Median PF <sup>(a)</sup> Monitoring	Median PF <sup>(b)</sup> Risk assessment	Median CF <sup>(c)</sup>	Malt sprouts	2	0.77	0.91	<b>1.18</b>	Brewer's malt	2	0.49	0.52	<b>1.05</b>	Brewer's grain	2	0.07	0.08	<b>1.10</b>	Hops draff	2	<b>0.35</b>	0.44	<b>1.23</b>	Brewer's yeast	2	0.10	0.11	<b>1.08</b>	Beer	2	0.08	0.08	<b>1.10</b>	Pearl barley rub off	2	<b>2.93</b>	2.87	<b>0.99</b>	Pearl barley	2	<b>0.12</b>	0.13	<b>1.10</b>			
Processed commodity	Number of studies	Median PF <sup>(a)</sup> Monitoring	Median PF <sup>(b)</sup> Risk assessment	Median CF <sup>(c)</sup>																																															
Malt sprouts	2	0.77	0.91	<b>1.18</b>																																															
Brewer's malt	2	0.49	0.52	<b>1.05</b>																																															
Brewer's grain	2	0.07	0.08	<b>1.10</b>																																															
Hops draff	2	<b>0.35</b>	0.44	<b>1.23</b>																																															
Brewer's yeast	2	0.10	0.11	<b>1.08</b>																																															
Beer	2	0.08	0.08	<b>1.10</b>																																															
Pearl barley rub off	2	<b>2.93</b>	2.87	<b>0.99</b>																																															
Pearl barley	2	<b>0.12</b>	0.13	<b>1.10</b>																																															

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 46/56

### Section 3 - Residues (B.7)

Other comments							
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations				
			Processed commodity	Number of studies	Median PF <sup>(a)</sup> Monitoring	Median PF <sup>(b)</sup> Risk assessment	Median CF <sup>(c)</sup>
(27)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (page 34, processing factors and correction factors for wheat): <ul style="list-style-type: none"> <li>- Conversion factors have to be estimated on same calculation basis for monitoring and risk assessment method (see above)</li> <li>- please correct value for white flour (0.33 instead of 0.36)</li> </ul> <p>=&gt; please consider that due to different rounding, slightly different values will occur for some of the conversion factors. However all CF are approx. 1 and the conclusion is that no conversion factor is needed.</p>	Semolina bran	2	5.17	4.99	0.97
			Semolina	2	0.95	0.98	1.03
			White flour bran	2	6.63	6.35	0.96
			White flour	2	<b>0.33</b>	0.36	1.10
			white bread	2	0.27	0.30	1.14
			Whole meal	2	1.50	1.48	0.98
			Whole meal bread	2	0.92	0.92	1.00
			Wheat germ	2	1.07	1.07	1.00
(28)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (page 34, Table 3-3b, wheat): <ul style="list-style-type: none"> <li>- Please correct header:</li> </ul> <p>Overview of the available processing studies with <b>wheat</b> (USA)</p>					
(29)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (page 34, Table 3-3b, wheat): <ul style="list-style-type: none"> <li>- Was the processing factor in the USEPA evaluation really calculated on the basis of the residue definition for monitoring? (In the dossier submitted by BCS, the residue definition for risk assessment was the basis).</li> <li>- it is not conclusive that for IT crops no conversion factor is calculated, but for the EU</li> </ul>					

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		crops => however if the conclusion from the EU trials is that no CF is needed, it is okay -the conclusion that the conversion factor monitoring/risk assessment will be set to 1 is missing – please add this in the conclusions	
(30)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (general remark): - No processing factors were described for lettuce, hops, peach, potato and sugar cane (these data were provided in the Annex II dossier)	
(31)	MRL Evaluation Report, 3.1.2 Rotational crops	BCS (page 41, 3.1.2.1 Preliminary considerations): Oilseed rape was also tested in a rotational crop study.	To further substantiate residues in representative succeeding crops, rotational crop field studies performed <del>with</del> -after application of 2x125 g flupyradifurone/ha to bare soil and short plant back intervals in potatoes, leeks, cucumbers, onion, French beans, <del>and</del> peas and <b>oilseed rape</b> which are evaluated in this Evaluation Report.
(32)	MRL Evaluation Report, 3.1.2 Rotational crops	BCS (page 41, 3.1.2.1 <i>Validation of the analytical method</i> ): - Typo in last paragraph - please add that method was also validated for crops with high oil content	Flupyradifurone residues in the rotational crop field studies were determined using method 01304. The method was validated for the determination of parent BYI 02960 and its metabolites difluoroacetic acid (DFA) and BYI 02960-difluoroethyl-amino furanone ( <b>DFEAF</b> ) in crops <b>with high water and high acid content, in dry-starch crops and in crops with high oil content.</b>
(33)	MRL Evaluation Report, 3.1.2 Rotational crops	BCS (page 41, 3.1.2.1 <i>Validation of the analytical method</i> ): - This paragraph refers only to the rotational field study conducted with three rotations ("main	The limit of quantitation (LOQ) for BYI 02960 and DFEAF, defined as the lowest validated fortification level, was 0.01 mg/kg in all matrices tested. All metabolite levels are expressed in parent equivalents. For DFA, the LOQ was 0.02 mg/kg in crop matrices high in acid and water content (e.g.

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>study"), however a lot of additional rotational field studies were conducted with a 30-day plant-back interval  =&gt; Please adapt the paragraph  - Please correct the LOQ information</p>	<p>oranges, tomatoes) or 0.05 mg/kg in dry/protein-rich matrices, fodder materials, and soybeans.</p> <p>⇒ Total calculated LOQ for crop matrices with high in acid and water content: 0.04 mg/kg</p> <p>⇒ Total calculated LOQ for dry/protein-rich matrices, fodder materials, and soybeans 0.07 mg/kg</p>
(34)	MRL Evaluation Report, 3.1.2.2 Nature of residues	<p>BCS (page 42, 3.1.2.2 Nature of residues):  - BYI 02960-difluoroethyl-aminofuranone (DFEAF) was only detected in higher amounts in the matrices of Swiss chard in the confined rotational crop studies (all rotations); in primary crops it was generally a minor metabolite.  Since DFEAF was not observed in the rat and the metabolism studies indicated that no other appropriate marker compound was present in rotational crops, BCS proposed to include this metabolite in the residue definition for risk assessment.</p>	<p>Due to the results of the confined rotational crop studies, DFEAF was included in the residue definition for risk assessment.</p> <p>However, the only residues of BYI 02960 that were consistently observed at significant levels across all primary and succeeding crops in <u>field studies</u> were the parent compound BYI 02960 and DFA, both of which are specific to BYI 02960 use.</p>
(35)	MRL Evaluation Report, 3.1.2.3 Magnitude of residues	<p>BCS (page 43, 3.1.2.2 Magnitude of residues, Table 3.1.2.3-01):  - harvest interval for carrot: 95-114 days</p>	
(36)	MRL Evaluation Report, 3.1.2.3 Magnitude of	<p>BCS (page 43-44, 3.1.2.2 Magnitude of residues, Table 3.1.2.3-03):</p>	

## Section 3 - Residues (B.7)

<b>Other comments</b>																														
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations																											
	residues	<ul style="list-style-type: none"> <li>- the residues given in the table are the sum of parent compound, <b>DFA and DFEAF</b> (all expressed in parent equivalents)</li> <li>- how were the mean values (mean of NEU and SEU) calculated?</li> <li>- how was the CF calculated? Based on mean values calculated according to the different residue definitions (monitoring/RA)?</li> <li>- cucumber DAT: <b>69-83</b></li> <li>- French bean: Residues in NEU: <b>0.59-1.1</b> Residues in SEU: <b>0.28-0.40</b></li> <li>- field pea DAT: <b>100-144</b></li> </ul>																												
(37)	MRL Evaluation Report, 3.1.2.3 Magnitude of residues	BCS (page 44, 3.1.2.2 Magnitude of residues, Table 3.1.2.3-03): <ul style="list-style-type: none"> <li>- the residues given in the table are the sum of parent compound, <b>DFA and DFEAF</b> (all expressed in parent equivalents) – at least for the first line...</li> <li>- how was the CF calculated?</li> <li>- a separate MRL for root vegetables could be calculated based on the residues in rotational carrots and turnips</li> </ul>	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th rowspan="2"><b>Crop</b></th> <th colspan="3"><b>Total residue (BYI 02960 + DFA + DFEAF, expressed as BYI 02960) in mg/kg</b></th> </tr> <tr> <th><b>STMR</b></th> <th><b>HR</b></th> <th><b>MRL</b></th> </tr> </thead> <tbody> <tr> <td>Root and <del>tuber</del> Tuber vegetables</td> <td>0.13</td> <td>0.27</td> <td><b>0.6</b></td> </tr> <tr> <td>Stem vegetables</td> <td><b>0.08</b></td> <td>0.25</td> <td><b>0.5</b></td> </tr> <tr> <td>Bulb vegetables</td> <td><b>0.08</b></td> <td>0.18</td> <td><b>0.3</b></td> </tr> <tr> <td>Fruiting vegetables</td> <td><b>0.32</b></td> <td>0.43</td> <td><b>0.9</b></td> </tr> <tr> <td>Sweet corn</td> <td><b>0.35</b></td> <td><b>0.65</b></td> <td><b>1.5</b></td> </tr> </tbody> </table>	<b>Crop</b>	<b>Total residue (BYI 02960 + DFA + DFEAF, expressed as BYI 02960) in mg/kg</b>			<b>STMR</b>	<b>HR</b>	<b>MRL</b>	Root and <del>tuber</del> Tuber vegetables	0.13	0.27	<b>0.6</b>	Stem vegetables	<b>0.08</b>	0.25	<b>0.5</b>	Bulb vegetables	<b>0.08</b>	0.18	<b>0.3</b>	Fruiting vegetables	<b>0.32</b>	0.43	<b>0.9</b>	Sweet corn	<b>0.35</b>	<b>0.65</b>	<b>1.5</b>
<b>Crop</b>	<b>Total residue (BYI 02960 + DFA + DFEAF, expressed as BYI 02960) in mg/kg</b>																													
	<b>STMR</b>	<b>HR</b>	<b>MRL</b>																											
Root and <del>tuber</del> Tuber vegetables	0.13	0.27	<b>0.6</b>																											
Stem vegetables	<b>0.08</b>	0.25	<b>0.5</b>																											
Bulb vegetables	<b>0.08</b>	0.18	<b>0.3</b>																											
Fruiting vegetables	<b>0.32</b>	0.43	<b>0.9</b>																											
Sweet corn	<b>0.35</b>	<b>0.65</b>	<b>1.5</b>																											

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 50/56

### Section 3 - Residues (B.7)

Other comments						
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations			
			legumes	<b>0.50</b>	1.1	<b>2.0</b>
			Leafy vegetables	<b>0.08</b>	<b>0.21</b>	<b>0.4</b>
			pulses	1.6	2.3	<b>5</b>
			oilseeds	0.10	0.17	<b>0.3</b>
			Cereal grains	<b>0.35</b>	<b>0.65</b>	<b>1.5</b>
(38)	MRL Evaluation Report, 3.2 Nature of the magnitude of residues in livestock	BCS (page 45ff, 3.2 Nature of the magnitude of residues in livestock) - Please refer to the remarks made for the DAR - Please align tables in the DAR and the MRL Evaluation Report				
(39)	MRL Evaluation Report, 4. Consumer risk assessment	BCS (page 60-62, Table 4-1 Input values for consumer risk assessment) - What is the reason for not using the IT-MRLs for the highly traded commodities: root & tuber vegetables; bulb vegetables; cattle and poultry matrices, except for milk and eggs? -				
(40)	MRL Evaluation Report, 4. Consumer risk assessment	BCS (page 62, Table 4-1 Input values for consumer risk assessment) - <u>Chronic RA</u> : Input values for poultry liver and milk were permuted milk: 0.3 mg/kg poultry liver: 1.0 mg/kg				

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<ul style="list-style-type: none"> <li>- Chronic and acute RA: Input values for goat and sheep milk should be <b>0.08 mg/kg</b></li> <li>- Chronic RA: Input values for all other commodities should be <b>0.03 mg/kg*</b></li> </ul>	
(41)	MRL Evaluation Report, 4. Consumer risk assessment	BCS (page 62, Table 5-1 Overview of the proposed EC MRLs) <ul style="list-style-type: none"> <li>- Numbering of Table? =&gt; Table 4.2</li> </ul>	
(42)	MRL Evaluation Report, 4. Consumer risk assessment	BCS (page 63, Table 5-1 Overview of the proposed EC MRLs) <p>According to guidance SANCO 7525/VI/95 rev 9 extrapolation</p> <ul style="list-style-type: none"> <li>- from apples to the whole crop group (pome fruit) is possible</li> <li>- from almonds or pecan to the whole group of closed nuts is possible</li> <li>- from cucumbers to the whole crop group (cucurbits, edible peel) is possible</li> <li>- from peas to the whole crop group (pulse) is possible</li> </ul>	
(43)	MRL Evaluation Report, 4. Consumer risk assessment	BCS (page 64, Table 5-1 Overview of the proposed EC MRLs) <p>Cotton seeds should be added (except from the other oilseeds). Proposed IT-MRL: <b>0.9 mg/kg</b></p>	
(44)	MRL Evaluation Report, Appendix A, Good Agricultural Practices	BCS (page 74, GAPs): <p>Pome fruit (home &amp; garden use):  application rate in EU-N:  <b>2 x 0.06 kg a.s./ha x mCH</b>  application rate in EU-S:</p>	

## Section 3 - Residues (B.7)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		1 x <b>0.06</b> kg a.s./ha x mCH	
	MRL Evaluation Report, Appendix A, Good Agricultural Practices	BCS (page 75, GAPs): Fruiting vegetables (greenhouse): missing PHI application rate: 2 x 0.1125 kg a.s./ha x mCH; <b>PHI = 3 days</b>	
(45)	MRL Evaluation Report, Appendix B, PRIMo	BCS (page 77ff, PRIMo): - Please refer to the remarks made for the DAR - Please align MRL Evaluation Report and DAR	

Section 4 - Environmental fate and behaviour (B.8)

**4. Environmental fate and behaviour (B.8)**

<b>Route and rate of degradation in soil (B.8.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>PEC in soil (B.8.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

## Comments of Applicant on the draft assessment report on flupyradifurone

(01.04.2014) 54/56

### Section 4 - Environmental fate and behaviour (B.8)

<b>PEC in surface water and ground water (B.8.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Fate and behaviour in air and PEC in air (B.8.7 – B.8.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Definition of the residues (B.8.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

## Section 5 - Ecotoxicology (B.9)

**5. Ecotoxicology (B.9)**

<b>Birds and mammals (B.9.1 and B.9.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

<b>Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier/applicant>>: <<comment>>	

## Section 5 - Ecotoxicology (B.9)

<b>Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <><>, <><>	<><>: <><>	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. #, <><>, <><>	<><>: <><>	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

**1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)**

**AT: not considered**

Section 2 - Mammalian toxicology (B.6)

**2. Mammalian toxicology (B.6)**

**AT: not considered**

Section 3 - Residues (B.7)

**3. Residues (B.7)**

**AT: not considered**

## Section 4 - Environmental fate and behaviour (B.8)

### **4. Environmental fate and behaviour (B.8)**

**AT: not considered**

## Section 5 - Ecotoxicology (B.9)

**5. Ecotoxicology (B.9)**

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.9.4.4.1	AT: The calculation of in-field and off-field HQ values for bees is not foreseen in the guidance document. The calculation of off-field HQs indicates that there might be no risk for bees in the off-field and hence a higher tier risk assessment is not required. Please clarify the purpose of the calculation of off-field HQ values.	
(2)	Vol. 3, B.9.5.2	AT: The table B.9.5.2-02 (p. 367) is not readable; please change the table.	

# Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 1/22

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

## 1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

<b>Identity (B.1, Annex C)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	C.1.1.2	FR: The table of synonyms and abbreviation is reported 2 times in this paragraph	
(2)	C.1.2.2 Table C.1.2.2-01	FR: the impurities 1, 5, 6, 11 and 13 are not specified but described in C.1.2.2  Please RMS explain why the other impurities not detected or <LOQ are nor described in C.1.2.2  Moreover, the number of impurities given in C.1.2.2 does not correspond to the number given in Table C.1.2.2-01 (ex in C.1.2.2 water is the impurity 15 and in the table it is the impurity 20)	
(3)	C.1.2.2 Table Justificationpf specified maximum purity of active substance and minimum content of impurities	FR: Please RMS explain why for some impurities, 2 specification limits are proposed.	
(4)	C.1.2.3Analytical methods	FR: Please RMS give the method used for the confirmation of the identity of each impurity	

## Physical and chemical properties of the active substance (B.2.1)

No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	B.2.1 Physical and	FR : For a better readability, the complete chemical	

## Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 2/22

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Physical and chemical properties of the active substance (B.2.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	chemical properties of the active substance	name of the metabolites should be reported	
(2)	B.2.1 Physical and chemical properties of the active substance	FR : Please RMS, explain why some physical and chemical properties are presented for 5 metabolites as they are not relevant	

<b>Physical, chemical and technical properties of the formulation (B.2.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	B.2.2 Physical and chemical properties of the plant protection product	FR : For a better readability, the minimum and maximum use concentrations and the commercial packaging should be reported	
(2)	B.2.2.14 Storage stability B.2.2.15 Shelf life	FR : For a better readability, physical and chemical properties after storage should be reported	

<b>Further information (B.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		-	

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	B.5.1.1 Technical active	FR: the concentration used for the precision test	

## Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 3/22

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

Methods of analysis (B.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	substance B.5.1.2 Plant protection product	should be provided to calculate Horwitz value	
(2)	B.5.2 Analytical methods (residue)	FR : For a better readability, residue definition should be reported	
(3)	B.5.2 Analytical methods (residue)	FR : For a better readability, the complete chemical name of the metabolite DFA should be reported	
(4)	B.5.2 Analytical methods (residue)	FR : The test facility of each study (primary methods and ILVs) should be reported	
(5)	B.5.2 Analytical methods (residue)	FR : The description of the methods should be detailed (column, ion mode ...)	
(6)	B.5.2 Analytical methods (residue)	FR : It is not necessary to report overall recovery of the 2 fortification levels	
(7)	B.5.2 Analytical methods (residue)	FR : Please RMS correct the values of the fortification level for hop (0.05 mg/kg instead of 0.01 mg/kg, and 0.5 mg/kg instead of 0.1 mg/kg)	
(8)	B.5.2 Analytical methods (residue)	FR: The modification M001 of the analytical method 01330 should be explained.	
(9)	B.5.3 Analytical methods (residue) soil	FR : For a better readability, residue definition should be reported	
(10)	B.5.3 Analytical methods (residue) soil	FR: Characteristics of the soil sample (e.g. soil type, pH and organic matter/carbon content) should be provided in the method description to support its selection	
(11)	B.5.3 Analytical methods (residue) soil	FR: The number of the samples used for the calibration should be reported	
(12)	B.5.3 Analytical methods (residue) soil	FR: Please RMS correct : "Untreated Control Samples.... 0.3xLOQ (1.5 µg/kg instead of Hg/kg)"	

## Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 4/22

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(13)	B.5.3 Analytical methods (residue) water	FR : For a better readability, residue definition should be reported	
(14)	B.5.3 Analytical methods (residue) water	In the method description the sampling site should be provided.  Validation quality data shall be provided to demonstrate that the sample is typical surface water in terms of its inorganic load (e.g. conductivity, hardness, pH) and its organic load (e.g. dissolved organic carbon content (DOC)).	
(15)	B.5.3 Analytical methods (residue) water	FR: Please RMS correct : "Limit of Quantification.... 0.05 µg/L instead of Hg/kg"	
(16)	B.5.3 Analytical methods (residue) water	FR: According to the regulation 283/2013, an ILV of the method for the determination of residues in drinking water should be provided	
(17)	B.5.3 Analytical methods (residue) water	FR: The analytical method allows to quantify the active substance flupyradifurone but not DFA and 6-CNA included in the residue definition (see LOEP)	
(17)	B.5.3 Analytical methods (residue) air	FR: It should be mentioned that as the active substance is not classified T, T+, Xi or Xn, no analytical method for the determination of residues in air is necessary	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	LOEP Method of analysis	FR: Please RMS correct the wavelength reported for the method for the determination of impurities in technical sa (210 nm instead of 20)	

## Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 5/22

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(2)	LOEP Method of analysis	FR: LOQ for flupyradifurone in fat, liver, kidney, muscle, egg and milk is 0.01 mg/kg and not 0.02 mg/kg	

## Section 2 -Toxicology

## 2. Mammalian toxicology (B.6)

<b>Acute toxicity (B.6.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.2.1 Acute toxicity Study 1	FR: According to mortalities observed at 2000 mg/kg bw (3/3 and 1/3 deaths), the LD50 would be below 2000 mg/kg. The conclusion on classification does not change.	
(2)	Vol. 3, B.6.2.2 Irritation and sensitisation Study 3	FR: Could you please clarify the highest tested dose in the LLNA study is 50% of BYI 02960? The preparation BYI 02960 SL 200g/L was found to be sensitizing (without any sensitizing substance in the composition), a highest dose could have been tested on flupyradifurone.	

<b>Short-term toxicity (B.6.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.3.1 28-day oral studies Study 1	FR: We suggest to set a LOAEL of 75 mg/kg bw/d based on observed effects on liver and clinical chemistry.	
(2)	Vol. 3, B.6.3.1 28-day oral studies Study 2	FR: We suggest to set a LOAEL of 500 ppm or 33.6 mg/kg bw/d based on observed effects on liver and clinical chemistry.	
(3)	Vol. 3, B.6.3.1 28-day oral studies Study 3	FR: Could you please explain why the effects on epididymis weight have not been taken into account from 300 ppm (statically decreased).	

# Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 7/22

## Section 2 -Toxicology

<b>Short-term toxicity (B.6.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(4)	Vol. 3, B.6.3.4 semichronic oral studies Study 1	FR: We suggest to set a NOAEL of 100 ppm or 6 mg/kg bw/d for male and 7.6 mg/kg bw/d for female, based on decreased of body weight and body weight gain at 500 ppm and 2500 ppm.	

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity Study 1	FR: In the liver, an increased in incidence and severity of alteration eosinophilic focus of hepatocellular and a higher incidence of centrilobular hepatocellular hypertrophy was found in male at 400 ppm and 2000 ppm. Furthermore in the thyroid, increased incidences of colloid alteration were noted in male at 400 ppm and 2000 ppm.  Due to observed effects on liver and thyroid, the NOAEL for general toxicity need to be discussed. France suggests setting the NOAEL at 80 ppm based on observed effects on liver and thyroid in male at 400 ppm and 2000 ppm.	

## Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 8/22

### Section 2 -Toxicology

<b>Reproductive toxicity (B.6.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.6.1 Reproductive toxicity Study 1	FR: The table 6.6.1-3 is the same as the table 6.6.1-4. Could you please update the study summary	
(2)	Vol. 3, B.6.6.1 Reproductive toxicity Study 2	FR: We suggest to set the parental systemic NOAEL and the offspring NOAEL at 100 ppm, based on decreased of body weight and body weight gain at 500 ppm and 1800 ppm in parental and F1 generation during premating, gestation and lactation and on offspring in F1 and F2 generation.	

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.9 Studies on metabolites B.6.9.1.1 Acute toxicity Difluoroacetic acid (DFA, BCS-AA56716,M44) Study 1	FR: Could you please harmonise the number of death at 2000 mg/kg between the text and the table 6.9.1.1-1.	
(2)	Vol. 3, B.6.9.1.3 Short term studies Difluoroacetic acid (DFA, BCS-AA56716,M44)	FR: We suggest to set a LOAEL of 500 ppm or 48 mg/kg bw/d for male and 51 mg/kg bw/d for female, based on decreased of glucose concentration in both sexes at 500 ppm, 2000 ppm and 8000 ppm.	

## Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 9/22

### Section 2 -Toxicology

Other toxicological studies & Medical data (B.6.8-B.6.9)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Study 1		
(3)	Vol. 3, B.6.9.1.3 Short term studies Difluoroacetic acid (DFA, BCS-AA56716,M44) Study 2	FR: We suggest to set a LOAEL of 200 ppm or 12.7 mg/kg bw/d for male and 15.6 mg/kg bw/d for female, based on decreased of glucose concentration in both sexes at 200 ppm, 1000 ppm and 6000 ppm.	
(4)	Vol. 3, B.6.9.2.2 Genotoxicity BYI 02960-difluoroethyl-amino-furanone (BCS-CC98193, BYI 02960-DFAEF,M34)	FR: In the study 3, the results of solvent controls are not in the range of historical solvent controls. In the study 4, a dose dependent increased is observed in the micronuclei test. Therefore, the result could be considered as equivocal.  For these reasons, the genotoxic potential of BYI 02960-DFAEF need to be discussed.	
(5)	Vol. 3, B.6.9.2.3 Short term studies Study 1	FR: We suggest to set a LOAEL of 1280 ppm or 135 mg/kg bw/d for male and female, based on decreased of glucose concentration at 1280 ppm, 3200 ppm, 8000 ppm and 20000 ppm.	
(6)	Vol. 3, B.6.9.2.3 Short term studies Study 2	FR: We suggest to set a NOAEL of 800 ppm or 68 mg/kg bw/d for male and 76 mg/kg bw/d for female, based on decreased of body weight in both sexes at 3000 ppm.	
(7)	Vol. 3, B.6.9.6 Applicant's Position papers on metabolites	FR: Considering the LOAEL of 200 ppm, based on decreased of glucose concentration in both sexes at 200 ppm, 1000 ppm and 6000 ppm, setting in the 28 days study on difluoroacetic acid (DFA);	

## Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 10/22

### Section 2 -Toxicology

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>the toxicity of this metabolite is not covered by the overall toxicological profile of the parent compound.</p> <p>It is the same for the metabolite BYI 02960-difluoroethyl-amino-furanone (BYI 02960-DFEAF) which genotoxic potential should be discussed.</p>	

<b>Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.11.3 ADI	FR: Pending the discuss on the NOAEL in the 2 years rat study, France suggests setting an ADI of 0.032 mg/kg bw/d on the basis of NOAEL of 3.17 mg/kg bw/d, applying a standard assessment factor of 100.	
(2)	Vol. 3, B.6.11.5 AOEL	<p>FR: We suggest to set an AOEL of 0.078 mg/kg bw/d on the basis of NOAEL of 7.8 mg/kg bw/d from the 1 year oral dog study, applying a standard assessment factor of 100.</p> <p>This AOEL can be supported by the NOAEL of 7.6 mg/kg bw/d from the 90-days oral rat study, the NOAEL of 7.8 mg/kg bw/d from the 2-generation rat study and by the NOAEL of 12 mg/kg bw/d from the 90-days oral dog study.</p>	

Section 3- Residues

**3. Residues (B.7)**

This section has not been peer reviewed

Section 4 - Environmental fate and behaviour (B.8)

**4. Environmental fate and behaviour (B.8)**

<b>Route and rate of degradation in soil (B.8.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	B.8.2 Adsorption, desorption and mobility in soil (IIA 7.1.2, 7.1.3, IIIA 9.1.2)  B.8.2.1 Batch sorption STUDY IIA, 7.4.1/03	FR : For flupyradifurone, Koc values were derived from soil which pH range is narrow (i.e. from 5.3 to 7.2). Please note that Koc values seem to decrease with higher pH values.  Then alkaline conditions may not be covered by this narrow pH range and risk assessment may not cover such conditions.	Alkaline conditions may have been investigated using the San Juan Bautista soil (used only for metabolite 6-chloronicotinic acid) having a soil pH value of 8.3.
	B.8.2 Adsorption, desorption and mobility in soil (IIA 7.1.2, 7.1.3, IIIA 9.1.2)  B.8.2.1 Batch sorption STUDY IIA, 7.4.1/03	FR : Koc values for both 6-chloronicotinic acid and BYI 02960-DFA were derived using soil which pH (H <sub>2</sub> O) range is narrow (respectively from 6.2 to 8.3 and 5.8 to 7.4).	

## Section 4 - Environmental fate and behaviour (B.8)

	<p>B.8.2 Adsorption, desorption and mobility in soil (IIA 7.1.2, 7.1.3, IIIA 9.1.2)</p> <p>B.8.2.1 Batch sorption STUDY IIA, 7.4.1/03</p>	<p>FR: FR agrees that time dependent sorption may be requested to adequately address pesticides leaching in soils as demonstrated in literature.</p> <p>The background information reviewed by RMS in its DAR would certainly be of interest for illustrating practical cases.</p> <p>Back to regulatory world, FR also agrees that no peer-review guidance on TDS have been adopted in Europe.</p> <p>Since there is no EU guidance on TDS, and for consistency with current risk assessment performed for PPP at EU level, TDS studies and following refinements based on TDS should be included as informative information only.</p>	<p>If refinements may be proposed at EU level using TDS, one may acknowledge that for consistency at EU level and following national decisions a common agreement should be achieved on how implementing TDS in PPP risk assessment.</p> <p>Please note that in the DAR the “ UK guidance” is from time to time taken as reference : <i>“The RMS concludes that the study has been well conducted and that its results (i.e. decline curves of BYI 02960) are in line with the draft guidance on time dependent sorption and are suitable to be used in a kinetic analysis to calculate time dependent sorption parameters”</i>; and sometimes not : <i>“The RMS was aware that in the guidance on how aged sorption studies for pesticides should be conducted, analysed and used in regulatory assessments () a different opinion is presented, i.e. not to combine the TDS and batch adsorption/desorption data »</i>.</p>
	<p>B.8.2 Adsorption, desorption and mobility in soil (IIA 7.1.2, 7.1.3, IIIA 9.1.2)</p> <p>B.8.2.1 Batch sorption STUDY IIA, 7.4.1/03</p>	<p>FR: The material and method to define accurate TDS parameters may not be accurate. For instance, the extraction performed may not accurately account for true available fraction. It may lead to underestimate the amount of available active substance and to overestimate adsorption. This may influence all the derived parameters and following calculations.</p> <p>TDS studies and following refinements based on TDS should be included as informative information only.</p>	<p>If refinements may be proposed at EU level for future PPP risk assessment using TDS, definition and agreement on a material and method to define accurate TDS parameters would be of importance.</p>

# Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 14/22

## Section 4 - Environmental fate and behaviour (B.8)

<b>PEC in soil (B.8.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

<b>PEC in surface water and ground water (B.8.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	B.8.6 Predicted environmental concentrations in surface water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3)  B.8.6.3 Predicted concentrations in groundwater (Annex IIIA 9.2.1)	Since there is no EU guidance on TDS, and for consistency with current risk assessment at EU level, TDS studies and following PEC gw refinements based on TDS should be included as informative information only and deleted from the LoEP.	
	B.8.6 Predicted environmental concentrations in surface water, in sediment and in	FR: It should be confirmed and indicated in the DAR that the mitigation factors used for runoff are according to FOCUS L&M.  It's not obvious which mitigations values were used	

## Section 4 - Environmental fate and behaviour (B.8)

<b>PEC in surface water and ground water (B.8.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3) B.8.6.1 Predicted concentrations in surface water (Annex IIIA 9.2.3)	for 10; 15 and 20 m vegetative buffer strips, please clarify.	
	B.8.6 Predicted environmental concentrations in surface water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3) B.8.6.1 Predicted concentrations in surface water (Annex IIIA 9.2.3)	FR: PECsw and sed provided for hops include at minimum a nozzle drift reduction of 25 %. Please provide additional values including no drift reduction for relevant uses.	In FR, mitigation measures based on nozzle drift reduction can not be proposed (only un-treated and vegetated buffer zones can be).
	B.8.6 Predicted environmental concentrations in surface water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3) B.8.6.1 Predicted concentrations in surface water (Annex IIIA 9.2.3)	FR: Please confirm that no PECsed accumulation are needed for the intended uses (see ecotox section).	

# Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 16/22

## Section 4 - Environmental fate and behaviour (B.8)

<b>Fate and behaviour in air and PEC in air (B.8.7 – B.8.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

<b>Definition of the residues (B.8.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	Vol1; LoEP	Since there is no EU guidance on TDS, and for consistency with current risk assessment of AS at EU level, TDS studies and following PEC gw refinements should be deleted from the LoEP	
	B.8.3 Predicted environmental concentrations in soil (PECs) (Annex IIIA, 9.1.3)  B.8.6 Predicted environmental concentrations in surface water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3)	FR: FR agrees with RMS that there are currently no agreed European guidelines for the assessment of exposure from the use in glasshouses the pragmatic approach assuming that the use in glasshouses is covered by the outdoor field use. Still, when checking the approach in the different compartments, the approach followed is not the same: For soil it is assumed that the use in glasshouses is covered by the outdoor field use (no PEC and no reference of the different use pattern); for GW, calculations were provided using specific GAP for indoor use (2 applications); and for SW it is assumed that the use in glasshouses is covered	

## Section 4 - Environmental fate and behaviour (B.8)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		by the outdoor field use even considering of the different use pattern. Please clarify.	
	Table B.8.3-01 Application pattern used for PECsoil calculations of BYI 02960; + GAP table in Vol1	FR: table footnotes; please check if "biannual" is the right wording.	
	B8	FR: FR thanks the RMS for producing a comprehensive DAR.	

## Section 5- Ecotoxicology

## 5. Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol 3, B.9.3 Effects on terrestrial vertebrates	FR: We agreed with RMS proposal to consider the NOEL of 34 mg/kg bw/d derived from the toxicological studies (B.6) for screening and tier 1 calculations.	
(2)	Vol 3, B.9.3 Effects on terrestrial vertebrates  Residue decline and 21d-Ftwa proposal  Vol. 1 2.6.1.2 Effects on mammals	FR: The mean 21d-Ftwa approach proposed for lettuce and hops uses should be discussed in expert meeting as the approach is quite new and need agreement to facilitate the assessment at national and zonal level. Therefore, the appropriateness of this approach should be discussed for single and multiple applications, <i>e.g.</i> case where moving “TWA x MAF” are required.  In addition, we agree with the RMS that due to the experimental conditions for the 17 trials carried out on lettuce further justifications are needed to consider that the trials also cover early application stages.	

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol 3, B.9.2 Effects on	FR: FR: There are some uncertainties regarding the	

## Section 5- Ecotoxicology

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	aquatic organisms  Vol. 1 2.6.2 Effects on aquatic organisms	term biannual associated with intended uses on lettuce. Could RMS precise if the term biannual in the DAR refers to two applications per year or one application every two years. In the last case biannual is wrongly used and the term biennial should be used.  Due to these uncertainties could RMS clarify whether PECsw Step 2 for use in lettuce two application per year or one application every two years? In addition, could you, please, also indicate the frequency of applications used for the estimation of the PECsw in Step 3 and Step 4. If the TER are based on one application every two years, then annual application could not be considered covered and the risk assessment could have to be revised.	
(2)	Vol 3, B.9.2 Effects on aquatic organisms	FR: In line with the e-fate comment regarding PECsw, could it be possible to add TER calculation with buffer zone (drift + run-off) only for uses in hops?	
(3)	Vol 3, B.9.2 Effects on aquatic organisms	FR: In line with the e-fate comment regarding PECsed, please confirm that no risk assessment for sediment dwelling organisms is needed?	

## Comments of France on the draft assessment report on Flupyradifurone

(07.04.2014) 20/22

### Section 5- Ecotoxicology

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1 and Vol 3 B.9.4, Effects on bees	FR: The data and risk assessment for bees is well-built, clear and agreed.	

<b>Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1 Vol. 3 B.9.6, B.9.7 and B.9.8 Effects on soil organisms	FR: To our understanding for glasshouse “soil bound” indicates that this structure could be set up on natural soils. If it the case, the risk assessment on lettuce for biannual applications (two applications per year) in glasshouse with soil bound may be performed as the GAP for field uses do not cover this intended use. New PEC accumulations calculations could be needed in case two applications per year have not been already considered.	

<b>Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	-	-	

## Section 5- Ecotoxicology

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1 (page 183) Vol 3 B.3 Table 3.3.1 Vol 3 B.9 Intended uses in Hops	<p>FR: For uses in hops, only one application per year was assessed in B.9 while biannual application (<i>i.e.</i> two applications per year) is reported in the last column of the summary of intended uses (Vol. 1 and Vol.3, B.3, Table 3.3.1). Could RMS clarify?</p> <p>If two applications in hops are possible, then the complete risk assessment should be revised.</p> <p>If the remark means one application every two years, then the term “biennial” should be used (or application every two year).</p>	
(2)	Vol. 1, 2.6	<p>FR: We have an editorial remark for Vol1. We are favourable to limit the detailed assessment to Vol 3 B.9 and to focus on validated assessment in Vol 1. This allows an easier reading of the Vol. 1.</p> <p>For example, all the justifications regarding the choice of the mammalian endpoint or the description of the method used to estimate a mean 21-d FTWA could have not been inserted in Vol 1. As this comment would not impact the conclusions, an update of the current Vol. 1 is not considered necessary.</p>	

## Section 5- Ecotoxicology

<b>Other comments</b>		
<u>Column 1</u>	<u>Column 2</u>	<u>Column 3</u>
Reference to assessment report	Comment (restricted to 500 characters, ca.10 lines)	Further explanations
Vol. 3, B.10 Efficacy, General comment.	FR: The RMS presented a well written evaluation report. As a very minor remark, there is a repetition of text in page 8 – line 4 of the B.10.	

# **Comment of Sweden on the Draft Assessment Report**

## **Flupyradifurone**

Rapporteur Member State: NL

### **Comments on the Sections**

- Proposed decision
- Physical/Chemical properties; Details of uses and further information; Methods of analysis
- Mammalian toxicology
- Residues
- Environmental fate and behaviour
- Ecotoxicology

07 April 2014

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

**1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)**

No comments on this section, not reviewed

Section 3 - Residues (B.7)

**2. Mammalian toxicology (B.6)**

No comments on this section, not reviewed.

Section 3 - Residues (B.7)

**3. Residues (B.7)**

No comments on this section, not reviewed.

Section 4 - Environmental fate and behaviour (B.8)

**4. Environmental fate and behaviour (B.8)**

No comments on this section, not reviewed.

## Section 5 - Ecotoxicology (B.9)

## 5. Ecotoxicology (B.9)

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, IIA, 8.3.2.2/01, Chronic endpoint for <i>C. riparius</i> . Comment also relevant for IIIA, 10.2.6.2/01, chronic chironomus endpoint for the formulation.	SE: We would hesitate to use the nominal concentrations to derive a NOEC since the mean measured concentrations in the test system is only 41% after 28 days. Especially since there is no information regarding fate of the study compound in the study summary, i.e. concentrations in the sediment.  Analytical measurements in the overlying water, pore water and sediment is listed as a minimum requirement in the OECD 219. Measurements should be performed at the start and at the end of the test in at least a higher and a lower concentration.	

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, KIIIA 10.4.5/01 and KIIIA 10.4.5/02, Honey bee field studies.	SE: It is noted that the flight intensity was quite low in the field trials, 0-2 bees /m <sup>2</sup> throughout the majority of the study. The low flight intensity was observed both in the controls and the treated fields.	
(2)	Vol 1, Risk assessment for honey bees, Exposure	SE: At applications at later growth stages there is a possibility that build-up of honeydew has	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	via honeydew.	occurred before spraying with flupyradifurone, hence honey bees may be exposed to honey dew.	

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

**1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)**

<b>Identity (B.1, Annex C)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 4, Method of manufacture, p.7	EFSA: the different impurity spectrum of the technical material used for the chronic studies means different impurities or different amounts of the same impurities?	
(2)	Vol. 4, Specification of impurities, p.20	EFSA: The specification can be considered as provisional taking into account the pilot plant production, however this specification should be revised when the full scale production is available	
(3)	Vol. 4, Specification of impurities, p.20	EFSA: usually sulphated ash is not part of a specification	
(4)	Vol. 4, Analytical methods, Method 5, p.34	EFSA: typo: AM015011MP1 is A GLC method not HPLC	

<b>Physical and chemical properties of the active substance (B.2.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

<b>Physical, chemical and technical properties of the formulation (B.2.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

## Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Further information (B.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.5.2 Residue methods for plants, method 01330 for BYI 02960, p.65	EFSA: it is not clear what is the meaning of the note in the FL column * 'fortified compound DFA determined as DFA'. Probably a typo, note belonging to the table for DFA	
(2)	Vol. 3, B.5.2 Residue methods for plants, method 01330 for BYI 02960 and DFA, p.64	EFSA: small note: it is slightly misleading how the information is presented about method 01330, as from reading the DAR, it is thought that there is one method used for quantifying the two compounds, however there are important differences: different columns, different gradient, elution temperatures... In practice there is a need to run two methods to be able to quantify the compounds of the residue definition.	
(3)	Vol. 3, B.5.2 Residue methods for plants, method 01330, p.64	EFSA: it is stated that method 01330 was validated according to SANCO/825/00 rev.7, while the ILV according to SANCO/825/00 rev. 8.1, however there is no mention, how the extraction efficiency was assessed.	
(4)	Vol. 3, B.5.2 Residue methods for animal matrices, method 01214, p.77	EFSA: it is stated that method 01214 was validated according to SANCO/825/00 rev. 8.1, however there is no mention, how the extraction efficiency was assessed.	
(5)	Vol. 3, B.5.3 Residue methods for soil, p.78	EFSA: small typo: water is missing from the composition of the extraction mixture: acetonitrile:	

# Comments of EFSA on the draft assessment report on flupyradifurone

(07.04.2014) 3/41

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		water (1:4)	
(6)	Vol. 3, B.5.3 Residue methods for soil, p.79 and p. 81	EFSA: small typo in the unit for LOQ (should be µg/kg)	
(7)	Vol. 3, B.5.3 Residue methods for water, p.80 and p. 81	EFSA: clarification is needed if the residue definition for monitoring is as presented in the LoEP, is this method able to quantify all the compounds of the residue definition?	

<b>Effectiveness against target organisms, Occurrence of Resistance, Effects on quality/Processes/Yield/Phytotoxicity/Succeeding and Adjacent crops</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.10, Effectiveness	EFSA: No comments	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1, LoEP Residue methods for soil, p.184	EFSA: small typo: the extraction is with acetonitrile:water	

## Section 2 - Mammalian toxicology (B.6)

## 2. Mammalian toxicology (B.6)

<b>Toxicokinetics (B.6.1)</b>			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.1.1, study 1, metabolites in urine and faeces, p. 13	EFSA: In the conclusion of the study, three major metabolites are mentioned, but only two major metabolites are found: BYI2960-OH and Hippuric acid (and six minor metabolites).	
(2)	Vol. 3, B.6.1.2, Toxicokinetic studies, repeated dose, oral route, p. 51	EFSA: data requirements state that repeated dose studies must be submitted, the OECD guideline also acknowledge that this test may be required by regulatory authorities and the test may provide more detailed information on bioaccumulation.  Considering the bi-phasic kinetic of flupyradifurone, low radioactive residues were still measured in almost all organ and tissues, day 7 (ref. p. 34).	
(3)	Vol. 1, LoEP, toxicokinetics	EFSA: it is proposed to add the following information in the LoEP, regarding:  <ul style="list-style-type: none"> <li>- rate and extent of oral absorption: based on comparison of pattern of excretion after oral and i.v. administration.</li> <li>- distribution: state higher levels found in organs or tissues</li> <li>- rate and extent of excretion: please state % eliminated in 24h (and/or 48h) and % by urine and by faeces.</li> <li>- metabolism: it is proposed to mention which metabolites are minor (or disregard these) and which are major metabolites (for which reference values of</li> </ul>	

## Comments of EFSA on the draft assessment report on flupyradifurone

(07.04.2014) 5/41

### Section 2 - Mammalian toxicology (B.6)

<b>Toxicokinetics (B.6.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		the parent would be applicable)	

<b>Acute toxicity (B.6.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1, LoEP, acute toxicity	<p>EFSA: Regarding rat oral LD50 it would be clearer to mention that it is between 300 and 2000 mg/kg bw (classification required: H302).</p> <p>Regarding rat LC50 by inhalation, mg/L units are usually used and type of exposure (nose-only).</p> <p>Please add the test used for skin sensitisation.</p>	

<b>Short-term toxicity (B.6.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.3.1, 28-day study in mouse, pp. 71-73	EFSA: Considering the effects observed at the high dose level (reduced bw gain by 15%, reduced relative and absolute epididymis weight and clinical chemistry changes), this dose should be set as the LOAEL of the study.	
(2)	Vol. 3, B.6.3.4, study 1, 90-day rat, pp. 78-82	EFSA: the 500 ppm dose level produced reduced bw gain (12%), increased relative and absolute thyroid weight by 20 and 17%, it should therefore be considered a LOAEL.	

## Section 2 - Mammalian toxicology (B.6)

<b>Short-term toxicity (B.6.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(3)	Vol. 1, LoEP, short term toxicity, relevant oral NOAEL in dogs	EFSA: as both the 90-day and 1-year studies in dogs are considered short term, only the most relevant one should be mentioned in the LoEP. It appears to be the 1-year, once a longer duration of exposure is tested (although considering dose spacing, the 12 mg/kg bw per day from the 90-day study may be discussed).	

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.5.1, study 1, 2-year, rat, pp. 108-115	EFSA: Table 6.5.1-1: it would be useful to have the actual values of bw/bw gain (or at least % of change) and haematological findings to be able to assess the RMS conclusion. The statistically significant values for controls would be related to HCD, but these are not provided and therefore cannot be used. Some effects at 400 ppm appear to be the first signs of substance-related adversity in the liver.	
(2)	Vol. 3, B.6.5.1, study 2, 18-month mouse study, pp. 115-120	EFSA: Table 6.5.1-7: please give the actual values of bw / bw gain (and % of change regarding controls).	

## Section 2 - Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.6.1, study 2, 2-generation, rat, pp.129-140	<p>EFSA: regarding parental toxicity, based on reduced bw gain in females (weeks 1-10) by &gt;20% in the P generation and by 16% in F1 parental generation, the parental NOAEL is proposed to be set at 100 ppm, LOAEL 500 ppm.</p> <p>It may be arguable whether all offspring/reproductive findings at the high dose level may be explained only by parental decrease in bw/bw gain (delay in preputial separation and vaginal patency; reduced brain, thymus and spleen weights; and reduced number of implantation sites). Or whether another MoA may be expected (endocrine mediated).</p>	
(2)	Vol. 3, B.6.6.2, developmental studies in rat (study 1 and 2) / LoEP	EFSA: the overall maternal NOAEL between the two studies is 50 mg/kg bw per day from study 1 as no sign of toxicity was found in study 2 up to the highest dose level of 30 mg/kg bw per day. It is also noted that increased liver weight of 13% without associated hepatotoxicity is generally not considered as adverse.	
(3)	Vol. 3, B.6.6.2, study3, developmental toxicity study in rabbit	EFSA: In view of reduced bw of 12% during the first days of treatment, the maternal NOAEL would be 15 mg/kg bw per day.	

## Section 2 - Mammalian toxicology (B.6)

<b>Neurotoxicity (B.6.7)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1, LoEP, repeated neurotoxicity	EFSA: please add the systemic toxicity NOAEL from the 90-day neurotoxicity study in rat in the LoEP.	
(2)	Vol. 3, B.6.7.3, study 1, developmental neurotoxicity, p. 169	EFSA: as bw change was not important, and changes in brain weight were also observed in other studies, it is not so straightforward that reduced brain weight is not treatment-related, although it is acknowledged that also the decreased brain weight was also not important and adversity may be discussed.  In the LoEP, it should be clarified that the NOAEL refers to maternal, developmental and developmental neurotoxicity.	

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.9, studies on metabolites, p. 177	EFSA: if metabolite BYI 02960-CHMP is common to other a.s. it may be worthwhile considering if specific reference values should be set for the metabolite.  Pending on the agreed consumer and groundwater assessments in the residue and fate sections, it should be clarified for which metabolites the reference values of the parent are applicable and/or for which metabolites further toxicological data may be necessary.	

## Section 2 - Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(2)	Vol. 3, B.6.9.6, applicant's position paper 2 on metabolites, p. 234	EFSA: metabolite 6-CNA is presumed to be an intermediate in the rat metabolism of flupyradifurone, this does not allow to conclude that it is covered by the toxicity studies conducted with the parent compound as it is unknown whether its potential intrinsic toxicity would have time to be expressed in the studies.	
(3)	Vol. 3, B.6, literature search	EFSA: Regulation (EC) No 1107/2009 requires a search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, to be conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092). Although acknowledged that flupyradifurone is a new a.s. and therefore may not be found in the open literature, this search should at least have been conducted on metabolites.	

## Section 2 - Mammalian toxicology (B.6)

<b>Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.11.3 ADI and B.6.11.5, AOEL, pp. 245-247	EFSA: considering the comments regarding 90-day, 2-year and multigeneration rat NOAELs, these may have an impact on the setting of the ADI and/or AOEL.	

<b>Dermal absorption (B.6.12)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1, LoEP, dermal absorption	EFSA: please add the value of dermal absorption set for the higher dilution (0.045 g/L) used in exposure risk assessment in the LoEP.	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 4, C.1.4, toxicological equivalence assessment of the technical specification with the material tested in toxicity studies, p. 42	EFSA: it is agreed that the batches used in toxicity studies appear to cover the (pilot plant scale) technical specification.  The relevance of the individual impurities in comparison with the toxicity profile of the parent has not been addressed.	

## Section 3 - Residues (B.7)

## 3. Residues (B.7)

<b>Metabolism in plants (B.7.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.7.1.1, Plant Metabolism, Study 10	EFSA: The Study 10 on paddy rice is stated as a "seed treatment" in page 49, while described as " <i>a granule application in the planting hole before seedling</i> " in the section "study design".	

<b>Metabolism in animals (B.7.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(2)	Vol. 3, B.7.2, Animal metabolism	EFSA is of the opinion that the input values in table 7.2-2 for DFA livestock burden calculations have to be reconsidered as not representative of an actual residue situation in rotational crops (see comment (18)).	

<b>Residue definition (B.7.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(3)	Vol. 3, B.7.3.1, Plant residue definition for monitoring.	EFSA: The residue definition for monitoring is questionable: - Parent flupyradifurone is a sufficient marker for residues as accounting for at least 20% to 88% of the TRR in primary crops. This point is confirmed by the supervised residue trial data, where	

## Section 3 - Residues (B.7)

<b>Residue definition (B.7.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>flupyradifurone residues are almost detected in all samples analysed for, irrespective of the PHIs.</p> <p>- DFA metabolite is effectively a better marker than the parent in rotational crops, however, the toxicological profile of the DFA metabolite was not discussed and it is therefore not possible to conclude whether DFA toxicity is effectively covered by the toxicological end points set for the parent. It is therefore not possible to conclude whether residues should be expressed as "sum parent + DFA expressed as parent" or if separate residue definitions have to be proposed to consider the different toxicological profiles of these two compounds.</p> <p>Residue definition for monitoring needs to be reconsidered.</p>	
(4)	Vol. 3, B.7.3.1, Plant residue definition for risk assessment	<p>EFSA: As mentioned above, the toxicological profile of the DFA metabolite should be addressed to conclude whether a single global residue definition has to be proposed for risk assessment or two separate ones.</p> <p>The inclusion of the DFEAF metabolite (M34) in the residue definition for risk assessment is questionable as almost not present in the metabolism studies on primary crops (&lt;4%TRR in potato tuber and apple fruit and present in significant level in tomato flower only). Moreover, M34 was never detected in the field rotational crop studies and was almost not detected</p>	

## Section 3 - Residues (B.7)

<b>Residue definition (B.7.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		in the supervised residue trials or at levels close to the LOQ of 0.01 mg/kg (expressed as flupyradifurone equivalent). As previously for DFA, the toxicological profile of the DFEAF metabolite has not been sufficiently addressed.	
(5)	Vol. 3, B.7.3.2, Animal residue definition for risk assessment.	EFSA: Similar comment as for plants. Toxicological profile of the DFA metabolite should be addressed to conclude whether a single residue definition including pyradifurone and DFA or if two separate residue definitions have to be proposed.	

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(6)	Vol. 3, B.7.6 and ER part I, 3.1.1.2, Residue trials	EFSA: All MRL proposals would have to be reconsidered if the peer review concludes on a different residue definition for monitoring (flupyradifurone only or 2 separate residue definitions for flupyradifurone and DFA respectively, having regard to the conclusion on the toxicological profile of these two compounds.	
(7)	Vol. 3, B.7.6 and ER part I, 3.1.1.2, Residue trials	EFSA: Conversion factor proposals are pending the conclusions on the residue definitions for monitoring and risk assessment.  Nevertheless, the CFs proposed by the RMS needs to be reconsidered, even if the residue definitions	

## Section 3 - Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		proposed by the RMS in the DAR are finally agreed in the course of the peer review. CFs should not be based on the values observed at the intended PHI only. CFs may be time dependent and the ratio parent/metabolites subject to significant changes over time. Therefore, the possible variations in the CF values at the different PHI time points should be considered. CFs have to be proposed considering the values derived at the different PHIs investigated in the residue trials.	
(8)	ER, Part I (point 3.1.1.2) and part II (table C.2.1.2), residue trials on grape	EFSA: Only 4 independent trials have been submitted for grape in SEU (see tables from page 106 to 109 in part II). In each of the 4 locations, data refer to 2 replicates/plots (??) where applications have been made on the same variety, with the same application dates and harvest date and therefore, cannot be considered as independent. No MRL can be proposed for SEU and 4 SEU trials should be requested.  Note: Last treatment date (26/06/2010) in Campo Arcis trial (SP) is probably wrong and needs to be corrected.	
(9)	ER, part I, 3.1.1.2 and part II (table C.3.2.1.2-8 to 11), residue trials cucumber and gherkin	EFSA: In part I page 15, it is mentioned that 4 outdoor trials have been conducted on cucumber and 4 on gherkin, while in part II and tables C.3.1.2.1-8 and C.3.1.2.1-11, 3 trials are referenced as conducted on cucumber and 5 on gherkin (trial on cucumber in Toulouse (FR), page 119 on variety <i>Marida</i> is	

## Section 3 - Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		referenced as "Gherkin"). This point should be clarified.	
(10)	ER, part I, 3.1.1.2 and part II (table C.3.2.1.2-12 to 15), residue trials on melon	EFSA: Three indoor trials (Part II, table C.3.1.2.1-14, page 133-134) were conducted with 2 applications at 250 g/ha, while the other ones at 113 g/ha. Are varieties <i>Haon</i> , <i>Talento</i> and <i>Jucar</i> , climbing varieties requiring dose rates as g/mCH? If not these trials should be disregarded.	
(11)	ER, part II (table C.3.2.1.2-19), residue trials on Tomato	EFSA: harvest date in trial Gualchos (SP) in table C.3.2.1.2-19 page 68 is probably wrong and needs to be corrected.	
(12)	ER, part II (table C.3.2.1.2-20 to 23), residue trials on apple	EFSA: As the residue levels observed in the 6 SEU trials conducted according to the NEU GAP (2 applications) are not significantly different (U-test, 5%) from the residue levels observed in the NEU trials, they can be merged together to derive an MRL proposal for apple.	
(13)	ER part III, US/Canadian Import tolerances	EFSA: Flupyradifurone is not yet registered in the USA and Canada. The setting of import tolerances at EU level is therefore pending the submission of the following information:  - Documentation evidencing that an authorisation has been granted for the active substance by the national authorities in the exporting countries.  - Details and documentation on the GAPs that have been effectively registered in the exporting	

## Section 3 - Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>countries.</p> <p>- MRL values that have been effectively published at national level in the exporting countries and references to the national legislation.</p> <p>Assessment of the import tolerance proposals in ER Part III is pending the submission of the information requested here above. EFSA conclusion will not consider the import tolerance request.</p>	
(14)	Vol. 3, B.7.6.4, Storage stability studies	<p>EFSA: As mentioned in the current EU guideline 7032/VI/95, "<i>individual results should not be corrected to 100% yield...</i>". This recommendation is indeed taken over in the OECD 506 guideline "<i>...results not adjusted by recoveries....</i>". Therefore, columns "<i>corrected % for recoveries</i>" in tables B.7.6.4-2, B.7.6.4-3, B.7.6.4-4 and B.7.6.4-2 (page 186) should be deleted and the rational concerning the stability of the residues reconsidered, based on uncorrected recovery values.</p>	

<b>Processing (B.7.7)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(16)	Vol. 3, B.7.7, Processing studies	EFSA: As already mentioned for primary crops, the inclusion of the DFEAF metabolite in the residue definition for processed commodities is questionable.	

## Section 3 - Residues (B.7)

<b>Processing (B.7.7)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		In the same way, for monitoring parent flupyradifurone seems to be a sufficient marker for the residues in processed commodities and the inclusion of the DFA metabolite seems superfluous and not in line with the "single marker concept". PFs and CFs would have to be reconsidered taking into account the possible changes in the residue definition proposals made in the course of the peer review.	
(17)	ER Part III, B.7.7, C.3.2.2.6 Study 6, Processing study on grape	EFSA: It is not stated whether processing to wine has been conducted on red or white wine. This point should be clarified. Having regard to the flow chart presented in page 861, process seems refer to white wine as fermentation takes place on the grape juice and not on the must as this should be done for red wine.  Processing studies on red wine, including eating of the must, are therefore required.	

<b>Succeeding/Rotational crops (B.7.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(18)	Vol. 3, B.7.9, Field rotational crop studies	EFSA: It is questionable whether the studies (referenced Study 2 to Study 7, table 7.9-4) are fully representative of the residue levels expected in	

## Section 3 - Residues (B.7)

<b>Succeeding/Rotational crops (B.7.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>rotational crops.</p> <p>All studies have been conducted with an application on bare soil with a PBI of <i>ca.</i> 30 days, representative or a <b>crop failure</b>. In practice and having regard to the use of flupyradifurone against aphids, the application will take place on a crop well established and therefore not subject to a crop failure in the vast majority of the cases. These studies are therefore a very worst case that do not reflect the actual residue situation in rotational crops.</p> <p>EFSA is therefore of the opinion that the use of the DFA residues levels observed in the studies 2 to 7 are not representative of the residues levels expected in practice in rotational crops, leading to an overestimation of the animal burdens as proposed in tables 7.2-2 and 7.12.2-4 and <b>therefore leading to the setting of MRLs for animal products higher than necessary.</b></p>	

## Section 3 - Residues (B.7)

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(19)	Vol. 3, B.7.12, MRL proposals	EFSA: EU MRL proposals are pending the final conclusions on the plant and animal residue definitions for monitoring.	
(20)	Vol. 3, B.7.13, MRL proposals	EFSA: Import tolerance proposals would have to be reconsidered once the information requested under comment (13) is submitted.	
(21)	Vol. 3, B.7.15, Consumer risk assessment	EFSA: As the setting on import tolerances is not possible at this stage, import tolerance values have to be removed from the consumer risk assessment.  Moreover, MRL values are pending the peer review conclusions on the residue definitions and on the toxicological end points applicable to flupyradifurone and DFA respectively.	

## Section 4 - Environmental fate and behaviour (B.8)

**4. Environmental fate and behaviour (B.8)**

<b>Route and rate of degradation in soil (B.8.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.8.1.2.2, Field studies, page 135 and B.8.1.3 Summary route and rate of degradation in soil pages 138 and 140.	EFSA: It is not clear to us that the conclusion that the field dissipation observed for flupyradifurone and metabolite DFA was comparable to that found within the standardised laboratory studies is appropriate. Looking at the DT50 and DT90 endpoints for parent flupyradifurone, it could be that the compound is more persistent under field conditions than is indicated by the available lab incubations. It is difficult to do this comparison when the field studies have not been normalised to reference conditions. A further consideration of the field dissipation behaviour in comparison to that which was apparent from laboratory incubations would appear appropriate.	

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(2)	Vol. 3, B.8.2.1, batch adsorption, pages 142 146 and 156. And B.8.2.4 summary adsorption, desorption and mobility in soil page 168.	EFSA: We note that the batch adsorption 1/n values for the 4 European soils are used in the tier 2b groundwater modelling in combination with the adsorption parameters from the time dependent adsorption experiment for 4 European soils with the same names. Though the soils have the same names they are from different batches and have slightly	

## Section 4 - Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		different measured properties. In particular the organic carbon contents are somewhat different. (Table B.8.1.1-01 page 4 and Table B.8.2.1-02 page 142). This puts in question and adds uncertainty to the use of the time dependent sorption (TDS) approach in the tier 2b groundwater modelling. This also means the statement on page 168 'arithmetic mean of the 1/n of the four soils used from the batch adsorption and identical as the soils used for TDS' is inaccurate / misleading.	
(3)	Vol. 3, B.8.2.1, batch adsorption, page 157.	EFSA: We would find it helpful if the fitting of the time dependent sorption parameters could present results where the quality measures identified as being important in Beulke and van Beinum (2012) and earlier drafts, (that the RMS indicated were not done) have been completed. (I.e. plotting apparent adsorption with time and optimising using different starting parameters / transparently reporting all these optimisations).	
(4)	Vol. 3, B.8.2.4 summary adsorption, desorption and mobility in soil page 168.	EFSA: We do not agree that 'For BYI 02960 a fitted mean Koc,eq of 80.2 L/kg (Kom,eq of 46.5 L/kg) and the Freundlich exponent 1/n of 0.8605 can be used in higher tier simulation runs' Neither the associated geometric mean DT50_eq or K_des derived from the TDS study. This is because these factors are all expected to be correlated and soil property dependent so averaging them before input into a leaching model is considered by the regulatory	

## Section 4 - Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		community to be questionable. (This was identified by Beulke and van Beinum (2012) and earlier drafts). The draft guidance indicates that simulations should be done using the substance properties for each investigated soil separately and then taking a median value of the 80th percentile leaching concentration. When this approach gives a higher value than the approach presented in the DAR then the draft guidance recommends that this value be compared to the regulatory trigger.	

<b>PEC in soil (B.8.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(5)	Vol. 3, B.8.3, PEC soil, page 173  And Vol. 1, List of endpoints, PEC soil, page 208	EFSA: Are the PEC calculated for the metabolites correct? Have they accounted for the accumulated concentration of parent flupyradifurone precursor from use over repeated years? If they have then the metabolite DT50 must have been accounted for in the calculations. If this was the case then the information as reported in the DAR is insufficient to understand exactly how the concentrations were calculated.	
(6)	Vol. 1, List of endpoints, PEC soil, page 207	EFSA: The PEC soil values for parent flupyradifurone in the list of endpoints are not consequent with the accumulated values calculated	

## Section 4 - Environmental fate and behaviour (B.8)

<b>PEC in soil (B.8.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		and presented in Table B.8.3-04 of Vol. 3 page 172. They should be. When updating this anomaly in the list of endpoints, further details / explanation is also required regarding mixing depths and depth assumed for the applications in the final year for the two crops.	

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(7)	Vol. 3, B.8.5, Impact on water treatment procedures, page 247.	EFSA: Article 4 (approval criteria for active substances) 3. (b) of Regulation (EC) No 1107/2009 requires that 'it shall have no immediate or delayed harmful effects on human health, including that of vulnerable groups, or animal health, ....through drinking water (taking into account substances resulting from water treatment)'. Information on the effect of water treatment processes on the nature of residues when surface water is abstracted for drinking water has not been presented or discussed in the DAR?	

## Section 4 - Environmental fate and behaviour (B.8)

<b>PEC in surface water and ground water (B.8.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(8)	Vol. 3, B.8.6.1, PEC in surface water, page 248.	EFSA: The statement 'There are currently no agreed European guidelines for the assessment of exposure of surface water from the use in glasshouses' is not accurate. FOCUS air guidance recommends that 0.2% emission from glasshouses to surface water is an exposure assumption that can be used. EFSA can however accept the approach taken of the assumption 'that the use in glasshouses on lettuce is covered by the outdoor field use even considering the different use pattern.', provided that the RMS can confirm that the mitigation considered for the field uses would mean that the exposure of surface water would be > than would occur assuming 0.2% emission from glasshouses (the currently note EU guidance).	
(9)	Vol. 3, B.8.6.1, PEC in surface water, pages 251-255.  Vol. 1, List of endpoints, PEC surface water and sediment, pages 212-216 and TER step 4 pages 231-232 and 236-238.	EFSA: Some of the FOCUS step 4 calculations presented that combine no spray buffer distances with drift reducing nozzles do not respect the upper limit on total drift reduction in FOCUS landscape and mitigation guidance that is a maximum drift reduction of 95%. PEC and TER where drift is mitigated by more than 95% should not have been presented in the DAR or list of endpoints.	
(10)	Vol. 3, B.8.6.1, PEC in groundwater, page 260.	EFSA: Footnotes indicate 'Data provided to justify that the plant uptake factor for the active substance and metabolites is 0.5'. What were these data? Where are they evaluated?	

## Section 4 - Environmental fate and behaviour (B.8)

<b>PEC in surface water and ground water (B.8.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	Vol. 1, List of endpoints, PEC groundwater, pages 219-220		
(11)	Vol. 3, B.8.6.1, PEC in groundwater, page 259-269.  Vol. 1, List of endpoints, PEC groundwater, pages 218-223	EFSA: We would not consider it appropriate to accept the tier 2b groundwater simulations regarding the parent flupyradifurone that are currently presented without further clarifications. Further to the EFSA comments above in the section 'Adsorption, desorption and mobility in soil (B.8.2)' EFSA would need further information from the applicant regarding the uncertainty created by the fact that the soils used in the batch aged adsorption experiments (from which 1/n was derived) are not 'identical' to those used in the TDS experiment, in particular OC content. We would also wish to have further detail / reassurance on the way that the pertinent parameters were fitted from the results of the TDS experiments on each of the soils. Finally we would also wish to see groundwater simulations at tier 2b where the results are expressed as a median of the 80 <sup>th</sup> percentile values with separate sets of simulations completed for each of the 4 soils, in addition to the current approach where averages of the substance input parameters from the 4 soils have been input to the model.	

## Section 4 - Environmental fate and behaviour (B.8)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(12)	General	EFSA: A search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, being conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) does not appear to be available. Searches need to have been done and consider both the active substance and identified metabolites.	

## Section 5 - Ecotoxicology (B.9)

## 5. Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>			
No.	<u>Column 1</u> <b>Reference to assessment report</b>	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. B.9.1, General	EFSA: It is noted that the short-term endpoints are considerable higher than the acute endpoints (mainly from encapsulated studies), which is a rather strange pattern. Is there any explanation for that?	
(2)	Vol. B.9.1.3, Long-term study on mallard	EFSA: EFSA shares the original concerns of the RMS regarding several reproductive parameters in the medium doses and considers that the further assessments (including considerations for outliers) were necessary for the conclusion and endpoint setting.	
(3)	Vol. B.9.1.3, Long-term study on quail	EFSA: It is just noted that it seems to be strange that for the parameter of eggs set/eggs laid (%) the higher difference in the lower concentration was not statistically different, while the lower average difference in the higher concentration was. It is assumed that the standard deviation of the data was significantly different.	
(4)	B.9.3.2, decline data from the lettuce residue trials	EFSA: It was considered that it is not possible to derive an overall average first order DT50 value, since the best fits were obtained from different models. However it would be possible just considering the slow phase DT50s from the DFOP kinetics.	
(5)	B.9.3.2, Generic field monitoring	EFSA: EFSA agrees that this is a good quality study, and note the remarks of the RMS especially the note regarding the possible effects of the surrounding	

## Section 5 - Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>			
No.	<u>Column 1</u> <b>Reference to assessment report</b>	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		habitat in the species composition in a crop.	
(6)	B.9.3.3, Endpoints for mammals	EFSA: EFSA welcomes the thorough assessments for the choice of the reproductive endpoint. However, EFSA is still wondering why the lower endpoint of 7.8 mg/kg bw can be omitted in the Tier 2 assessment as this endpoint is based on effects on offspring (as indicated in Table B.9.3.3-1), which should be considered as relevant effects for these risk assessments.	It is further noted (already noted by the RMS) that this lower endpoint is not included in the mammalian tox. part of the LoEP under the rat 2 generation study. However and endpoint of 7.8 mg/kg bw is included for a 1-year dog study.

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(7)	B.9.2.1.2, Study by Bowers L.M. & Lam C.V. (1998) and general for tests on AO	EFSA: It is noted that no analytical confirmation was done for the test water in this study. However, EFSA agrees that read across from other studies with the same metabolite is possible. It can generally be concluded that the a.s. and the metabolites indicated a good stability in the test waters of all the aquatic studies. Is this statement agreed?	
(8)	B.9.2.2.1, Study by Matlock D. & Lam C.V. (2011)	EFSA: Please confirm that the larval survival of 88.8% at the 4.41 mg/L test concentration versus the control results of 93.8% is not considered as biologically relevant.	
(9)	B.9.2.2.1, Study by	EFSA: Although a clear concentration-effect	

## Section 5 - Ecotoxicology (B.9)

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	Riebschläger T. (2012)	relationship can be seen, all biological parameters were worse in all of the treated concentrations than the results from the control. Please comment whether at least the results for the number of offsprings are or are not considered as biologically relevant.	
(10)	B.9.2.2.1, Study by Claude M.B. <i>et al.</i> (2011)	EFSA: EFSA welcomes the further analysis and careful control of the assessments on the results of these studies by the RMS. However EFSA still considers that ~30% difference on average from the control might be considered as biologically relevant. If it is believed that no robust endpoint can be derived from this study than it maybe considered to repeat the test.	
(11)	B.9.2.5, RA for AO	EFSA: Please note that when a FOCUS scenario has more than one water body, EFSA considers this scenario as 'safe' only if a low risk was proven for all the linked water bodies.	
(12)	B.9.2.5, RA for AO	EFSA: Please clarify that when 'R' is indicated for a buffer type in a table of this chapter, whether it indicates runoff mitigation or runoff mitigation and spray drift mitigation. Please also clarify how to understand the mitigation regime in Table B.9.2.5.5-12 (buffer zone + nozzle for D scenarios and nozzle + VFS for R scenarios without spray drift buffer zone??)	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(13)	Vol. 3, B.9.4.1.3.1, Chronic adult tests and larval test	<p>EFSA: EFSA welcomes to have these 'new type' of tests in the dossier. EFSA also considers that the way of the evaluations of these studies by the RMS, in general, was very good.</p> <p>However, please consider the following related comments.</p>	
(14)	Vol. 3, B.9.4.1.3.1, Chronic adult tests and Vol. 1, LoEP	<p>EFSA: As general remark, the control mortality should always be clearly reported, especially if it was used for correction, what is not particularly supported by relevant EFSA documents. In relation to that EFSA is unsure on the statistically derived (here from corrected mortality data) NOEC values (i.e. NOEC is established where there were some mortalities, sometimes even higher than in the control). As in the future the LC50 will be used, EFSA is of the opinion that it is enough to include only the LC50 values in the LoEP (also expressed in ug/bee/day).</p> <p>The results on the analytical findings were not always reported. Were the test items stable in the feed items?</p>	
(15)	Vol. 3, B.9.4.1.3.1, Chronic adult tests	EFSA: It is noted that the first study was invalidated due to relatively high control mortality. It is further noted that the temperature used in this test was lower than in the second test (considered as valid).	
(16)	Vol. 3, B.9.4.1.3.1, Chronic adult tests	EFSA: It is noted that the chronic endpoint on adults for the a.s. is higher than the acute, which is a rather surprising result. Provided that this conclusion is	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>valid, it might indicate that no accumulative effects is expected for this a.s.</p> <p>Some uncertainty on the used test item in the acute test is noted.</p>	
(17)	Vol. 3, B.9.4.1.3.1 (B.9.4.1.3.2 ?), larval test Vol. 1, LoEP	<p>EFSA: It is noted that the exposure of the larvae was only between days 3 and 6 in the test. The young larvae did not feed on the treated food in the first 2 days, therefore this part of the exposure is not covered by this test. It is acknowledged that this design is indeed in line with the latest developments from OECD.</p> <p>Please express the endpoint in mass/larvae (accumulated test item intake/larvae) and include this value in the LoEP. The unit of the existing value in the LoEP needs also an amendment.</p> <p>Additionally, it would be interesting to see, what was the mortality in the larval phase (e.g. by day 7).</p> <p>Were the discarded runs valid considering only the larval phase?</p>	
(18)	Vol. 3, B.9.4.1.4. Foliage residue trial	EFSA: RMS has indicated that it is unclear how this study can be used in the risk assessment, therefore it was not evaluated. This type of study might be useful to see persistence of effects and if some risk mitigation measure is needed to be established (e.g. restriction to evening application).	
(19)	Vol. 3, B.9.4.2, Semi-field studies	EFSA: It is noted that significant food store (not contaminated) was available for the colonies at the start of the tests. It is further noted that 2 of these	As general remarks, the EFSA opinion on bees noted that the semi-field trials are suitable to observe immediate effects (e.g. large acute contact effects), but have only limited usefulness to study long-term effects. The

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		studies had no GLP certificate. RMS has indicated that the EFSA opinion concluded that the main exposure route for bee brood is via pollen. Indeed, in general, pollen samples had higher residue levels than nectar samples (on the basis of the data that were available). However honey bee larvae are fed with significantly more nectar than pollen.	foraging area thus the potentially collected and stored food is limited. This was also observed in these studies. The fate of the colonies were monitored for cca. one month, but not followed until overwintering. It is noted that the RMS has captured these notes in Vol. 3. B.9.4.4.
(20)	Vol. 3, B.9.4.2, Semi-field studies	EFSA: It is not clear from all summaries whether there were or not significant rainfalls after the application(s) and if so whether these could influence the exposure. Could you please indicate this?	
(21)	Vol. 3, B.9.4.2, Semi-field studies, Study by Schnorbach, H. (2012a)	EFSA: It is agreed that no apparent (i.e. no large, no medium) effects on the bee colonies were observed in this trial. EFSA however not sure that slight effects was not indicated e.g. for brood, adult abundance and hive weight in the 150 g/ha group.	
(22)	Vol. 3, B.9.4.2, Semi-field studies, Study by Schnorbach, H. (2012b)	EFSA: EFSA does not share the RMS's view on this study. Some effects on forager mortality (supported by the fact of short-lived reduced foraging activity) seem to be apparent (on the basis of the provided averages). Please provide more detailed information on the forager mortality from this trial. Some slight effects also cannot be excluded on the larvae on the basis of day 14 data (Figure 9.4.2-13) and that the reference group of Insegar also did not indicated any apparent effect.	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(23)	Vol. 3, B.9.4.2, Semi-field studies, Study by Rentschler,S. (2012a)	<p>EFSA: It is agreed that some effects on mortality and on foraging activity was indicated in this study. However, Figure 9.4.2-17 includes larvae and pupa mortality. Would the picture be similar if only the forager mortality were presented?</p> <p>Also, on the basis of Figure 9.4.2-20 some effects on larvae cannot be excluded. Please provide more detailed information at least on the larval abundance.</p>	
(24)	Vol. 3, B.9.4.2, Semi-field studies, Study by Pröbsting, A. (2012a)	EFSA: EFSA shares the concerns of the RMS regarding this study. It is noted that pollen and nectar samples for residue analysis were taken from the combs, therefore dilution from uncontaminated stored food cannot be excluded.	
(25)	Vol. 3, B.9.4.2, Semi-field studies	<p>EFSA: Some slight, temporary effects on forager mortality cannot absolutely be excluded. The number of bees was slightly lower at the second hive assessment in the treated group (similarly to the reference). Repellent effects were apparent in this study. At the second hive assessment practically there was no larvae in the treated groups. These might be due to the shortage of pollen, but can also be indication of toxic effects (or the combination of them).</p> <p>Please provide more detailed information at least on the forager mortality.</p> <p>Was the crop in good condition in this trial?</p>	
(26)	Vol. 3, B.9.4.2, Semi-field studies , Study by	EFSA: The mortality was practically continuously higher in the treated group than in the control, with	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	Rentschler,S. (2012b)	<p>continuously less flower visits in the treated tunnels. This is a clear indication of (at least a slight) potential effect of the a.s. Please clarify if pupae mortality was indeed combined with forager mortality in Figure 9.4.2-29 and if so, how important was this. Also some sublethal intoxication symptoms were noted.</p> <p>It is just noted that the colonies originates from 2 beekeepers. The pollen and nectar samples for residue analysis were taken from the combs, therefore dilution from uncontaminated stored food cannot be excluded.</p> <p>Please clarify the used Guideline.</p>	
(27)	Vol. 3, B.9.4.2, Residue trials	<p>EFSA: EFSA welcomes the residue data on pollen and nectar. Could you please clarify how exactly the foragers were sampled (e.g. collected in front of the hive, in the hive, in the crop) in the study Rexter 2013.</p> <p>The trials with drenching and non EU representative crops – although also welcomed – are less relevant for the current assessments.</p>	
(28)	Vol. 3, B.9.4.3, Field studies, Study by Rexter 2012a	<p>EFSA: EFSA agrees that some increase in forager mortality is apparent for a few days after the 3<sup>rd</sup> application (day 13 data might be statistically different). Also some sublethal intoxication symptoms were noted. Also agreed that the average hive weight was somewhat lower for the treated hives after the 2<sup>nd</sup> and 3<sup>rd</sup> spray applications, while</p>	<p>It is acknowledge that in terms of a.s. treatments (4 different treatments), the study can be considered as worst case. However the severity of the study in terms of residue dilution of the collected food from the surroundings is unknown (might be typical but likely not worst case). Also, the impact of the comb(s) removal is unknown.</p>

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>this parameter was very similar before this period. An important element that the surroundings of the fields were checked and major flowering crops were not present within 2 kms of the treated fields.</p> <p>However attractive wild trees and shrubs were foraged as indicated by the pollen analysis.</p> <p>In general, EFSA agrees with the assessments of the RMS ('Remarks by the evaluator').</p> <p>Please confirm that the 2<sup>nd</sup> application was on Day 6 and the 3<sup>rd</sup> on Day 12. Please also clarify if there was any significant rain after the 2<sup>nd</sup> and 3<sup>rd</sup> spray applications in the fields.</p>	
(29)	Vol. 3, B.9.4.3, Field studies, Study by Rexer 2012b	<p>EFSA: It is noted (already noted by the RMS) that the average forager mortality was continuously slightly higher in the treated field in the last period of the exposure, however this phenomenon was not observed shortly after the applications.</p> <p>Some decrease in brood (queen loss ?) of one treated hive was observed in late of the season.</p> <p>One control pollen sample contained the a.s. (this was not noted on page 279 only on page 289).</p> <p>Again, in general, EFSA agrees with the assessments of the RMS ('Remarks by the evaluator') including the noted uncertainties.</p> <p>Please confirm that the 2<sup>nd</sup> application was on Day 1 and the 3<sup>rd</sup> on Day 10. Please also clarify if there was any significant rain after the 2<sup>nd</sup> and 3<sup>rd</sup> spray applications in the fields.</p>	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(30)	Vol. 3, B.9.4.3, Field studies, Study by Nikolakis, Krieg et al. 2012	<p>EFSA: Again, EFSA agrees with the assessments of the RMS ('Remarks by the evaluator') including the noted uncertainties.</p> <p>Please confirm also whether the food supplements placed inside the hive in periods when honey bees did not sufficiently forage were also spiked. It is noted that no reference treatment was used in this study.</p> <p>The adult mortality in T1 was definitely higher than in the other groups, what most likely originates from the elevated mortality of one colony (No. 8 in tunnel 13). It was also argued (page 294) that this colony had disease-like symptoms. Could you please clarify that it is believed that this elevated mortality was not linked with the a.s. consumption.</p> <p>Reading across of some parameters, but mainly considering the average data on colony strength, some delayed effects in group T3 cannot be excluded. A same trend (lower abundance from September) can be observed also for T1 and T2. The colony strength after overwintering was clearly lower in all treated groups than in the control (22-33%).</p> <p>It is acknowledged that this special feeding study represents quite severe conditions in terms of oral exposure of a honey bee colony (up to 10 mg/kg a.s. in pollen and nectar).</p>	
(31)	Vol. 3, B.9.4.4, RA for	EFSA: In general, EFSA agrees with the conclusions	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	bees	<p>of the RMS and welcomes the overview tables for the higher tier studies. However please consider specific comments above, and in line with those, please consider to amend the entries in the LoEP (especially for the higher tier studies).</p> <p>EFSA notes that a kind of calculation method for the oral exposure for lower tier RAs (which allow to use the endpoints from the laboratory data) was used for the RA for the neonicotinoids (published in January 2013 by EFSA). These may be used if needed.</p>	
(32)	Vol. 3, B.9.5.1, Aged residue studies on NTAs	<p>EFSA: The aging processes were conducted in semi-natural conditions in both trials. It seems that the temperature was very high (at least occasionally). Was not the degradation accelerated too much in these conditions?</p> <p>It is noted that the effects on the reproduction on 42DAT2 is considerable higher than on day 28DAT2.</p>	
(33)	Vol. 3, B.9.5.2, Field studies for NTAs	EFSA: It is noted that the checkerboard design could be favourable for the re-colonisation of the test plots. A relatively undisturbed habitat (grassland) with little agricultural impact may have not represent well a typical NTA communities of typical agricultural habitats. Although it is acknowledged that the study sites were surrounded by agricultural fields.	
(34)	Vol. 3, B.9.5.3, RA for NTAs	EFSA: It is noted that a correction factor of 5 was used in the Tier 2 HQ off-field calculations; however a factor of 10 is recommended in ESCORT 2.	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		It is also noted that for hops, risk mitigation (i.e. 20 ms buffer zone) measures are recommended to manage the off-field risk.	

<b>Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(35)	Vol. 3, B.9.6.1, General	EFSA: It is noted that in some studies the results of the reference item (2-chloroacetamide) was out of the range of the recommendation LC50 being between 20-80 mg/kg soil by the very similar ISO test guideline.	
(36)	Vol. 3, B.9.6.1, Study by Leicher T. (2010a)	EFSA: There were two test run in this study, but results only for one control were reported. Please confirm that a control was used for both runs and they performance were sufficiently comparable to each other.	
(37)	Vol. 3, B.9.6.2, Lab. sublethal studies on earthworms	EFSA: Please confirm that the differences in reproductive parameters seen at the established NOECs compared to the control are not considered as biologically relevant. It is noted that these differences expressed in % using the average data were ~ 6.7% in the formulation study and for the metabolites > 13%.	
(38)	Vol. 3, B.9.6.4 (3?), Study by Menke, 2012	EFSA: It is noted that although reductions in abundance/biomass of some categories even after 11	

## Section 5 - Ecotoxicology (B.9)

<b>Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		month were observed with the available data, these differences were not considered as biologically relevant. The main reasons for these were the relative low abundance within those categories (even in the control), the lack of dose-effect relationship and the natural variation.	
(39)	Vol. 3, B.9.6.4, RA for earthworms	EFSA: EFSA is wondering, why it is justified to calculate the PECs for lettuce for 20 cm.	

<b>Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(40)	Vol. 3, B.9.9.2	EFSA: It is noted that a study (although non GLP) was available that indicated that difluoroacetic acid has no insecticidal efficacy compared to parent. This kind of information should be available for all metabolites which has high potential to leaching to GW (i.e. PECgw > 0.1 ug/L).	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(40)	Vol. 3, B.9, General	EFSA: It is noted that many of the study summaries are rather short (especially for the aquatic organisms). A very detailed test description is indeed	

## Section 5 - Ecotoxicology (B.9)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		not necessary for the highly standardised laboratory tests if there are no deviations from the test guideline. Deviations or the lack of deviations from the test guidelines however were not indicated by the RMS. Can the indication of 'acceptable' be considered as there were no major deviations from the TGs?	
(41)	Vol. 3, B.9, General	EFSA: Could you please confirm that the bathes used in the ecotoxicological studies are equivalent with the technical specification?	
(42)	Vol. 3, B.9 and Vol.1, General	EFSA: It is noted that no detailed discussion/assessment was available on the approval criterion (cut-off criterion) including potential for endocrine activity. However it is noted that some potential effects on the endocrine system was indicated in the mammalian toxicology section (e.g. on thyroid). Specific assessment on this issue in B.9 was not available.	
(43)	Vol. 3, B.9, General	EFSA: A search of the scientific peer-reviewed open literature relevant to the scope of the application for amendment to the conditions of approval, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, to be conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of	

## Section 5 - Ecotoxicology (B.9)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092).	
(44)	Vol. 1, LoEP, General	EFSA: Please include always the correct name of the test item in the LoEP, i.e. 'G' is usually missing from the end of the name of the formulation (compared to the name indicated in B.9).	
(45)	Vol. 1, LoEP, box for birds	EFSA: The included long-term endpoint from the mallard study is based on the measured food concentration, while for the quail study the nominal value is included. It might be considered to harmonise or clearly indicate the bases of each endpoint.	
(46)	Vol. 1, LoEP, box for birds & mammals	EFSA: Please indicate everywhere the 'kind of endpoints' (e.g. LD50, NOEC) in this box.	
(47)	Vol. 1, LoEP, box for RA for birds	EFSA: The DDD and the TER values for the 'pigeon' scenario are not the same as reported in B.9. Please clarify this.	
(48)	Vol. 1, LoEP, box for AO	EFSA: Please consider to indicate all the data for <i>chironomus</i> under 'sediment dwelling organisms'. Please also indicate if the test used water spiking.	
(49)	Vol. 1, LoEP, box for bumble bee	EFSA: The name of the test item used in the text is not the same as indicated in B.9. Please correct it.	
(50)	Vol. 3, B.9, General	EFSA: Generally, EFSA considers that the RMS did a comprehensive risk assessment even undertaking unusual, extra assessments where it was necessary.	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 1/28

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

### 1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

<b>Identity (B.1, Annex C)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 4,	DE: The approach of the RMS that in case the data of the industrial scale process cannot be included, the identified issues regarding the specification should remain open, is fully supported.	

<b>Physical and chemical properties of the active substance (B.2.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.2 oxidising properties.	DE: Although in the summary in B.2.3.1 it is mentioned that the oxidising properties are not critical, it seems that the respective annex point has not been addressed in table B.2.1.1.	

<b>Physical, chemical and technical properties of the formulation (B.2.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Further information (B.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 2/28

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1, 2.4.1 definition of the residue relevant to MRLs, animal products and vol. 1, list of endpoints, residue definition for monitoring purposes	DE: The residue definition for monitoring in animal products in volume 1, 2.4.1 includes the parent compound and DFA metabolite whereas in the list of endpoints only the parent compound is listed. Please bring in accordance.	
(2)	Vol. 1, 2.5.1 definition of the residue relevant for the environment and vol. 1, list of endpoints, residue definition for monitoring purposes	DE: The residue definition for monitoring in surface water and drinking/ground water in volume 1, 2.5.1 includes the parent compound only whereas in the list of endpoints the parent compound and the metabolites DFA and 6-CAN are listed. Please bring in accordance.	
(3)	Vol. 1, list of endpoints, analytical methods for food/feed of plant origin,	DE: The LOQ cited in the list of endpoints is valid for flupyradifurone only. The LOQ for DFA was given in volume 3, B.5.2 as 0.02 mg/kg for lettuce, rape seed, orange fruit and wheat grain and 0.1 mg/kg for hop cone. Please add the LOQ for DFA.	
(4)	Vol. 1, list of endpoints, analytical methods for food/feed of animal origin,	DE: The LOQ cited in the list of endpoints is valid for DFA only. The LOQ for flupyradifurone was given in volume 3, B.5.2 (study 7 and 8) as 0.01 mg/kg for animal matrices. Please add the LOQ for flupyradifurone.	
(5)	Vol. 3, B.5.2, study 5 and 6	DE: The method description is incomplete. The column used for flupyradifurone was not mentioned. The calibration range for flupyradifurone and DFA, a statement about blank	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 3/28

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		values and ionisation type and MS/MS transition for DFA are missing. Please add. There is a typo for the fortified level for flupyradifurone in hop cones. The levels are 0.05 and 0.5 mg/kg, respectively.	
(6)	Vol. 3, page 70, Tables without headline	DE: The tables list studies KIIA 4.3/10 (Schulte &Teubner, 2012) and KIIA 4.3/11 (Konrad, 2012) which are not mentioned in the list of references and are neither described nor evaluated in the vol. 3, B.5.2. Either delete the tables or describe the studies if modifications of methods accepted before are needed.	
(7)	Vol. 3, table B.5.2-2	DE: What is the reason for citing methods RARVP013 (01304) and 012012 in the 2 <sup>nd</sup> and 3 <sup>rd</sup> line in table B.5.2-2? The methods are not described and not evaluated in the vol. 3, B.5.2.	
(8)	Vol. 3, chapter B.5.2	DE: The statement about extraction efficiency of the proposed monitoring method is missing. A corresponding study of Justus (2011) is mentioned in the references (section 5.6) but not evaluated. Please add an evaluation of this study.	
(9)	Vol. 3, B.5.2, study 7 and 8	DE: The method description is incomplete. The HPLC column used for flupyradifurone was not mentioned. The calibration range for flupyradifurone and DFA, a statement about blank values and ionisation type and MS/MS transition for DFA are missing. Please add.	
(10)	Vol. 3, B.5.3, study 9, section Description of	DE: The parent ion of the selected MRM transitions is not reported in the method description and	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 4/28

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	methods	should be added.	
(11)	Vol. 3, B.5.3, study 9, section linearity	DE: There is a typo in the unit for calibrated range in soil: 2 to 200 <b>pg</b> /kg should read as 2-200 <b>µg</b> /kg. Please correct.	
(12)	Vol. 3, B.5.3, study 9, section Untreated control samples	DE: There is a typo in the unit for residues in control soil: 1.5 <b>Hg</b> /kg should read as 1.5 <b>µg</b> /kg. Please correct.	
(13)	Vol. 3, B.5.3, study 9, section Recovery rates	DE: The recovery and precision data of the method for residues of flupyradifurone in soil are missing. The mentioned tables presenting these data for both transitions should be added.	
(14)	Vol. 3, B.5.3, study 10, section Description of methods	DE: The mentioned “following table” presenting the LC-MS/MS parameter is missing and should be added.	
(15)	Vol. 3, B.5.3, study 10, section LOQ	DE: There is a typo in the unit for LOQ: 0.05 <b>Hg</b> /kg should read as 0.05 <b>µg</b> /kg. Please correct.	
(16)	Vol. 3, B.5.3, study 10, section Recovery rates	DE: The recovery and precision data of the method for residues of flupyradifurone in water are missing. The mentioned tables presenting these data for both transitions should be added.	
(17)	Vol. 3, B.5.3, study 10	DE: It should be added which water samples were used for validation. Were the water samples characterized?	
(18)	Vol. 3, B.5.3, study 10	DE: Please clarify that a valid method for the water metabolites DFA and 6-CAN is missing (given that the residue definition for monitoring in the list of endpoints is correct).	
(19)	Vol. 3, B.5.3, study 11;	DE: In the references for all studies described before	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 5/28

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	page 82, reference of method	under “Type of study” the title of a study is presented. Therefore, the phrase “Analytical methods for soil, air and water” should be deleted.	
(20)	Vol. 3, B.5.3, study 11	DE: Information with respect to the calibration range, breakthrough and the column type is missing and should be added.	
(21)	Vol. 3, B.5.3, study 11; Table Recovery Results: Extraction Efficiency and Storage Stability	DE: The headlines of the last four columns should be revised.	
(22)	Vol. 3, B.5.3, study 11; Table Recovery Results: Retention Recoveries	DE: The headlines of the last four columns should be revised.	
(23)	Vol. 3, B.5.5, evaluation and Assessment	DE: The assessment of the reported studies seems to be too slim. We would prefer a tabular overview on residue definitions, action values and acceptable methods (i.e. according to table 5 in the SANCO/825/00 rev. 8.1). Probably, the unclear residue definitions would have been noticed in that case.	
(24)	Vol. 3, B.5.6, References relied on	DE: The list does not contain two studies mentioned on page 70 (Schulte & Teubner, 2012 and Konrad, 2012).	
(25)	Vol. 3, B.5.6, References relied on	DE: The list contains two studies, which are not mentioned in the text before (Li & Schoening, 2011 and Justus, 2011).	
(26)	Vol. 3, B.5.6, References relied on	DE: In two cases (Schulte & Bauer, 2012 and Konrad, 2012) the referenced Annex Points are different to the Annex Points mentioned during	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 6/28

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

<b>Methods of analysis (B.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		method description. Furthermore, the two studies of Schulte & Bauer should be indicated as 2012a and 2012b and the two studies of Konrad should also be indicated as 2012a and 2012b.	

<b>Effectiveness against target organisms</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Occurrence of Resistance, Effects on quality/Processes/Yield/Phytotoxicity/Succeeding and Adjacent crops/Plants for propagation</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

# Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 7/28

## Section 2 - Mammalian toxicology (B.6)

### 2. Mammalian toxicology (B.6)

<b>Toxicokinetics (B.6.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.1.3, List of identified metabolites	DE: Metabolism in the rat was extensively investigated. What about the comparative <i>in vitro</i> study on different species as mentioned in the new data requirements?	

<b>Acute toxicity (B.6.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Short-term toxicity (B.6.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Genotoxicity (B.6.4)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.4.1, <i>In vitro</i>	DE: A negative HGPRT test in CHO cells is reported (study 4). Surprisingly, it is stated in the conclusion, in addition, that no UDS was induced	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 8/28

### Section 2 - Mammalian toxicology (B.6)

<b>Genotoxicity (B.6.4)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		but this was not tested. Is the description of a further study lacking in the DAR or was it a technical error?	

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.5.1, Chronic toxicity or carcinogenicity, rat study, editorial remark	DE: It was noted that in the tables B.6.5.1-4, B.6.5.1-5 and B.6.5.1-6 statistical significances were indicated for certain histopathological findings in the control group of the long-term study in rats. Can you explain that or was it simply an error?	
(2)	Vol. 3, B.6.5.1., Chronic toxicity or carcinogenicity, study in mice	DE: In the kidney, there were histopathological findings pointing to a less pronounced occurrence of mostly age-related changes (less mineralization, less vacuolation) in male mice. On one hand, they should not be mentioned to support the NOAEL (that is based on liver toxicity). On the other hand, is there an explanation for this "beneficial" effect on the kidneys?	

<b>Reproductive toxicity (B.6.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 9/28

### Section 2 - Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.62, Teratogenicity studies; Vol. 3, B.6.11.2, Toxicodynamics (Summary)	DE: It is not clear to us why a second developmental study in rats became necessary to be performed because a robust maternal NOAEL was obtained in the first one. However, taking both studies together, the overall NOAEL for maternal toxicity would be 50 mg/kg bw/day rather than 30 mg/kg bw/day.	

<b>Neurotoxicity (B.6.7)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Summary of mammalian toxicology and setting ADI, AOEL, ARfD (B.6.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 10/28

### Section 2 - Mammalian toxicology (B.6)

<b>Toxicity of the product(s) (B.6.11)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Dermal absorption (B.6.12)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.13, Overall conclusion comparative dermal absorption	DE: The approach taken by the RMS and the derived values (0.4% / 3 % / 8%) are supported. However, the use of the pro-rata calculation for a more diluted product (see 6.16) giving 17% seems questionable although mathematically correct. There was no linear increase in dermal absorption (in particular when also the rat data were considered) and there were large inter individual differences in some experiments. Thus, it is suggested to use 17% for this highest dilution (0.045 g/L) for the moment but to require a further <i>in vitro</i> study as "confirmatory data".	

<b>Toxicity of non-active substances (B.6.13)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 11/28

### Section 2 - Mammalian toxicology (B.6)

<b>Exposure data (B.6.14)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.6.16.3, Resident exposure	DE: We use higher drift values in DE assuming minimum distances of 1 m for applications in field crops and 3 m for applications in high crops, i.e. 2.77 % drift for application on lettuce (or 2.38 % drift for two applications on lettuce) and 19.33 % drift for application in hops. In this case, however, this has no impact on the outcome of the risk assessment.	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1, 2.3.1.2, Toxicodynamics, Short-term toxicity; Vol. 3, 6.11., Toxicodynamics, Short-term toxicity; editorial remark	DE: With regard to the 28-day study in mice, erroneously a wrong NOAEL was given. At least, the mentioned dose of 33.6 mg/kg bw/d was not tested. The study description in Vol. 3 is not entirely clear but it seems that the most correct NOAEL might be 166 mg/kg bw/d (1200 ppm). In the 90-day study in mice, the NOAEL was stated to be 80.6 mg/kg bw/d but the dietary intake at the respective dietary concentration was 81 mg/kg bw/d, according to the same paragraph and also to the LEP.  If this paragraph is revised, the “micropathology findings” in the one-year dog study should be specified. (Quite often, only Vol. 1 will be read.)	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 12/28

### Section 2 - Mammalian toxicology (B.6)

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(2)	Vol. 1, 2.3.1.2, Toxicodynamics, Long-term toxicity; Vol. 3, 6.11., Toxicodynamics; editorial remark	DE: A statement on the carcinogenic potential in mice should be included. As it is now, the information that no neoplastic lesions were observed is confined to the long-term study in rats. The LEP is more clear in this respect.	
(3)	Vol. 3, B.6.8.1; Vol. 1, 2.3.1.2 and Vol. 3, B.6.11., Toxicodynamics, Further toxicological studies, Biokinetic study, General remark	DE: Apparently, this study was performed to meet the new data requirement of measuring toxicokinetic parameters as part of toxicological studies. The results allow a comparison of plasma concentrations following repeated dietary and single gavage administration in the ADME studies. This data is useful but, for the future, it would be more relevant to measure not only plasma levels but also organ/tissue residues following much longer exposure periods.	

# Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 13/28

## Section 3 - Residues (B.7)

### 3. Residues (B.7)

<b>Storage Stability (B.7.0)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Metabolism in plants (B.7.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Metabolism in livestock (B.7.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Residue definition (B.7.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.7.3 Residue definition in plant matrices for enforcement purposes	DE: The inclusion of DFA into the residue definition for enforcement purposes needs further consideration.	DE: Tetraconazole also contains a DFA related moiety. In soil photolysis and soil metabolism studies tetraconazole-DFA was a minor intermediate but tetraconazole-alcohol missing the DFA part was a major residue. Since DFA was not radiolabelled, the amount released was not measured. However, it seems plausible that DFA was released from tetraconazole, making it a non-specific marker for flupyradifurone. In view of the very

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 14/28

### Section 3 - Residues (B.7)

<b>Residue definition (B.7.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
			high levels of DFA in rotational crops resulting from application of flupyradifurone, it should be discussed whether the contribution from tetaconazole is relevant or covered by the current approach. Since MRLs based on rotational crops are proposed for nearly all crops, "false" MRL-exceedances due to tetaconazole seem unlikely, but further explanation is required.
(2)	Vol. 3, B.7.3 Residue definition in plant matrices for risk assessment purposes	DE: The reasoning for an inclusion of DFEAF is unclear. The levels found in field trials are insignificant compared to parent and DFA. In rotational crops residues are also expected to be <0.01 mg/kg. RMS concluded, that a CF of 1 is appropriate, since no residues of DFEAF are found. Why is it included in the RD at all?	
(3)	Vol. 3, B.7.3 Residue definition in animal matrices for enforcement purposes	DE: Although DFA is also an environmental metabolite for tetaconazole, its levels are unlikely to cause a significant carry-over into farm animals. The proposed RD is supported, irrespective of the discussion for plant matrices.	

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 15/28

### Section 3 - Residues (B.7)

<b>Processing (B.7.7)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Livestock feeding (B.7.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol.3 B.7.8 TF for DFA	DE: The practical relevance of the approach to estimate TFs for metabolites is unclear.	DE: TFs normally consist of several aspects combined in an overall factor. Besides the systemic distribution the bioavailability is of major importance. Since it is unclear, whether DFA found in animal matrices is formed in the GI tract before being taken up via the lumen or is a metabolite formed in the animal organism after uptake of the parent, the derived factors are guesswork when applied to DFA in feed crops for the estimation of residue levels in animal commodities. Therefore the use of such an approach is unclear. The same applies to TFs for other metabolites.

<b>Succeeding/Rotational crops (B.7.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol.3 B.7.9 Calculation of residues in rotational crops	DE: The basis of 2 x 0.125 kg as/ha for the estimation of residues in rotational crops is from a GAP on protected lettuce. Field lettuce is treated only once with 0.125 kg as/ha while hops is considered a permanent crop. It seems unlikely that many of the crops listed for MRLs are relevant for crop rotation under protected	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 16/28

### Section 3 - Residues (B.7)

<b>Succeeding/Rotational crops (B.7.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		conditions. Further consideration is needed whether the GAP for protected lettuce is relevant for any rotational crops grown indoors. If it is not, the estimation of STMRs/HRs/MRLs for rotational crops, the livestock animal dietary burden and the consumer risk assessment need to be reconsidered and should rely on the relevant field GAP.	

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol.3 B.7.10	DE: MRLs for rotational crops need to be reconsidered – see comment under section Vol.3 B.7.9.	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

Section 4 - Environmental fate and behaviour (B.8)

**4. Environmental fate and behaviour (B.8)**

<b>Route and rate of degradation in soil (B.8.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3,B 8.1, rate of degradation (Study IIA, 7.2.3/01)	DE: A table with soil characteristics and a table with the measured residues of the metabolite in the samples should be added to the summary of the study Lowden et al (1997).	
(2)	Vol 1, Appendix 3, List of Endpoints, chapter 2.5	DE: Please add the soil names additionally to the soil types to the tables on degradation rate in soil, this will allow an easier attribution of the DT <sub>50</sub> and DT <sub>90</sub> values to the respective study summaries in Vol 3, B 8.	
(3)	Vol 1, Appendix 3, List of Endpoints, chapter 2.5	DE: Since the DFOP kinetics evaluation of the active substance's degradation data are used later on for higher tier groundwater modelling and for PEC <sub>soil</sub> calculations, the parameters k <sub>1</sub> , k <sub>2</sub> and g of the kinetics should be added to the table on degradation and dissipation rates of flupyradifurone in the laboratory and in the field.	

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B 8.2, adsorption in soil (Study IIA, 7.1.2/01)	DE: A table with soil characteristics and a table with the concentration of the metabolite in the solid and liquid phase should be added to the summary of the study Lui (1997).	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 18/28

### Section 4 - Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(2)	Vol 1, Appendix 3, List of Endpoints, chapter 2.5	DE: Please add the soil names additionally to the soil types to the tables on the adsorption parameters in soil, this will allow an easier attribution of the parameters to the respective study summaries in Vol 3, B 8.	

<b>PEC in soil (B.8.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B 8.4.3.2, degradation in water-sediment systems (Study IIA, 7.8.3/04)	DE: Has it been tested during or before the study, if the active substance does not adsorb to the plastic foil used to line the ponds? Were the residues in the biota (e.g. the lentils) analyzed? If yes, could this information please be added to the summary? Such studies might be used at some point to decide on the fulfilment of the P-criteria for PBT substances, this information is therefore important to evaluate if the dissipation of the active substance is actually mainly degradation.	

# Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 19/28

## Section 4 - Environmental fate and behaviour (B.8)

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(2)	Vol. 3, B 8.4.3.2, degradation in water-sediment systems (Study IIA, 7.8.3/04)	DE: The column headers in Table B.8.4.3.2-38 are mixed up and need to be corrected.	

<b>PEC in surface water and ground water (B.8.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B 8.6.3, predicted concentrations in groundwater	DE: An application of a PPP only every 2 <sup>nd</sup> year to a permanent crop like hops will be very difficult for risk management to implement and to control; we thus suggest to delete this refinement option here and to generally only apply it to non-permanent crops that are generally cultivated in crop rotations.	
(2)	Vol. 3, B 8.6.3, predicted concentrations in groundwater	DE: No tier 2A and 2B groundwater modelling was performed for the metabolite 6-CNA; however refinement modelling for the metabolite DFA shows that the simulated decrease in groundwater concentration for the active substance is correlated with an increase in groundwater concentration for the metabolites. Since the tier 2A and 2B groundwater modelling is considered more realistic it should also be performed for 6-CNA to ensure that the concentrations of this metabolite remain <0.1 µg/L.	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 20/28

### Section 4 - Environmental fate and behaviour (B.8)

<b>Fate and behaviour in air and PEC in air (B.8.7 – B.8.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Definition of the residues (B.8.9)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 1, Level 3, proposed decision on POP, PBT, vPvB, candidate for substituition	DE: An evaluation as to the question whether the active substance has POP, vPvB or PBT properties and whether it should be regarded as a candidate for substitution is missing. This evaluation should be included to Volume 1, Level 3 according to Guidance Document SANCO/12592/2012 –rev. 0 November 2012 (Template to be used for Assessment Reports); please also include short explanatory notes how the decisions were derived and which data were used to decide on the separate criteria.	

## Section 5 - Ecotoxicology (B.9)

## 5. Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, Table B.9.2.4.02, p. 55/56  Vol. 1, Point 2.6.2 “Effects on Aquatic species” and  Vol. 1, Appendix 3, chapter 2.6	DE: Typing error: The duration of the acute test with the test substance 6-CNA on <i>Chironomus tentans</i> according to the ASTM and EPA guidelines took 96 hours. Please correct time-scale in table B.9.2.3.02 of Vol. 3 (last line on page 80) and write 96 h instead of 48 h.	
(2)	Vol. 3, B.9.2.5, Risk assessment Invertebrates and Point 2.6.2 “Effects on Aquatic species”	DE: We acknowledge that the more sensitive species of the tested aquatic invertebrates is <i>Chironomus</i> . Accordingly, please use <i>Chironomus</i> data for the acute and chronic TER calculations for the 4 relevant metabolites (DFA, 6-CNA, BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide). Nevertheless, metabolites are less toxic to aquatic invertebrates compared to the active substance.	
(3)	Vol. 3, B.9.2.5, Risk assessment on aquatic	DE: Even if the butenolide flupyradifurone (nicotinic acetylcholine receptor (nAChR) agonist) is not as	

# Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 22/28

## Section 5 - Ecotoxicology (B.9)

<b>Aquatic organisms (B.9.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	insects	toxic to <i>Chironomides</i> as the closely related neonicotinoids, such as imidacloprid, the concerns about possible effects on mayflies (Ephemeroptera) should be investigated and discussed further because mayflies show higher sensitivity to neonicotinoids compared to <i>Chironomides</i> . The aquatic risk could be well addressed exploring sensitivity of mayflies to the a.s.	

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.9.4., Effects on wild pollinators	DE: Even if the butenolide flupyradifurone (nicotinic acetylcholine receptor (nAChR) agonist) is not as toxic as the closely related neonicotinoids, such as imidacloprid, the concerns about possible sublethal effects on wild pollinators such as bumble bees and wild bees (e.g. due to persistence, potency, systemic properties, bioavailability, mobility and findings in pollen of succeeding crops) should be investigated and discussed further. Concerns about long term sublethal effects on brood development or queen production cannot be excluded per se and possible	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>effects could cause unacceptable damage for the population of wild pollinators.</p> <p>For the risk assessment of wild pollinators only ecotoxicological studies with honey bees are available (except for one bumble bee study for pollen collection).</p> <p>Thus, there is insufficient data provided for the risk assessment of wild bees and solitary bees.</p> <p>The risk assessment for wild bees should be discussed.</p>	
(2)	Vol. 3, B.9.5.3, Refined off-field risk assessment	<p>DE: The two non-target arthropod field studies (off-crop) from the authors Aldershof S. and Bakker, F. (2012) are quite comprehensive and a summary of it is obviously labour-intensive. Nevertheless, in the study summary more readable (e.g. Table on page 367) as well as more detailed information will be necessary to understand the visualised results and especially the data standing behind it (e.g. validity criterion). It will also be helpful to provide more information within the summary to avoid misinterpretation of the results.</p> <p>Furthermore, there are some shortcomings of the studies that question the applicability for the refinement in off-crop risk assessment as well as the reliability of the selected endpoints:</p> <p>(1) In an off-crop field study suitable for the refinement of the off-field risk assessment it</p>	

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>has to be shown that toxic effects are not overlaid by re-colonisation, but the studies were conducted to show NOER/NOEAER by recovery, thus the focus was different influencing the design and outcome of the study. In the two conducted (off-crop) field studies the plots were established in a checkerboard design with open (uncovered) plots, which makes it difficult to conclude on the reliability of the study results on toxic effects. Furthermore, arthropods were sampled one, two, four and eight weeks after treatment. Thus, overlaying of toxic effects by re-colonisation cannot be excluded, and a clear separation of NTA-communities between treated and non-treated plots in the off-field is missed.</p> <p>(2) The off-crop field studies were performed only on grassland and are, therefore, insufficient as surrogate for the variability of possible off-field habitats around arable land. The study is not representative for 100% of existing worst case landscape. Standing alone, these field studies are insufficient for the refinement of the NTA off-crop risk assessment (please see DE comment 3, below "reduction of the correction factor").</p>	

# Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 25/28

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>(3) The study design is not suitable to show time and concentration related trends of toxic effects. Therefore, reliability of population related endpoints, such as NOER and NOEAER is questionable and conclusions on recovery and dose effect relationships are not reliable</p> <p>(4) Information on the mode of action as well as physical-chemical properties of the test substance flupyradifurone and the reference substance lambda-cyhalothrin should be used to underline and interpret the results in observations of treated plots.</p>	
(3)	Vol. 3, B.9.5.3, Refined potential exposure, Table 2.6.3.2-08	<p>DE: Reduction of the correction factor for the off-field PEC calculations from 5 to 1 is not acceptable, considering the shortcomings of the available off-crop field studies (please see DE comment (1) above). The uncertainty concerning the sensitivity of off-field arthropod species cannot be clarified. A correction factor of 5 will clearly result in a risk for off-crop NTAs. A study design for the refinement with a correction factor of 1 for the off-crop community requires a clear separation of toxic effects, recovery and re-colonisation as well as a 100% covering of a existing worst case landscape.</p> <p>The refined risk assessment for off-field arthropods should be discussed.</p>	

# Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 26/28

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(4)	Vol. 3, B.9.5.3, Refined off-field risk assessment, Reference product, page 365  Aldershof, S. and Bakker, F. Date: 17.2.2012 Study No.: <b>B154FFN</b> ; Figure A8-1, page 123	DE: “ <i>The validity criterion for the reference treatment was clearly met (at least 50% effect on at least one sample date for at least 10% of the taxa evaluated; De Jong et al., 2010)</i> ”  In the summary, more detailed information was missed to be able to follow the conclusion on the validity of the study. The study report (B154FFN) was available and the following results were found: 16.2%, 47.8%, 40.6%, 47.3% and 16.9% at the analysed sample dates (week -1, 1, 2, 4 and 8, respectively). Accordingly, the validity criterion 50% has not been reached in this field study from 2012. Thus, the validity of the study should be discussed.	

<b>Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.9.6.4, Earthworm field study, Menke,U. (2012), p. 407	DE: The field study from Menke, U. (2012, report number NMU/RG-F-8/12) shows some shortcomings that question the acceptability for the refined chronic risk assessment.  (1) Possibly inappropriate timing of substance application. The 25 <sup>th</sup> of May 2010 might have been too late for the study performance. The results gained 4 weeks after application	

## Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 27/28

### Section 5 - Ecotoxicology (B.9)

Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		<p>(end of June) are less representative because there are few earthworms present. The recorded mean (!) temp. of 18°C was higher than long term recording and mean precipitation of 12.3 mm far less compared to long term precipitation of 77.5 mm. Thus, reliability of the results 4 weeks after treatment is questionable.</p> <p>(2) The effects of the test substance on the number and the biomass of juveniles of <i>Lumbricus terrestris</i> are significant and constant over the test period of 11 months showing a concentration dependent trend. No recovery is shown during the whole test for <i>L. terrestris</i> juveniles at 300, 600 and 1500 g ai/ha. We do not support the conclusion stating that no effects are present at the end of the study. A NOER of 300 g ai/ha (0.271 µg ai/kg soil) for <i>L. terrestris</i> juvenile survival/ <i>L. terrestris</i> reproduction can be derived from the study.</p>	
(2)	Vol. 3, B.9.6.4.1-04, TER <sub>long-term</sub> calculations for earthworms	<p>DE: Based on the available earthworm field study from Menke, U. (2012), page 407 ff., the new relevant value for the chronic risk assessment is the NOER of 300 g ai/ha (corresponding to 0.271 mg a.i/kg soil) for the endpoints <i>L. terrestris</i> survival of juveniles and <i>L. terrestris</i> reproduction, (please see comment (1) above). Regarding the chronic risk assessment for</p>	

# Comments of Germany on the draft assessment report on Flupyradifurone

(07.04.14) 28/28

## Section 5 - Ecotoxicology (B.9)

<b>Earthworms and other soil non-target organisms (macro and micro) (B.9.6, B.9.7 and B.9.8)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		earthworms, we preliminarily calculate a TER long-term of 1.7 (Trigger = 5). Thus, the chronic risk assessment for earthworms should be discussed.	
(3)	Vol. 3, B.9.6.4, Earthworms field studies, IIIA 10.6.4/01, reference: Menke, U. (2012), “Remarks”, p. 421	DE:” ...low numbers of anecic earthworms ( <i>L. terrestris</i> ) is considered to be a feature of the test plots...” and “...low residues of the a.s. were found in the control plots...”: Please provide more information about the aim of the study as well as the study design in the study summary, to avoid misinterpretation of the results.	

<b>Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

<b>Other comments</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)		DE: no comment	

## Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

**1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)**

<b>Data on application (B.3)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	B.3.1.	Nature et Progrès Be  From points B.3.1.2 and B.3.1.3. it appears that flupyradifurone acts exactly as other neonicotinoids (imidacloprid, clothianidine, thiamethoxam) that are now suspended because of lacks pointed by EFSA in the assessment dossiers.  In such a context releasing another neonicotinoid in the environment seems to be irrelevant.	Imidacloprid, clothianidin and thiamethoxam were suspended because of data gaps in the assessment; one of these data gaps was the absence of assessment of risks to other pollinators (wild bees) in the DAR of these substances. A same data gap is present in the DAR of flupyradifurone.
(2)	B.3.1.5. Control of aphids in lettuce and hop were chosen as representative uses for the representative formulation, the product Sivanto	Nature et Progrès Be  Following point 1.5.3 of vol1, lettuce and hops are the intended uses applied for. Here these two crops are chosen as representative. Does the applicant intend to use the active substance (in Sivanto or other products) on other crops? It is not clear.	Because of the residues levels in pollen and nectar and the effects on pollinators (see below) from our point of view the substance cannot be authorized neither for flowering crops neither for crops producing honeydew or guttation. Only very limited uses are acceptable.  Moreover the uses applied for are not relevant for assessing risks linked to uses in seed dressing or on flowering crops.

## Section 5 - Ecotoxicology (B.9)

## 5. Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	B.9.4. Effects on bees	Nature et Progrès Be  Bees are a livestock and should be considered in the framework of assessment of risks to animal health, that is to say: residues studies, sublethal effects studies leading to the definition of ARfD, definition of LMRs in pollen and nectar.	
(2)	B.9.4. Effects on bees	Nature et Progrès Be  Chronic toxicity tests were performed as well as larvae tests. This is a great improvement of assessment of the risk to bees!	
(3)	B.9.4.1.3. Chronic toxicity of the active substance and metabolites	Nature et Progrès Be  Behavioural effects are present in some trials; there is no dose-response pattern (in Kling 2011). Absence of dose-response patterns should lead assessors to consider with caution the idea that a substance has no harmful effects below a dose for which no effects appeared; effects can appear when insects are exposed to lower doses.	Absence of dose-response patterns is described in peer-review studies for bees and other arthropods:  <ul style="list-style-type: none"> <li>- Charpentier G, Louat F et al. 2014: Lethal and sublethal effects of imidacloprid, after chronic exposure, on the insect model <i>Drosophila melanogaster</i>, <i>Environ. Sci. Technol.</i>, Just Accepted Manuscript • DOI: 10.1021/es405331c</li> <li>- Suchail S, Guez D and Belzunces LP, 2000: Characteristics of Imidacloprid toxicity in two <i>Apis mellifera</i> subspecies, <i>Environmental Toxicology and Chemistry</i>: 19(7): 1901–1905</li> <li>- Suchail, S., Guez, D., and Belzunces, L.P., 2001: Discrepancy between acute and chronic toxicity induced by Imidacloprid and its metabolites in <i>Apis mellifera</i>, <i>Environmental Toxicology and Chemistry</i> 20, 2482 – 2486</li> </ul>
(4)	B.9.4.1.3.1. Chronic toxicity on honeybee	Nature et Progrès Be  Since no statistically significant effects are reported,	

## Comments of Nature et Progrès BE on the draft assessment report on Flupyradifurone

(10.04.2014) 3/4

### Section 5 - Ecotoxicology (B.9)

Bees and non-target arthropods (B.9.4 and B.9.5)			
No.	Column 1 Reference to assessment report	Column 2 Comment (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	larvae	it is concluded from the larvae test that both NOEC and LOEC are > 10 000 microg/bee (the highest concentration used in the trial). However, from raw data (Table 9.4.1.3-09 p. 176) it appears that mortality was generally higher in the treated items than in control items even for the lowest concentration (150 microg/bee). Even when the Abbott-corrected mortality reaches 25% this additional mortality is not statistically significant. What is the statistical power of this test? Which level of additional mortality is it able to discriminate?	
(5)	B.9.4.2. Semi-field studies, Rexer 2013 p. 239 and following studies	Nature et Progrès Be Residues levels as high as 3 mg/kg and 70 mg/kg (70 ppm) are present in nectar and pollen from forager bees, respectively. Since behavioural effects exist without dose-response pattern the innocuousness of the substance for pollinators is not proved.	
(6)	<i>B.9.4.5. p. 340: Repellence of flupyradifurone leads to decreased flight intensity. In that way bees will minimize exposure of the hive to flupyradifurone.</i>	Nature et Progrès Be Reduction of flight intensity is not always due to repellence. Knock-down effects may lead to a reduction of flight intensity too. These two situations are different since in the first case bees are not intoxicated; in the second one they are intoxicated and other effects may appear.	When pyrethroids are usually considered to be repellent, scientific studies have shown that the stopping of foraging was actually due to a knock-down effect. Effects on temperature regulation may lead to bees' mortality depending on temperature of the place where the bee has to overnight. Cox RL and Wilson WT, 1984: Effects of permethrin on the behavior of individually tagged honey bees, <i>Apis mellifera L</i> (Hymenoptera : Apidae), <i>Environ. Entomol.</i> 13: 375-378

## Section 5 - Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B.9.4 and B.9.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
			Rieth JP, 1986 : The repellent effect of pyrethrinoids insecticides on honey bees, <i>Physiological Entomology</i> 13(2): 213–218

# **Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone**

(14. 04. 2014) 1/9

---

Section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of analysis (B.1 – B.5)

## **1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)**

No comments to this section

# **Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone**

(14. 04. 2014) 2/9

---

Section 2 - Mammalian toxicology (B.6)

## **2. Mammalian toxicology (B.6)**

No comments to this section

# **Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone**

(14. 04. 2014) 3/9

---

Section 3 - Residues (B.7)

## **3. Residues (B.7)**

No comments to this section

# Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone

(14. 04. 2014) 4/9

## Section 4 - Environmental fate and behaviour (B.8)

### 4. Environmental fate and behaviour (B.8)

<b>Route and rate of degradation in soil (B.8.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies	<b>Igor Kondzielski – IEP-NRI, Warsaw, Poland:</b> In the introductory paragraph to this whole section RMS declared that the kinetic analysis was performed using KinGUI tool. Could RMS specified which version of the tool – KinGUI 1 or KinGUI 2 was used? It might be of minor relevance, but while the KinGUI 1 offers only one fit option – OLS, the KinGUI 2 gives s possibility of choice between 3 – OLS, IRLS and MCMC, what may be considered as an additional refinement step. It might be useful, in case KinGUI 2 was used, to list the fit option selected as well.	
(2)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies	<b>Igor Kondzielski – IEP-NRI, Warsaw:</b> There seems to be inconsistency In approach reggrading to the selection of best fit made by the RMS. While in the first study – II A 7.2.1/01 (Menke U, 2011) the proposed by the Applicant selection of DFOP as best fit for AH and DD soil was rejected by the RMS and FOMC identified as returning the best fit, for the following studies such Applicant's approach was accepted by the RMS. Moreover in the latter cases the exactly same justification for selecting DFOP above FOMC even though the latter returned statistically better fit, was accepted,	

# Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone

(14. 04. 2014) 5/9

## Section 4 - Environmental fate and behaviour (B.8)

<b>Route and rate of degradation in soil (B.8.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		while for the first study it was rejected. This looks like an inconsistent approach. Could RMS explain this?	
(3)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies	<i>Igor Kondzielski – IEP-NRI, Warsaw:</i> the criteria of selection of the modelling endpoints for the parent compound seems to be not very clear. When examining the best-fit kinetics RMS declared that DFOP should be selected as returning the modeling endpoints and the slow phase should be used for this purpose. Were it so, why, for the same studies, in case of some soils this changed to SFO? This looks like inconsistent and confusing approach. Maybe it would be better to use the identified best-fit model to derive modeling endpoints instead of looking once again for them? Would RMs be so kind and explain this?	
(4)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies – rate of degradation of metabolite 6CNA	<i>Igor Kondzielski – IEP-NRI, Warsaw:</i> study by Lowden, Oddy and Jones (1997) is very briefly summarised with no information on soils used in examination, nor the experimental results. Probably more extent summary of this study can be found in the original (old) DAR for Flupyradifuron, never the less it might be a good idea to transfer them into this document.	
(5)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil,	<i>Igor Kondzielski – IEP-NRI, Warsaw:</i> could RMS comment on such a huge difference of DT <sub>50</sub>	

# Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone

(14. 04. 2014) 6/9

## Section 4 - Environmental fate and behaviour (B.8)

<b>Route and rate of degradation in soil (B.8.1)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
	Laboratory studies – rate of degradation of metabolite 6CNA	values (8-10 fold) for 6-CAN obtained in studies II A 7.2.3/03 (Sur Dorn 2012) and IIA 7.2.3/04 (Shepherd, 2011). The results of one of them may not be fully reliable.  Additionally, could RMS comment on why the results for 6-CNA in the study by Sur and Dorn (2012) were kinetically examined at all? These are very low levels of the compound detected, so the uncertainty related to so determined kinetic endpoints may be significant.	

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol.3, B.8.2.1- Batch sorption, the adsorption/desorption of metabolite 6-CNA	<b>Igor Kondzielski – IEP-NRI, Warsaw:</b> The summary of the study by Lui (1997) reports the results of the examination of batch soil sorption of 6-CAN. However, in the table B.8.2.1-18 summarising the key results of this study one crucial soil property – soil pH is missing. This may be of particular importance for 6-CAN, which is a difluoroanalogue of acetic acid – one of the stronger organic acids, therefore prone to ionisation at favourable pH. For this reason the pH-dependence of the adsorption of this	

# Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone

(14. 04. 2014) 7/9

## Section 4 - Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
		compound onto soil cannot be excluded and hence should be examined, what may be not possible without the information of soil pH. Could RMS insert these data into the indicated table?	

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4 – B.8.5)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 8.5, Impact on water treatment procedures	<b>Igor Kondzielski – IEP-NRI, Warsaw:</b> Only the potential impact of the residues of the Flupyradifuron on the wastewater treatment procedures was addressed. There is however no mention what could be a possible influence of the residues of this compound, itself or its degradation products on the processes of the abstraction of drinking water. It was demonstrated that the aqueous photolysis may be a relevant process of transformation of the active substance in water, therefore it may become important if the residues of the parent reach the disinfection stage of drinking water purification. Would RMS be so kind and address the issue?	

# Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone

(14. 04. 2014) 8/9

## Section 4 - Environmental fate and behaviour (B.8)

<b>PEC in surface water and ground water (B.8.6)</b>			
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations
(1)	Vol. 8.6.1, Predicted Environmental Concentrations in SW – calculations for the parent compound	<b>Igor Kondzielski – IEP-NRI, Warsaw:</b> The calculations were performed at Steps 1-4 using a standard set of FOCUS tools plus SWAN 1.1.4 for Step 4 calculations. At Step 4 one of the mitigation measures was the application of 15-meter buffer zone for spray drift and runoff in case of lettuce (e.g table B.8.6.1-11). Could RMS explain what reduction factors were used for runoff for 15-metres buffer zone and how this possibly complies with the recommendations given by FOCUS L&M Guidelines?	

# **Comments of Igor Kondzielski – IEP-NRI, Warsaw, Poland on the draft assessment report on Flupyradifurone**

(14. 04. 2014) 9/9

---

Section 5 - Ecotoxicology (B.9)

## **5. Ecotoxicology (B.9)**

No comments to this section

## TABLE OF CONTENTS

	<b>Document</b>
00	Cover page
01	Comments on the assessment report
<b>02</b>	<b>Reporting table</b>
03	Pesticides peer review meeting reports
04	Evaluation table
05	Comments on the additional information assessment
06	Comments on the draft EFSA conclusion

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

## 1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

<b>Identity (B.1, Annex C)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 4, Method of manufacture, p.7	EFSA: the different impurity spectrum of the technical material used for the chronic studies means different impurities or different amounts of the same impurities?	<b>APPL (04/2014): the different impurity spectrum of the technical material used for the chronic studies means both: different impurities as well as different amounts of the same impurity.</b>  NL (May 2014): Agreed with the applicant.	See data requirement in comment 2(54).
1(2)	Vol. 4, Specification of impurities, p.20	EFSA: The specification can be considered as provisional taking into account the pilot plant production, however 25.04.2014 Dok prepared by Isabelle - will be uploaded to DART	<b>APPL (04/2014): agreed</b>  NL (May 2014): Agreed.	Addressed.  See also comment 1(5)
1(3)	Vol. 4, Specification of impurities, p.20	EFSA: usually sulphated ash is not part of a specification	<b>APPL (04/2014): the inorganic impurities have to be seen as part of the specification and these impurities are given as a sum parameter as sulphated ash.</b>  NL (May 2014): Agreed with the applicant.	Addressed: The inorganic impurities can be part of the specification, expressed as sulphated ash
1(4)	Vol. 4, Analytical methods, Method 5, p.34	EFSA: typo: AM015011MP1 is A GLC method not HPLC	<b>APPL (04/2014): agreed - AM015011MP1 is A GLC method</b>  NL (May 2014): Typo, will be corrected.	Addressed.

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Identity (B.1, Annex C)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(5)	Vol. 4,	DE: The approach of the RMS that in case the data of the industrial scale process cannot be included, the identified issues regarding the specification should remain open, is fully supported.	<b>APPL (04/2014) agreed – data of industrial scale process cannot be included, so final specification will be concluded, when data from full scale production are available.</b>  NL(May 2014): Agreed.	Addressed. See also comment 1(2).

<b>Physical and chemical properties of the active substance (B.2.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(6)	C.1.1.2	FR: The table of synonyms and abbreviation is reported 2 times in this paragraph	<b>APPL (04/2014): the table is reported 2 times – one table can be deleted</b>  NL(May 2014): OK, 1 table of reported 2 times, will be deleted.	Addressed.
1(7)	C.1.2.2 Table C.1.2.2-01	FR: the impurities 1, 5, 6, 11 and 13 are not specified but described in C.1.2.2  Please RMS explain why the other impurities not detected or <LOQ are nor described in C.1.2.2  Moreover, the number of impurities given in C.1.2.2 does not correspond to the number given in Table C.1.2.2-01 (ex in C.1.2.2 water is the impurity 15 and in the table it is	<b>APPL (04/2014): In C 1.2.2 all impurities are described, which were detected. The described impurities 1, 5, 6 and 13 were not specified, as their values were below the LOQ.</b>  <b>Only those impurities which were not detected, are not described in C 1.2.2.</b>  <b>In table C 1.2.2-01 the results of the 5 batch analysis are given. So all impurities are</b>	Addressed.

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Physical and chemical properties of the active substance (B.2.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		the impurity 20)	mentioned, which are analysed with the analytical methods, described in C 1.2.3, independent if they were detected or not. This is the reason, why the total number of impurities is different.  NL(May 2014): Agreed with the applicant.	
1(8)	C.1.2.2 Table Justification of specified maximum purity of active substance and minimum content of impurities	FR: Please RMS explain why for some impurities, 2 specification limits are proposed.	APPL (04/2014): The applicant proposed lower specification limits for some impurities, as it is expected, that in the full scale production lower values of these impurities can be expected. In addition these lower limits are covered by the CMR batch.  As the RMS did not follow the proposal of the lower limits and suggested the values given in bold, which were derived with the 3fold standard deviation.  So for some impurities two limits are given: the one proposed by the applicant and the one proposed by the RMS.  NL(May 2014): Agreed with explanation of the applicant of 2 specification limits. Since full production scale might not be final during the dossier, the limits are not expected to be lowered.	Addressed:  The specification proposed by the applicant can be accepted and should be revised when the full scale production data are available.
1(9)	C.1.2.3Analytical	FR: Please RMS give the method used for	APPL (04/2014): for the organic impurities	Addressed.

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Physical and chemical properties of the active substance (B.2.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	methods	the confirmation of the identity of each impurity	<p>the MS-UV confirmatory method, for all solvents and volatile impurities the GC-MS confirmatory technique is used. This is described in the report of 5 batch analysis (M-420122-01-1).</p> <p>NL(May 2014): Agreed. Will be checked and added accordingly where appropriate.</p>	
1(10)	B.2.1 Physical and chemical properties of the active substance	FR : For a better readability, the complete chemical name of the metabolites should be reported	<p>APPL (04/2014): the list of metabolites with all used synonyms and the complete names can be found in Volume 3 B7 –Annex 1, page 303ff</p> <p>NL(May 2014): Agreed, and already addressed in B7.</p>	Addressed.
1(11)	B.2.1 Physical and chemical properties of the active substance	FR : Please RMS, explain why some physical and chemical properties are presented for 5 metabolites as they are not relevant	<p>APPL (04/2014): the available phys/chem data for metabolites which are relevant for risk assessment may be required/helpful for risk assessment and is therefore included in the summary where it is available.</p> <p>NL(May 2014): Agreed with the applicant.</p>	Addressed.
1(12)	Vol. 3, B.2 oxidising properties.	DE: Although in the summary in B.2.3.1 it is mentioned that the oxidising properties are not critical, it seems that the respective annex point has not been addressed in table B.2.1.1.	<p>APPL (04/2014) agreed - respective annex point has not been addressed in table B.2.1.1</p> <p>However the study about the oxidizing properties was submitted (Smeykal, H.</p>	Open point:  RMS to update table B.2.1.1 with the report of the oxidising property in an

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Physical and chemical properties of the active substance (B.2.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			Report No.: 20110197.06, Edition Number: M-414253-01-1) and is also mentioned in the reference list B.2.4 (KIIA 2.15/01)  NL(May 2014): Study will be included.	addendum to Vol.3..

<b>Physical, chemical and technical properties of the formulation (B.2.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(13)	B.2.2 Physical and chemical properties of the plant protection product	FR : For a better readability, the minimum and maximum use concentrations and the commercial packaging should be reported	APPL (04/2014): the information of the minimum and maximum use concentrations can be found in  NL(May 2014): Will be added.	Open point:  RMS to include the information concerning the minimum and maximum use concentrations and the commercial packaging in an addendum to Vol.3...
1(14)	B.2.2.14 Storage stability B.2.2.15 Shelf life	FR : For a better readability, physical and chemical properties after storage should be reported	APPL (04/2014): summary table of the results after storage, taken from report M- 402996-02-1, could be added   Summary table Storage and Shelf-life	Open point:  RMS to include the summary of the results after storage in an addendum to Vol.3..  Data requirement: Applicant to submit the report M- 402996-02-1, if not already submitted

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Physical, chemical and technical properties of the formulation (B.2.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL(May 2014): Summary will be added.	in the dossier.

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(15)	Vol B.3.1.2 Vol B.3.1.3	Nature et Progrès Be:  From points B.3.1.2 and B.3.1.3. it appears that flupyradifurone acts exactly as other neonicotinoids (imidacloprid, clothianidine, thiamethoxam) that are now suspended because of lacks pointed by EFSA in the assessment dossiers.  In such a context releasing another neonicotinoid in the environment seems to be irrelevant.	Imidacloprid, clothianidin and thiamethoxam were suspended because of data gaps in the assessment; one of these data gaps was the absence of assessment of risks to other pollinators (wild bees) in the DAR of these substances. A same data gap is present in the DAR of flupyradifurone.  <b>APPL (APR/2014): There are to date no harmonised test guidelines on how to reproducibly test non-Apis bees for risk assessment purposes, however, the international bee testing community under the auspices of ICPPR and OECD are currently developing these test systems (laboratory and higher tier) with first activities in 2014. From the envisaged non-Apis test systems, the acute bumble bee contact laboratory toxicity test is most progressed, and for flupyradifurone, tested via Flupyradifurone SL 200, no intrinsic</b>	Addressed.  Whether flupyradifurone will be approved or not will be a risk management decision. EFSA will present all available data that is scientifically evaluated as valid in the conclusion for flupyradifurone.

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>sensitivity differences were found between Bombus (LD50 &gt;100 µg a.s./bee; Vergé, 2012; KIIA 8.7.1/07) and Apis (LD50 = 15.7 µg a.s./bee; Schmitzer, 2009; KIIIA 10.4.2.1 /01); in the Bombus laboratory study (Vergé, 2012; KIIA 8.7.1/07), no behavioural abnormalities or sub-lethal effects were recorded throughout the entire test period.</p> <p>Regarding the chemical class of agrochemicals, for example, carbamates and organophosphates are both acetylcholinesterase (AChE) inhibitors, but simply due to an identical/similar mode of action, a carbamate insecticide is not an organophosphate insecticide and vice versa. The same holds true for flupyradifurone, which acts on the nicotinic acetylcholine receptor (nAChR). Due to its identical/similar mode of action, it does <u>not</u> become a neonicotinoid insecticide. For example, also spinosad, which is derived from naturally occurring bacteria (actinomycetes) acts on nAChR and is approved for use in organic agriculture by numerous countries.</p> <p>Moreover, also IRAC (Insecticide Resistance Action Committee) allocated flupyradifurone to the group of butenolides (IRAC sub-group 4D), whereas imidacloprid, clothianidin, thiamethoxam are allocated to the group of neonicotinoids (IRAC sub-group 4A). For illustration, the above mentioned carbamates</p>	

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>belong to the IRAC sub-group 1A, whereas the organophosphates belong to the IRAC sub-group 1 B.</p> <p>NL (May 2014): See applicant's response. In addition, please note that the toxicity to honeybees of flupyradifurone is others of magnitude less than that of the neonicotinoids imidacloprid, clothianidin and thiamethoxam. In section B.9 it is nevertheless proposed that the wild bee risk assessment is discussed in an expert meeting.</p>	

<b>Data on application (B.3)</b>				
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(15) a	B.3.1.	<p>Nature et Progrès Be</p> <p>From points B.3.1.2 and B.3.1.3. it appears that flupyradifurone acts exactly as other neonicotinoids (imidacloprid, clothianidine, thiamethoxam) that are now suspended because of lacks pointed by EFSA in the assessment dossiers.</p> <p>In such a context releasing another neonicotinoid in the environment seems to be irrelevant.</p>	<p><b>APPL (APR/2014): There are to date no harmonised test guidelines on how to reproducibly test non-<i>Apis</i> bees for risk assessment purposes, however, the international bee testing community under the auspices of ICPPR and OECD are currently developing these test systems (laboratory and higher tier) with first activities in 2014. From the envisaged non-<i>Apis</i> test systems, the acute bumble bee contact</b></p>	

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Data on application (B.3)</b>				
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>laboratory toxicity test is most progressed, and for flupyradifurone, tested via Flupyradifurone SL 200, no intrinsic sensitivity differences were found between Bombus (LD50 &gt;100 µg a.s./bee; Vergé, 2012; KIIA 8.7.1/07) and Apis (LD50 = 15.7 µg a.s./bee; Schmitzer, 2009; KIIIA 10.4.2.1 /01); in the Bombus laboratory study (Vergé, 2012; KIIA 8.7.1/07), no behavioural abnormalities or sub-lethal effects were recorded throughout the entire test period.</p> <p>Regarding the chemical class of agrochemicals, for example, carbamates and organophosphates are both acetylcholinesterase (AChE) inhibitors, but simply due to an identical/similar mode of action, a carbamate insecticide is not an organophosphate insecticide and vice versa. The same holds true for flupyradifurone, which acts on the nicotinic acetylcholine receptor (nAChR). Due to its identical/similar mode of action, it does become a neonicotinoid insecticide. For example, also spinosad, which is derived from naturally occurring bacteria (actinomycetes) acts on nAChR and is approved for use in organic agriculture by numerous countries.</p> <p>Moreover, also IRAC (Insecticide Resistance Action Committee) allocated flupyradifurone to the group of butenolides (IRAC sub-group 4D), whereas imidacloprid, clothianidin, thiamethoxam are allocated to the group of</p>	

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Data on application (B.3)</b>				
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>neonicotinoids (IRAC sub-group 4A). For illustration, the above mentioned carbamates belong to the IRAC sub-group 1A, whereas the organophosphates belong to the IRAC sub-group 1 B.</p> <p>NL (May 2014): See applicant's response.</p>	
1(15)b	B.3.1.5. Control of aphids in lettuce and hop were chosen as representative uses for the representative formulation, the product Sivanto	<p>Nature et Progrès Be</p> <p>Following point 1.5.3 of vol1, lettuce and hops are the intended uses applied for. Here these two crops are chosen as representative. Does the applicant intend to use the active substance (in Sivanto or other products) on other crops? It is not clear.</p>	<p>Because of the residues levels in pollen and nectar and the effects on pollinators (see below) from our point of view the substance cannot be authorized neither for flowering crops neither for crops producing honeydew or guttation. Only very limited uses are acceptable.</p> <p>Moreover the uses applied for are not relevant for assessing risks linked to uses in seed dressing or on flowering crops.</p> <p>APPL (APR/2014): A high number of (semi-)field studies, including long-term exposure scenarios, were conducted in highly bee attractive crops and have consistently not shown any evidence of acute, short-term or long-term adverse effects on individual honey bees and/or on the honey bee colony level, including over-wintering performance and bee-health, up to the highest envisaged application rate(s) of flupyradifurone in agronomically relevant crops. These (semi-)field studies confirmed the conclusions as derived from laboratory studies, which have consistently shown no delayed or chronic</p>	

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Data on application (B.3)</b>				
No.	<u>Column 1</u> Reference to assessment report	<u>Column 2</u> Comment (restricted to 500 characters, ca.10 lines)	<u>Column 3</u> Further explanations	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>effects, neither on individual adult honey bees nor on honey bee larvae.</p> <p>NL (May 2014): In the DAR, only the risk of the representative uses is assessed, which in this case are lettuce and hops. Whether other uses will be applied for at national levels is not relevant for the risk assessment in the European peer review process.</p>	

**Classification and labelling (B.4)**

For comments on classification and labelling see the relevant sections.

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(16)	Vol. 3, B.5.2, analytical methods for plants, plant products...	<u>BCS</u> (page 70): Recovery results of method 01330/ <b>M001</b> (modification of method for commodities with high oil content = rape, seed), submitted in November 2012 in the updated version of the Annex II dossier, are not included, neither for the method (KIIA 4,3/10) nor the ILV (KIIA 4.3/11). The modification of the method showed improved recoveries for DFA in rape, seed.	NL(May 2014): Recovery results will be checked and included where appropriate.  The table was moved to the end of the section.	Open point: RMS to include the recovery results of method 01330/M001 submitted in November 2012 in the updated version of the Annex II dossier, presented in the col. 3 of the RT in an updated Vol.3.  See also comment 1(68).
1(17)	Vol. 3, B.5.2 Residue methods for plants, method 01330 for BYI 02960, p.65	EFSA: it is not clear what is the meaning of the note in the FL column * 'fortified compound DFA determined as DFA'. Probably a typo, note belonging to the table for DFA	<b>APPL (04/2014):</b> <u>Typo:</u> The asterisk should include the following explanation: <b>Fortified compound: BYI 02960 / determined as BYI 02960 / expressed as BYI 02960</b> <b>The FL is always expressed in BYI 02960 equivalents, thus for DFA recoveries it has to be</b> <b>Fortified compound: DFA / determined as DFA / expressed as BYI 02960</b>  NL(May 2014): Clarification will be included.	Open point: RMS to update the note in B.5.2 Residue methods for plants, method 01330 for BYI 02960 according to the entry in col. 3 of the RT in an updated Vol.3.
1(18)	Vol. 3, B.5.2 Residue methods for plants, method 01330 for BYI 02960 and DFA, p.64	EFSA: small note: it is slightly misleading how the information is presented about method 01330, as from reading the DAR, it is thought that there is one method used for	<b>APPL (04/2014):</b> <b>New proposal:</b> <b>The residues were extracted twice from 5 g of plant material with acetonitrile/water (4/1,</b>	Open point: RMS to update the Vol. 3 with the information from col.3 of the RT concerning residue method 01330 for

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		quantifying the two compounds, however there are important differences: different columns, different gradient, elution temperatures...In practice there is a need to run two methods to be able to quantify the compounds of the residue definition.	<p>v/v) with 2.2 mL/L formic acid. The materials tested included lettuce (head), rape (seed), orange (fruit), wheat (grain), and hop (cone), representing a wide variety of crops/crop types as requested by EU guidance. After dilution, each aliquot of the raw extract was filtered for separate measurement of BYI 02960 and DFA. The solutions were analyzed by HPLC-MS/MS using either a C18-column (BYI 02960) or a ZIC®-HILIC SeQuant™ or a Hypercarb column (DFA); residues were quantified against matrix-matched standards.</p> <p>NL(May 2014): Additional information will be included regarding clarification on the methods.</p>	BYI 02960 and DFA
1(19)	Vol. 3, B.5.2 Residue methods for plants, method 01330, p.64	EFSA: it is stated that method 01330 was validated according to SANCO/825/00 rev.7, while the ILV according to SANCO/825/00 rev. 8.1, however there is no mention, how the extraction efficiency was assessed.	<p><b>APPL (04/2014):</b> Please refer to the paragraph in the Annex II dossier (p. 14): The extraction efficiency of the residue method for the determination of the relevant residues of BYI 02960 in plant matrices, consisting of the parent compound and its metabolite DFA, was assured by choosing the same extraction procedures as used in the plant metabolism studies (cf. chapter 6.2.1 of the Annex II dossier). In addition, an extraction efficiency study (see KIIA 4.3/04) was conducted using</p>	Open point: RMS to include the information concerning the extraction efficiency of the methods for plants presented in col.3 of the RT in an updated Vol.3.  See also comments 1(46), 1(49)

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>method 01304. As the extraction procedures for method 01330 are the same as for 01304, the results of the study prove satisfactory extraction efficiency with method 01330 in all matrices. The extraction efficiency was conducted in agreement with SANCO/825/00 rev. 8.1.</p> <p>NL(May 2014): Information regarding the extraction efficiency will be included.</p>	
1(20)	Vol. 3, B.5.2 Residue methods for animal matrices, method 01214, p.77	EFSA: it is stated that method 01214 was validated according to SANCO/825/00 rev. 8.1, however there is no mention, how the extraction efficiency was assessed.	<p><b>APPL (04/2014):</b> Please refer to the paragraph in the Annex II dossier (p. 55), but please correct typos: The extraction efficiency of the residue method for the determination of the relevant residues of BYI 02960 in animal matrices, consisting of the parent compound and its metabolite DFA, was assured by choosing the same extraction procedures as used in the livestock metabolism studies (cf. chapter 6.2.2 and 6.2.3 of the Annex II dossier). In addition an extraction efficiency examination was conducted as part of the poultry (KIIA 4.3/09) and cattle (KIIA 4.3/08) feeding studies. Aged residues in respective samples were analysed using procedures described in method RV-004-A11-04 and, in parallel, using the procedures described in the metabolism studies (cf. chapter 6.1 of the</p>	<p>Open point: RMS to include the information concerning the extraction efficiency of the methods for animal matrices presented in col.3 of the RT in an updated Vol.3.</p> <p>See also comment 1(49).</p>

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>Annex II dossier). As the extraction procedures for method RV-004-A11-04 are the same as for 01214, the results of the study prove satisfactory extraction efficiency with method 01214 in all matrices. The sample materials were eggs, fat, liver, and muscle in the poultry report, and kidney and milk in the ruminant report. The extraction efficiency was conducted in agreement with SANCO/825/00 rev. 8.1.</p> <p>NL(May 2014): Agreed with the applicant, information regarding extraction efficiency will be included and typos will be corrected.</p>	
1(21)	Vol. 3, B.5.3 Residue methods for soil, p.78	EFSA: small typo: water is missing from the composition of the extraction mixture: acetonitrile: water (1:4)	<p>NL(May 2014): Typo will be corrected.</p>	Addressed.
1(22)	Vol. 3, B.5.3 Residue methods for soil, p.79 and p. 81	EFSA: small typo in the unit for LOQ (should be µg/kg)	<p>NL(May 2014): Typo will be corrected.</p>	See open point in comment 1(52).
1(23)	Vol. 3, B.5.3 Residue methods for water, p.80 and p. 81	EFSA: clarification is needed if the residue definition for monitoring is as presented in the LoEP, is this method able to quantify all the compounds of the residue definition?	<p>APPL (04/2014): the proposed residue definition for monitoring of water is parent only. The method presented has been validated for the parent</p> <p>NL(May 2014): Agreed with the applicant.</p>	<p>Open point: RMS to harmonise the residue definition for monitoring for water in the LoEP with the residue definition proposed.</p> <p>See also comments 1(36), 1(40),</p>

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
				1(43), 1(59)
1(24)	B.5.1.1 Technical active substance B.5.1.2 Plant protection product	FR: the concentration used for the precision test should be provided to calculate Horwitz value	<p>APPL (04/2014): The mean concentration of the TGAS used for the precision is 979 g/kg. As the Horwitz criteria is 1.34 for this concentration, we pass with a RSD of 0.30 %, as given in report M-409002-01-1.</p> <p>The concentration of the active substance in the formulated product used for the precision is nominal 200 g/L. As the Horwitz criteria is 1.76 for this concentration, we pass with a RSD of 0.31 %, as given in report M-395374-01-1.</p> <p>NL(May 2014): Details can be included.</p>	Addressed.
1(25)	B.5.2 Analytical methods (residue)	FR : For a better readability, residue definition should be reported	<p>APPL (04/2014); The proposed residue definition for monitoring residues in food of plant or animal origin is the sum of parent flupyradifurone and its metabolite difluoroacetic acid (DFA), expressed in parent compound equivalents</p> <p>NL(May 2014): Agreed.</p>	<p>Open point: RMS to harmonise the residue definition for monitoring for food of plant and animal origin in the LoEP with the residue definition proposed. See also comment 1(42)</p>
1(26)	B.5.2 Analytical methods (residue)	FR : For a better readability, the complete chemical name of the metabolite DFA should be reported	NL(May 2014): Noted, can be added.	<p>Open point: RMS to include the complete chemical name of the metabolite DFA in an updated Vol.3</p>

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(27)	B.5.2 Analytical methods (residue)	FR : The test facility of each study (primary methods and ILVs) should be reported	<p>APPL (04/2014):  <u>Study 5 (primary method 01330 plus modified method 01330 M001) and Study 7 (primary method 01214):</u>  Test facility: Bayer CropScience AG,  D-40789 Monheim am Rhein</p> <p><u>Study 6 (ILV of method 01330 and 01330 M001) and</u>  <u>Study 8 (ILV of method 01214):</u>  Test facility: Currenta GmbH &amp; Co. OHG,  D-51368 Leverkusen</p> <p>NL(May 2014):  Information will be included.</p>	Addressed.
1(28)	B.5.2 Analytical methods (residue)	FR : The description of the methods should be detailed (column, ion mode ...)	<p>APPL (04/2014): see Commenting Table DE &amp; EFSA</p> <p>NL(May 2014): See response to comment 1(45).</p>	See open point in comment 1(46).
1(29)	B.5.2 Analytical methods (residue)	FR : It is not necessary to report overall recovery of the 2 fortification levels	NL(May 2014): Noted.	Addressed.
1(30)	B.5.2 Analytical methods (residue)	FR : Please RMS correct the values of the fortification level for hop (0.05 mg/kg instead of 0.01 mg/kg, and 0.5 mg/kg instead of 0.1 mg/kg)	NL(May 2014): Will be checked and amended accordingly where appropriate.	See open point in comment 1(16).
1(31)	B.5.2 Analytical methods (residue)	FR: The modification M001 of the analytical method 01330 should be explained.	APPL (04/2014): see Commenting Table DE & EFSA	See open point in comment 1(18)

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL(May 2014): See response to comment 1(17).	
1(32)	B.5.3 Analytical methods (residue) soil	FR : For a better readability, residue definition should be reported	<b>APPL (04/2014); The proposed residue definition is parent only.</b>  NL(May 2014): Agreed with the applicant.	Addressed.
1(33)	B.5.3 Analytical methods (residue) soil	FR: Characteristics of the soil sample (e.g. soil type, pH and organic matter/carbon content) should be provided in the method description to support its selection	<b>APPL (04/2014): The two soil types used (silt and sandy loam) are mentioned, which should be enough for a methods summary) further details are available if considered necessary.</b>  NL(May 2014): Agreed with the applicant.	Addressed.
1(34)	B.5.3 Analytical methods (residue) soil	FR: The number of the samples used for the calibration should be reported	<b>APPL (04/2014): The number of the samples used for the calibration is 6 per soil.</b>  NL(May 2014): Will be included.	Addressed.
1(35)	B.5.3 Analytical methods (residue) soil	FR: Please RMS correct : "Untreated Control Samples.... 0.3xLOQ (1.5 µg/kg instead of Hg/kg)"	<b>APPL (04/2014): this typo occurs at several points in the DAR</b>  NL(May 2014): Typo will be corrected.	See open point in comment 1(52).
1(36)	B.5.3 Analytical methods (residue) water	FR : For a better readability, residue definition should be reported	<b>APPL (04/2014) : The proposed residue definition is parent only.</b>	See open point in comment 1(23).

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>																
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)												
			NL(May 2014): Agreed.													
1(37)	B.5.3 Analytical methods (residue) water	In the method description the sampling site should be provided.  Validation quality data shall be provided to demonstrate that the sample is typical surface water in terms of its inorganic load (e.g. conductivity, hardness, pH) and its organic load (e.g. dissolved organic carbon content (DOC)).	<p>APPL (04/2014. For method validation surface water from the river Rhine sampled at Leverkusen-Hitdorf was used.</p> <p>Characteristics of the test system are listed in following table.</p> <p>Characteristics of Surface Water from River Rhine, Sampled on 2007-07-29 at LEV-Hitdorf (GER):</p> <table border="1"> <thead> <tr> <th>Parameter</th><th>Value</th></tr> </thead> <tbody> <tr> <td>Total organic carbon (TOC)</td><td>2 mg/L</td></tr> <tr> <td>Dissolved organic carbon (DOC)</td><td>2 mg/L</td></tr> <tr> <td>Conductivity</td><td>448 µS/cm</td></tr> <tr> <td>pH</td><td>7.3</td></tr> <tr> <td>Water hardness</td><td>9.9 °dH</td></tr> </tbody> </table>	Parameter	Value	Total organic carbon (TOC)	2 mg/L	Dissolved organic carbon (DOC)	2 mg/L	Conductivity	448 µS/cm	pH	7.3	Water hardness	9.9 °dH	<p>Addressed:</p> <p>See also comment 1(58)</p>
Parameter	Value															
Total organic carbon (TOC)	2 mg/L															
Dissolved organic carbon (DOC)	2 mg/L															
Conductivity	448 µS/cm															
pH	7.3															
Water hardness	9.9 °dH															

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>						
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)		
			<p>Dry residue after filtration</p> <table border="1"> <tr> <td></td> <td>290 mg/L</td> </tr> </table> <p>NL(May 2014): Details will be included.</p>		290 mg/L	
	290 mg/L					
1(38)	B.5.3 Analytical methods (residue) water	FR: Please RMS correct : "Limit of Quantification.... 0.05 µg/L instead of Hg/kg"	<p>NL(May 2014): Agreed.</p>	See open point in comment 1(52).		
1(39)	B.5.3 Analytical methods (residue) water	FR: According to the regulation 283/2013, an ILV of the method for the determination of residues in drinking water should be provided	<p><b>APPL (04/2014): This requirement was not in place at submission of the dossier (July 2012) and hence does not form part of the registration requirements,</b></p> <p>NL(May 2014): As the dossier has been submitted before 31th of December 2013, this Regulation does not apply to this dossier. Agreed with the applicant.</p>	<p>Addressed:</p> <p>In the peer review the monitoring methods are assessed against the European Commission Guidance document on pesticide residue analytical methods. SANCO/825/00 rev. 8.1 (16 November 2010), and in the case of water methods there is no need for ILV.</p>		
1(40)	B.5.3 Analytical methods (residue) water	FR: The analytical method allows to quantify the active substance flupyradifurone but not DFA and 6-CNA included in the residue definition (see LOEP)	<p><b>APPL (04/2014): the residue definition proposed for monitoring is parent only.</b></p> <p>NL(May 2014): Agreed with the applicant.</p>	See open point in comment 1(23).		
1(41)	B.5.3 Analytical methods (residue) air	FR: It should be mentioned that as the active substance is not classified T, T+, Xi or Xn,	<p><b>APPL (04/2014): This would appear to be incorrect as we understand that a method for</b></p>	Addressed.		

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		no analytical method for the determination of residues in air is necessary	monitoring of air is always required within the EU. Residue definition for monitoring of air is parent only.  NL(May 2014): Agreed with the applicant.	
1(42)	Vol. 1, 2.4.1 definition of the residue relevant to MRLs, animal products and vol. 1, list of endpoints, residue definition for monitoring purposes	DE: The residue definition for monitoring in animal products in volume 1, 2.4.1 includes the parent compound and DFA metabolite whereas in the list of endpoints only the parent compound is listed. Please bring in accordance.	<b>APPL (04/2014): Agreed; monitoring method for animal matrices has to include flupyradifurone and DFA</b>  NL(May 2014): Agreed, will be included.	See open point in comment 1(25).
1(43)	Vol. 1, 2.5.1 definition of the residue relevant for the environment and vol. 1, list of endpoints, residue definition for monitoring purposes	DE: The residue definition for monitoring in surface water and drinking/ground water in volume 1, 2.5.1 includes the parent compound only whereas in the list of endpoints the parent compound and the metabolites DFA and 6-CAN are listed. Please bring in accordance.	<b>APPL (04/2014): The residue definition for monitoring of surface water and drinking/ground water is flupyradifurone, only.</b>  NL(May 2014): Residue definition will be made consistent throughout the DAR.	See open point in comment 1(23).
1(44)	Vol. 1, list of endpoints, analytical methods for food/feed of plant origin,	DE: The LOQ cited in the list of endpoints is valid for flupyradifurone only. The LOQ for DFA was given in volume 3, B.5.2 as 0.02 mg/kg for lettuce, rape seed, orange fruit and wheat grain and 0.1 mg/kg for hop cone. Please add the LOQ for DFA.	<b>APPL (04/2014): Please note that separate LOQs have to be reported for flupyradifurone and DFA: Plant matrices: flupyradifurone 0.01 mg/kg (hops: 0.05 mg/kg) DFA: 0.02 mg/kg (hops: 0.10 mg/kg)</b>	Open point: RMS to update the LOQs for the analytical methods for food/feed of plant origin in the LoEP

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL(May 2014): Will be included.	
1(45)	Vol. 1, list of endpoints, analytical methods for food/feed of animal origin,	DE: The LOQ cited in the list of endpoints is valid for DFA only. The LOQ for flupyradifurone was given in volume 3, B.5.2 (study 7 and 8) as 0.01 mg/kg for animal matrices. Please add the LOQ for flupyradifurone.	<b>APPL (04/2014): Please note that separate LOQs have to be reported for flupyradifurone and DFA:</b> Animal matrices: flupyradifurone 0.01 mg/kg DFA: 0.02 mg/kg  NL(May 2014): Will be included.	Open point: RMS to update the LOQs for the analytical methods for food/feed of animal origin in the LoEP.
1(46)	Vol. 3, B.5.2, study 5and 6	DE: The method description is incomplete. The column used for flupyradifurone was not mentioned. The calibration range for flupyradifurone and DFA, a statement about blank values and ionisation type and MS/MS transition for DFA are missing. Please add. There is a typo for the fortified level for flupyradifurone in hop cones. The levels are 0.05 and 0.5 mg/kg, respectively.	<b>APPL (04/2014): See also proposal in EFSA commenting table</b> The residues were extracted twice from 5 g of plant material with acetonitrile/water (4/1, v/v) with 2.2 mL/L formic acid. The materials tested included lettuce (head), rape (seed), orange (fruit), wheat (grain), and hop (cone), representing a wide variety of crops/crop types as requested by EU guidance. After dilution, each aliquot of the raw extract was filtered for separate measurement of BYI 02960 and DFA. The solutions were analyzed by HPLC-MS/MS using either a C18-column (BYI 02960) or a ZIC®-HILIC SeQuantTM or a Hypercarb column (DFA); residues were quantified against matrix-matched standards.	Open point: RMS to include the information from the col.3 of the RT concerning B.5.2, studies 5and 6 in an updated Vol.3  See also comments 1(19), 1(28)

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>Please add additional paragraphs from the method as summarized in the Annex II dossier KIIA 4.3/01 &amp; 02</p> <p>Linearity, LOQ, Repeatability, Reproducibility, Extraction Efficiency</p> <p><u>Blank value of untreated control samples:</u> From each sample material, one untreated control sample was examined. All residues of BYI 02960 and difluoroacetic acid (expressed as parent equivalents) were well below 30% of the corresponding LOQ level.</p> <p><u>Ionisation type and MS/MS transition:</u> The experiments were performed on a triple-quadrupole mass spectrometer system, fitted with an electrospray interface operated in the positive ion mode for BYI 02960 and in negative mode for difluoroacetic acid under MRM conditions.</p> <p>BYI 02960: ESI positive      1<sup>st</sup> MRM: 289 =&gt; 126 (quantification)     2<sup>nd</sup> MRM: 289 =&gt; 90 (confirmatory)</p> <p>DFA: ESI negative      1<sup>st</sup> MRM: 95 =&gt; 51</p> <p>The wrong fortification level for flupyradifurone in hop cones was already in the Annex II dossier – sorry! DE is right, the</p>	

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			levels are 0.05 and 0.5 mg/kg  NL(May 2014): See also response to comment 1(18). Information will be included.	
1(47)	Vol. 3, page 70, Tables without headline	DE: The tables list studies KIIA 4.3/10 (Schulte & Teubner, 2012) and KIIA 4.3/11 (Konrad, 2012) which are not mentioned in the list of references and are neither described nor evaluated in the vol. 3, B.5.2. Either delete the tables or describe the studies if modifications of methods accepted before are needed.	<b>APPL (04/2014): Please describe method modification. Due to a request from Ctgb to improve the recoveries for oilseed, a modification of the method was submitted in the updated version of the DAR (see also BCS comments).</b>  NL(May 2014): Modification will be added.	Open point: RMS to describe the studies KIIA 4.3/10 (Schulte & Teubner, 2012) and KIIA 4.3/11 (Konrad, 2012) in an updated Vol.3..
1(48)	Vol. 3, table B.5.2-2	DE: What is the reason for citing methods RARVP013 (01304) and 01212 in the 2 <sup>nd</sup> and 3 <sup>rd</sup> line in table B.5.2-2? The methods are not described and not evaluated in the vol. 3, B.5.2.	<b>APPL (04/2014): RARVP013 (01304) and 01212 are data generation methods for plant matrices, as well as method RV-004-A11-04 which is a data generation method for animal matrices</b>  NL(May 2014): Agreed, is supplementary information.	Addressed.
1(49)	Vol. 3, chapter B.5.2	DE: The statement about extraction efficiency of the proposed monitoring method is missing. A corresponding study of Justus (2011) is mentioned in the references (section 5.6) but not evaluated. Please add an evaluation of this study.	<b>APPL (04/2014): KIIA 4.3/1 and KIIA 4.3/10 The extraction efficiency of the residue method (and its modification) for the determination of the relevant residues of BYI 02960 in plant matrices, consisting of the parent compound and its metabolite DFA,</b>	See open points 1(20) and 1(21).

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>was assured by choosing the same extraction procedures as used in the plant metabolism studies. In addition, an extraction efficiency study was conducted using method 01304. As the extraction procedures for method 01330 are the same as for 01304, the results of the study prove satisfactory extraction efficiency with method 01330 (see KIIA 4.3/04).</p> <p>NL(May 2014): Additional information will be added.</p>	
1(50)	Vol. 3, B.5.2, study 7 and 8	DE: The method description is incomplete. The HPLC column used for flupyradifurone was not mentioned. The calibration range for flupyradifurone and DFA, a statement about blank values and ionisation type and MS/MS transition for DFA are missing. Please add.	<p><b>APPL (04/2014): Please add additional paragraphs from the method as summarized in the Annex II dossier KIIA 4.3/06 &amp; 07 Specificity, Accuracy, Linearity, LOQ, Repeatability, Reproducibility, Stability of Analytes</b></p> <p><b>Principle of the method</b></p> <p>The residues were extracted twice from 5 g of animal-based material with acetonitrile/water (4/1, v/v), with the addition of n-heptane in the cases of fat and milk. The materials tested included bovine muscle, liver, kidney, and milk; and chicken fat and egg, representing the variety of matrix types requested by EU guidance. After the addition of formic acid and dilution, an aliquot of the raw extract was filtered for measurement. After dilution, each aliquot of</p>	<p>Open point: RMS to update the Vol.3 with the information presented in col.3 of the RT concerning B.5.2, studies 7 and 8.</p>

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>the raw extract was filtered for separate measurement of BYI 02960 and DFA. The solutions were analyzed by HPLC-MS/MS <i>using either a C18-column (BYI 02960) or a ZIC®-HILIC SeQuantTM or a Hypercarb column (DFA)</i>; residues were quantified against matrix-matched standards.</p> <p><b><u>Extraction Efficiency</u></b></p> <p>The extraction efficiency of the residue method for the determination of the relevant residues of BYI 02960 in animal matrices, consisting of the parent compound and its metabolite DFA, was assured by choosing the same extraction procedures as used in the livestock metabolism studies (cf. chapter 6.2.2 and 6.2.3 of the Annex II dossier). In addition an extraction efficiency examination was conducted as part of the poultry (KIIA 4.3/09) and cattle (KIIA 4.3/08) feeding studies. Aged residues in respective samples were analysed using procedures described in method RV-004-A11-04 and, in parallel, using the procedures described in the metabolism studies (cf. chapter 6.1 of Annex II dossier). As the extraction procedures for method RV-004-A11-04 are the same as for method 01214, the results of the study prove satisfactory extraction efficiency with method 01214. The sample</p>	

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>materials were eggs, fat, liver, and muscle in the poultry report, and kidney and milk in the ruminant report.</p> <p><u>Blank value of untreated control samples:</u> From each sample material, two untreated control samples were examined. All residues of BYI 02960 and difluoroacetic acid (expressed as parent equivalents) were well below 30% of the corresponding LOQ level.</p> <p><u>Ionisation type and MS/MS transition:</u> The experiments were performed on a triple-quadrupole mass spectrometer system, fitted with an electrospray interface operated in the positive ion mode for BYI 02960 and in negative mode for difluoroacetic acid under MRM conditions.</p> <p>BYI 02960: ESI positive      1<sup>st</sup> MRM: 289 =&gt; 126 (quantification)        2<sup>nd</sup> MRM: 289 =&gt; 90 (confirmatory)</p> <p>DFA: ESI negative      1<sup>st</sup> MRM: 95 =&gt; 51</p> <p>NL(May 2014): Additional information will be included.</p>	
1(51)	Vol. 3, B.5.3, study 9, section Description of methods	DE: The parent ion of the selected MRM transitions is not reported in the method description and should be added.	<p>APPL (04/2014) agreed.</p> <p>NL(May 2014):</p>	<p>Open point: RMS to report the parent ion of the selected MRM transitions for B.5.3,</p>

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			Agreed, will be added.	study 9 in an updated Vol.3
1(52)	Vol. 3, B.5.3, study 9, section linearity	DE: There is a typo in the unit for calibrated range in soil: 2 to 200 <b>pg</b> /kg should read as 2-200 <b>µg</b> /kg. Please correct.	<b>APPL (04/2014) That typo related to <b>µ</b> seems to occur several times on the dossier</b>  NL(May 2014): Agreed, typo will be corrected throughout the dossier.	Open point: RMS to correct the typos concerning the units in an updated Vol.3.
1(53)	Vol. 3, B.5.3, study 9, section Untreated control samples	DE: There is a typo in the unit for residues in control soil: 1.5 <b>Hg</b> /kg should read as 1.5 <b>µg</b> /kg. Please correct.	<b>APPL (04/2014): see above.</b>  NL(May 2014): Agreed, typo will be corrected throughout the dossier.	See open point in comment 1(52).
1(54)	Vol. 3, B.5.3, study 9, section Recovery rates	DE: The recovery and precision data of the method for residues of flupyradifurone in soil are missing. The mentioned tables presenting these data for both transitions should be added.	<b>APPL (04/2014) Tables as follows might be helpful:</b>  The table was moved to the end of this section  NL(May 2014): Tables will be included.	Open point: RMS to include the information from the col.3 of the RT concerning B.5.3, study 9 in an updated Vol.3..
1(55)	Vol. 3, B.5.3, study 10, section Description of methods	<b>DE: The mentioned "following table" presenting the LC-MS/MS parameter is missing and should be added.</b>	NL(May 2014): Will be checked and added where appropriate.	Open point: RMS to update the Vol. 3 with the LC-MS/MS parameters of B.5.3 study 10 .
1(56)	Vol. 3, B.5.3, study 10, section LOQ	DE: There is a typo in the unit for LOQ: 0.05 <b>Hg</b> /kg should read as 0.05 <b>µg</b> /kg. Please	<b>APPL (04/2014). That typo related to <b>µ</b> occurred more often the entire document.</b>	See open point in comment 1(52).

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>						
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)		
		correct.	NL(May 2014): Typo will be corrected throughout the dossier.			
1(57)	Vol. 3, B.5.3, study 10, section Recovery rates	DE: The recovery and precision data of the method for residues of flupyradifurone in water are missing. The mentioned tables presenting these data for both transitions should be added.	<p><b>APPL (04/2014). Tables as follows might be helpful:</b></p> <p><b>The tables were moved to the end of this section.</b></p> <p>NL(May 2014): Tables will be included.</p>	Open point: RMS to update the Vol.3 with the information presented in col.3 of the RT concerning B.5.3, study 10		
1(58)	Vol. 3, B.5.3, study 10	DE: It should be added which water samples were used for validation. Were the water samples characterized?	<p><b>APPL (04/2014) The water samples have been characterised and the details are available.</b></p> <p><b>Characteristics of Surface Water from River Rhine, Sampled at LEV-Hitdorf (GER)</b></p> <table border="1"> <thead> <tr> <th>Parameter</th> <th>Value</th> </tr> </thead> </table>	Parameter	Value	Addressed:  See also comment 1(37).
Parameter	Value					

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>																
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)												
			<table border="1"> <tr><td>Total organic carbon (TOC)</td><td>2 mg/L</td></tr> <tr><td>Dissolved organic carbon (DOC)</td><td>2 mg/L</td></tr> <tr><td>Conductivity</td><td>448 µS/cm</td></tr> <tr><td>pH</td><td>7.3</td></tr> <tr><td>Water hardness</td><td>9.9 °dH</td></tr> <tr><td>Dry residue after filtration</td><td>290 mg/L</td></tr> </table> <p>NL(May 2014): Details will be included.</p>	Total organic carbon (TOC)	2 mg/L	Dissolved organic carbon (DOC)	2 mg/L	Conductivity	448 µS/cm	pH	7.3	Water hardness	9.9 °dH	Dry residue after filtration	290 mg/L	
Total organic carbon (TOC)	2 mg/L															
Dissolved organic carbon (DOC)	2 mg/L															
Conductivity	448 µS/cm															
pH	7.3															
Water hardness	9.9 °dH															
Dry residue after filtration	290 mg/L															
1(59)	Vol. 3, B.5.3, study 10	DE: Please clarify that a valid method for the water metabolites DFA and 6-CAN is missing (given that the residue definition for monitoring in the list of endpoints is correct).	<p>APPL (04/2014) The list of endpoints should be revised, the proposed residue definition for monitoring of water is parent only.</p> <p>NL(May 2014): See response to comment 1(42).</p>	See open point in comment 1(23)												
1(60)	Vol. 3, B.5.3, study 11; page 82, reference of method	DE: In the references for all studies described before under "Type of study" the title of a study is presented. Therefore, the phrase "Analytical methods for soil, air and water" should be deleted.	<p>NL(May 2014): Will be deleted.</p>	Addressed.												
1(61)	Vol. 3, B.5.3, study 11	DE: Information with respect to the calibration range, breakthrough and the column type is missing and should be added.	<p>NL(May 2014): Will be checked and revised accordingly where appropriate.</p>	<p>Open point: RMS to update the information concerning B.5.3, study 11 in an updated Vol.3.</p>												

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(62)	Vol. 3, B.5.3, study 11; Table Recovery Results: Extraction Efficiency and Storage Stability	DE: The headlines of the last four columns should be revised.	NL(May 2014): Will be checked and revised accordingly where appropriate.	Open point: RMS to update the word processing errors of the tables concerning B.5.3, study 11 in an updated Vol.3.
1(63)	Vol. 3, B.5.3, study 11; Table Recovery Results: Retention Recoveries	DE: The headlines of the last four columns should be revised.	NL(May 2014): Will be checked and revised accordingly where appropriate.	See open point 1(62).
1(64)	Vol. 3, B.5.5, evaluation and Assessment	DE: The assessment of the reported studies seems to be too slim. We would prefer a tabular overview on residue definitions, action values and acceptable methods (i.e. according to table 5 in the SANCO/825/00 rev. 8.1). Probably, the unclear residue definitions would have been noticed in that case.	<b>APPL (04/2014): Proposed table for plant and animal matrices:</b>   Summary analytical methods.pdf  NL(May 2014):	Open point: RMS to update B.5.5, Evaluation and assessment with the information from col.3 of the RT in an updated Vol.3  Data requirement: Applicant to submit the table for plant and animal matrices, if not already included in the dossier.
1(65)	Vol. 3, B.5.6, References relied on	DE: The list does not contain two studies mentioned on page 70 (Schulte & Teubner, 2012 and Konrad, 2012).	NL(May 2014): Will be checked and and revised accordingly where appropriate.	See open point in comment 1(47).
1(66)	Vol. 3, B.5.6, References relied on	DE: The list contains two studies, which are not mentioned in the text before (Li & Schoening, 2011 and Justus, 2011).	NL(May 2014): Will be checked and and revised accordingly where appropriate.	Addressed.
1(67)	Vol. 3, B.5.6, References relied on	DE: In two cases (Schulte & Bauer, 2012 and Konrad, 2012) the referenced Annex Points are different to the Annex Points mentioned during method description.	NL(May 2014): Will be checked and and revised accordingly where appropriate.	See open point in comment 1(47).

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Methods of analysis (B.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		Furthermore, the two studies of Schulte & Bauer should be indicated as 2012a and 2012b and the two studies of Konrad should also be indicated as 2012a and 2012b.		

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(68)	Vol. 3, B.5.2, analytical methods for plants, plant products...	<u>BCS (page 71):</u> Please include method 01330/M001	Matrix: Plant Analyte: BYI 02960, DFA Method: 01330/M001 Method principle: HPLC-MS/MS LOQ: BYI 02960: 0.01 mg/kg; DFA: 0.02 mg/kg Reference: IIA 4.3/10 & IIA 4.3/10  NL(May 2014): Will be included.	See open point in comment 1(16).
1(69)	Vol. 3, B.5.2, analytical methods for plants, plant products...	<u>BCS (page 71):</u>  Please include the reference to method RARVP013 (= method 01304) and the respective extraction efficiency study	Reference: IIA 4.3/3 & IIA 4.3/4  NL(May 2014): Will be included.	See open point in comment 1(19).

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
1(70)	Vol. 3, B.5.2, analytical methods for plants, plant products...	BCS (page 71):  <u>Please indicate that methods RARVP013 &amp; 01212 (plant) and method RV-004-AII-04 (animal) are data collection methods</u>	NL(May 2014): Will be included.	Open point: RMS to indicate in an updated Vol. 3 that methods RARVP013 & 01212 (plant) and method RV-004-AII-04 (animal) are data collection methods.
1(71)	Vol. 1, LoEP Residue methods for soil, p.184	EFSA: small typo: the extraction is with acetonitrile:water	NL(May 2014): Typo will be corrected.	Addressed.
1(72)	LOEP Method of analysis	FR: Please RMS correct the wavelength reported for the method for the determination of impurities in technical sa (210 nm instead of 20)	NL(May 2014): Typo will be corrected.	Open point: RMS to correct the typo in the LoEP concerning the used wavelength.
1(73)	LOEP Method of analysis	FR: LOQ for flupyradifurone in fat, liver, kidney, muscle, egg and milk is 0.01 mg/kg and not 0.02 mg/kg	<b>APPL (04/2014):</b> <b>Residue definition for monitoring purposes:</b> Food of <i>plant</i> origin: Flupyradifurone, DFA LOQ (flupyradifurone): 0.01 mg/kg, except hop (0.05 mg/kg) LOQ (DFA): 0.02 mg/kg, except hop (0.10 mg/kg)  Food of <i>animal</i> origin: Flupyradifurone, DFA LOQ (flupyradifurone): 0.01 mg/kg LOQ (DFA): 0.02 mg/kg  NL(May 2014): Agreed with the applicant.	Open point: RMS to update the LOQs for the analytical methods in the LoEP.

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

**Table from row 1(15):**

In order to improve the recoveries for rape, seed, a modification of method 01330 was submitted in the updated version of the Annex II dossier (November 2012):

Method 01330/M001: Recoveries for BYI 02960

Sample material	FL* [mg/kg]	Individual values [%]					Mean value [%]	RS D [%]	LOQ [mg/kg]
<i>QUANTIFICATION MRM (289/126)</i>									
rape / seed	0.01	104	106	100	97	99	101	3.7	0.01
	0.10	95	99	91	99	99	97	3.7	
	<i>Overall recovery (n = 10)</i>					99	4.2		
<i>CONFIRMATORY MRM (289/90)</i>									
rape / seed	0.01	107	105	107	104	103	105	1.7	0.01
	0.10	99	102	95	102	101	100	3.0	
	<i>Overall recovery (n = 10)</i>					103	3.6		

Method 01330/M001: Recoveries for DFA

Sample material	FL* [mg/kg]	Individual values [%]					Mean value [%]	RS D [%]	LO Q [mg/kg]
<i>HILIC COLUMN (PRIMARY)</i>									
rape / seed	0.02	84	84	80	85	85	84	2.5	0.02
	0.20	71	74	77	71	74	73	3.4	
	<i>Overall recovery (n = 10)</i>					79	7.4		

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

<i>HYPERCARB COLUMN (CONFIRMATORY)</i>								
rape / seed	0.02	73	78	80	82	82	79	4.7
	0.20	94	80	89	81	90	88	8.8
	<i>Overall recovery (n = 10)</i>				83	8.8		

## ILV of method 01330/M001: Recoveries for BYI 02960

Sample material	FL [mg/kg]	Individual values [%]	Mean value [%]	RSD [%]	LOQ [mg/kg]
<i>QUANTIFICATION MRM (289/126)</i>					
rape / seed	0.01	76 85 83 83 78	81	4.7	0.01
	0.10	93 94 94 89 93	93	2.4	
	<i>Overall recovery (n = 10)</i>				7.7
<i>CONFIRMATORY MRM (289/90)</i>					
rape / seed	0.01	77 84 85 82 81	82	3.9	0.01
	0.10	94 93 92 88 95	92	2.8	
	<i>Overall recovery (n = 10)</i>				7.2

## ILV of method 01330/M001: Recoveries for DFA

Sample material	FL [mg/kg]	Individual values [%]	Mean value [%]	RSD [%]	LOQ [mg/kg]
<i>HILIC COLUMN (PRIMARY)</i>					
rape / seed	0.02	96 103 107 108 98	103	5.1	0.01
	0.20	95 102 102 97 100	99	3.0	
	<i>Overall recovery (n = 10)</i>				4.3
<i>HYPERCARB COLUMN (CONFIRMATORY)</i>					
rape / seed	0.02	90 102 94 110 92	97	8.6	0.01
	0.20	86 92 93 87 92	90	3.3	
	<i>Overall recovery (n = 10)</i>				7.6

## section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1–B.5)

Table form row 1(56):

## Recoveries for BYI 02960 Quantifier Mass Transition (m/z 126) RSD: Relative Standard Deviation

### Recoveries for BYI 02960 Confirmatory Mass Transition (m/z 99) RSD: Relative Standard Deviation

section 1 – Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)

**Table from row 1(59):**

Recoveries for BYI 02960 Quantifier Mass Transition (m/z 126); RSD = Relative Standard Deviation

Fortification [µg/L]	Matrix (measured by)	Single values [%]					Mean [%]	RSD [%]
0.05 0.5 Mean	Surface Water (matrix matched standards)	82	88	87	80	79	83	4.7
		84	88	86	84	89	86	5.7
		Mean single values					85	4.1
0.05 0.5 Mean	Surface Water (solvent standards)	76	82	81	75	74	78	4.7
		81	84	83	73	77	80	5.7
		Mean single values					79	5.1

Recoveries for BYI 02960 Confirmatory Mass Transition (m/z 90); RSD = Relative Standard Deviation

Fortification [µg/L]	Matrix (measured by)	Single values [%]	Mean [%]	RSD [%]
0.05 0.5 Mean	Surface Water (matrix matched standards)	9 94 9 90 90 4 4	92	2.4
		8 82 7 84 84 1 9	82	2.6
		Mean single values		87
0.05 0.5 Mean	Surface Water (solvent standards)	7 78 7 74 74 8 8	76	2.9
		7 78 7 72 72 7 4	75	3.7
		Mean single values		76

## section 2 – Mammalian toxicology (B.6)

## 2. Mammalian toxicology

<b>Toxicokinetics (B.6.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(1)	Vol. 3, B.6.1.1, study 1, metabolites in urine and faeces, p. 13	EFSA: In the conclusion of the study, three major metabolites are mentioned, but only two major metabolites are found: BYI2960-OH and Hippuric acid (and six minor metabolites).	<b>APPL (04/2014):</b> <b>6-CNA was also considered major since it was found in one dose group at a level of &gt; 5%</b>  NL (May 2014): See comment applicant.	Expert consultation MS to discuss whether the metabolite 6-CAN can be regarded as a major metabolite or not  Data requirement: 6-CNA cannot be regarded as a major metabolite in the rat studies (the level of 6.3% of the administered dose was obtained only in males treated with 200 mg/kg bw and was indiscriminately found in urine and faeces). Pending on the fate and behaviour section conclusion on 6-CNA calculated levels in groundwater, further toxicological data may be needed for this metabolite.
2(2)	Vol. 3, B.6.1.2, Toxicokinetic studies, repeated dose, oral route, p. 51	EFSA: data requirements state that repeated dose studies must be submitted, the OECD guideline also acknowledge that this test may be required by regulatory authorities and the test may provide more detailed information on bioaccumulation.  Considering the bi-phasic kinetic of flupyradifurone, low radioactive residues were still measured in almost all organ and	<b>APPL (04/2014):</b> <b>A bioaccumulation is considered highly unlikely for different reasons:</b> - The plasma curves clearly show a constant decline of total radioactivity - The concentration of radioactivity in the organs at sacrifice are lower than in the blood - The high water solubility / low	Expert consultation: MSs to discuss the possibility of waiving toxicokinetic study with repeated dosing.

## section 2 – Mammalian toxicology (B.6)

<b>Toxicokinetics (B.6.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		tissues, day 7 (ref. p. 34).	<p>lipophilicity of BYI 2960 and metabolites</p> <p>- The results of the quantitative whole-body autoradiography study demonstrating the concentrations fell for most organs and tissues below 5% of the maximum after one day and below the LOQ after 7 days</p> <p>NL (May 2014): Metabolism in the rat is very extensively investigated. All the design requirements of the kinetic studies are addressed with the single dose studies. The single dose toxicokinetic and tissue distribution data adequately determine the potential for accumulation. A repeated dose study is not considered relevant.</p>	
2(3)	Vol. 3, B.6.1.3, List of identified metabolites	DE: Metabolism in the rat was extensively investigated. What about the comparative <i>in vitro</i> study on different species as mentioned in the new data requirements?	<p><b>APPL (April/2014): At the time of dossier submission (May 2012 and Nov. 2012) these data requirements were not applicable, they entered into force at January 1<sup>st</sup>, 2014. It should also be noted that up to now no guideline or guidance document is existing on how to conduct such a study.</b></p> <p>NL (May 2014): Agreed with applicant. Furthermore, in SANCO/10181/2013-rev 2.1, it is clearly stated that in cases where “<i>test methods or guidance documents are not yet available for particular data requirements</i></p>	Addressed.

## section 2 – Mammalian toxicology (B.6)

<b>Toxicokinetics (B.6.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			[...] waiving of these particular data requirement points is considered acceptable as long as no test methods or guidance documents are published in form of an update of the Commission Communications 2013/C 95/01 and 2013/C 95/02."	
2(4)	Vol. 1, LoEP, toxicokinetics	EFSA: it is proposed to add the following information in the LoEP, regarding: - rate and extent of oral absorption: based on comparison of pattern of excretion after oral and i.v. administration. - distribution: state higher levels found in organs or tissues - rate and extent of excretion: please state % eliminated in 24h (and/or 48h) and % by urine and by faeces. - metabolism: it is proposed to mention which metabolites are minor (or disregard these) and which are major metabolites (for which reference values of the parent would be applicable)	<b>APPL (04/2014):</b> <b>Rate and extent of absorption:</b> BYI 02960 was fast and almost completely absorbed within 48 h (75-90% of administered radioactivity was detected in urine after oral administration and 76% was detected after i.v. administration) <b>Distribution:</b> Maximum plasma concentration was reached approx. 1 h (2-4 h) after administration of a low dose (high dose); fast clearance from blood and distribution mainly into liver (metabolism) and kidney (excretion); after reaching the peak concentrations, a fast decline of RA was observed for all organs and tissues, concentrations in all organs/tissues were < LOQ seven days after administration. <b>Rate and extent of excretion:</b> Excretion was very fast, mainly renal and almost completed after 24 h (approx. 77-97% within 24 hours and 82-100% within 48 h); 75-90% of administered radioactivity was	Open point: RMS to revise the LoEP adding some relevant information regarding toxicokinetics and metabolism of flupyradifurone.

## section 2 – Mammalian toxicology (B.6)

<b>Toxicokinetics (B.6.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>excreted via the urine within 48 h.</p> <p><u>Metabolism:</u> Moderate metabolism; main metabolites detected in urine (accounting for &gt;10% of the dose administered) were BYI 02960-OH and BYI 02960-hippuric acid (only high dose, male); metabolites 6-CNA and DFA were detected in urine at levels &gt;5% of the dose administered.</p> <p>The principal metabolic reactions of BYI 02960 in rats were:</p> <ul style="list-style-type: none"> <li>• hydroxylation followed by conjugation with glucuronic acid or sulfate,</li> <li>• cleavage of the difluoroethyl group forming BYI 02960-des-difluoroethyl, and difluoroacetic acid (DFA),</li> <li>• cleavage of the molecule at the pyridinylmethylene bridge forming BYI 02960-difluoroethyl-amino-furanone and 6-CNA, which was further conjugated with glycine to BYI 02960-hippuric acid.</li> </ul> <p>These main metabolic reactions were also ob</p> <p>NL (May 2014): Additional information will be added in a revised addendum.</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Acute toxicity (B.6.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(5)	Vol. 3, B.6.2.1 Acute toxicity Study 1	FR: According to mortalities observed at 2000 mg/kg bw (3/3 and 1/3 deaths), the LD50 would be below 2000 mg/kg.  The conclusion on classification does not change.	APPL (April/2014): The applicant agrees that the LD50 should be considered below 2000 mg/kg with no impact on the classification.  NL (May 2014): Agreed, Cat 4 LD50 >300-2000 mg/kg bw. Will be revised in a revised DRAR.	See open point in 2(7)
2(6)	Vol. 3, B.6.2.2 Irritation and sensitisation Study 3	FR: Could you please clarify the highest tested dose in the LLNA study is 50% of BYI 02960?  The preparation BYI 02960 SL 200g/L was found to be sensitizing (without any sensitizing substance in the composition), a highest dose could have been tested on flupyradifurone.	APPL (April/2014): A 100% (w/v) (1 g/mL) formulation of BYI 02960 in DMF was tested in a preliminary study but there was only a partial dissolution, whereas a clear solution was obtained with a formulation at 50% (w/v) (0.5 g/mL). Another solvent (acetone/olive oil) had already been tested without success. Therefore the main study was done with a formulation at 50%.  NL (May 2014): See comment applicant.	Addressed.
2(7)	Vol. 1, LoEP, acute toxicity	EFSA: Regarding rat oral LD50 it would be clearer to mention that it is between 300 and 2000 mg/kg bw (classification required: H302).  Regarding rat LC50 by inhalation, mg/L units are usually used and type of exposure (nose-only).	APPL (April/2014): The applicant agrees that the LD50 should be considered below 2000 mg/kg with no impact on the classification, Category 4 H302.  The inhalation study was effectively done under nose only conditions for 4 hours and the LC50 was higher than 4.7 mg/L	Open point: RMS to revise the LoEP regarding the acute oral, acute inhalation and skin sensitisation endpoints.  See also 2(5)

## section 2 – Mammalian toxicology (B.6)

<b>Acute toxicity (B.6.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		Please add the test used for skin sensitisation.	<b>The table was moved to the end of this section</b>  NL (May 2014): Agreed, Cat 4 LD50 >300-2000 mg/kg bw with H302. Will be revised in a revised DRAR.	

<b>Short-term toxicity (B.6.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(8)	Vol. 3, B.6.3.1 28-day oral studies Study 1	FR: We suggest to set a LOAEL of 75 mg/kg bw/d based on observed effects on liver and clinical chemistry.	<b>APPL (April/2014): The only statistically significant effect seen in clinical chemistry parameters is a decrease in total bilirubin concentration at 75 mg/kg/day in males. This effect is due to one animal only and is therefore not considered relevant. Liver findings at 75 mg/kg/day are limited to prominent liver lobulation in one male without associated microscopic findings or liver weight increase. This is therefore considered incidental. The applicant</b>	Expert consultation: MSs to discuss the NOAEL/LOAEL of the 28-day oral study in rat by gavage (study 1).

## section 2 – Mammalian toxicology (B.6)

<b>Short-term toxicity (B.6.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>considers 75 mg/kg/day as a NOAEL and not a LOAEL.</p> <p>NL (May 2014): A decrease in total bilirubin is not considered adverse. As explained by the applicant this effect is due to one animal only. In conclusion the significant effects seen at 75 mg/kg are not considered adverse.</p>	
2(9)	Vol. 3, B.6.3.1 28-day oral studies Study 2	FR: We suggest to set a LOAEL of 500 ppm or 33.6 mg/kg bw/d based on observed effects on liver and clinical chemistry.	<p>APPL (April/2014): There are no statistically significant effects seen at 500 ppm in any clinical chemistry parameters. 2/5 males showed prominent lobulation at 500 ppm but this was not associated with liver weight increase and not associated with microscopic findings. Therefore this finding was not considered adverse.</p> <p>NL (May 2014): The non significant clinical chemistry effect without any histological effects are not considered adverse. The macroscopy liver lobulation, which was not associated with any microscopic finding is also no considered adverse.</p>	<p>Expert consultation:</p> <p>MSs to discuss the NOAEL/LOAEL of the 28-day dietary study in rat (study 2).</p>
2(10)	Vol. 3,B.6. 3.1, 28-day oral studies, study 3	DK: There is a statistically significant decrease in absolute and/or relative epididymis weights in all 3 dose groups.	APPL (April/2014): Lower epididymis weights were found in treated animals when compared to controls but this change was	<p>Data requirement:</p> <p>Applicant to provide the historical control data regarding epididymis</p>

## section 2 – Mammalian toxicology (B.6)

<b>Short-term toxicity (B.6.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		Rapporteur considers this effect not relevant because no relevant histological findings were observed. However, this effect seems to be dose related.	<p>considered not to be relevant since it was not clearly dose-related and not associated with relevant histological findings.</p> <p>Furthermore, the epididymis weights were within historical control data.</p> <p>NL (May 2014): The epididymis weights in the 300 ppm group and higher dosage are indeed significantly decreased however the effect was not considered adverse since there is no histological finding. Based on the figures in the DAR the dose effect relation is not clear, because of the low absolute weight and the rounded figures. Nonetheless, the weights are within the historical control data (See 2(11)) and since significant lower epididymis weights are not found in any of the other studies the significant effect is considered a chance observation.</p>	weights for the 28-day study in mice.  Expert consultation: MSs to discuss the NOAEL of the 28-day study in an experts meeting.  See also 2(11), 2(12)
2(11)	Vol. 3, B.6.3.1 28-day oral studies Study 3	FR: Could you please explain why the effects on epididymis weight have not been taken into account from 300 ppm (statistically decreased).	<p>APPL (April/2014): Lower epididymis weights were found in treated animals when compared to controls but this change was considered not to be relevant since it was not clearly dose-related and not associated with relevant histological findings.</p> <p>Furthermore, the epididymis weights were within historical control data.</p>	See 2(10)

## section 2 – Mammalian toxicology (B.6)

<b>Short-term toxicity (B.6.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			 HCD epididymis C57 28day.pdf  NL (May 2014): See 2(10).	
2(12)	Vol. 3, B.6.3.1, 28-day study in mouse, pp. 71-73	EFSA: Considering the effects observed at the high dose level (reduced bw gain by 15%, reduced relative and absolute epididymis weight and clinical chemistry changes), this dose should be set as the LOAEL of the study.	<b>APPL (April/2014):</b> The body weight gain decrease observed in the males during the first week of treatment was not considered adverse because it was a transient effect limited to the first week of the study (body weight gain was higher than in the controls during the following weeks), with no statistically significant impact on total body weight and limited to one sex. Lower epididymis weights were found in treated animals when compared to controls but this change was considered not to be relevant since it was not clearly dose-related and not associated with relevant histological findings. Furthermore, the epididymis weights were within historical control data. The slight increase in alanine aminotransferase and alanine phosphatase observed in the females at 1200 ppm were not considered relevant because there was no dose-related relationship, this was limited to one sex and there was no histological changes in the liver. Therefore we believe that 1200 ppm	See 2(10)

## section 2 – Mammalian toxicology (B.6)

<b>Short-term toxicity (B.6.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>should be considered as a NOAEL.</p>  <p>HCD epididymis C57 28day.pdf</p> <p>NL (May 2014): See 2(10). Regarding the clinical chemistry the variation of the individual values and the lack of a clear dose response these changes were considered not to be treatment-related.</p>	
2(13)	Vol. 3, B.6.3.4, study 1, 90-day rat, pp. 78-82	EFSA: the 500 ppm dose level produced reduced bw gain (12%), increased relative and absolute thyroid weight by 20 and 17%, it should therefore be considered a LOAEL.	<p><b>APPL (April/2014): The only finding observed at 500 ppm in females was a slight body weight gain decrease which was statistically significant during the first week and the last week of treatment but without any significant impact on body weight. The mean thyroid gland to body weight ratio was statistically significantly higher in males at 500 ppm but was not associated with any relevant microscopic finding neither in the thyroid nor in the liver. The applicant therefore believes that 500 ppm should be considered as a NOAEL.</b></p> <p>NL (May 2014): As explained by the applicant the reduced bw gain in females without effects on the bw is not considered</p>	<p>Expert consultation: MSs to discuss the NOAEL of the 90-day study in rat (study 1) in an experts meeting.</p> <p>See also 2(14), 2(15)</p>

## section 2 – Mammalian toxicology (B.6)

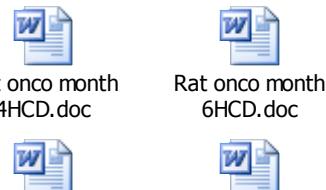
<b>Short-term toxicity (B.6.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			adverse. Regarding the thyroid gland only effects are seen relative to body weight in males. Since there is no effect on bw in males the absolute thyroid gland weight is more relevant. No significant effects are found in the absolute thyroid gland.	
2(14)	Vol. 3. B.6.3.4 Semichronic oral studies, study 1	DK: relative thyroid weight was also statistically significantly increased in the 500 ppm group but without histopathological findings which were observed at the higher dose of 2500 ppm. However, there seems to be dose response, supporting an effect at 500 ppm, making NOAEL 100 ppm.	<b>APPL (April/2014): The mean thyroid gland to body weight ratio was statistically significantly higher in males at 500 ppm but was not associated with any relevant microscopic finding neither in the thyroid nor in the liver. The applicant therefore believes that 500 ppm should be considered as a NOAEL.</b>  <b>NL (May 2014): See 2(13)</b>	See 2(13)
2(15)	Vol. 3, B.6.3.4 semichronic oral studies Study 1	FR: We suggest to set a NOAEL of 100 ppm or 6 mg/kg bw/d for male and 7.6 mg/kg bw/d for female, based on decreased of body weight and body weight gain at 500 ppm and 2500 ppm.	<b>APPL (April/2014): 100 ppm is a real NOEL in this study as no treatment-related findings were seen at this dose level. The only finding observed at 500 ppm in females was a slight body weight gain decrease which was statistically significant during the first week and the last week of treatment but without any significant impact on body weight. The applicant therefore believes that 500 ppm can be still considered as a NOAEL.</b>	See 2(13)

## section 2 – Mammalian toxicology (B.6)

<b>Short-term toxicity (B.6.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL (May 2014): See 2(13)	
2(16)	Vol. 1, LoEP, short term toxicity, relevant oral NOAEL in dogs	EFSA: as both the 90-day and 1-year studies in dogs are considered short term, only the most relevant one should be mentioned in the LoEP. It appears to be the 1-year, once a longer duration of exposure is tested (although considering dose spacing, the 12 mg/kg bw per day from the 90-day study may be discussed).	<b>APPL (April/2014): the applicant suggests to mention both studies.</b>  NL (May 2014): Because the ADI and AOEL are based on both the 90-d dog and 1-y dog study it is proposed to show both studies in the LoEP	See expert consultation in 2(45)

<b>Genotoxicity (B.6.4)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(17)	Vol. 3, B.6.4.1, <i>In vitro</i>	DE: A negative HGPRT test in CHO cells is reported (study 4). Surprisingly, it is stated in the conclusion, in addition, that no UDS was induced but this was not tested. Is the description of a further study lacking in the DAR or was it a technical error?	<b>APPL (April/2014): this is effectively a technical error. No UDS was triggered for the parent.</b>  NL (May 2014): Probably a copy paste error. Will be removed in a revised DAR.	Addressed: RMS to consider in a revised DAR or corrigendum.

## section 2 – Mammalian toxicology (B.6)

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>								
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)				
2(18)	Vol. 3, B.6.5.1, study 1, 2-year, rat, pp. 108-115	EFSA: Table 6.5.1-1: it would be useful to have the actual values of bw/bw gain (or at least % of change) and haematological findings to be able to assess the RMS conclusion. The statistically significant values for controls would be related to HCD, but these are not provided and therefore cannot be used. Some effects at 400 ppm appear to be the first signs of substance-related adversity in the liver.	<p><b>APPL (April/2014):</b></p> <p><b>The table has been moved to the end of this section.</b></p> <p><b>Haematological findings in the males:</b> All the data are within historical control data except for the white blood cell and neutrophil counts after 24 months, but the mean values are within the range of HCD.</p> <p><b>Haematological findings in females :</b> All the data are within historical control data except for the lymphocyte counts after 4 months and haemoglobin concentration and haematocrit after 12 months but the mean values are within the range of HCD.</p>  <table> <tr> <td>Rat onco month 4HCD.doc</td> <td>Rat onco month 6HCD.doc</td> </tr> <tr> <td>Rat onco month 12HCD.doc</td> <td>Rat onco month 18HCD.doc</td> </tr> </table>	Rat onco month 4HCD.doc	Rat onco month 6HCD.doc	Rat onco month 12HCD.doc	Rat onco month 18HCD.doc	<p>Data requirement: Applicant to provide the tabled results of body weight/body weight gain and haematological findings of the 2-year rat study and relevant historical control data.</p> <p>Expert consultation: MSs to discuss the NOAEL of the 2-year rat study in an experts meeting.</p> <p>See also 2(19), 2(20), 2(21)</p>
Rat onco month 4HCD.doc	Rat onco month 6HCD.doc							
Rat onco month 12HCD.doc	Rat onco month 18HCD.doc							

## section 2 – Mammalian toxicology (B.6)

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			 Rat onco month 24HCD.doc <p>There was no increased incidence or severity in eosinophilic foci in the liver at 400 ppm, but an increased incidence in colloid alteration in the thyroid with no increased severity compared to control males. The findings observed in the males at 2000 ppm (liver histopathological findings and colloid alteration) were considered adverse because the hepatocellular hypertrophy was associated with pre-neoplastic findings (eosinophilic foci in the liver). Whereas the findings observed the liver at 400 ppm were considered adaptative: the hypertrophy was minimal, there was no liver weight effects, no pre-neoplastic or clinical chemistry changes. The thyroid effects which have been demonstrated to be secondary to liver induction were therefore not considered adverse. The applicant would still recommend a NOAEL at 400 ppm</p> <p>*: Dunnett LSD Test significant at 0.05 level  ++: Dunn Rank Sum Test significant at 0.01 level  +: Dunn Rank Sum Test significant at 0.05</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p><b>level</b></p> <p>NL (May 2014): Bw and bwg data and HCD data will be included in a revised DAR. Increased incidence of colloid alteration occurs naturally in aging rats and was not associated with follicular hypertrophy at 400 ppm.</p> <p>The only effect is the minimal centrilobular hypertrophy in 6 male animals without any increase of foci of alteration or hepatocellular macrovacuolation and is therefore not considered adverse.</p>	
2(19)	Vol. 3, B6.5.1, Chronic toxicity and carcinogenicity, study 1	<p>DK: the increased incidence of colloid alteration in the thyroid was not considered adverse in the 400 ppm group because it was argued that it occurs with age in rats and was not associated with relevant follicular hypertrophy. The incidence of colloid alteration was 38 and 40 in the 400 ppm and 2000 ppm groups, respectively, taken together with an incidence of follicular cell hypertrophy of 1 and 3 in the 400 ppm and 2000 ppm groups, respectively.</p> <p>The effect in the two highest doses is very similar. It should be considered if the effect observed in both dose groups is adverse or not adverse.</p>	<p><b>APPL (April/2014): There was no increased incidence or severity in eosinophilic foci in the liver at 400 ppm, but an increased incidence in colloid alteration in the thyroid with no increased severity compared to control males. The findings observed in the males at 2000 ppm (liver histopathological findings and colloid alteration) were considered adverse because the hepatocellular hypertrophy was associated with pre-neoplastic findings (eosinophilic foci in the liver). Whereas the findings observed the liver at 400 ppm were considered adaptative: the hypertrophy was minimal, there was no liver weight effects, no pre-</b></p>	See 2(18)

## section 2 – Mammalian toxicology (B.6)

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			neoplastic or clinical chemistry changes. The thyroid effects which have been demonstrated to be secondary to liver induction were therefore not considered adverse. The applicant would still recommend a NOAEL at 400 ppm  NL (May 2014): See 2(18) and comment from the applicant.	
2(20)	Vol. 3, B.6.5.1, Chronic toxicity or carcinogenicity, rat study, editorial remark	DE: It was noted that in the tables B.6.5.1-4, B.6.5.1-5 and B.6.5.1-6 statistical significances were indicated for certain histopathological findings in the control group of the long-term study in rats. Can you explain that or was it simply an error?	APPL (April/2014): This is an error.  NL (May 2014): Will be removed in a revised DAR.	See 2(18)
2(21)	Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity Study 1	FR: In the liver, an increased in incidence and severity of alteration eosinophilic focus of hepatocellular and a higher incidence of centrilobular hepatocellular hypertrophy was found in male at 400 ppm and 2000 ppm. Furthermore in the thyroid, increased incidences of colloid alteration were noted in male at 400 ppm and 2000 ppm.  Due to observed effects on liver and thyroid, the NOAEL for general toxicity need to be discussed.  France suggests setting the NOAEL at 80	APPL (April/2014): There was no increased incidence or severity in eosinophilic foci in the liver at 400 ppm, but an increased incidence in colloid alteration in the thyroid with no increased severity compared to control males. The findings observed in the males at 2000 ppm (liver histopathological findings and colloid alteration) were considered adverse because the hepatocellular hypertrophy was associated with pre-neoplastic findings (eosinophilic foci in the liver). Whereas the findings observed the liver at 400 ppm were considered adaptative : the hypertrophy was minimal,	See 2(18)

## section 2 – Mammalian toxicology (B.6)

<b>Long-term toxicity and carcinogenicity (B.6.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		ppm based on observed effects on liver and thyroid in male at 400 ppm and 2000 ppm.	there was no liver weight effects, no pre-neoplastic or clinical chemistry changes. The thyroid effects which have been demonstrated to be secondary to liver induction were therefore not considered adverse. The applicant would still recommend a NOAEL at 400 ppm  NL (May 2014): See 2(18) and comment from the applicant.	
2(22)	Vol. 3, B.6.5.1, study 2, 18-month mouse study, pp. 115-120	EFSA: Table 6.5.1-7: please give the actual values of bw / bw gain (and % of change regarding controls).	<b>APPL (April/2014):</b>  <b>The table was moved to the end of this section.</b>  NL (May 2014): Will be included in a revised DAR.	Addressed: RMS to consider in a revised DAR or corrigendum.
2(23)	Vol. 3, B.6.5.1., Chronic toxicity or carcinogenicity, study in mice	DE: In the kidney, there were histopathological findings pointing to a less pronounced occurrence of mostly age-related changes (less mineralization, less vacuolation) in male mice. On one hand, they should not be mentioned to support the NOAEL (that is based on liver toxicity). On the other hand, is there an explanation for this "beneficial" effect on the kidneys?	<b>APPL (April/2014): there is no explanation for the "beneficial" effect on the kidneys</b>  NL (May 2014): NL is of the opinion that only effects which are adverse should be mentioned along with the NOAEL.	Addressed.

## section 2 – Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(24)	Vol. 3, B.6.6.1, study 2, 2-generation, rat, pp.129-140	<p>EFSA: regarding parental toxicity, based on reduced bw gain in females (weeks 1-10) by &gt;20% in the P generation and by 16% in F1 parental generation, the parental NOAEL is proposed to be set at 100 ppm, LOAEL 500 ppm.</p> <p>It may be arguable whether all offspring/reproductive findings at the high dose level may be explained only by parental decrease in bw/bw gain (delay in preputial separation and vaginal patency; reduced brain, thymus and spleen weights; and reduced number of implantation sites). Or whether another MoA may be expected (endocrine mediated).</p>	<p>APPL (April/2014): the applicant appreciates that there is good scientific argumentation for proposing a parental NOAEL at both 100 ppm as suggested by EFSA or 500 ppm as suggested by the RMS. Taking the conservative approach would be acceptable to the applicant.</p> <p>As stated in the paper of Melching-Kollmuss et al. (Anti-androgenicity can only be evaluated using a weight of evidence approach, Regulatory Toxicology and Pharmacology 68(2014) 175-192) there is a significant chance that delayed preputial separation is observed in the rat 2-generation reproduction study as a result of general systemic toxicity rather than a consequence of an endocrine disruption mode of action, as the test guideline requires that systemic toxicity is evident, at least at the highest dose level. Pup body weight at day 21 pp correlated best with the age at PPS, presumably because any potentially confounding variation due to lactation differences as a result of litter size at birth was minimized by pup culling at ay 4 pp and the subsequent comparable lactation condition. In the rat 2 generation reproduction study 13% and 12.5% decrease</p>	<p>Data requirement:</p> <p>Applicant to provide clarification on the possible endocrine-mediated MoA of flupyradifurone. The information embedded in column 3 of the reporting table should be included.</p> <p>Expert consultation:</p> <p>MSs to discuss the parental, reproductive and offspring NOAEL of the multigeneration study in an experts meeting and the potential for an endocrine-mediated MoA.</p> <p>See also 2(25), 2(27)</p>

## section 2 – Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>in body weight was observed in male and female F1 pups from the 1800 ppm dose group, respectively, on LD21. This body weight decrease can therefore explain the delay in PPS and VP, as seen in the tables below and in the attached document.</p> <p>Table 1: Mean body weight at day of complete preputial separation</p> <p><b>The table was moved to the end of this section.</b></p> <p>Table 2 : Mean body weight at day of complete vaginal separation</p> <p><b>The table was moved to the end of this section.</b></p> <p> Delay in PPS and VP.pdf     PPS_article2014_mel ching-Kollmuss.pdf</p> <p>The effects on brain, thymus or spleen weights can also be explained by lower body weights as seen in the tables in the document attached below.</p> <p><u>Brain weights:</u></p> <p>In F1 pups on LD21, a slight decrease in</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>absolute brain weight was observed in males (-3.93%) and females (-3.3%) at 1800 ppm (only one male was outside the control range) and a slight increase in brain weight to body weight ratio was observed due to lower body weight (+9.5% in males and +9.07% in females). 9 males from 7 litters and 12 females from 7 litters were outside the control range but they had lower body weight compared to control animals.</p> <p>In F2 pups, statistically significant decrease in absolute brain weight was observed in females only (-3%) with only one animal outside the control range. Statistically significant increase in brain weight to body weight ratio was observed in males (+11.5%) with 6 animals from the same litter outside the control range and in females (+11.4%) with only one animal outside the control range.</p> <p><u>Thymus weights</u></p> <p>F1 pups at 1800 ppm: Statistically significant thymus weight changes were observed in males for absolute weights (-11.3%, all animals within control range) and in females for thymus weight to body weight ratio (+6.8% with 3 animals outside the control range).</p> <p>F2 pups at 1800 ppm: Statistically significant decrease in absolute thymus weight in</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>females (-10.96%) with 12 animals from 5 litters. No significant changes were observed in thymus weight to body weight ratio.</p> <p><u>Spleen weights</u></p> <p>F1 pups at 1800 ppm: A statistically significant decrease in absolute spleen weight was observed in males only (- 17.98%) with all animals within the control range and no significant effect on spleen weight to body weight ratio. This could be explained by lower body weight.</p> <p>F2 pups at 1800 ppm: Statistically significant decrease in absolute spleen weight in both males (-14.98%) with 6 animals from one litter outside the control range due to lower body weight and females (-15.48%) with 6 animals from 3 litters outside the control range due to lower body weight. No significant effect on spleen weight to body weight ratio in both sexes.</p> <p> Rat 2 generation - Pup organ weights fin</p> <p><u>Reduced implantation sites:</u> A statistically significant decrease in the total number of implantation sites was effectively observed at 1800 ppm in the second generation.</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>However, if this effect was linked to endocrine disrupting properties, endocrine effects should have been seen during the rat carcinogenicity study (M-428257-01-1) in the high dose group (2000 ppm). This is not the case, as effects were only seen in the liver and the thyroid in both sexes and in the lung in the females only. The thyroid effects are secondary to liver enzyme inductions as demonstrated in a 28-day rat study (M-297120-01-2) where increased TSH and decreased T4 levels were observed at 5000 ppm (385 mg/kg/day) with an increase in BROM and UDPGT activities. Therefore, based on the data available there is no reason to suspect an endocrine MoA for the active substance.</p> <p>NL (May 2014): Agreed that the reduced bwg with a significant reduced bw is considered as an adverse effect. Parental NOAEL will be adapted to 100 ppm. Reproductive findings should be discussed in a meeting of experts.</p>	
2(25)	Vol.3, B.6.6.1 Reproductive toxicity, study 2	DK: A statistically significantly decreased body weight PND 14-21 and a reduced weight gain in F2 generation in the mid- and high dose group was observed. In the F1 generation a significant decreased body	<p>APPL (April/2014): Taking the conservative approach would be acceptable to the applicant: parental female systemic LOAEL at 500 ppm (39.2 mg BYI 02960/kg bw/day), based on decreased body weight (F1) and</p>	See 2(24)

## section 2 – Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		weight week 10 of premating and during gestation and lactation in the mid – and high dose group was reported. The NOAEL should therefore be 100 ppm instead of 500 ppm.  The argument for not using this effect at 100 ppm is that the decrease is < 10 % but there seems to be dose- response and the effect in the F1 generation is persistent.	body weight gain (P and F1) during premating, decreased body weight during gestation (F1) and lactation (F1). Also observed were terminal body weight declines for the F1-females; the parental female systemic NOAEL at 100 ppm (7.8 mg BYI 02960/kg bw/day).  NL (May 2014): NL is of the opinion that a sole observation of bw decrease <10% although significant is not considered as an adverse effect (as has been concluded in previous DARs).	
2(26)	Vol. 3, B.6.6.1 Reproductive toxicity Study 1	FR: The table 6.6.1-3 is the same as the table 6.6.1-4. Could you please update the study summary	APPL (April/2014): Mean Body Weight and Food Consumption – Gestation  <b>The table was moved to the end of this section.</b>  NL (May 2014): Will be updated in a revised DAR.	Open point: RMS to revise tabled results of body weight and food consumption of the multigeneration study in rats in an addendum to the DAR.
2(27)	Vol. 3, B.6.6.1 Reproductive toxicity Study 2	FR: We suggest to set the parental systemic NOAEL and the offspring NOAEL at 100 ppm, based on decreased of body weight and body weight gain at 500 ppm and 1800 ppm in parental and F1 generation during premating, gestation and lactation and on offspring in F1 and F2 generation.	APPL (April/2014): The applicant appreciates that there is good scientific argumentation for proposing a parental NOAEL at both 100 ppm as suggested by France or 500 ppm as suggested by the RMS. Taking the conservative approach would be acceptable to the applicant.	See 2(24)

## section 2 – Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL (May 2014): See comment 2 (24) and 2 (25).	
2(28)	Vol. 3, B.6.6.2, developmental studies in rat (study 1 and 2) / LoEP	EFSA: the overall maternal NOAEL between the two studies is 50 mg/kg bw per day from study 1 as no sign of toxicity was found in study 2 up to the highest dose level of 30 mg/kg bw per day. It is also noted that increased liver weight of 13% without associated hepatotoxicity is generally not considered as adverse.	NL (May 2014): The combination decreased bw and increased liver weight was considered sufficient for the parental “worst-case” LOAEL at 150 mg/kg bw/d because no microscopic observations are performed.	See 2(30)
2(29)	Vol. 3, B.6.6.2, study3, developmental toxicity study in rabbit	EFSA: In view of reduced bw of 12% during the first days of treatment, the maternal NOAEL would be 15 mg/kg bw per day.	<b>APPL (April/2014): the applicant appreciates that there is good scientific argumentation for proposing a maternal NOAEL at both 15 mg/kg/day as suggested by EFSA or 40 mg/kg/day as suggested by the RMS. Taking the conservative approach would be acceptable to the applicant.</b>  NL (May 2014): The reduced bw of 12% is borderline. To be consistent with the NOAEL in the reproductive study the NOAEL should be 15 mg/kg bw/d.	Addressed: The maternal NOAEL of the rabbit developmental study is 15 mg/kg bw per day.  Open point: RMS to revise the LoEP regarding the relevant maternal NOAEL of the rabbit developmental study.
2(30)	Vol. 3, B.6.62, Teratogenicity studies; Vol. 3, B.6.11.2, Toxicodynamics	DE: It is not clear to us why a second developmental study in rats became necessary to be performed because a robust maternal NOAEL was obtained in the first	<b>APPL (April/2014): The second developmental toxicity study was conducted to have a better idea of the effect of the compound on maternal body weight: mean</b>	Addressed: Reduced maternal body weight gain (GD 6-8) by 49% justifies keeping the overall rat maternal NOAEL at 30

## section 2 – Mammalian toxicology (B.6)

<b>Reproductive toxicity (B.6.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	(Summary)	one. However, taking both studies together, the overall NOAEL for maternal toxicity would be 50 mg/kg bw/day rather than 30 mg/kg bw/day.	<b>maternal body weight gain reduced by 49% and mean food consumption reduced by 8% between GD 6-8 at 50 mg/kg/day in the first study.</b>  NL (May 2014): See comment notifier.	mg/kg bw per day (as stated in the LoEP) for the developmental toxicity studies.  See also 2(28)

<b>Neurotoxicity (B.6.7)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(31)	Vol. 1, LoEP, repeated neurotoxicity	EFSA: please add the systemic toxicity NOAEL from the 90-day neurotoxicity study in rat in the LoEP.	<b>APPL (April/2014): Systemic toxicity NOAEL from the 90-day neurotoxicity study in rat is 500 ppm (equating to 29.4 and 34.8 mg/kg/day in males and females, respectively) based on body weight and food consumption effects at 2500 ppm.</b>  NL (May 2014): Agreed will be updated in Vol. 3 and Vol 1.	Open point: RMS to add the systemic NOAEL of the neurotoxicity study and its basis in the LoEP.
2(32)	Vol. 3, B.6.7.3, study 1, developmental neurotoxicity, p. 169	EFSA: as bw change was not important, and changes in brain weight were also observed in other studies, it is not so straightforward that reduced brain weight is not treatment-related, although it is acknowledged that also	<b>APPL (April/2014): There was a slight trend of decline in terminal body weights at 1200 ppm (-5% as compared to controls) in PND 75 (<math>\pm</math> 5 days) non-perfused rats. There was also a decrease (-5%) in fresh brain weights</b>	Addressed regarding changes in brain weight.  Open point: RMS to revise the LoEP clarifying

## section 2 – Mammalian toxicology (B.6)

<b>Neurotoxicity (B.6.7)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>the decreased brain weight was also not important and adversity may be discussed.</p> <p>In the LoEP, it should be clarified that the NOAEL refers to maternal, developmental and developmental neurotoxicity.</p>	<p>at 1200 ppm as compared to controls in PND 75 (<math>\pm</math> 5 days) non-perfused rats. This change was considered not directly related to test substance administration since it was related to decline in terminal body weights. The brain weight range for the non-perfused males was 1.769 g to 2.050 g and the range for the non-perfused 1200 ppm treated males was 1.739 g to 1.993 g with only two animals with a brain weight outside the control range.</p> <p>The maternal NOAEL was 500 ppm (equating to 42.4 mg/kg/day) based on decreased body weight and body weight gain and the developmental neurotoxicity NOAEL was 500 ppm (equating to 42.4 mg/kg/day) based increased startle amplitude in females only on PND 60 and increased motor and locomotor activity on PND 13 in males only.</p> <p>NL (May 2014): See comment from applicant. Agreed will be updated in Vol 3 and Vol 1.</p>	maternal, developmental and developmental neurotoxicity NOAELs.

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(33)	Vol. 3, B.6, literature search	EFSA: Regulation (EC) No 1107/2009 requires a search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, to be conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092).  Although acknowledged that flupyradifurone is a new a.s. and therefore may not be found in the open literature, this search should at least have been conducted on metabolites.	APPL (April/2014): A literature search was already presented in the applicant dossier in Document N  NL (May 2014): Conclusions from the literature search will be in the updated DAR.	Open point: RSM to include the assessment of the literature search performed by the applicant in an addendum to the DAR.
2(34)	Vol. 3, B.6.9, studies on metabolites, p. 177	EFSA: if metabolite BYI 02960-CHMP is common to other a.s. it may be worthwhile considering if specific reference values should be set for the metabolite.  Pending on the agreed consumer and groundwater assessments in the residue and fate sections, it should be clarified for which metabolites the reference values of the parent are applicable and/or for which metabolites further toxicological data may be necessary.	APPL (04/2014): Metabolite BYI 02960-CHMP and its corresponding conjugates (BYI 02960-CHMP-glyc, BYI 02960-CHMP-di-glyc, BYI 02960-CHMP-glyc-di-SA, BYI 02960-CHMP-glyc-tri-SA and BYI 02960-CHMP-serinate) were minor metabolites (<10% of the TRR and <0.01 mg/kg) in all edible livestock and plant matrices, except in tomato fruits. In tomato fruits, metabolite BYI 02960-CHMP-di-glyc accounted for 37.1% of the TRR (0.048 mg a.s. equivalents/kg).	Expert consultation: Considering that the metabolite DFA is a major metabolite in rotational crops and in poultry, and is found above 0,75 µg/L in groundwater, MSs to discuss the reference values applicable to the metabolite in an expert meeting.  See also 3(36), 2(37), 2(43)

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>Therefore the toxicological profile of the aglycon BYI 02960-CHMP was evaluated based on available data.</p> <p>Available toxicological data on BYI 02960-CHMP:</p> <ul style="list-style-type: none"> <li>- <i>in-vitro</i> genotoxicity: Bacterial assay for gene mutation =&gt; negative</li> <li>- acute oral toxicity =&gt; LD<sub>50</sub> (males): 1842 mg/kg; LD<sub>50</sub> (females): 1483 mg/kg</li> <li>- subchronic toxicity: Oral 90-day toxicity in the rat =&gt; The no observed effects level (NOEL) was 800 ppm (48.9 mg/kg/day) in males, and 4000 ppm (275.9 mg/kg/day) in females. When the NOEL is expressed in BYI 02960 equivalents, it equates to 97.8 and 551.8 mg/kg/day. Therefore, BYI 02960-CHMP was shown to be less toxic than BYI 02960 after subchronic administration to the rat.</li> </ul> <p>An overview on the flupyradifurone metabolites was given in the Annex II dossier KII A 5.10 (Toxicological coverage of BYI 02960 plant and livestock metabolites): The metabolites were assigned to different groups</p> <p>(1) Metabolites with no toxicological</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>concern (natural compounds)</p> <p>(2) Metabolites with no consumer exposure (&lt;0.01 mg/kg in food items and &lt;0.05 mg/kg in feed items)</p> <p>(3) Metabolites with exposure below the threshold of 1.5 µg/kg bw (TTC concept)</p> <p>(4) Metabolites covered by rat ADME (<math>\geq 10\%</math> of administered radioactivity)</p> <p>(5) Metabolites with additional toxicity testing</p> <ul style="list-style-type: none"> <li>- <b>DFA</b> (major metabolite in soil, water, plant and animal matrices)           <p>=&gt; accounted for approx. 6% of the administered dose in urine, however was the dominating metabolite in the 24 hours samples of plasma, organs and tissues (accounting for more than 50% of the radioactivity) in the rat study on metabolism in organs and tissues</p> <p>=&gt; was a systemic metabolite in the rat contributing to the toxicity effects of parent</p></li> <li>- <b>DFEAF</b> (major metabolite in rotational Swiss chard matrices in metabolism studies; not confirmed in field studies)</li> <li>=&gt; was detected in the urine of the rat ADME study at low levels (up to 3.5% of administered dose), but also in plasma and all organs/tissues of rat samples collected 6 h after administration</li> <li>=&gt; was a systemic metabolite in the rat</li> </ul>	

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>contributing to the toxicity effects of parent</p> <p>- <b>CHMP</b> (minor metabolite in plant matrices, was subjected to conjugation; BYI 02960-CHMP-di-glyc was a major metabolite in tomato fruits)</p> <p>=&gt; was not detected in the urine of the rat ADME study, however the subsequent metabolites 6-CNA and BYI 02960-hippuric acid</p> <p>=&gt; was most probably a systemic metabolite in the rat</p> <p>=&gt; additional toxicity tests showed that the toxicological profile of BYI 02960-CHMP is less critical compared to the one of the parent and is thus covered by the endpoints derived for the parent</p> <p>- <b>6-CNA</b> (major metabolite in tomato fruits and potato tubers)</p> <p>=&gt; was detected in the urine of the rat ADME (up to 6% of administered dose), together with the subsequent metabolite BYI 02960-hippuric acid, the metabolites accounted for more than 10% of the administered dose</p> <p>=&gt; was a systemic metabolite in the rat contributing to the toxicity effects of parent</p> <p>=&gt; additional test on acute toxicity showed a less critical acute toxicity compared to the parent.</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL (May 2014): For the residue section only parent (and DFA, under discussion) are considered relevant for risk assessment. For metabolites in GW it is considered worst-case to add the residue found in gw and compare them to the parent ADI.	
2(35)	Vol. 3, B.6.9 Studies on metabolites B.6.9.1.1 Acute toxicity Difluoroacetic acid (DFA, BCS-AA56716,M44) Study 1	FR: Could you please harmonise the number of death at 2000 mg/kg between the text and the table 6.9.1.1-1.	<b>APPL (April/2014): updated table:</b>  <b>The table was moved to the end of this section.</b>  NL (May 2014): Will be in the updated in a revised DAR.	Addressed: RMS to consider in a revised DAR or corrigendum.
2(36)	Vol. 3, B.6.9.1.3 Short term studies Difluoroacetic acid (DFA, BCS-AA56716,M44) Study 1	FR: We suggest to set a LOAEL of 500 ppm or 48 mg/kg bw/d for male and 51 mg/kg bw/d for female, based on decreased of glucose concentration in both sexes at 500 ppm, 2000 ppm and 8000 ppm.	<b>APPL (April/2014): DFA induces effectively a significant decrease in glucose which however did not cause any change in the behaviour of the animals nor did it cause any functional impairment. A decrease in glucose was also observed in the 90-day study after administration of BYI 02960 at 2500 ppm and this decrease in glucose was reversible as no significant change was observed at the end of a 28-day recovery period. Also, in the 2-year rat study, a decrease in glucose was observed in both males and females treated at 2000 ppm</b>	See 2(34)

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>after 3 months of administration and in males only after 6 months, but no significant variations were observed thereafter. Based on these observations, the applicant believes that a NOAEL can be set at 500 ppm.</p> <p>NL (May 2014): Significant changes in clinical chemistry is not considered adverse without any other effects (bw, organ weight, pathology or histochemical changes).</p>	
2(37)	Vol. 3, B.6.9.1.3 Short term studies Difluoroacetic acid (DFA, BCS-AA56716,M44) Study 2	FR: We suggest to set a LOAEL of 200 ppm or 12.7 mg/kg bw/d for male and 15.6 mg/kg bw/d for female, based on decreased of glucose concentration in both sexes at 200 ppm, 1000 ppm and 6000 ppm.	<p>APPL (April/2014): DFA induces effectively a significant decrease in glucose which however did not cause any change in the behaviour of the animals nor did it cause any functional impairment. A decrease in glucose was also observed in the 90-day study after administration of BYI 02960 at 2500 ppm and this decrease in glucose was reversible as no significant change was observed at the end of a 28-day recovery period. Also, in the 2-year rat study, a decrease in glucose was observed in both males and females treated at 2000 ppm after 3 months of administration and in males only after 6 months, but no significant variations were observed thereafter. Based on these observations, the applicant believes that a NOAEL can be set at 200</p>	See 2(34)

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>ppm.</p> <p>NL (May 2014): Significant changes in clinical chemistry is not considered adverse without any other effects (bw, organ weight, pathology or histochemical changes).</p>	
2(38)	Vol. 3, B.6.9.2.2 Genotoxicity BYI 02960-difluoroethyl-amino-furanone (BCS-CC98193, BYI 02960-DFAEAF, M34)	<p>FR: In the study 3, the results of solvent controls are not in the range of historical solvent controls.</p> <p>In the study 4, a dose dependent increased is observed in the micronuclei test.</p> <p>Therefore, the result could be considered as equivocal.</p> <p>For these reasons, the genotoxic potential of BYI 02960-DFAEAF need to be discussed.</p>	<p><b>APPL (April/2014): All results of solvent controls from study 3 are well within the historical range of solvent controls: number of mutant colonies per <math>10^6</math> cells.</b></p> <p><b>The table was moved to the end of this section.</b></p> <p><b>In the <i>in vitro</i> Chromosome aberration test, BCS-CC98193 showed effectively a clastogenic potential in the absence of metabolic activation. To better understand the genotoxic potential of this metabolite, two <i>in vivo</i> studies (a micronucleus assay in bone marrow cells of the mouse and <i>in vivo</i> unscheduled DNA synthesis in rat hepatocytes) were performed. As none of these two <i>in vivo</i> studies were positive, it can be stated that on a weight of evidence, BCS-CC98193 has no genotoxic potential.</b></p>	<p>Data requirement:</p> <p>Applicant to provide historical control data for the <i>in vivo</i> micronucleus assay performed with BYI 02960-difluoroethyl-amino-furanone (study 4).</p> <p>See also 2(43)</p>

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL (May 2014): Agreed with the applicant that the results from the solvent controls are well within the HC range (see column 5 in the tables in the DAR).  Regarding study 4, although a dose dependent increase is observed the results are far below the positive control and well within the HC. Furthermore, in the highest dosage the result comes from one isolated increased value.	
2(39)	Vol. 3, B.6.9.2.3 Short term studies Study 1	FR: We suggest to set a LOAEL of 1280 ppm or 135 mg/kg bw/d for male and female, based on decreased of glucose concentration at 1280 ppm, 3200 ppm, 8000 ppm and 20000 ppm.	<b>APPL (April/2014): This study was only designed to choose dose levels for the 28-day rat study.</b>  NL (May 2014): In the 1280 ppm dosage only significant changes in clinical chemistry is observed. At the next dosage of 3200 ppm also bw changes are observed. Significant changes in clinical chemistry is not considered adverse without any other effects (bw, organ weight, pathology or histochemical changes).	Addressed.
2(40)	Vol. 3, B.6.9.2.3 Short term studies Study 2	FR: We suggest to set a NOAEL of 800 ppm or 68 mg/kg bw/d for male and 76 mg/kg bw/d for female, based on decreased of body weight in both sexes at 3000 ppm.	<b>APPL (April/2014): There was a slight but not statistically significant trend towards lower body weights at 3000 ppm in both sexes (5 - 6% below control at termination). There were statistically significantly lower</b>	Open point for EFSA to conclude on the NOAEL of the 28-day rat study with BYI 02960-difluoroethyl-amino-furanone.

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			weight gains in both sexes in the first week of the study, up to approximately - 18% in the 3000 ppm males and - 38% in the females, although without a clear dose response (- 31.82% lower than control mean body weight gain values were noted in the 3000 ppm females) and 33.33% higher than control mean value during the following week. The overall weight gains for the study duration were not statistically different. With no other findings the applicant therefore considers the dose of 3000 ppm as a NOAEL.  NL (May 2014): Agreed with the applicant. A sole non significant decrease in bw <10% is not considered adverse.	
2(41)	Vol. 3.B.6.9.5 Summary of toxicity studies with the metabolites	DK: Table 6.9.5-1 Summary of toxicity studies with the metabolites: 90-day dietary study  Nukui T., Ikeyama S.; 1993 amended in 1997: it should be NOAEL instead of NOEL	APPL (April/2014): agreement for NOAEL instead of NOEL  NL (May 2014): Agreed, will be amended in a revised DAR.	Addressed: RMS to consider in a revised DAR or corrigendum.
2(42)	Vol. 3, B.6.9.6, applicant's position paper 2 on metabolites, p. 234	EFSA: metabolite 6-CNA is presumed to be an intermediate in the rat metabolism of flupyradifurone, this does not allow to conclude that it is covered by the toxicity studies conducted with the parent compound	APPL (04/2014): The metabolism of BYI 02960 in organs and tissues was not examined in the rat after application of [pyridinylmethyl- <sup>14</sup> C]BYI 02960 and no data on the concentration in organs	Addressed.

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		as it is unknown whether its potential intrinsic toxicity would have time to be expressed in the studies.	<p>and tissues of rat is available. However, significant 6-CNA concentrations were detected in the organs/tissues of the laying hen (1.8% of the TRR in fat, 6.4% in liver, 7.2% in eggs and 8.8% in muscle) indicating that the metabolite has a certain retention time in the body of the animals and thus contributes to the overall toxicity of the parent compound.</p> <p>NL (May 2014): The metabolite 6-CNA was not measured in tissue of rat, however the metabolite 6-CNA is found up to 6.3% of the dose in male rats faeces and urine assuming some systemic exposure. It is however, questionable if a maximum of 6.3 % is sufficient to cover it's intrinsic toxicity potential also assuming that 6-CNA will be quickly conjugated with glycine.</p>	
2(43)	Vol. 3, B.6.9.6 Applicant's Position papers on metabolites	FR: Considering the LOAEL of 200 ppm, based on decreased of glucose concentration in both sexes at 200 ppm, 1000 ppm and 6000 ppm, setting in the 28 days study on difluoroacetic acid (DFA); the toxicity of this metabolite is not covered by the overall toxicological profile of the parent compound.	<p><b>APPL (April/2014): BCS believes that the toxicological profile of DFA is covered by the toxicological profile of the parent BYI 02960 as shown in a comparative assessment of the findings: Metabolic changes observed with difluoroacetic acid were also observed with BYI 02960 in a 28-day rat study at 5000 ppm, where a marked decrease in total bilirubin and glucose and a significant increase in urea and total cholesterol</b></p>	See 2(34) and 2(38)

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>It is the same for the metabolite BYI 02960-difluoroethyl-amino-furanone (BYI 02960-DFA) which genotoxic potential should be discussed.</p>	<p>compared to controls were observed at 5000 ppm. The most significant effect detected for DFA is the decrease in glucose which however did not cause any change in the behaviour of the animals nor did it cause any functional impairment. A decrease in glucose was also observed in the 90-day study after administration of BYI 02960 at 2500 ppm and this decrease in glucose was reversible as no significant change was observed at the end of a 28-day recovery period. Also, in the 2-year rat study, a decrease in glucose was observed in both males and females treated at 2000 ppm after 3 months of administration and in males only after 6 months, but no significant variations were observed thereafter.</p> <p>Even if estimating an ADI for DFA based on 90-day rat study and considering that the low dose (200 ppm) is the LOAEL (and not the NOAEL), the estimated value is very close to the parent ADI, confirming that a separate risk assessment for DFA is not warranted.</p> <p>In the scenario where the low dose of 200 ppm is not considered as a NOAEL in the 90-day rat study but as a LOAEL, it is preferable to use the bench mark dose (BMD) approach instead of applying an additional uncertainty factor to the LOAEL,</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>as recommended by EFSA (EFSA Scientific Committee, 2012).</p> <p>The lower confidence limit of bench mark dose (BMDL) has been calculated based on the glucose data from the 90-day rat study. The combined data set used to calculate the BMDL included combined glucose values for males and females at all doses, but dropping the highest dose for males and females since none of the data sets met the criteria of model acceptability. Three models were deemed to be the best fit, with the Hill model giving the lowest BMD/BMDL (2.99 / 2.07 mg/kg bw/day). Using the BMD approach, no extra uncertainty factor (UF) is needed and only the default inter-/intra-species extrapolation UF of 100 has to be applied resulting in an ADI proposal of 0.021 mg DFA/kg bw/day. Using the two other models an ADI of 0.029 mg/kg results. Thus the estimated ADI for DFA ranges between 0.062 and 0.088 mg/kg bw/day when expressed in BYI 02960 equivalents and which is in very good agreement with the initial ADI proposal of 0.078 mg/kg bw/day for BYI 02960.</p> <p>When considering the low dose (200 ppm) as NOAEL (clinical chemistry changes observed at the low dose are considered to be non-adverse in the absence of other</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Other toxicological studies &amp; Medical data (B.6.8-B.6.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>evidence of systemic toxicity), the following ADI would be calculated:</p> <p>NOAEL = 200 ppm (NOAEL = 200 ppm (12.7/15.6 mg/kg/day))</p> <p>Extrapolation from subchronic to chronic duration: UF = 2</p> <p>Default inter-/intra-species extrapolation: UF =100</p> <p>=&gt; ADI = 12.7 /(2 x 100) = 0.064 mg DFA/kg bw/day;</p> <p>corresponding to 0.191 mg BYI 02960 equiv./kg bw/day</p> <p> BYI 02960-difluoroethyl-amino-furanone is not a genotoxic compound as demonstrated in this dossier. Although clastogenic potential was observed in absence of metabolic activation in an <i>in vitro</i> study (chromosome aberration assay), the two other <i>in vitro</i> studies were negative as were the two <i>in vivo</i> studies.</p> <p> NL (May 2014): Significant changes in clinical chemistry is not considered adverse without any other effects (bw, organ weight, pathology or histochemical changes) as also concluded in other DARs.</p>	

## section 2 – Mammalian toxicology (B.6)

<b>Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(44)	Vol.3, B.6.11.1 Toxicokinetics	DK: in the summary of 90-day dietary study by Nukui T., Ikeyama S.; 1993. NOEL should be corrected to NOAEL	APPL (April/2014): agreement for NOAEL instead of NOEL  NL (May 2014): Agreed, will be revised.	Addressed: RMS to consider in a revised DAR or corrigendum.
2(45)	Vol. 3, B.6.11.3 ADI and B.6.11.5, AOEL, pp. 245- 247	EFSA: considering the comments regarding 90-day, 2-year and multigeneration rat NOAELs, these may have an impact on the setting of the ADI and/or AOEL.	NL (May 2014): To be discussed in a meeting.	Expert consultation: MSs to discuss the ADI and AOEL in an expert meeting.  See also 2(16), 2(46), 2(47)
2(46)	Vol. 3, B.6.11.3 ADI	FR: Pending the discuss on the NOAEL in the 2 years rat study, France suggests setting an ADI of 0.032 mg/kg bw/d on the basis of NOAEL of 3.17 mg/kg bw/d, applying a standard assessment factor of 100.	APPL (April/2014): The applicant would still recommend a NOAEL at 400 ppm (15.8 mg/kg/day) for the 2 year rat study.  NL (May 2014): See (45)	See 2(45)
2(47)	Vol. 3, B.6.11.5 AOEL	FR: We suggest to set an AOEL of 0.078 mg/kg bw/d on the basis of NOAEL of 7.8 mg/kg bw/d from the 1 year oral dog study, applying a standard assessment factor of 100.  This AOEL can be supported by the NOAEL of 7.6 mg/kg bw/d from the 90-days oral rat study, the NOAEL of 7.8 mg/kg bw/d from the 2-generation rat study and by the NOAEL of 12 mg/kg bw/d from the 90-days oral dog study.	APPL (April/2014): Based on the relevant toxicological studies, the most sensitive species is the dog with the Lowest Observed Adverse Effect Level (LOAEL) obtained in the 90-day dog study: 33 mg/kg/day or the 1 year dog study: 28.1 mg/kg/day, based on myofiber atrophy seen in skeletal muscle. The second lowest LOEL is obtained in the rat 2 generation study: 39.2 mg/kg/day, based on slight body weight effects. Thus, the most sensitive endpoint is seen in the dog. Therefore it is more appropriate to use the 90-day dog study to set up the AOEL, which provides the highest NOAEL below the LOAEL.	See 2(45)

## section 2 – Mammalian toxicology (B.6)

<b>Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL (May 2014): See (45)	

<b>Dermal absorption (B.6.12)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(48)	Vol. 1, LoEP, dermal absorption	EFSA: please add the value of dermal absorption set for the higher dilution (0.045 g/L) used in exposure risk assessment in the LoEP.	APPL (04/2014): in case the dermal absorption figure for the higher dilution is added to the LoEP it should be also clearly stated that this figure is a mathematical <i>pro-rata</i> extrapolation.  NL (May 2014): Agreed	Open point: RMS to revise the LoEP regarding the dermal absorption for the highest dilution.
2(49)	Vol. 3, B.6.13, Overall conclusion comparative dermal absorption	DE: The approach taken by the RMS and the derived values (0.4% / 3 % / 8%) are supported. However, the use of the pro-rata calculation for a more diluted product (see 6.16) giving 17% seems questionable although mathematically correct. There was no linear increase in dermal absorption (in particular when also the rat data were considered) and there were large inter individual differences in some experiments. Thus, it is suggested to use 17% for this	APPL (04/2014): The value of 17% is overly conservative given the observed trend from the study results. Using mean potentially absorbable values for human skin there is a 2.4-fold increase in dermal absorption for a 6.3-fold decrease in concentration (0.625 g/L to 0.1 g/L). The decrease from 0.1 g/L to 0.045 g/L is only 2.2-fold suggesting that a value of 17% is quite conservative. Furthermore a recent publication (Aggarwal et al. (2014). Regul Toxicol Pharmacol. Jan	Addressed.

## section 2 – Mammalian toxicology (B.6)

<b>Dermal absorption (B.6.12)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		highest dilution (0.045 g/L) for the moment but to require a further <i>in vitro</i> study as "confirmatory data".	31;68(3):412-423) also clearly demonstrated that the increase in dermal absorption with increasing dilution is less than linear. Given that the risk assessment results were acceptable using the conservative 17% value it is not currently clear why an additional study should be required.  NL (May 2014): NL agrees with the applicant that the value of 17% is sufficiently conservative and that no additional study is required.	

<b>Exposure data (B.6.14)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(50)	Vol. 3, B.6.16.3, Resident exposure	DE: We use higher drift values in DE assuming minimum distances of 1 m for applications in field crops and 3 m for applications in high crops, i.e. 2.77 % drift for application on lettuce (or 2.38 % drift for two applications on lettuce) and 19.33 % drift for application in hops. In this case, however, this has no impact on the outcome of the risk assessment.	NL (May 2014): Indeed the resident exposure assessment was not performed with the most worst-case parameters. During review a distance of 10 m for residents was considered sufficient. Since a worst-case assessment does not have effect on the overall conclusion (no risk for residents), NL is of the opinion that the current assessment is acceptable.	Addressed.

## section 2 – Mammalian toxicology (B.6)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
2(51)	Vol. 1, 2.3.1.2, Toxicodynamics, Long- term toxicity; Vol. 3, 6.11., Toxicodynamics; editorial remark	DE: A statement on the carcinogenic potential in mice should be included. As it is now, the information that no neoplastic lesions were observed is confined to the long-term study in rats. The LEP is more clear in this respect.	NL (May 2014): Agreed, will be included in revised DAR	Addressed: RMS to consider in a revised DAR or corrigendum.
2(52)	Vol. 1, 2.3.1.2, Toxicodynamics, Short- term toxicity; Vol. 3, 6.11., Toxicodynamics, Short-term toxicity; editorial remark	DE: With regard to the 28-day study in mice, erroneously a wrong NOAEL was given. At least, the mentioned dose of 33.6 mg/kg bw/d was not tested. The study description in Vol. 3 is not entirely clear but it seems that the most correct NOAEL might be 166 mg/kg bw/d (1200 ppm).  In the 90-day study in mice, the NOAEL was stated to be 80.6 mg/kg bw/d but the dietary intake at the respective dietary concentration was 81 mg/kg bw/d, according to the same paragraph and also to the LEP.  If this paragraph is revised, the “micropathology findings” in the one-year dog study should be specified. (Quite often, only Vol. 1 will be read.)	NL (May 2014): Agreed, will be included in revised DAR	Addressed: RMS to consider in a revised DAR or corrigendum.
2(53)	Vol. 3, B.6.8.1; Vol. 1, 2.3.1.2 and Vol. 3, B.6.11., Toxicodynamics, Further toxicological studies, Biokinetic study, General remark	DE: Apparently, this study was performed to meet the new data requirement of measuring toxicokinetic parameters as part of toxicological studies. The results allow a comparison of plasma concentrations following repeated dietary and single gavage administration in the ADME studies. This	NL (May 2014): Agreed, it should be noted however that data requirements at the time of performing the studies were not clear.	Addressed.

## section 2 – Mammalian toxicology (B.6)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		data is useful but, for the future, it would be more relevant to measure not only plasma levels but also organ/tissue residues following much longer exposure periods.		
2(54)	Vol. 4, C.1.4, toxicological equivalence assessment of the technical specification with the material tested in toxicity studies, p. 42	EFSA: it is agreed that the batches used in toxicity studies appear to cover the (pilot plant scale) technical specification.  The relevance of the individual impurities in comparison with the toxicity profile of the parent has not been addressed.	<p><b>APPL (April/2014): The toxicological equivalence of the technical specification has been already assessed in the EU Annex II dossier under Document J (KIIA 1.11.1/02).</b></p> <p>NL (May 2014): The relevance of the impurities should be determined by the applicant according to SANCO/10597/2003. It should be noted however that genotoxicity of the impurities is addressed under Vol. 4 C1.4.</p> <p><i>Relevant impurities are all impurities of toxicological and/or ecotoxicological or environmental concern compared with the active substance, even if present in technical material at &lt; 1 g/kg. Considering the Regulation, the following definition is proposed for relevant impurities: such substances include, but are not limited to, substances meeting the criteria to be classified as hazardous in accordance with Regulation (EC) No. 1272/2008 [extract from Art. 3(4)] or the available information (e.g.</i></p>	Data requirement:  Applicant to provide historical control data for the in vivo micronucleus assay performed with BYI 02960-difluoroethyl-amino-furanone (study 4).

## section 2 – Mammalian toxicology (B.6)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<i>(Q)SAR, genotoxicity) indicates that the impurity has a toxicological hazard. Relevant impurities have the inherent capacity to cause harmful/unacceptable effects within the meaning of Article 4(2) and (3). Compared to the active substance, relevant impurities show additional (or more severe) toxic properties (in the sense of the above given properties).</i>	

Table from row 2(7):

Table 6.2.3.3 Classification

Type of study	Species	Results	Classification (proposed)
Oral route	Rat	Mortalities observed at 2000 mg/kg; none at 300 mg/kg	Category 4 H302 (300<LD <sub>50</sub> < 2000 mg/kg)
Dermal route	Rat	LD <sub>50</sub> > 2 000 mg/kg	Category 5 / Unclassified
Inhalation	Rat	LC <sub>50</sub> at 4 hours > 4.671 mg/L	Category 5 / Unclassified
Primary skin irritation	Rabbit	Non irritating	Category 5 / Unclassified
Eye irritation	Rabbit	Slight redness of the conjunctivae, reversed within 48 hours	Category 5 / Unclassified
Skin sensitization (LLNA)	Mouse	Not sensitizing	Category 5 / Unclassified

## section 2 – Mammalian toxicology (B.6)

**Table from row 2(18)****Table 6.5.1-1 : Body weight and body weight gain additional data**

Dose (ppm )	0		80		400		2000		dr
	m	f	m	f	m	f	m	f	
BW W10- 6	65 3	421	623 (-5%)	437 (+4%)	655	444 (+5%)	616 (-6%)	364 ds (-13%)	
BWG W1- 106	41 6	256	392 (-6%)	271 (+6%)	420	275 (+1%)	379 (-9%)	198 ds (-23%)	

## section 2 – Mammalian toxicology (B.6)

Parameters	Dose levels in ppm				Historical control data
	0	80	400	2000	
Month 4 Males					
White blood cell counts	14.79±	14.66±	14.58±	15.67±	13.15±2.89 [5.2-24.5]±
Neutrophil counts	2.68±	2.17±	2.14±	2.38±	1.96±0.633 [0.8-7.5]±
Lymphocyte counts	11.30±	11.75±	11.62±	12.51±	10.42±2.31 [3.9-20.1]±
Month 6 Males					
White blood cell counts	12.13±	12.39±	12.91±	14.07±	12.43±2.433 [7.5-23.0]±
Neutrophil counts	1.85±	2.00±	1.94±	2.28±	1.98±0.558 [1.0-4.2]±
Lymphocyte counts	9.36±	9.60±	10.17±	10.93±	9.73±2.108 [5.6-19.4]±
Month 12 Males					
White blood cell counts	10.55±	11.27±	11.73±	12.91**	10.93±2.262 (+22.4%)± [6.5-17.3]±
Neutrophil counts	2.05±	2.18±	2.19±	2.79**	2.18±0.670 (+36.1%)± [4.3-13.4]±
Lymphocyte counts	7.8±	8.44±	8.86±	9.31++	8.07±1.913 (+19.4%)± [4.3-13.4]±
Month 18 Males					
White blood cell counts	8.92±	10.01±	9.03±	11.68**	10.60±2.404 (+30.9%)± [5.8-17.5]±
Neutrophil counts	2.07±	2.16±	1.87±	2.63±	2.67±0.763 [1.2-4.6]±
Lymphocyte counts	6.32±	7.25±	6.70±	8.37**	7.24±1.828 (+32.4%)± [3.9-13.0]±
Month 24 Males					
White blood cell counts	11.10±	11.10†	11.68±	18.06++	11.37±4.643† (+62.7%)± [5.1-29.3]±
Neutrophil counts	3.58±	3.60±	4.11±	8.69++	4.04±2.343† (143%)± [1.4-13.7]±
Lymphocyte counts	6.81±	6.72±	6.80±	8.38±	6.70±2.822† [2.2-19.9]±

Counts expressed in  $10^9/L$ 

\*\*\*: Dunnett LSD Test significant at 0.01 level → \*: Dunnett LSD Test significant at 0.05 level

++: Dunn Rank Sum Test significant at 0.01 level → †: Dunn Rank Sum Test significant at 0.05 level

\*: Dunn Rank Sum Test significant at 0.05 level

## section 2 – Mammalian toxicology (B.6)

Parameters	Dose levels in ppm				Historical control data
	0	80	400	2000	
<b>Month 4 Females</b>					
HGB (g/dL)♂	15.55±	15.77±	15.55±	15.46±	15.68±0.548 <sup>¶</sup> [14.2-17.4]♂
HCT (L/L)♂	0.4518±	0.4555±	0.4493±	0.4518±	0.4572±0.00219 <sup>¶</sup> [0.408-0.545]♂
MCV (fL)♂	52.4±	52.2±	52.2±	51.3* <sup>¶</sup> (-2%)♂	53.3±1.7% [49-58]♂
MCH (pg)♂	18.03±	18.06±	18.11±	17.57++ <sup>¶</sup> (-2.6%)♂	17.94±0.391 <sup>¶</sup> [16.3-19.4]♂
Platelet (10 <sup>9</sup> /L)♂	1192.8±	1190.8±	1182.6±	1390.1* <sup>¶</sup> (+16.5%)♂	1204.6±138.01 <sup>¶</sup> [732-1603]♂
White blood cell count (10 <sup>9</sup> /L)♂	8.12±	8.43±	8.34±	10.64** <sup>¶</sup> (+31%)♂	8.33±2.289 <sup>¶</sup> [3.7-19.8]♂
Lymphocytes (10 <sup>9</sup> /L)♂	6.65±	6.69±	7.19±	8.90** <sup>¶</sup> (+33.8%)♂	8.63±1.963 <sup>¶</sup> [2.6-17.3]♂
<b>Month 6 Females</b>					
HGB (g/dL)♂	15.14±	15.36±	15.33±	14.48** <sup>¶</sup> (-6.3%)♂	15.33±0.653 <sup>¶</sup> [13.8-16.9]♂
HCT (L/L)♂	0.4453±	0.4537±	0.4535±	0.4323+ <sup>¶</sup> (-2.9%)♂	0.4555±0.00201 <sup>¶</sup> [0.408-0.512]♂
MCV (fL)♂	53.4±	53.2±	53.5±	52.3* <sup>¶</sup> (-2.07%)♂	53.3±1.69% [49-59]♂
MCH (pg)♂	18.16±	18.04±	18.08±	17.49** <sup>¶</sup> (-3.7%)♂	17.92±0.376 <sup>¶</sup> [16.6-19.5]♂
Platelet (10 <sup>9</sup> /L)♂	1238.8±	1214.9±	1199.9±	1451.8* <sup>¶</sup> (+17.2%)♂	1209.1±181.33 <sup>¶</sup> [111-1663]♂
White blood cell count (10 <sup>9</sup> /L)♂	6.33±	7.17±	7.02±	8.31** <sup>¶</sup> (+34.44%)♂	7.12±1.835 <sup>¶</sup> [3.4-13.1]♂
Lymphocytes (10 <sup>9</sup> /L)♂	4.84±	5.64±	5.40±	6.85** <sup>¶</sup> (+41.53%)♂	5.57±1.587 <sup>¶</sup> [2.5-11.2]♂
<b>Month 12 Females</b>					
HGB (g/dL)♀	14.59±	14.36±	15.01±	14.04** <sup>¶</sup> (-3.8%)♀	15.72±0.397 <sup>¶</sup> [13.2-17.3]♀
HCT (L/L)♀	0.4296±	0.4380±	0.4389±	0.4144** <sup>¶</sup> (-3.5%)♀	0.4730±0.00189 <sup>¶</sup> [0.418-0.515]♀
MCV (fL)♀	52.7±	52.5±	52.4±	51.1* <sup>¶</sup> (-3.04%)♀	52.0±1.55% [48-55]♀
MCH (pg)♀	17.88±	17.83±	17.93±	17.32++ <sup>¶</sup> (-3.13%)♀	17.26±0.669 <sup>¶</sup> [15.6-19.3]♀
Platelet (10 <sup>9</sup> /L)♀	1101.9±	1127.2±	1171.7±	1306.4** <sup>¶</sup> (+18.6%)♀	1168.2±193.78 <sup>¶</sup> [597-1693]♀
White blood cell count (10 <sup>9</sup> /L)♀	5.77±	6.09±	6.33±	6.44±	10.95±2.262 <sup>¶</sup> [6.5-17.3]♀
Lymphocytes (10 <sup>9</sup> /L)♀	4.08±	4.27±	4.58±	4.64±	8.07±1.913 <sup>¶</sup> [4.3-13.4]♀

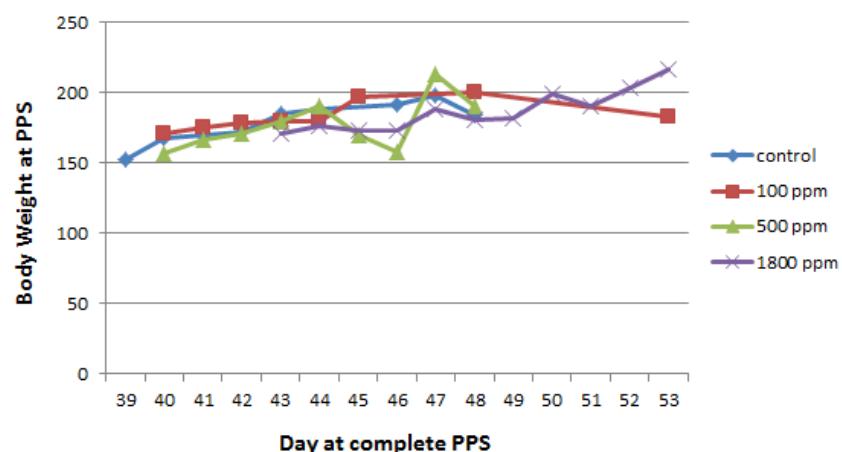
¶

## section 2 – Mammalian toxicology (B.6)

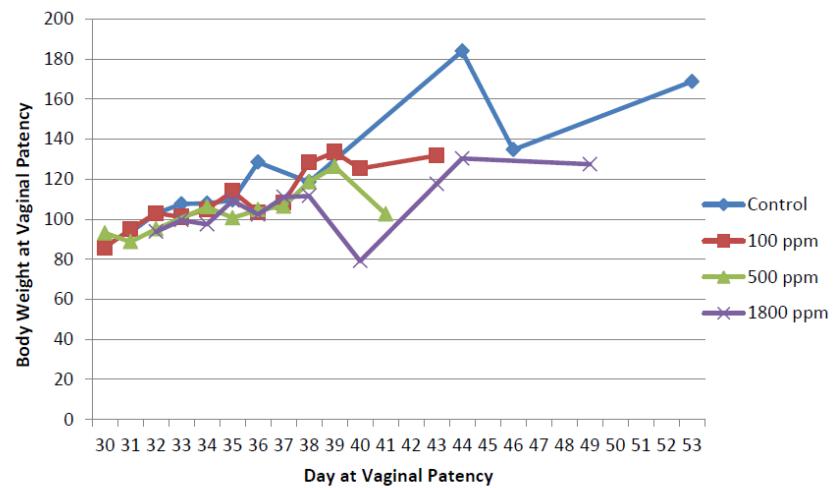
**Table from row 2(22):**

Table 6.5.1-7: Body weight and body weight gain additional data

Dose (ppm )	0		70		300		1500		dr
	m	f	m	f	m	f	m	f	
BW W78	31. 2	28.5	30.9 (- 1%)	28.4	30.7 (- 1%)	27.1 (- 5%)	29.4 (- 6%)	26.6 (- 7%)	
BWG W1- 78	10. 8	11.2	10.4 (- 4%)	11.5 (+3 %)	10.2 d (- 6%)	10.1 d (- 10%)	8.7 ds (- 19%)	9.7 ds (- 13%)	

**Table from row 2(24):**

## section 2 – Mammalian toxicology (B.6)



## section 2 – Mammalian toxicology (B.6)

**Table from row 2(26):**

Observations/study week	P Generation Females - Gestation			
	Control 0 ppm	LDT 200 ppm	MDT 700 ppm	HDT 2000 ppm
Mean body weight (g) - Day 0 S.E.	233.5 4.33	231.3 6.22	225.5 4.69	206.4** 4.47
Mean body weight (g) - Day 6 S.E.	249.4 5.26	251.8 6.06	241.2 4.09	225.0** 3.85
Mean body weight (g) - Day 13 S.E.	274.7 5.15	274.8 7.39	261.4 4.26	241.6** 4.38
Mean body weight (g) - Day 20 S.E.	334.8 6.45	337.8 10.78	315.5 6.10	295.9** 4.42
Mean weight gain (g) - Days 0-20 S.E.	101.4 5.30	106.5 6.14	90.0 3.98	89.5 3.15
Mean food consumption (g/animal/day) Days 0–20	18.6	20.1	17.4	18.6
Mean food consumption (g/kg/day) Days 0–20	73.8	80.1	71.8	83.4

\*\* : Statistically different from control,  $p \leq 0.01$

**Table from row 2(35):****Table 6.8.4.1-1 Mortality:**

Dose mg/kg bw	Mortality	Time of death
1 <sup>st</sup> 300	0/3	--
2 <sup>nd</sup> 2000	2/3	1h
3 <sup>rd</sup> 300	0/3	--

## section 2 – Mammalian toxicology (B.6)

**Table from row 2(38):**

Treatment	HC range	Experiment I		Experiment II	
		Culture 1	Culture 2	Culture 1	Culture 2
-S9/4 hours	4.4 – 42.9	6.4	9.6	-	-
+S9/4 hours	3.3 – 45.3	7.4	18.9	24.2	8.2
-S9/24 hours	2.6 – 40.3	-	-	17.5	30.0

## section 3 – Residues (B.7)

## 3. Residues

<b>Storage Stability (B.7.0)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
3(1)	Vol. 3, B.7.6.4, Storage stability studies	EFSA: As mentioned in the current EU guideline 7032/VI/95, " <i>individual results should not be corrected to 100% yield...</i> ". This recommendation is indeed taken over in the OECD 506 guideline "... <i>results not adjusted by recoveries....</i> ". Therefore, columns "corrected % for recoveries" in tables B.7.6.4-2, B.7.6.4-3, B.7.6.4-4 and B.7.6.4-2 (page 186) should be deleted and the rational concerning the stability of the residues reconsidered, based on uncorrected recovery values.	NL (May 2014): text and tables to be amended in revised DAR. Residues can still be considered to be stable during frozen storage.  <b>APPL (04/2014):</b> New proposal for the text: At day 0, average residue recoveries of BYI 02960 ranged from 91-111% of nominal; of DFEAF ranged from 101-110% of nominal; and of DFA ranged from 79-101% of nominal. In samples analysed after approximately 18 months of frozen storage (556-560 days), the apparent storage stability recoveries ranged from 89-100% for BYI 02960, 87-147% for DFA, and from 85-104% for DFEAF. The concurrent recoveries (= procedural recovery for freshly spiked control samples) after approx. 18 months ranged from 80-102% for BYI 02960, from 79-107% for DFA and from 83-114% for DFEAF. At all sampling dates and in all sample materials, the relevant components of the residue of BYI 02960 were above 70%. Even in the case of the lower values in the given ranges, there was no evidence of any continued degradation of any of the analytes in any of the sample materials.	Open point RMS, to amend the section B.7.6.4 on storage stability in a revised DAR (overall recoveries following storage under frozen conditions not corrected from procedural recoveries).

## section 3 – Residues (B.7)

<b>Storage Stability (B.7.0)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			Thus, all analytes can be considered stable in all relevant plant matrix types for a period of at least 18 months (556 to 560 days).	
<b>Metabolism in plants (B.7.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
3(2)	Vol. 3, B.7.1.1, Plant Metabolism, Study 10	EFSA: The Study 10 on paddy rice is stated as a "seed treatment" in page 49, while described as "a granule application in the planting hole before seedling" in the section "study design".	NL (May 2014): agrees that it should not be considered as a seed treatment, to be amended in revised DAR  <b>APPL (04/2014):</b> The application technique used was a granule application during transplanting of the seedling. Possible residues expected after this kind of soil application should be very similar to residues after seed treatment. Nevertheless, the comment is valid and the application should be named as "granule application".	Open point RMS to mentioned in a revised DAR that study 10 on paddy rice was conducted following soil granule application (instead of seed dressing).
3(3)	Vol. 3, B.7.1.1, Metabolism study in apple	BCS (page 26; Table 7.1.1-8): DFEAF was not detected in the conventional extract of apple fruits; residue values are not correctly assigned to metabolites  Table 7.1.1-8: Distribution of radioactivity in	NL (May 2014): agreed. The results in study report MEF-11/499 appear to give different results. To be amended in revised DAR.	Open point Table 7.1.1-8 should be amended in a revised DAR considering BCS comment in column 2.

## section 3 – Residues (B.7)

<b>Metabolism in plants (B.7.1)</b>																																																	
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																													
		apple fruit and leaves after a single foliar application of [furanone-4- <sup>14</sup> C]flupyradifurone <table border="1"> <thead> <tr> <th></th> <th colspan="2">apple fruits</th> </tr> </thead> <tbody> <tr> <td>TRR [mg a.s. equiv/kg] =</td> <td colspan="2">0.28</td> </tr> <tr> <td>BYI 02960-</td> <td>% TRR</td> <td>mg/kg</td> </tr> <tr> <td colspan="3"><i>Conventional extraction</i></td></tr> <tr> <td>parent compound</td> <td>7.4</td> <td>0.02</td> </tr> <tr> <td>glucose/carbohydrates (M45)</td> <td>50.3</td> <td>1</td> </tr> <tr> <td>---</td> <td>---</td> <td>0.14</td> </tr> <tr> <td>DFEAF (M34)</td> <td>0.3</td> <td>1</td> </tr> <tr> <td>acetic acid-glyc (M16)</td> <td>0.4</td> <td>---</td> </tr> <tr> <td>OH-glyc (M8)</td> <td>0.2</td> <td>0.00</td> </tr> <tr> <td>acetic acid (M15)</td> <td>---</td> <td>1</td> </tr> <tr> <td>difluoroethyl-OH-glyc (M11)</td> <td>---</td> <td>0.00</td> </tr> <tr> <td>OH (M3)</td> <td>---</td> <td>1</td> </tr> <tr> <td>Subtotal identified</td> <td><b>58.7</b></td> <td><b>0.16</b></td> </tr> <tr> <td></td> <td></td> <td>4</td> </tr> </tbody> </table>		apple fruits		TRR [mg a.s. equiv/kg] =	0.28		BYI 02960-	% TRR	mg/kg	<i>Conventional extraction</i>			parent compound	7.4	0.02	glucose/carbohydrates (M45)	50.3	1	---	---	0.14	DFEAF (M34)	0.3	1	acetic acid-glyc (M16)	0.4	---	OH-glyc (M8)	0.2	0.00	acetic acid (M15)	---	1	difluoroethyl-OH-glyc (M11)	---	0.00	OH (M3)	---	1	Subtotal identified	<b>58.7</b>	<b>0.16</b>			4		
	apple fruits																																																
TRR [mg a.s. equiv/kg] =	0.28																																																
BYI 02960-	% TRR	mg/kg																																															
<i>Conventional extraction</i>																																																	
parent compound	7.4	0.02																																															
glucose/carbohydrates (M45)	50.3	1																																															
---	---	0.14																																															
DFEAF (M34)	0.3	1																																															
acetic acid-glyc (M16)	0.4	---																																															
OH-glyc (M8)	0.2	0.00																																															
acetic acid (M15)	---	1																																															
difluoroethyl-OH-glyc (M11)	---	0.00																																															
OH (M3)	---	1																																															
Subtotal identified	<b>58.7</b>	<b>0.16</b>																																															
		4																																															
3(4)	Vol. 3, B.7.1.2, Confined rotational crop study	BCS (page 99; Table 7.1.2-35): Table 7.1.2-35 has to be re-named into Table 7.1.2-15	NL (May 2014): agreed. To be amended in revised DAR.	Open point, Table number in page 99 should be corrected (7.1.2-15 instead of 7.1.2-35)																																													

## section 3 – Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
3(5)	Vol. 3, B.7.2, Animal metabolism	EFSA is of the opinion that the input values in table 7.2-2 for DFA livestock burden calculations have to be reconsidered as not representative of an actual residue situation in rotational crops (see comment (18)).	NL (May 2014): see 3(41). RMS considers that the dietary burden calculation represent a realistic worst case.  <b>APPL (04/2014):</b> <b>Due to the possibility to apply flupyradifurone at early growth stages (e.g. BBCH 12 for lettuce or fruiting crops), the applicant is of the opinion that the worst-case scenario (PBI of 30 days) has to be considered.</b> <b>Please see also remark to comment (18).</b>	See expert consultation 3(40)
3(6)	Vol. 3; B.7.2, Dietary burden of livestock	BCS (page 115 ff; Table 7.2-1 & 7.2-2): It's more conclusive to calculate the dietary burden based on (1) the <u>total BYI 02960 residues</u> (BYI 02960, DFA and DFEAF) detected in the field trials and (2) <u>separate</u> the residues into <u>BYI 02960</u> and <u>DFA</u> residues in the worst-case diet to estimate the different transfer of the two compounds in animal matrices on the basis of the different transfer factors determined in the feeding studies.  Input data to calculate dietary burdens for poultry and ruminants	NL (May 2014): totals were considered, see table 7.2-2. However, exposure to DFEAf was considered not to be relevant for dietary burden calculation because they were at or below LOQ.  Separate values were needed for the calculations of the MRLs in Table 7.12.2-4. RMS will take the input values in column 2 into consideration during revision of the DAR RMS prefers that the dietary burden is calculated based on a 100% contribution to total DM intake.	Open point  RMS: Tables 7.2-1, 7.2-2 and B.7.2-3 should be reconsidered in a revised DAR, taking into account the BCS comment in column 2 and the conclusion of the expert consultations 3(13), 3(29), 3(40) on residue definitions, feeding studies/transfer factors, rotational crops and the comment in open point 3(53).  See also comment in 3(7)

## section 3 – Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>					
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant		Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Commodity	Total residue* [mg/kg] [ apple, pomace wet x 1.34) <i>Primary crops</i> apple, pomace wet x 1.34) <i>Rotational crops</i> grass rape forage silage cereal grain cereal grain, bran cereal straw cereal hay	STMR-p; STMR (fruit) PF = 1.34 HR (barley forage) HR (barley forage) HR (barley forage) STMR (barley grain) STMR-p STMR (barley grain); PF (wheat white flour bran) = 6.4 <sup>1</sup> HR (barley straw) HR (barley straw)	

## section 3 – Residues (B.7)

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		cabbage, kale	0.21	HR (lettuce at commercial harvest)
		root vegetable s, roots	0.14	HR (turnip, roots)
		root vegetable s, tops	0.24	HR (turnip, tops)
		potato, tuber	0.27	HR
		oilseed rape, meal	0.10	STMR of RAC; PF <1
		pulses	1.55	STMR (field pea)
	<p>* total residue (calc.) = sum of parent BYI 0296, DFA and DFEAF</p> <p>† below LOQ</p> <p><sup>1</sup> average EU processing factor of 6.4 for wheat was used as worst-case scenario, NAFTA processing factor accounted for 1.6</p> <p>=&gt; processing factors for <u>total residue</u> can</p>			

## section 3 – Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>																																			
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant			Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																													
		<p>be used when estimating the worst-case diet</p> <p><b>Poultry</b></p> <p>(1) Worst-case diet for poultry</p> <table border="1"> <thead> <tr> <th>Co mmo dity</th><th>DM intake (%)</th><th>Residue intake over DM intake</th><th>Actua l contri butio n to total DM intake (%)</th><th>Actua l contri butio n to total residue intake (mg/kg bw/d)</th></tr> </thead> <tbody> <tr> <td>Whe at bran</td><td>15</td><td>0.001 590</td><td>15</td><td>0.023 844</td></tr> <tr> <td>Peas (dry )</td><td>30</td><td>0.001 138</td><td>30</td><td>0.034 149</td></tr> <tr> <td>Pota toes</td><td>20</td><td>0.001 137</td><td>20</td><td>0.022 737</td></tr> <tr> <td>Cab bag e</td><td>5</td><td>0.000 947</td><td>5</td><td>0.004 737</td></tr> <tr> <td>Rap</td><td>10</td><td>0.000</td><td>10</td><td>0.000</td></tr> </tbody> </table>	Co mmo dity	DM intake (%)	Residue intake over DM intake	Actua l contri butio n to total DM intake (%)	Actua l contri butio n to total residue intake (mg/kg bw/d)	Whe at bran	15	0.001 590	15	0.023 844	Peas (dry )	30	0.001 138	30	0.034 149	Pota toes	20	0.001 137	20	0.022 737	Cab bag e	5	0.000 947	5	0.004 737	Rap	10	0.000	10	0.000			
Co mmo dity	DM intake (%)	Residue intake over DM intake	Actua l contri butio n to total DM intake (%)	Actua l contri butio n to total residue intake (mg/kg bw/d)																															
Whe at bran	15	0.001 590	15	0.023 844																															
Peas (dry )	30	0.001 138	30	0.034 149																															
Pota toes	20	0.001 137	20	0.022 737																															
Cab bag e	5	0.000 947	5	0.004 737																															
Rap	10	0.000	10	0.000																															

## section 3 – Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>											
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant			Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)					
		e see d	073	734	<p><b>Su m</b></p> <p>⇒ Maximum dietary burden: 0.0862013 mg/kg bw/d = 1.364854 mg/kg dry feed</p> <p>⇒ Highest contributor: pea (dry)</p> <p>(2) Calculation of the proportion of the individual components (BYI 02960 and DFA) in the relevant residue in poultry worst-case diet</p> <table border="1"> <thead> <tr> <th>Cr o p</th><th>Residue levels (mg/kg)</th><th>Level s in dry matte r</th><th>D M i n t</th><th>Dietar y burde n</th></tr> </thead> </table>	Cr o p	Residue levels (mg/kg)	Level s in dry matte r	D M i n t	Dietar y burde n	
Cr o p	Residue levels (mg/kg)	Level s in dry matte r	D M i n t	Dietar y burde n							

## **Reporting table, flupyradifurone**

24.06.2014

99/311

---

### section 3 – Residues (B.7)

Metabolism in livestock (B.7.2)											
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant							Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant		
		t o t a l r e s · ·	YI 0 2 9 6 0 · ·	D F A	% i n c r o p	re si d u e ( m g/ kg )	a k e ( % )	m g /k g b w / d	( m g /k g f e d )		
		<b>Poultry</b>									
	W he at br an	2 .2 4	0. 06		8 9	0 .0 6 7	1 5	0 .0 0 1	0 .0 0 1		
	P ea s (d ry )	1 .5 5	<0 .0 1		8 6	0 .0 1 2	5 0	< 0 .0 0 1	0 .0 0 1		
	P ot at oe s	0 .2 7	<0 .0 1		1 5	0 .0 6 7	2 0	0 .0 0 1	0 .0 0 1		
	C ab	0 .·	0. ·		1	0 .·	3	0 .·	0 .·		

## section 3 – Residues (B.7)

Metabolism in livestock (B.7.2)											
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant								Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		ba ge	2 1	08		4	5 7 1	0	0 1 1	1 7 1	
	R ap e se ed	0 .0 1 0	<0 0 1		8 6	0	1 0	< 0 0	0 .0 0	0 .0 1	
	<i>Subtotal</i> BYI 02 960:		0. 17					0 .0 1 2	0 .0 1 9 7		
	W he at br an	2 .2 4		2 .1 1	8 9	2 .3 7 1	1 5	0 .0 2 2	0 .0 3 5 6		
	P ea s (d ry )	1 .5 5		1 .5 5	8 6	1 .8 0 2	5	0 .0 0 0 6	0 .0 0 9 0		
	P ot at	0 .2		0 .2	1 5	1 .6	2 0	0 .0	0 .0 3		

## **Reporting table, flupyradifurone**

24.06.2014

101/311

### section 3 – Residues (B.7)

## section 3 – Residues (B.7)

Metabolism in livestock (B.7.2)							
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant			Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)	
		Co mm o-dity	DM intake (%)	Residue intake over DM intake	Actual contribution to total DM intake (%)	Actual contribution to total residue intake (mg/kg bw/d)	
		Whe at bran	20	0.0009 15	20	0.0183 04	
		Grass (fres h)	100	0.0007 45	80	0.0596 36	
		<b>Su m</b>			<b>100</b>	<b>0.0779 41</b>	<p>⇒ Maximum dietary burden: 0.077941 mg/kg bw/d = 2.143371 mg/kg dry feed</p> <p>⇒ Highest contributor: grass (fresh)</p> <p>(2) Calculation of the proportion of the individual components (BYI 02960 and DFA) in the relevant residue in ruminant worst-case diet</p>

## **Reporting table, flupyradifurone**

24.06.2014

103/311

---

### section 3 – Residues (B.7)

## **Reporting table, flupyradifurone**

24.06.2014

104/311

### section 3 – Residues (B.7)

## section 3 – Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>																																															
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																											
		<p>(comprising BYI 02960 and DFA) to poultry in a ratio relevant to the actual residues expected in feed commodities:</p> <table border="1"> <thead> <tr> <th>Dietary burden (mg/kg feed)</th> <th>Matrix</th> <th>Transfer factor</th> <th>Resulting residue (mg/kg)</th> </tr> </thead> <tbody> <tr> <td align="center" colspan="4"><i>BYI 02960</i></td></tr> <tr> <td align="center" rowspan="5">0.093</td><td>milk</td><td>0.009<sup>1</sup></td><td>0.001</td></tr> <tr> <td>muscle</td><td>0.013<sup>1</sup></td><td>0.001</td></tr> <tr> <td>fat</td><td>0.009<sup>1</sup></td><td>0.001</td></tr> <tr> <td>liver</td><td>0.036<sup>1</sup></td><td>0.003</td></tr> <tr> <td>kidney</td><td>0.037<sup>1</sup></td><td>0.003</td></tr> <tr> <td align="center" colspan="4"><i>DFA</i></td></tr> <tr> <td align="center" rowspan="5">1.954</td><td>milk</td><td>0.030<sup>2</sup></td><td>0.059</td></tr> <tr> <td>muscle</td><td>0.097<sup>2</sup></td><td>0.190</td></tr> <tr> <td>fat</td><td>0.086<sup>2</sup></td><td>0.168</td></tr> <tr> <td>liver</td><td>0.097<sup>2</sup></td><td>0.190</td></tr> <tr> <td>kidney</td><td>0.131<sup>2</sup></td><td>0.256</td></tr> </tbody> </table> <p><sup>1</sup> TF for total residue for enforcement/risk assessment = parent BYI 02960 plus DFA; determined for 1X dose level in cattle feeding study</p>	Dietary burden (mg/kg feed)	Matrix	Transfer factor	Resulting residue (mg/kg)	<i>BYI 02960</i>				0.093	milk	0.009 <sup>1</sup>	0.001	muscle	0.013 <sup>1</sup>	0.001	fat	0.009 <sup>1</sup>	0.001	liver	0.036 <sup>1</sup>	0.003	kidney	0.037 <sup>1</sup>	0.003	<i>DFA</i>				1.954	milk	0.030 <sup>2</sup>	0.059	muscle	0.097 <sup>2</sup>	0.190	fat	0.086 <sup>2</sup>	0.168	liver	0.097 <sup>2</sup>	0.190	kidney	0.131 <sup>2</sup>	0.256	
Dietary burden (mg/kg feed)	Matrix	Transfer factor	Resulting residue (mg/kg)																																												
<i>BYI 02960</i>																																															
0.093	milk	0.009 <sup>1</sup>	0.001																																												
	muscle	0.013 <sup>1</sup>	0.001																																												
	fat	0.009 <sup>1</sup>	0.001																																												
	liver	0.036 <sup>1</sup>	0.003																																												
	kidney	0.037 <sup>1</sup>	0.003																																												
<i>DFA</i>																																															
1.954	milk	0.030 <sup>2</sup>	0.059																																												
	muscle	0.097 <sup>2</sup>	0.190																																												
	fat	0.086 <sup>2</sup>	0.168																																												
	liver	0.097 <sup>2</sup>	0.190																																												
	kidney	0.131 <sup>2</sup>	0.256																																												

## section 3 – Residues (B.7)

Metabolism in livestock (B.7.2)														
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)										
		<sup>2</sup> TF for DFA, only; determined for 49X dose level in cattle feeding study												
3(7)	Vol. 3; B.7.2, Dietary burden of livestock	<p><u>BCS</u> (page 117; Table 7.2-2): Table 7.2-2 has to be re-named into Table 7.2-3 Proposal: Use the worst-case dietary burden calculated above.</p> <p><b>Table 7.2-3</b> Theoretical dietary intake calculations for livestock for total flupyradifurone residues</p> <table border="1"> <thead> <tr> <th></th> <th>Maximum dietary burden mg/kg bw/d (mg/kg dry feed)</th> <th>Median dietary burden mg/kg bw/d (mg/kg dry feed)</th> <th>Highest contributing commodity</th> <th>Dietary burden triggered?</th> </tr> </thead> <tbody> <tr> <td>Total BYI 02960 residue (BYI 02960, DFA and DFEAF)</td> <td>Dairy ruminate 1 (2.143371)</td> <td>0.0779429 (0.971546)</td> <td>Grass (fresh)</td> <td>Y</td> </tr> </tbody> </table>		Maximum dietary burden mg/kg bw/d (mg/kg dry feed)	Median dietary burden mg/kg bw/d (mg/kg dry feed)	Highest contributing commodity	Dietary burden triggered?	Total BYI 02960 residue (BYI 02960, DFA and DFEAF)	Dairy ruminate 1 (2.143371)	0.0779429 (0.971546)	Grass (fresh)	Y	NL (may 2014): <ul style="list-style-type: none"> <li>- agreed</li> <li>- RMS will consider the calculations by BCS during the amendment of the DAR</li> </ul>	See open point 3(6)
	Maximum dietary burden mg/kg bw/d (mg/kg dry feed)	Median dietary burden mg/kg bw/d (mg/kg dry feed)	Highest contributing commodity	Dietary burden triggered?										
Total BYI 02960 residue (BYI 02960, DFA and DFEAF)	Dairy ruminate 1 (2.143371)	0.0779429 (0.971546)	Grass (fresh)	Y										

## section 3 – Residues (B.7)

<b>Metabolism in livestock (B.7.2)</b>						
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant			<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		Meat ruminal na nt	0.09185 9 (2.1433 71)	0.0478 80 (1.1171 98)	Grass (fres h)	Y
		Pig	0.08454 3 (2.1135 87)	0.0499 02 (1.2475 57)	Pea (dry)	Y
		Poultry	0.08620 1 (1.3648 54)	0.0587 28 (0.9298 54)	Pea (dry)	Y

<b>Residue definition (B.7.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
3(8)	Vol. 3, B.7.3 Residue definition in plant matrices for enforcement purposes	DE: The inclusion of DFA into the residue definition for enforcement purposes needs further consideration.  Tetraconazole also contains a DFA	NL (May 2014): Agrees with the reasoning of Bayer Crop Science below. It is considered that the DFA will occur solely from the use of flupyradifurone.	Expert consultation  The plant residue definition for enforcement and risk assessment should be discussed in a meeting of

## section 3 – Residues (B.7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		related moiety. In soil photolysis and soil metabolism studies tetaconazole-DFA was a minor intermediate but tetaconazole-alcohol missing the DFA part was a major residue. Since DFA was not radiolabelled, the amount released was not measured. However, it seems plausible that DFA was released from tetaconazole, making it a non-specific marker for flupyradifurone. In view of the very high levels of DFA in rotational crops resulting from application of flupyradifurone, it should be discussed whether the contribution from tetaconazole is relevant or covered by the current approach. Since MRLs based on rotational crops are proposed for nearly all crops, "false" MRL-exceedances due to tetaconazole seem unlikely, but further explanation is required.	<p><b>APPL (04/2014):</b>  <b>BCS agrees that tetaconazole could theoretically be a source of DFA, however it has not been identified as such in any soil metabolism studies therefore a potential formation is pure speculation. The release of DFA from metabolite tetaconazole-DFA is not very probable, and since the theoretical formation of tetaconazole-alcohol (possible counterpart of DFA) is rather low (max. 4.3%), no significant release of DFA is expected. Thus the contribution from tetaconazole-related DFA would be significantly lower than the contribution from flupyradifurone, if at all.</b></p> <p><b>BCS did a literature search looking for occurrence of DFA as a pesticide metabolite and got no hits. The analysis of the control samples from all the residue trials used confirmed our assumption that no background level of DFA is present at the moment. The DFA levels detected in the presented rotational crop studies are purely flupyradifurone-related.</b></p>	experts, considering the following points: <ul style="list-style-type: none"> <li>- the conclusion of the review on the toxicological property of the DFA metabolite.</li> <li>- the DE comment on DFA to be specific to flupyradifurone only (contribution from tetaconazole unlikely)</li> </ul> See also comments 3(9), 3(11), 3(12)
3(9)	Vol. 3, B.7.3 Residue definition in plant matrices for risk	DE: The reasoning for an inclusion of DFEAF is unclear. The levels found in field trials are insignificant compared to parent	NL (May 2014): in view of the proposed CF of 1 and the very low residue levels of DFEAf found in crops (below or around LOQ of 0.01	See expert consultation 3(8)

## section 3 – Residues (B.7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	assessment purposes	and DFA. In rotational crops residues are also expected to be <0.01 mg/kg. RMS concluded, that a CF of 1 is appropriate, since no residues of DFEAF are found. Why is it included in the RD at all?	mg/kg), it does not seem necessary to include DFEAF in the residue definition for RA. To be amended.  <b>APPL (04/2014):</b> BCS agrees that DFEAF does not have to be included in the residue definition for risk assessment.  The initial reason for the inclusion in the data collection method was to have a marker compound in rotational crops (as indicated by the confined rotational crop studies with radiolabelled flupyradifurone). However, the field rotational crop studies showed high concentrations of DFA as possible marker and no residues of DFEAF above the LOQ. Therefore, there is no longer a reason to keep this marker compound in the residue definition for risk assessment.	
3(10)	Vol. 3, B.7.3 Residue definition in animal matrices for enforcement purposes	DE: Although DFA is also an environmental metabolite for tetraconazole, its levels are unlikely to cause a significant carry-over into farm animals. The proposed RD is supported, irrespective of the discussion for plant matrices.	NL (May 2014): agrees  <b>APPL (04/2014):</b> There is no evidence that DFA is a significant environmental metabolite of tetraconazole hence there is no relevance for farm animals.	Addressed The possible contribution of the active substance tetraconazole to DFA animal intakes is considered negligible when compare to flupyradifurone contribution.
3(11)	Vol. 3, B.7.3.1, Plant residue definition for	EFSA: The residue definition for monitoring is questionable:	NL (May 2014): Not only is DFA present in rotational crops, it also forms an important	See expert consultation 3(8)

## section 3 – Residues (B.7)

<b>Residue definition (B.7.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	monitoring.	<p>- Parent flupyradifurone is a sufficient marker for residues as accounting for at least 20% to 88% of the TRR in primary crops. This point is confirmed by the supervised residue trial data, where flupyradifurone residues are almost detected in all samples analysed for, irrespective of the PHIs.</p> <p>- DFA metabolite is effectively a better marker than the parent in rotational crops, however, the toxicological profile of the DFA metabolite was not discussed and it is therefore not possible to conclude whether DFA toxicity is effectively covered by the toxicological end points set for the parent. It is therefore not possible to conclude whether residues should be expressed as "sum parent + DFA expressed as parent" or if separate residue definitions have to be proposed to consider the different toxicological profiles of these two compounds.</p> <p>Residue definition for monitoring needs to be reconsidered.</p>	<p>part of the residues in primary crops, with levels increasing over time.</p> <p>In Vol 3, B.6.9.1.1, studies on the toxicity of DFA are evaluated and two position papers by the applicant were assessed under B.6.9.6. It can be concluded that the toxicity of DFA is covered by the ADI and ARfD of the parent.</p> <p>RMS maintains that DFA should be included in the residue definition for monitoring</p> <p><b>APPL (04/2014):</b></p> <p>The predominant, if not the only residue detected in rotational crops was DFA (DFA was the only residue detected in the field rotational crop studies on carrot, potato, leek, cucumber, onion, French beans and field peas. No parent compound residues above the LOQ were detected, whereas DFA residues ranged from &lt;0.02-2.3 mg/kg). If only parent residues would be monitored, no marker compound would be available to trace the flupyradifurone related residues, which can account for residues up to 2.3 mg/kg.</p> <p>In order to have a harmonized residue definition for primary and rotational crops, BCS proposes to include DFA in the residue definition for monitoring.</p>	

## section 3 – Residues (B.7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>Apart from the rotational crop situation, also several primary crops show increasing DFA residues with the time. Although parent compound is generally the main compound at the intended PHI, samples collected at later time points show increasing DFA values (until reaching a maximum or a plateau level) whereas BYI 0296 residues decrease. To consider this increase of DFA with time, BCS proposed to include this compound in the residue definition for monitoring.</p> <p>If DFA will not be included in the residue definition for monitoring and a combined risk assessment for flupyradifurone and DFA will be done, a CF has to be established. The estimation of a CF (monitoring =&gt; risk assessment) will be challenging since DFA residues increase with the time whereas BYI 02960 residues decrease with the time. Thus, the CF will be different for different time points (and different for different crops). Which CF should be applied to the monitoring data (the highest CF, the median value)?</p> <p><b>Example:</b> CF for <u>cucumber samples in S-EU</u> (field trials)  CF = (sum of residues of a.s. and DFA) / (residue of a.s.)  CF at day 3: 1.3-5.3 (median = 2.5; n = 8)</p>	

## section 3 – Residues (B.7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>CF at day 5: 3.0-5.5 (median = 3.9; n = 4)  CF at day 7: 3.4-21 (median = 6.5; n= 8)  CF at day 10: 4.1-13 (median = 7.8; n= 4)  CF at day 10: 5.4-45 (median = 8.3; n= 4)</p> <p>BCS submitted a position paper in which the comparison of the toxicological profiles of parent compound and metabolite DFA is evaluated. This position paper is discussed in the Annex II dossier (please refer to KIIA 5.10/03 (Lasserre, D.; 2012) and in the DAR (B.6.9.6).  A tiered argumentation is given which confirms that the DFA toxicity is covered by the toxicological endpoints set for the parent.  (1) Comparison of the toxicological profiles  - similar acute toxicity (GHS category IV), no clinical signs or neurotoxic effects after DFA administration  - both compounds show no genotoxic potential  - 90-day rat study: Metabolic changes observed with difluoroacetic acid were also observed with BYI 02960 in a 28-day rat study at 5000 ppm, where a marked decrease in total bilirubin and glucose and a significant increase in urea and total cholesterol compared to controls were observed at 5000 ppm. The most significant</p>	

## section 3 – Residues (B.7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>effect detected for DFA is the decrease in glucose which however did not cause any change in the behaviour of the animals nor did it cause any functional impairment. A decrease in glucose was also observed in the 90-day study after administration of BYI 02960 at 2500 ppm and this decrease in glucose was reversible as no significant change was observed at the end of a 28-day recovery period. Also, in the 2-year rat study, a decrease in glucose was observed in both males and females treated at 2000 ppm after 3 months of administration and in males only after 6 months, but no significant variations were observed thereafter.</p> <p>=&gt; similar toxicological profiles suggest that end points for parent are also driven by its metabolite DFA</p> <p>(2) Estimation of ADI for DFA based on 90-day rat study if low dose is considered as NOAEL (clinical chemistry changes observed at the low dose are considered to be non-adverse in the absence of other evidence of systemic toxicity)  NOAEL = 200 ppm (NOAEL = 200 ppm (12.7/15.6 mg/kg/day)  Extrapolation from subchronic to chronic duration: UF = 2  Default inter-/intra-species extrapolation: UF =100  =&gt; ADI = 12.7 /(2 x 100) = 0.064 mg DFA/kg</p>	

## section 3 – Residues (B.7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>bw/day; corresponding to <b>0.191 mg BYI 02960 equiv./kg bw/day</b> =&gt; estimated ADI is less critical compared to the ADI derived for the parent flupyradifurone</p> <p>(3) Estimation of ADI for DFA based on 90-day rat study if low dose (200 ppm) is not considered as NOAEL =&gt; EFSA recommends the bench mark dose (BMD) concept =&gt; the lower confidence limit of the bench mark dose (BMDL) has been calculated based on the glucose data from the 90-day rat study =&gt; BMDL values for the models with the best fit range between 2.07 and 2.94 mg/kg bw/day =&gt; ADI ranges between 0.021 and 0.029 mg DFA/kg bw/day; corresponding to <b>0.062 to 0.088 mg BYI 02960 equiv./kg bw/day</b> =&gt; estimated ADI is in the same range as the parent ADI proposed by the notifier (0.078 mg/kg bw/day)</p> <p>Based on a literature review, it seems that there are no significant other sources of DFA. No background levels are detected in soil, water or plant matrices. Thus it can be</p>	

## section 3 – Residues (B.7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			considered that DFA is a metabolite specific to flupyradifurone and a combined risk assessment would be appropriate.	
3(12)	Vol. 3, B.7.3.1, Plant residue definition for risk assessment	EFSA: As mentioned above, the toxicological profile of the DFA metabolite should be addressed to conclude whether a single global residue definition has to be proposed for risk assessment or two separate ones.  The inclusion of the DFEAF metabolite (M34) in the residue definition for risk assessment is questionable as almost not present in the metabolism studies on primary crops (<4%TRR in potato tuber and apple fruit and present in significant level in tomato flower only). Moreover, M34 was never detected in the field rotational crop studies and was almost not detected in the supervised residue trials or at levels close to the LOQ of 0.01 mg/kg (expressed as flupyradifurone equivalent). As previously for DFA, the toxicological profile of the DFEAF metabolite as not been sufficiently addressed.	NL (May 2014): In Vol 3, B.6.9.1.1, studies on the toxicity of DFA are evaluated and two position papers by the applicant were assessed under B.6.9.6. It can be concluded that the toxicity of DFA is covered by the ADI and ARfD of the parent.  RMS maintains that DFA should be included in the residue definition for monitoring  DFEAF: see comment 3(9). To be removed from residue definition for RA.  <b>APPL (04/2014):</b> <b>DFA:</b> Please consider the position paper concerning the comparison of the toxicological profiles of parent compound and metabolite DFA as described in KIIA 5.10/03 (Lasserre, D.; 2012) or DAR B.6.9.6 and the comments to remark (3).  <b>DFEAF:</b> BCS agrees that the residue definition for risk assessment does not need to include	See expert consultation 3(8)

## section 3 – Residues (B.7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>DFEAF. DFEAF appeared to be a suitable marker for estimating residue levels of other metabolites in rotational crops and therefore it was included in the data collection method</p> <p>- however, DFEAF was not detected in virtually all samples and since DFA is always present in high amounts, DFEAF is no longer needed as marker compound for risk assessment.</p> <p>Nevertheless, the toxicological profile of DFEAF was addressed in several studies:</p> <ul style="list-style-type: none"> <li>- <i>in vitro</i> genotoxicity (<i>Salmonella</i> Typhimurium, Reverse mutation assay; <i>in vitro</i> chromosome aberration test with Chinese Hamster V79 cells; gene mutation assay in Chinese Hamster V79 cells <i>in vitro</i> (V79/HPRT); micronucleus assay in the bone marrow cells of the mouse; <i>in vivo</i> unscheduled DNA synthesis in rat hepatocytes</li> <li>- acute oral toxicity</li> <li>- subchronic toxicity (90-day range finding test, 28 day final test)</li> </ul> <p>Based on these studies it can be concluded that metabolite DFEAF is less toxic than the parent flupyradifurone. In addition, the study on the metabolism in organs and tissues of male and female rat after a single oral administration of 3 mg/kg bw [furanone-4-</p>	

## section 3 – Residues (B.7)

<b>Residue definition (B.7.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<sup>14</sup> C]BYI 02960 showed that DFEAF is an important metabolite in the rat, although it accounted for less than 10% of the administered dose in urine. DFEAF was detected in plasma and all organs and tissues (3.7% of the TRR in liver to 7.7% of the TRR in plasma) besides very high concentrations of parent compound. Thus it can be considered that the toxicology of DFEAF is covered by the endpoints determined for the parent.	
3(13)	Vol. 3, B.7.3.2, Animal residue definition for risk assessment.	EFSA: Similar comment as for plants. Toxicological profile of the DFA metabolite should be addressed to conclude whether a single residue definition including pyradifurone and DFA or if two separate residue definitions have to be proposed.	NL (may 2014): see 3(12)  <b>APPL (04/2014):</b> <b>DFA:</b> Please consider the position paper concerning the comparison of the toxicological profiles of parent compound and metabolite DFA as described in KIIA 5.10/03 (Lasserre, D.; 2012) or DAR B.6.9.6 and the comments to remark (3).	Expert consultation Animal residue definitions should be discussed in a meeting of experts, considering the conclusion of the review on the toxicological property of the DFA metabolite.

## section 3 – Residues (B.7)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(14)	Vol. 3, B.7.4, Use pattern	BCS (page 146, Table 7.4-1): Add frames in line 3 of table	NL (May 2014): To be amended in revised DAR.	Open point RMS to amend Table 7.4-1 in a revised DAR according BCS comment in column 2
3(15)	Vol. 3, B.7.5, Critical GAPs	BCS (page 148, Table 7.5-1): Add frames in line 3 of table  Add "home and garden use" as critical GAP  The "home and garden field use" represents the critical <u>field use</u> for lettuce. It was agreed with the RMS to conduct the field residue trials according to this cGAP since this GAP is more critical in respect to possible residues compared to the "agricultural field use". Thus it could be the driver for the MRL. Therefore this field use (2x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; max. 1 use per <b>12 months</b> ) should be added in the table.	NL (May 2014): To be amended in revised DAR.  The "home and garden use" was not considered as critical GAP, since it was not reported in the original submission of the dossier (Document D1 of 06-01-2014, M- 421862-01-1) This comment was only given for residues, but applies to all aspects. Hence, other aspects should also reconsider their evaluation and risk assessments.  It is considered for the MRL.	Open point RMS to amend Table 7.4-1 in a revised DAR according BCS comment in column 2. However, the following clarification is requested.  1 - BCS comment on "home and garden field use" does not result in a change to the cGAP, since the cGAP for lettuce was already defined in Table 7.5-1 as 2x 125 g/ha, interval 10 d, PHI 3 d and maximum 2 uses per 12 months. Is EFSA understanding the correct one?  2 – To avoid any misunderstanding, could the RMS confirm that " <i>max. 2 uses/12 months</i> " means " <i>maximum 2 times 2 applications at 125 g/ha/yea = total 500 g/ha/year</i> " ( <b>and not</b> <i>maximum 2 applications at 125 g/ha/year, total 250 g/ha/year</i> )
3(16)	Vol. 3, B.7.6, Residue trials	BCS (page 164, Table 7.6.2-1): Header is not in line with outdoor results shown	NL (May 2014): since the home and garden use is part of the MRL dossier, the table can be amended to include this worst-case use	Open point RMS to amend Table 7.6.2-1 in a revised DAR according BCS comment

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		=> residue values of "home and garden use" (2 x 0.125 g a.s./ha, interval = 10 days, PHI = 3 days) should be shown instead of values of "agricultural use" (1 x 0.125 g a.s./ha, PHI = 10 days) <b>2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; SEU:</b> Risk assessment: 0.39; 0.43; 0.53; 0.78; 1.2; 1.6; 2.2; 2.7; 3.2 mg/kg Enforcement: 0.38; 0.42; 0.53; 0.76; 1.1; 1.6; 2.2; 2.7; 3.2 mg/kg  <b>2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; NEU:</b> Risk assessment: 0.14; 0.40; 0.47; 0.61; 0.71; 0.87; 1.0; 1.6; 3.0 mg/kg Enforcement: 0.13; 0.39; 0.46; 0.60; 0.70; 0.85; 1.0; 1.5; 3.0 mg/kg	for completeness.	in column 2. See comment in 3(15)
3(17)	Vol. 3, B.7.6, Residue trials	<u>BCS</u> (page 165, Table 7.6.2-2): Add results of trials conducted according to the "home and garden" use pattern <b>2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; SEU:</b> Risk assessment: 0.39; 0.43; 0.53; 0.78; 1.2; 1.6; 2.2; 2.7; 3.2 mg/kg Enforcement: 0.38; 0.42; 0.53; 0.76; 1.1; 1.6; 2.2; 2.7; 3.2 mg/kg	NL (May 2014): since the home and garden use is part of the MRL dossier, the table can be amended to include this worst-case use for completeness.	Open point RMS to amend Table 7.6.2-1 in a revised DAR according BCS comment in column 2.  See comment in 3(15)

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<b>2 x 0.125 kg a.s./ha, interval = 10 days, PHI = 3 days; NEU:</b> Risk assessment: 0.14; 0.40; 0.47; 0.61; 0.71; 0.87; 1.0; 1.6; 3.0 mg/kg Enforcement: 0.13; 0.39; 0.46; 0.60; 0.70; 0.85; 1.0; 1.5; 3.0 mg/kg		
3(18)	Vol. 3, B.7.6 and ER part I, 3.1.1.2, Residue trials	EFSA: All MRL proposals would have to be reconsidered if the peer review concludes on a different residue definition for monitoring (flupyradifurone only or 2 separate residue definitions for flupyradifurone and DFA respectively, having regard to the conclusion on the toxicological profile of these two compounds.	NL (may 2014): noted	Open point MRL proposals are pending the conclusion on the plant residue definitions.  see expert consultation in 3(8).
3(19)	Vol. 3, B.7.6 and ER part I, 3.1.1.2, Residue trials	EFSA: Conversion factor proposals are pending the conclusions on the residue definitions for monitoring and risk assessment.  Nevertheless, the CFs proposed by the RMS needs to be reconsidered, even if the residue definitions proposed by the RMS in the DAR are finally agreed in the course of the peer review. CFs should not be based on the values observed at the intended PHI only. CFs may be time dependent and the ratio parent/metabolites subject to significant changes over time. Therefore, the possible variations in the CF values at the different PHI time points should be considered. CFs have to be proposed considering the values	NL (may 2014): agrees that CFs need to be assessed for different PHIs. Looking at the sheer number of residue trials and various uses in the MRL dossier, this would mean a very large number of CFs.  RMS is of the opinion that the proposed residue definition of parent + DFA for both monitoring and RA is the most preferable solution.  <b>APPL (04/2014):</b> <b>Based on the Annex II dossier and the DAR, the difference between the proposed residue definition for risk assessment and monitoring</b>	Open point CF proposals are pending the conclusion on the plant residue definitions. As stated by EFSA in column 2, the possible variations in the CF values at the different PHI time points should be considered.

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		derived at the different PHIs investigated in the residue trials.	<p>is the determination of the metabolite DFEAF, which was detected at levels &lt;0.01 mg/kg in virtually all samples, independent if determined at the PHI or at later time points. Thus, the proposed CF of 1 could be remained if the residue definition for monitoring will include parent flupyradifurone and metabolite DFA.</p> <p>BCS agrees that it is not necessary to include metabolite DFEAF in the residue definition for risk assessment. A CF would be no longer needed if the residue definition for monitoring and risk assessment will be identical.</p> <p>As a consequence the following considerations need to be discussed:</p> <p>Monitoring method: Flupyradifurone, only</p> <p>Risk assessment: Separate risk assessments for flupyradifurone and DFA would be more appropriate</p> <p>=&gt; Advantages: no CF needed, future additional sources of DFA would be already considered</p> <p>=&gt; Disadvantages: DFA residues (related to the use of flupyradifurone) would not be considered; despite rather high DFA residues, no MRLs would be set for rotational crops</p> <p>or</p> <p>Monitoring method: Flupyradifurone and</p>	

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>DFA</p> <p>Risk assessment: Combined risk assessment for flupyradifurone and DFA would be more appropriate</p> <p>=&gt; Advantages: no CF needed, DFA residues in rotational crops would be covered</p> <p>=&gt; Disadvantages: Future additional sources of DFA could lead to MRL exceedances, if present at high concentrations (not expected)</p> <p>An example showing the variability of the CF is given under comment (3) of (B.7.3) and thus the difficulty to establish an appropriate CF. Therefore the need of CFs should be avoided.</p>	
3(20)	ER, Part I (point 3.1.1.2) and part II (table C.2.1.2), residue trials on grape	<p>EFSA: Only 4 independent trials have been submitted for grape in SEU (see tables from page 106 to 109 in part II). In each of the 4 locations, data refer to 2 replicates/plots (??) where applications have been made on the same variety, with the same application dates and harvest date and therefore, cannot be considered as independent. No MRL can be proposed for SEU and 4 SEU trials should be requested.</p> <p>Note: Last treatment date (26/06/2010) in Campo Arcis trial (SP) is probably wrong and needs to be corrected.</p>	<p>NL (May 2014): agrees. To be reviewed and to be amended in revised ER</p> <p><b>APPL (04/2014):</b></p> <p>Table C.3.1.2.1-4 does not include the correct data for the trials conducted in 2011; please refer to the Annex II dossier KIIA 6.3.1.4, Table 6.3.1.4-5a (Note: Wrong trial parameters were submitted in the tier 1 summary forms!)</p> <p>11-2090-01: France, 47550 Boé (Ugni blanc; white variety)</p>	<p>Open point</p> <p>RMS to reconsider in a revised DAR the MRL proposal for grape, considering EFSA and BCS comments in column 2 and 3. See also expert consultation 3(8) on plant residue definitions and BCS comments 3(80) and 3(81)</p> <p>Data requirement:</p> <p>Applicant to submit the embedded files in column 3, if not already</p>

## section 3 – Residues (B.7)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>11-2090-02: Spain, 46352 Campo Arcis (Bobal; red variety)            11-2090-03: Spain, 08784 La Fortesa – Piera (Xarelo; white variety)            11-2090-04: Italy, 41030 San Prospero (Lambrusco; red variety)            ⇒ all trial parameters have to be changed; residue results are correct and refer to the 2011 trials            11-2090-02 (Campo Arcis): application dates = 08.08.2011 &amp; 22.08.2011            8 valid trials were submitted for grapes in S-EU</p> <p style="text-align: center;">  _SL_200_SEU_Tier I.pdf                 _grape_SL_200_SEU_Tier I.pdf         </p>	included in the dossier.
3(21)	ER, part I, 3.1.1.2 and part II (table C.3.2.1.2-8 to 11), residue trials cucumber and gherkin	EFSA: In part I page 15, it is mentioned that 4 outdoor trials have been conducted on cucumber and 4 on gherkin, while in part II and tables C.3.1.2.1-8 and C.3.1.2.1-11, 3 trials are referenced as conducted on cucumber and 5 on gherkin (trial on cucumber in Toulouse (FR), page 119 on variety Marida is referenced as "Gherkin"). This point should be clarified.	NL (May 2014): in the trial report (10-2184) it is reported that the test system concerns gherkin, whilst the variety is called Marida Gherkin. The other four trials (report 11-2066) were reported to be in a gherkin test system, whilst two varieties were called Raider F1 Cucumber (11-2066-01, FR) and Potomac short cucumber (11-2066-02, ES). Considering the use on snack cucumbers/small cucumber varieties, all trials can be consider for MRL setting for	Open point RMS to clarify in a revised DAR what are the studies conducted on gherkin and on cucumber. BCS comment in column 3 should be considered indeed.

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>cucurbits with edible peel.</p> <p>To be clarified in amended ER</p> <p><b>APPL (04/2014):</b> According to SANCO 7525/VI/95 rev. 9, residue trials in cucumbers can be used to extrapolate to the whole crop group cucurbits – edible peel.</p> <p>To properly represent a typical array of sizes of cucumber, residue trials were conducted in cucumbers, small "snack cucumbers" or gherkins.</p> <p>The variety does not always clearly indicate the size of the crop –there are cucumber varieties (Vers petit de Paris) where the individual weight of the crop ranged between 49 and 101 g whereas the individual weight of a gherkin variety (Cetriolino do parigi) ranged between 75 and 200 g.</p> <p>It would be more appropriate to mention that the trials were conducted using different cucumber varieties (including gherkins) to represent the typical array of sizes possible in cucumbers.</p> <p>10-2184-01: weight of individual crops: 177-258 g 10-2184-02: weight of individual crops: 430-494 g</p>	

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>10-2184-03: weight of individual crops: 190-277 g</p> <p>10-2184-04: weight of individual crops: 49-101 g</p> <p>11-2066-01: weight of individual crops: 524-650 g (=&gt; maximum)</p> <p>11-2066-02: weight of individual crops: not given</p> <p>11-2066-03: weight of individual crops: 11-39 g (=&gt; minimum)</p> <p>11-2066-04: weight of individual crops: 75-200 g</p> <p>The variety (Raider F1) is more a cucumber than a gherkin, however it can also be harvested at a very small size. There is no clear guideline definition of a gherkin or a snack cucumber – nevertheless the supervised residue trials were designed in a manner to represent all possible crop sizes. Therefore all trials results have to be considered when calculating an MRL for cucumbers.</p>	

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(22)	ER, part I, 3.1.1.2 and part II (table C.3.2.1.2-12 to 15), residue trials on melon	EFSA: Three indoor trials (Part II, table C.3.1.2.1-14, page 133-134) were conducted with 2 applications at 250 g/ha, while the other ones at 113 g/ha. Are varieties Haon, Talento and Jucar, climbing varieties requiring dose rates as g/mCH? If not these trials should be disregarded.	NL (May 2014): see applicant's response below. To be clarified in amended ER.  <b>APPL (04/2014):</b> <b>In 2010, 3 trials were conducted in melons in the greenhouse (in the Netherlands, Italy, Spain) to support the use of BYI 02960 SL 200 (Uceda, 2012, KIIA 6.3.1.8/03). Two applications were made at intervals of 10 days at a nominal rate of 0.625 L/(haxm), corresponding to 125 g/(haxm) BYI 02960 a.s.; the water rate was 750 L/(haxm), reflecting local practice in the trial regions. All three varieties (Haon, Talento and Jucar) are climbing varieties. The treated foliage height at all applications was 2 m in all trials. Since BCS decided to support watermelon only, all additional trials were conducted in varieties of watermelon. Watermelon plants are not commonly cultivated into high plants in greenhouses, thus height adjustment was no longer necessary. The intended GAP for watermelons does no longer request a height adaption.</b>	Open point Varieties Haon, Talento and Jucar are climbing varieties. Application rates were therefore calculated taking into account the plant height (2 m), resulting in an application rate of ca 250 g/ha/treatment.  The residue levels observed in the trials conducted on climbing melons are significantly higher than the levels observed in non-climbing varieties (U-Test, 5%). Since watermelons are not climbing varieties, it seems not appropriate to take into account the values observed on climbing melon to derive a MRL for watermelon.
3(23)	ER, part II (table C.3.2.1.2-19), residue trials on Tomato	EFSA: harvest date in trial Gualchos (SP) in table C.3.2.1.2-19 page 68 is probably wrong and needs to be corrected.	NL (May 2014): agreed.  <b>APPL (04/2014):</b> <b>Dates of treatments:</b>	Open point Dates in trial Gualchos (SP) in table C.3.2.1.2-19 page 68 have to be corrected.

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<b>03-06-2011</b> <b>14-06-2011</b>	
3(24)	ER, part II (table C.3.2.1.2-20 to 23), residue trials on apple	EFSA: As the residue levels observed in the 6 SEU trials conducted according to the NEU GAP (2 applications) are not significantly different (U-test, 5%) from the residue levels observed in the NEU trials, they can be merged together to derive an MRL proposal for apple.	<p>NL (May 2014): since U-test shows datasets are comparable, the results will be combined.</p> <p>Considering that the establishment of MRLs in EU might precede the setting of MRLs in Canada/USA with regard to import tolerances, an EU-based MRL needs to be assessed</p> <p><b>APPL (04/2014):</b> When considering the residue results from SEU and NEU (NEU GAP) an MRL proposal of 0.4 mg/kg results (OECD calculator). However, for this crop group, uses are planned outside of the EU which are import-relevant. As a consequence the MRL will be driven by an import tolerance. Question: A sufficient number of residue trials is available for NEU – what would be the reason to include the SEU trials? (larger dataset?)</p>	<p>Open point RMS to reconsider the MRL proposal for apple taking into account the NEU and SEU data sets. MRL proposal should also consider the conclusion of the expert consultation on plant residue definition (see Expert consultation 3(8)).</p> <p>Note to the applicant: Since statistical calculations are more reliable when based on a larger data set, the pooling of the NEU and SEU trials is recommended (if not significantly different).</p>
3(25)	ER part III, US/Canadian Import tolerances	EFSA: Flupyradifurone is not yet registered in the USA and Canada. The setting of import tolerances at EU level is therefore pending the submission of the following	<p>NL (May 2014): noted.</p> <p><b>APPL (04/2014):</b> The aim of submitting import tolerances in</p>	<p>Open point. RMS to reconsider in an Evaluation Report (ER), the Import Tolerance (IT) proposals, once the documentation</p>

## section 3 – Residues (B.7)

<b>Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<p>information:</p> <ul style="list-style-type: none"> <li>- Documentation evidencing that an authorisation has been granted for the active substance by the national authorities in the exporting countries.</li> <li>- Details and documentation on the GAPs that have been effectively registered in the exporting countries.</li> <li>- MRL values that have been effectively published at national level in the exporting countries and references to the national legislation.</li> </ul> <p>Assessment of the import tolerance proposals in ER Part III is pending the submission of the information requested here above. EFSA conclusion will not consider the import tolerance request.</p>	<p>parallel to the EU uses was to minimize the workload for the RMS and EFSA and to avoid trade barriers after authorization of flupyradifurone in major export markets, e.g. the USA. Flupyradifurone was submitted for a global joint review (Canada, USA, Mexico, Australia and Brazil) in October 2012 and the European dossier (including the import tolerance data) was submitted in November 2012. Since Ctgb was assigned as an observer in the GJR process it was assumed that they are always informed about the GJR evaluation. However, this process did not work properly and Ctgb was not involved in the evaluation process. Therefore BCS can understand that the import tolerances can be evaluated only at a later time point. For information purposes: BCS plans to submit a JMPR dossier for flupyradifurone end of 2014. All globally intended uses (based on valid labels only) will be included for evaluation.</p>	<p>evidencing that authorisations have been granted in the exporting countries is provided. IT proposals should be consistent with the MRL values effectively published at national level in the exporting countries, and the residue definitions finally adopted for flupyradifurone.</p> <p>By the time being, evaluation and MRL proposals are limited to the EU GAPs proposed for:</p> <p><b>Representative uses:</b></p> <ul style="list-style-type: none"> <li>- hops,</li> <li>- lettuce,</li> </ul> <p><b>MRL application:</b></p> <ul style="list-style-type: none"> <li>- apple (pear)</li> <li>- grape,</li> <li>- pepper,</li> <li>- cucumber, gherkins (zucchini)</li> <li>- water melon</li> <li>- tomato (egg plant)</li> </ul>

## section 3 – Residues (B.7)

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(26)	Vol. 3, B.7.7, Processing studies	<p>EFSA: As already mentioned for primary crops, the inclusion of the DFEAF metabolite in the residue definition for processed commodities is questionable. In the same way, for monitoring parent flupyradifurone seems to be a sufficient marker for the residues in processed commodities and the inclusion of the DFA metabolite seems superfluous and not in line with the "single marker concept".</p> <p>PFs and CFs would have to be reconsidered taking into account the possible changes in the residue definition proposals made in the course of the peer review.</p>	NL (may 2014): see 3(9) and 3(11).	<p>Expert consultation</p> <p>Member states to discuss the residue definitions for processed commodities, considering the conclusion on the toxicity of the BFA metabolite.</p>
3(27)	ER Part III, B.7.7, C.3.2.2.6 Study 6, Processing study on grape	<p>EFSA: It is not stated whether processing to wine has been conducted on red or white wine. This point should be clarified. Having regard to the flow chart presented in page 861, process seems refer to white wine as fermentation takes place on the grape juice and not on the must as this should be done for red wine.</p> <p>Processing studies on red wine, including eating of the must, are therefore required.</p>	<p>NL (may 2014): processing study evaluation to be reported in more detail to clarify the processing process and the type of wine.</p> <p><b>APPL (04/2014):</b>  <b>Processing to wine was done on red (2 trials) and white grape varieties (2 trials):</b>  <b>10-3406-01: red variety (Blauer Spaetburgunder)</b>  <b>=&gt; must, juice (pasteurized), wine, jelly</b>  <b>10-3406-02: red variety (Blauer Spaetburgunder)</b></p>	<p>Open point</p> <p>RMS to reconsider in a revised DAR, the processing studies on wine, taking into account the clarification given by the applicant in column 3. Red and white wine processes should be assessed separately. Conclusion of the expert consultations 3(8) and 3(26) on residue definitions should be considered indeed.</p>

## section 3 – Residues (B.7)

<b>Processing (B.7.7)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>=&gt; must, wine 10-3406-03: white variety (Riesling) =&gt; must, juice (pasteurized), wine, jelly, raisin 10-3406-04: white variety (Mueller-Thurgau) =&gt; must, wine, raisin</p> <p>No clear differentiation between must and raw juice was done in the dossier and in the ER.</p> <p>The detailed description of the red wine production is summarized in the GLP report 10-3406:</p> <p>The unwashed red grape bunches were crushed in a stalk separator mill, which removed the stalks from the rest of the mash. Subsequently, K<sub>2</sub>S<sub>2</sub>O<sub>5</sub> (SO<sub>2</sub>) was added. Sulphur addition is important to protect the grape must from oxidation and unwanted bacterial growth and to retard the influence of enzymes and it is vital for the preservation of the fresh and fruity taste of the wine. Following crushing, the mash was heated up to 60 °C (2 minutes). During heating, the mash was stirred. Subsequent to the cooling phase (up to approximately 20 hours), the mash was pressed to extract the liquid. A specimen of pomace, grape (without stalks) was taken. After clarification, specimens of must were taken.</p> <p>Subsequently, the must (raw juice) was</p>	

## section 3 – Residues (B.7)

<b>Processing (B.7.7)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<b>pasteurized at 83-87 °C for approximately 2 minutes. A specimen of juice, pasteurized was sampled.</b>	
3(28)	Vol. 3, B.7.7, Processing	BCS (page 190, Table 7.7.2-1): Add frame lines in table	NL (may 2014): to be amended in revised DAR	Open point RMS to amend Table 7.7.2-1 in a revised DAR according to applicant comment in column 2.

<b>Livestock feeding (B.7.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Vol.3 B.7.8 TF for DFA	DE: The practical relevance of the approach to estimate TFs for metabolites is unclear. TFs normally consist of several aspects combined in an overall factor. Besides the systemic distribution the bioavailability is of major importance. Since it is unclear, whether DFA found in animal matrices is formed in the GI tract before being taken up via the lumen or is a metabolite formed in the animal organism after uptake of the parent, the derived factors are guesswork when	NL (may 2014): agrees that where DFA is formed is of minor importance, since the exposure via tissues/milk/eggs is of importance. The approach is new, but since other OECD countries accept only studies performed with parent substance and not with a combined dose and with the idea of test animal reduction, only studies with the parent were performed.  RMs considers the approach chosen the most suitable option.	Expert consultation. Member states to discuss whether the feeding studies conducted with the parent compound flupyradifurone are appropriate to estimate DFA residue levels in animal matrices. The approach to derived MRLs for products of animal origin should be discussed indeed (use of transfer factors, ...). See comment in 3(55)  <b>EFSA Note:</b> RMS comment on

## section 3 – Residues (B.7)

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		applied to DFA in feed crops for the estimation of residue levels in animal commodities. Therefore the use of such an approach is unclear. The same applies to TFs for other metabolites.	<p><b>APPL (04/2014):</b> DFA is a prominent constituent of flupyradifurone related residues in animal feed items. Therefore DFA may be consumed with feed by farm animals and may be absorbed by the intestinal tract into the systemic circulation.</p> <p>In the presented feeding studies flupyradifurone was fed - and not DFA. However in the rat organ metabolism studies with [ethyl-1-<sup>14</sup>C]BYI 02960 it was shown that flupyradifurone is intensively metabolized. In the 24 hours samples of plasma, organs and tissues, DFA was by far the dominating metabolite accounting for more than 50% of the radioactivity. DFA itself is not subjected to further metabolism and is thus terminal.</p> <p>Based on this information, the amount of DFA which is systemically available in the animal (in organs, tissue and urine) can be equated to a minimum dose theoretically fed to the animals. This theoretical dose does not consider the part of the dose which is not bioavailable (faeces). However, it can be assumed</p>	<p>OECD studies limited to the parent active substance is surprising, as it is clearly stated in the OECD guideline 503 on metabolism in livestock that "<i>If a plant metabolite comprises a major portion of the TRR on a feed item, a livestock metabolism study involving dosing with the plant metabolite may be needed</i>". Moreover, in the guideline 505 on residues in livestock it is mentioned "<i>Livestock are dosed with the representative component(s) of the residue as defined in the feed, which is derived from crop metabolism, confined rotational crop and processing studies. The residue definition of a pesticide might consist of parent compound plus one or more metabolites, or a single or several metabolites or degradation products</i>".</p> <p>In addition, it is also mentioned in the current EU guidance on livestock feeding studies 7031/VI/95 rev.4 "<i>The initial active substance is often the relevant part</i></p>

## section 3 – Residues (B.7)

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>that DFA, as a small and polar molecule is well bioavailable (well absorbed by the GI tract) and therefore the dose fed should be almost identical with the portion systemically available. Data from literature for dichloroacetic acid (DCA) confirm this assumption (Lin et al., 1993; Larson and Bull, 1992).</p> <p>For the calculation of the theoretical dose of DFA it is not important to know if DFA was formed from BYI 02960 in the GI tract or in the metabolizing organs liver and kidney. Both portions form together the systemically available part which will lead to DFA residues in the animal matrices. If DFA would be fed, only the absorbed amount would represent the systemically available part since no further metabolism is expected.</p>	<i>of the residue. In other instances, a metabolite or metabolite mix may also be used in the trial."</i>
3(29)	Vol. 3, B.7.8.1, Livestock feeding studies	BCS (page 199, Table 7.8.1-2): Add frame lines in table	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2
3(30)	Vol. 3, B.7.8.1, Livestock feeding studies	BCS (page 204, wrong dose level mentioned) The estimation of the dose of DFA [...] was conducted on the basis of the data collected for the highest dose group ( <b>49N</b> in EU), ...	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2

## section 3 – Residues (B.7)

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(31)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 211, wrong dose level mentioned) Additional 25-day milk was collected [...] from one control cow and three of the <b>49N</b> dose group cows.	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2
3(32)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 216, wrong range of RSD) As the relative standard deviations [...] in the range of 1-13% - all...	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2
3(33)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 216, please correct residue value for kidney in the 3 <sup>rd</sup> paragraph): [...] were as follows: 0.063 mg/kg in muscle, 0.041 mg/kg in fat, 0.165 mg/kg in liver, and <b>0.176 mg/kg in kidney</b> , respectively. In milk taken on day 28, total residues in the 2N group were 0.043 mg/kg.	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2
3(34)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 216, wrong dose level mentioned in 4 <sup>th</sup> paragraph) In addition to the general testing [...] samples from the <b>49N</b> dose group...	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2
3(35)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 219, wrong Table No.) Please change: Table 7.8.1-12 has to be <b>Table 7.8.1-14</b> ; the numbering of all succeeding tables has to be changed as well.	NL (may 2014): to be amended in revised DAR	Open point Table numbering in section B.7.8.1 has to be reconsidered.

## section 3 – Residues (B.7)

<b>Livestock feeding (B.7.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(36)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 219, wrong dose level mentioned in 1st paragraph) [...] at average <i>actual</i> dose rates of 4.8 mg/kg feed (2N dose), 23 mg/kg feed (8N, which approximated a nominal NAFTA 1N dose), 50 mg/kg feed (18N), and 135 mg/kg feed ( <b>49N</b> ).	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2
3(37)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 219, wrong dose level mentioned in 3 <sup>rd</sup> paragraph): Highest residue were determined at day 17 in the <b>49N</b> milk samples,...	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2
3(38)	Vol. 3, B.7.8.1, Livestock feeding studies	<u>BCS</u> (page 223, Table 7.8.1-14 or Table 7.8.1-16 after correction of numbering): Add frame lines in table for 2N dose	NL (may 2014): to be amended in revised DAR	Open point RMS, point to be amended in a revised DAR according to BCS comment in column 2

<b>Succeeding/Rotational crops (B.7.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(39)	Vol.3 B.7.9 Calculation of residues in rotational crops	DE: The basis of 2 x 0.125 kg as/ha for the estimation of residues in rotational crops is from a GAP on protected lettuce. Field lettuce is treated only once with 0.125 kg as/ha while hops is considered a permanent crop. It seems unlikely that many of the	NL (may 2014): since in the ER for setting of MRLs for flupyradifurone a number of other, more critical, GAPs are evaluated, the estimation based on a more critical GAP is warranted.	Expert consultation Member states to discussed if the rotational crop studies conducted with a dose rate of 2x 125 g/ha and a PBI of 30 days, are appropriate to estimate the residue levels expected in food

## section 3 – Residues (B.7)

Succeeding/Rotational crops (B.7.9)																																		
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																														
		crops listed for MRLs are relevant for crop rotation under protected conditions. Further consideration is needed whether the GAP for protected lettuce is relevant for any rotational crops grown indoors. If it is not, the estimation of STMRs/HRs/MRLs for rotational crops, the livestock animal dietary burden and the consumer risk assessment need to be reconsidered and should rely on the relevant field GAP.	<p>APPL (04/2014): The GAP chosen for the rotational crop investigations is the more critical field GAP for the "home &amp; garden use" and not the greenhouse GAP for the agricultural use. The "home &amp; garden uses" are intended to be registered at the same time or shortly after the agricultural uses. It was agreed to consider these "home &amp; garden uses" in the Annex II dossier, in order to avoid re-calculation of all MRLs as soon as these uses are registered.</p> <p>As an example, the following table summarizes all intended uses for lettuce:</p> <table border="1"> <thead> <tr> <th>Description</th> <th>F/G</th> <th>N.o. of applic.</th> <th>Application rate per treatment (g a.s./ha)</th> <th>per season (g a.s./ha)</th> <th>Intervala (days)</th> <th>PHI (days)</th> </tr> </thead> <tbody> <tr> <td>Agricultural use*</td> <td>F<sup>†</sup></td> <td>1</td> <td>125</td> <td>125</td> <td>--</td> <td>10</td> </tr> <tr> <td></td> <td>G</td> <td>2</td> <td>125</td> <td>250</td> <td>10</td> <td>3</td> </tr> <tr> <td>home &amp; garden **</td> <td>F<sup>†</sup></td> <td>2</td> <td>125</td> <td>250</td> <td>10</td> <td>3</td> </tr> </tbody> </table>	Description	F/G	N.o. of applic.	Application rate per treatment (g a.s./ha)	per season (g a.s./ha)	Intervala (days)	PHI (days)	Agricultural use*	F <sup>†</sup>	1	125	125	--	10		G	2	125	250	10	3	home & garden **	F <sup>†</sup>	2	125	250	10	3	commodities and in the feed commodities used for the animal burden calculations.	See also comment 3(5), 3(41) and 3(47)	
Description	F/G	N.o. of applic.	Application rate per treatment (g a.s./ha)	per season (g a.s./ha)	Intervala (days)	PHI (days)																												
Agricultural use*	F <sup>†</sup>	1	125	125	--	10																												
	G	2	125	250	10	3																												
home & garden **	F <sup>†</sup>	2	125	250	10	3																												

## section 3 – Residues (B.7)

<b>Succeeding/Rotational crops (B.7.9)</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>* agricultural use based on an SL 200 formulation</p> <p>** "home &amp; garden" uses with an SL 50 formulation (available to the general public via retail sale)</p> <p>† uses in both the northern and southern residue regions (EU-N and EU-S)</p>	
3(40)	Vol. 3, B.7.9, Field rotational crop studies	<p>EFSA: It is questionable whether the studies (referenced Study 2 to Study 7, table 7.9-4) are fully representative of the residue levels expected in rotational crops.</p> <p>All studies have been conducted with an application on bare soil with a PBI of ca. 30 days, representative or a <b>crop failure</b>. In practice and having regard to the use of flupyradifurone against aphids, the application will take place on a crop well established and therefore not subject to a crop failure in the vast majority of the cases. These studies are therefore a very worst case that do not reflect the actual residue situation in rotational crops.</p> <p>EFSA is therefore of the opinion that the use of the DFA residues levels observed in the studies 2 to 7 are not representative of the residues levels expected in practice in rotational crops, leading to an overestimation of the animal burdens as proposed in tables 7.2-2 and 7.12.2-4 and <b>therefore leading to</b></p>	<p>NL (may 2014): there is no guidance on how MRLs should be set for residues in rotational crops.</p> <p>Flupyradifurone can be applied from early growth stages to late growth stages (e.g. BBCH 12 up to BBCH 87). It is therefore possible in practice that the primary crop is treated before crop failure occurs. Hence, a succeeding crop can be planted and be exposed to residues in the soil. RMS considers that the studies represent a realistic worst case</p> <p><b>APPL (04/2014):</b> Flupyradifurone can be applied at very early growth stages, e.g. in lettuce and all fruiting crops from <b>BBCH 12</b> onwards (please refer to the GAP table). Thus crop failure (e.g. by hail, damage by geese, slugs...) and replanting of new crops 30 days after the</p>	See expert consultation 3(40)

## section 3 – Residues (B.7)

<b>Succeeding/Rotational crops (B.7.9)</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<b>the setting of MRLs for animal products higher than necessary.</b>	<p>application of the failed crop is a realistic scenario which was considered in studies 2 to 7.</p> <p>Since no clear guidance is available for the "small rotational crop studies" with only one PBI, the study design and the crops to be replanted were discussed and agreed on with the RMS and also with another Member State based on a lecture presented by a representative of an European authority at the 8<sup>th</sup> International Fresenius Conference (February 2010).</p>	
3(41)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 245, plant-back interval for potato): Specify range of plant-back interval in 1 <sup>st</sup> paragraph: Potatoes were planted <b>25-33 DAT</b> and harvested 98-137 DAT.	NL (may 2014): to be amended in revised DAR	Open point RMS: section B.7.9.1, to be amended in a revised DAR according applicant comment in column 2.
3(42)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 246, harvest interval for leek): Please correct harvest interval: Leek was planted 26-33 DAT and harvested <b>97-130 DAT</b> (BBCH 49)	NL (may 2014): to be amended in revised DAR	Open point RMS: section B.7.9.1, to be amended in a revised DAR according applicant comment in column 2.
3(43)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 247, plant-back interval for cucumber and growth stage at harvest): Please correct: Cucumbers were planted <b>25-30 DAT</b> and harvested 69-83 DAT (BBCH 71-79)	NL (may 2014): to be amended in revised DAR	Open point RMS: section B.7.9.1, to be amended in a revised DAR according applicant comment in column 2.
3(44)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 248, plant-back interval for onion):	NL (may 2014): to be amended in revised DAR	Open point RMS: section B.7.9.1, to be amended

## section 3 – Residues (B.7)

<b>Succeeding/Rotational crops (B.7.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Please correct: Onion was [...] sown directly on the plot (northern trials) <b>25-33 DAT...</b>		in a revised DAR according applicant comment in column 2.
3(45)	Vol. 3, B.7.9.1, Field rotational crops	<u>BCS</u> (page 256-261, trial numbers, plant- back interval and interval between treatment and harvest): Please correct the following trial numbers and the plant-back intervals 11-2250 => <b>11-2550</b> (PBI = 31; 33; <b>25</b> ; 30 days) 11-2251 => <b>11-2551</b> 11-2252 => <b>11-2552</b> 11-2253 => <b>11-2553</b> (PBI = 30; 33; 25; <b>28 d</b> ) 11-2255 => <b>11-2555</b>	NL (may 2014): to be amended in revised DAR	Open point RMS: section B.7.9.1, to be amended in a revised DAR according applicant comment in column 2.

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(46)	Vol.3 B.7.10	DE: MRLs for rotational crops need to be reconsidered – see comment under section Vol.3 B.7.9.	NL (May 2014): see 3(40). Since there are numerous other GAPs applied for in the parallel MRL evaluation report, the more critical GAP used in the rotation crop field trials is warranted.  <b>APPL (04/2014): see remark under section Vol.3 B.7.9.</b>	Open point LMRs for rotational crops are pending the conclusion of the expert meeting requested under 3(40) and related to the dose rate and PBI considered in the DAR.

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(47)	Vol. 3, B.7.12, MRL proposals	EFSA: EU MRL proposals are pending the final conclusions on the plant and animal residue definitions for monitoring.	NL (May 2014): see 3(11)	Open point EU MRL proposals are pending the conclusions of the expert meeting on plant residue definitions requested under comment 3(8)
3(48)	Vol. 3, B.7.13, MRL proposals	EFSA: Import tolerance proposals would have to be reconsidered once the information requested under comment (13) is submitted.	NL (May 2014): see 3(25)	See open point 3(25)
3(49)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	<p>BCS (page 266, proposed import tolerances): dry bean and dry pea seeds should be summarized as “pulses”.</p> <p>Proposed IT (pulses): <b>10 mg/kg</b> =&gt; estimated based on EU rotational data and AUS seasonal rate of 450 g a.s./ha and applying a soil accumulation factor</p> <p>Residue data from EU limited rotational crop study with field peas (<math>2 \times 0.125 \text{ g a.s./ha} = 250 \text{ g a.s./ha}</math>): 2.3; 1.0; 0.67; 2.1 mg/kg =&gt; extrapolation to AUS rate (<math>3 \times 150 \text{ g a.s./ha} = 450 \text{ g a.s./ha}</math>) =&gt; multiplication with factor 1.8: 4.14; 1.8; 1.21; 3.78 mg/kg =&gt; considering a soil accumulation factor of 1.2 (probably requested by AUS): 4.97; 2.16; 1.45; 4.54 mg/kg =&gt; MRL proposal according OECD: 10</p>	NL (May 2014): to be considered in ER/DAR. It will only result in a proposal. Eventually, the established import tolerance in AUS, USA, CAN etc will drive the MRL	<p>Open point to be considered in a revised ER, once the information requested under 3(28) provided.</p> <p>Moreover, conclusion of the expert consultation on residue definition and rotational crop studies should also be considered (see Expert consultations 3(8) and 3(40)).</p>

## section 3 – Residues (B.7)

<b>MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		mg/kg		
3(50)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	<u>BCS</u> (page 266, proposed import tolerances): field corn grain => in accordance with sweet corn an EC MRL of 1.5 mg/kg should be proposed (based on rotational data for cereals)	NL (May 2014): agreed, discrepancy between DAR and ER	Open point To be considered in a revised DAR/ER, once the information requested under 3(28) provided.  Moreover, conclusion of the expert consultations on residue definition and rotational crop studies should also be considered (see Expert consultations 3(8) and 3(40))
3(51)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	<u>BCS</u> (page 266, proposed import tolerances): legume vegetables => no import tolerance is needed for legume vegetables since there is no significant trade => EC MRL of 2 should apply	NL (May 2014): agreed, discrepancy between DAR and ER. MRL of 10 for legume vegetables should have been assigned to pulses (see 3(50))	Open point To be considered in a revised ER, once the information requested under 3(28) provided.  Moreover, conclusion of the expert consultations on residue definition and rotational crop studies should also be considered (see Expert consultations 3(8) and 3(40))
3(52)	Vol. 3, B.7.12, proposed MRLs (animal matrices)	<u>BCS</u> (page 267, dietary burden according to notifier): The text refers to the dietary burden calculated by BCS in the Annex II dossier. This calculation considers also future uses. Either include this dietary burden calculation or refer to the dietary burden calculated in B.7.2.	NL (May 2014): see 3(6). RMS to consider the (revised) calculations by BCS during amendment of the DAR	Open point RMS to reconsider in a revised DAR the animal dietary burden based on the representative uses, the EU uses related to the MRL application and the residues expected in rotational crops. Conclusion of the expert meeting on rotational crops should be considered

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																																
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant					Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>			Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																						
		<p>Proposal: Use dietary burden calculation and the estimated ratio of BYI 02960 and DFA in the worst-case diet as proposed in this commenting table.</p> <p><b>Poultry:</b> Calculation of the proportion of the individual components (BYI 02960 and DFA) in the relevant residue in poultry worst-case diet</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th rowspan="2">Crop</th> <th colspan="3">Residue levels (mg/kg)</th> <th colspan="2">Levels in dry matter</th> <th rowspan="2">Dietary intake (%)</th> <th colspan="2">Dietary burden</th> </tr> <tr> <th>t o t a l</th> <th>B Y I</th> <th>D F A</th> <th>% i n c r o p</th> <th>re s i d u e ( m g / k g )</th> <th>m g / k g b w / d</th> <th>( m g / k g f e e d )</th> </tr> </thead> <tbody> <tr> <td>*</td> <td>0 2 9 6 0</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td></td> <td colspan="8"><b>Poultry</b></td></tr> <tr> <td></td> <td>W he</td> <td>2 .</td> <td>0 0 6</td> <td>8 9</td> <td>0 .</td> <td>1 5</td> <td>0 .</td> <td>0 .</td> <td></td> </tr> </tbody> </table>	Crop	Residue levels (mg/kg)			Levels in dry matter		Dietary intake (%)	Dietary burden		t o t a l	B Y I	D F A	% i n c r o p	re s i d u e ( m g / k g )	m g / k g b w / d	( m g / k g f e e d )	*	0 2 9 6 0								<b>Poultry</b>									W he	2 .	0 0 6	8 9	0 .	1 5	0 .	0 .		<p>(See expert consultation in 3(40)). See also comments in 3(6)</p> <p>Possible contribution of the residues resulting from the setting of import tolerances on food/feed commodities would have to be considered in a revised ER, once the information requested under 3(28) provided.</p>		
Crop	Residue levels (mg/kg)			Levels in dry matter		Dietary intake (%)	Dietary burden																																									
	t o t a l	B Y I	D F A	% i n c r o p	re s i d u e ( m g / k g )		m g / k g b w / d	( m g / k g f e e d )																																								
*	0 2 9 6 0																																															
	<b>Poultry</b>																																															
	W he	2 .	0 0 6	8 9	0 .	1 5	0 .	0 .																																								

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)										
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant							Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		at br an	2 4			0 6		0 0 1 0		
		P ea s (d ry )	1 .5 5	<0 .0 1	8 6 0	5	< 0 .0 0 0 1	0 .0 0 0 1		
		P ot at oe s	0 .2 7	<0 .0 1	1 5 0 6 7	2 0	0 .0 0 0 1	0 .0 0 0 1		
		C ab ba ge	0 .2 1	0. 08	1 4 0 5 7 1	3 0	0 .0 0 1 1	0 .0 0 1 1		
		R ap e se ed	0 .1 0	<0 .0 1	8 6 0 .0 1 2	1 0	< 0 .0 0 0 1	0 .0 0 0 1		
	Subtotal BYI 02 960:		0. 17					0 .0 1	0 .1 9	

## **Reporting table, flupyradifurone**

24.06.2014

144/311

### section 3 – Residues (B.7)

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																																																																										
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant						Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																																																																	
		<table border="1"> <tr> <td><i>Subtotal</i></td> <td></td> <td>4</td> <td></td> <td></td> <td></td> <td>0</td> <td>1</td> </tr> <tr> <td><i>al DFA:</i></td> <td></td> <td>.</td> <td></td> <td></td> <td></td> <td>0</td> <td>.</td> </tr> <tr> <td></td> <td></td> <td>1</td> <td></td> <td></td> <td></td> <td>0</td> <td>0</td> </tr> <tr> <td></td> <td></td> <td>1</td> <td></td> <td></td> <td></td> <td>6</td> <td>4</td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>6</td> <td>6</td> </tr> </table> <table border="1"> <tr> <td><i>Totals:</i></td> <td></td> <td></td> <td></td> <td></td> <td>8</td> <td>0</td> <td>1</td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td>0</td> <td>0</td> <td>2</td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td>7</td> <td>7</td> <td>4</td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td>8</td> <td>2</td> <td>2</td> </tr> </table> <p>Estimation of theoretical residues resulting from feeding grown BYI 02960 residues (comprising BYI 02960 and DFA) to poultry in a ratio relevant to the actual residues expected in feed commodities =&gt; corresponds to <b>Table 7.12.1-3 (chicken):</b></p> <table border="1"> <thead> <tr> <th>Dietary burden (mg/kg feed)</th> <th>Matrix</th> <th>Transfer factor*</th> <th>Resulting residue (mg/kg)</th> </tr> </thead> <tbody> <tr> <td>B Y I 0 2960</td> <td></td> <td></td> <td></td> </tr> <tr> <td rowspan="2">0.197</td> <td>egg</td> <td>0.038<sup>#</sup></td> <td>0.007</td> </tr> <tr> <td>muscle</td> <td>0.062<sup>#</sup></td> <td>0.012</td> </tr> </tbody> </table>	<i>Subtotal</i>		4				0	1	<i>al DFA:</i>		.				0	.			1				0	0			1				6	4							6	6	<i>Totals:</i>					8	0	1						0	0	2						7	7	4						8	2	2	Dietary burden (mg/kg feed)	Matrix	Transfer factor*	Resulting residue (mg/kg)	B Y I 0 2960				0.197	egg	0.038 <sup>#</sup>	0.007	muscle	0.062 <sup>#</sup>	0.012	
<i>Subtotal</i>		4				0	1																																																																																			
<i>al DFA:</i>		.				0	.																																																																																			
		1				0	0																																																																																			
		1				6	4																																																																																			
						6	6																																																																																			
<i>Totals:</i>					8	0	1																																																																																			
					0	0	2																																																																																			
					7	7	4																																																																																			
					8	2	2																																																																																			
Dietary burden (mg/kg feed)	Matrix	Transfer factor*	Resulting residue (mg/kg)																																																																																							
B Y I 0 2960																																																																																										
0.197	egg	0.038 <sup>#</sup>	0.007																																																																																							
	muscle	0.062 <sup>#</sup>	0.012																																																																																							

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																							
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																			
		<table border="1"> <tr> <td></td><td>fat</td><td>0.026<sup>#</sup></td><td>0.005</td></tr> <tr> <td></td><td>offal</td><td>0.076<sup>#</sup></td><td>0.015</td></tr> <tr> <td></td><td><i>DFA</i></td><td></td><td></td></tr> <tr> <td>1.046</td><td>egg</td><td>0.097</td><td>0.101</td></tr> <tr> <td></td><td>muscle</td><td>0.172</td><td>0.180</td></tr> <tr> <td></td><td>fat</td><td>0.060</td><td>0.063</td></tr> <tr> <td></td><td>offal</td><td>0.216</td><td>0.226</td></tr> </table> <p>* Transfer factor determined for 1x dose level in poultry feeding study  # TF for total residue for enforcement/risk assessment = parent BYI 02960 plus DFA</p> <p>Levels of the relevant residue of BYI 02960 (comprising BYI 02960 and DFA) in poultry tissues and eggs expected after feeding a worst-case diet containing residues due to treatment of crops with BYI 02960  =&gt; corresponds to <b>Table 7.12.1-4 (chicken):</b></p> <table border="1"> <thead> <tr> <th>Dietary burden (mg/kg feed)</th><th>Matrix</th><th>Resulting residue (sum of a.s. &amp; DFA) [mg a.s. equiv./kg]</th><th>MRL proposal EU / global [mg/kg]</th></tr> </thead> <tbody> <tr> <td colspan="4"><i>Total residue (BYI 02960 plus</i></td></tr> </tbody> </table>		fat	0.026 <sup>#</sup>	0.005		offal	0.076 <sup>#</sup>	0.015		<i>DFA</i>			1.046	egg	0.097	0.101		muscle	0.172	0.180		fat	0.060	0.063		offal	0.216	0.226	Dietary burden (mg/kg feed)	Matrix	Resulting residue (sum of a.s. & DFA) [mg a.s. equiv./kg]	MRL proposal EU / global [mg/kg]	<i>Total residue (BYI 02960 plus</i>				
	fat	0.026 <sup>#</sup>	0.005																																				
	offal	0.076 <sup>#</sup>	0.015																																				
	<i>DFA</i>																																						
1.046	egg	0.097	0.101																																				
	muscle	0.172	0.180																																				
	fat	0.060	0.063																																				
	offal	0.216	0.226																																				
Dietary burden (mg/kg feed)	Matrix	Resulting residue (sum of a.s. & DFA) [mg a.s. equiv./kg]	MRL proposal EU / global [mg/kg]																																				
<i>Total residue (BYI 02960 plus</i>																																							

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant		Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)															
		<b>DFA)</b> <table border="1"> <tr> <td>1.242 (<b>0.197</b> + <b>1.046</b>)</td><td>egg</td><td>0.109</td><td>0.15 / <b>0.50</b></td></tr> <tr> <td></td><td>mus cle</td><td>0.192</td><td>0.20 / <b>0.80</b></td></tr> <tr> <td></td><td>fat</td><td>0.068</td><td>0.07 / <b>0.30</b></td></tr> <tr> <td></td><td>offal</td><td>0.241</td><td>0.30 / <b>1.00</b></td></tr> </table>		1.242 ( <b>0.197</b> + <b>1.046</b> )	egg	0.109	0.15 / <b>0.50</b>		mus cle	0.192	0.20 / <b>0.80</b>		fat	0.068	0.07 / <b>0.30</b>		offal	0.241	0.30 / <b>1.00</b>	
1.242 ( <b>0.197</b> + <b>1.046</b> )	egg	0.109	0.15 / <b>0.50</b>																	
	mus cle	0.192	0.20 / <b>0.80</b>																	
	fat	0.068	0.07 / <b>0.30</b>																	
	offal	0.241	0.30 / <b>1.00</b>																	
		<b>Ruminants</b> (1) Worst-case diet for dairy ruminants		<table border="1"> <thead> <tr> <th>Co mm o- dity</th><th>DM inta ke (%)</th><th>Resid ue intake over DM intake</th><th>Actual contri butio n to total DM intake (%)</th><th>Actual contri butio n to total residu e inta ke (mg/k g bw/d)</th></tr> </thead> <tbody> <tr> <td>Whe at bran</td><td>20</td><td>0.0009 15</td><td>20</td><td>0.0183 04</td></tr> <tr> <td>Gras s</td><td>100</td><td>0.0007 45</td><td>80</td><td>0.0596 36</td></tr> </tbody> </table>	Co mm o- dity	DM inta ke (%)	Resid ue intake over DM intake	Actual contri butio n to total DM intake (%)	Actual contri butio n to total residu e inta ke (mg/k g bw/d)	Whe at bran	20	0.0009 15	20	0.0183 04	Gras s	100	0.0007 45	80	0.0596 36	
Co mm o- dity	DM inta ke (%)	Resid ue intake over DM intake	Actual contri butio n to total DM intake (%)	Actual contri butio n to total residu e inta ke (mg/k g bw/d)																
Whe at bran	20	0.0009 15	20	0.0183 04																
Gras s	100	0.0007 45	80	0.0596 36																

## **Reporting table, flupyradifurone**

24.06.2014

148/311

---

### section 3 – Residues (B.7)

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)											
No.	Column 1 Reference to DAR (vol., point, page)	Comments from Member States or applicant								Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		W he at br an	2. 2 4	0. 06		8 9	0. 0 6 7	2 0	< 0. 0 0 1	0. 0 0 3	
		Gr as s (fr es h)	0. 4 1	0. 02		2 0	0. 1 0 0	8 0	0. 0 0 3	0. 0 0 8 0	
		<i>Subtotal</i> <i>BYI 02</i> <i>960:</i>							0. 0 0 3	0. 0 0 3	
		W he at br an	2. 2 4		2. 1 1	8 9	2. 3 7 1	2 0	0. 0 0 1 7	0. 0 0 4 7 4	
		Gr as s (fr es h)	0. 4 1		0. 3 7	2 0	1. 8 5 0	8 0	0. 0 0 5 4	1. 0 4 8 0	
		<i>Subtotal</i>							0. 0	1. 9	

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																																												
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant						Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>																																																				
		<i>al DFA:</i> <table border="1" style="margin-left: auto; margin-right: auto;"> <tr> <td style="background-color: #cccccc;"></td><td></td><td></td><td></td><td></td><td></td><td>7</td><td>5</td> </tr> <tr> <td></td><td></td><td></td><td></td><td></td><td></td><td>1</td><td>4</td> </tr> <tr> <td colspan="6"></td><td></td><td></td> </tr> </table> <b>Totals:</b> <table border="1" style="margin-left: auto; margin-right: auto;"> <tr> <td></td><td></td><td></td><td></td><td></td><td>1</td><td>0.</td><td>2.</td> </tr> <tr> <td></td><td></td><td></td><td></td><td></td><td>0</td><td>0</td><td>0</td> </tr> <tr> <td></td><td></td><td></td><td></td><td></td><td>0</td><td>7</td><td>4</td> </tr> <tr> <td></td><td></td><td></td><td></td><td></td><td>4</td><td>4</td><td>8</td> </tr> </table>							7	5							1	4														1	0.	2.						0	0	0						0	7	4						4	4	8		
						7	5																																																					
						1	4																																																					
					1	0.	2.																																																					
					0	0	0																																																					
					0	7	4																																																					
					4	4	8																																																					

Estimation of theoretical residues resulting from feeding grown BYI 02960 residues (comprising BYI 02960 and DFA) to poultry in a ratio relevant to the actual residues expected in feed commodities  
=> corresponds to **Table 7.12.1-3 (cattle):**

Dietary burden (mg/kg feed)	Matrix	Transfer factor	Resulting residue (mg/kg)
BYI 0 2960			
0.093	milk	0.009 <sup>1</sup>	0.001
	muscle	0.013 <sup>1</sup>	0.001
	fat	0.009 <sup>1</sup>	0.001

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																																	
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																													
		<table border="1"> <tr> <td></td><td>liver</td><td>0.036<sup>1</sup></td><td>0.003</td><td></td></tr> <tr> <td></td><td>kidney</td><td>0.037<sup>1</sup></td><td>0.003</td><td></td></tr> <tr> <td></td><td>DFA</td><td></td><td></td><td></td></tr> <tr> <td></td><td></td><td>milk</td><td>0.030<sup>2</sup></td><td>0.059</td></tr> <tr> <td></td><td></td><td>muscle</td><td>0.097<sup>2</sup></td><td>0.190</td></tr> <tr> <td></td><td>1.954</td><td>fat</td><td>0.086<sup>2</sup></td><td>0.168</td></tr> <tr> <td></td><td></td><td>liver</td><td>0.097<sup>2</sup></td><td>0.190</td></tr> <tr> <td></td><td></td><td>kidney</td><td>0.131<sup>2</sup></td><td>0.256</td></tr> </table> <p><sup>1</sup> TF for total residue for enforcement/risk assessment = parent BYI 02960 plus DFA; determined for 1X dose level in cattle feeding study</p> <p><sup>2</sup> TF for DFA, only; determined for 49X dose level in cattle feeding study</p> <p>Levels of the relevant residue of BYI 02960 (comprising BYI 02960 and DFA) in ruminant tissues and milk expected after feeding a worst-case diet containing residues due to treatment of crops with BYI 02960</p> <p>=&gt; corresponds to <b>Table 7.12.1-4 (cattle):</b></p> <table border="1"> <tr> <td>Dietary burden (mg/</td><td>Matr ix</td><td>Resulting residue (sum of</td><td>MRL proposal EU /</td></tr> </table>		liver	0.036 <sup>1</sup>	0.003			kidney	0.037 <sup>1</sup>	0.003			DFA						milk	0.030 <sup>2</sup>	0.059			muscle	0.097 <sup>2</sup>	0.190		1.954	fat	0.086 <sup>2</sup>	0.168			liver	0.097 <sup>2</sup>	0.190			kidney	0.131 <sup>2</sup>	0.256	Dietary burden (mg/	Matr ix	Resulting residue (sum of	MRL proposal EU /			
	liver	0.036 <sup>1</sup>	0.003																																														
	kidney	0.037 <sup>1</sup>	0.003																																														
	DFA																																																
		milk	0.030 <sup>2</sup>	0.059																																													
		muscle	0.097 <sup>2</sup>	0.190																																													
	1.954	fat	0.086 <sup>2</sup>	0.168																																													
		liver	0.097 <sup>2</sup>	0.190																																													
		kidney	0.131 <sup>2</sup>	0.256																																													
Dietary burden (mg/	Matr ix	Resulting residue (sum of	MRL proposal EU /																																														

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																	
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant			Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																											
		<table border="1"> <thead> <tr> <th>kg feed)</th><th></th><th>a.s. &amp; DFA) [mg a.s. equiv./kg]</th><th>global [mg/kg]</th></tr> </thead> <tbody> <tr> <td colspan="4"><i>Total residue (BYI 02960 plus DFA)</i></td></tr> <tr> <td>2.048 (0.093 + 1.954</td><td>milk</td><td>0.059</td><td>0.08 / <b>0.3</b></td></tr> <tr> <td></td><td>mus cle</td><td>0.191</td><td>0.30 / <b>1.0</b></td></tr> <tr> <td></td><td>fat</td><td>0.169</td><td>0.30 / <b>0.5</b></td></tr> <tr> <td></td><td>liver</td><td>0.193</td><td>0.30 / <b>2.0</b></td></tr> <tr> <td></td><td>kidn ey</td><td>0.259</td><td>0.40 / <b>2.0</b></td></tr> </tbody> </table>				kg feed)		a.s. & DFA) [mg a.s. equiv./kg]	global [mg/kg]	<i>Total residue (BYI 02960 plus DFA)</i>				2.048 (0.093 + 1.954	milk	0.059	0.08 / <b>0.3</b>		mus cle	0.191	0.30 / <b>1.0</b>		fat	0.169	0.30 / <b>0.5</b>		liver	0.193	0.30 / <b>2.0</b>		kidn ey	0.259	0.40 / <b>2.0</b>
kg feed)		a.s. & DFA) [mg a.s. equiv./kg]	global [mg/kg]																														
<i>Total residue (BYI 02960 plus DFA)</i>																																	
2.048 (0.093 + 1.954	milk	0.059	0.08 / <b>0.3</b>																														
	mus cle	0.191	0.30 / <b>1.0</b>																														
	fat	0.169	0.30 / <b>0.5</b>																														
	liver	0.193	0.30 / <b>2.0</b>																														
	kidn ey	0.259	0.40 / <b>2.0</b>																														
3(53)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	BCS (page 269, plant MRLs): STMR, HR and MRL should be taken from the same data set (either using the residue definition for RA or monitoring for calculation) – otherwise the data is not comprehensible			NL (May 2014): agreed. To amend in revised DAR	Open point RMS to amend in a revised DAR Table in page 269.  <b>EFSA note:</b> according to WHO/FAO definition, STMR and HR refer to the median and highest residue level, <i>"including the residue components for estimation of the dietary intake"</i> (= calculated according to the residue definition for risk assessment).																											
3(54)	Vol. 3, B.7.12, proposed MRLs (plant matrices)	BCS (page 269, plant MRLs): Rotational root vegetables => MRL proposal of 0.6 mg/kg is based on succeeding trials with potatoes, thus the			NL (May 2014): since the carrot trials were performed with 1x 200 g/ha whilst the potato trials were performed at 2x 225 g as/ha, RMS considers that the potato trials	Open point MRL proposals for rotational crops should be reconsidered, taking into																											

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<p>MRL should refer to Rotational root <b>and tuber</b> vegetables =&gt; or separate into</p> <p><b>Rotational root vegetables</b> (turnips and carrots): MRL = 0.3 mg/kg</p> <p><b>Rotational tuber vegetables</b> (potatoes): MRL = 0.6 mg/kg</p> <p>Total BYI 02960 residues</p> <ul style="list-style-type: none"> <li>• Carrots &amp; turnips (PBI = 25-30 days): 0.05, 0.07; 0.08; 0.14 mg/kg =&gt; MRL proposal: 0.3 mg/kg</li> <li>• Potatoes (PBI = 25-33 days): 0.048; 0.056; 0.21; 0.27 mg/kg =&gt; MRL proposal: 0.6 mg/kg</li> </ul>	<p>represent the cGAP better. Hence, the MRL for rotational tuber vegetables needs to be increased in the ER, not decreased in the DAR.</p>	<p>account the conclusion of the expert consultations on residue definitions and rotational crops (see Expert consultation 3(8) and 3(40))</p>
3(55)	Vol. 3, B.7.12, proposed MRLs (animal matrices)	<p>BCS (page 269, animal MRLs): Residues detected in the animal matrices in the livestock feeding study cannot be used to estimate the MRLs (even after normalizing to 1N dose) since animals were fed with BYI 02960 only and a realistic diet will consist of BYI 02960 and DFA =&gt; transfer factors for the two compounds – estimated in the feeding studies – have to be applied to the calculate residues in animal matrices.</p>	<p>NL (May 2014): the normalisation to 1N was not used. Table can be removed to avoid confusion</p>	<p>Open point RMS, to reconsider the MRL proposals for products of animal origin, taking into account, conclusion of the expert consultations on the residue definitions 3(13), the animal feeding studies 3(29), and the rotational crop studies 3(40).</p> <p>See also comments 3(53), 3(57) and 3(58)</p>
3(56)	Vol. 3, B.7.12, proposed MRLs (animal matrices)	BCS (page 271, Table 7.12.2-4, estimation of animal MRLs according to RMS):	NL (May 2014):	See open point 3(56)

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																										
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant			Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>			Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																		
		<p>- for wheat grain and pea (dry) the STMR values and not the HR values should be used;</p> <p>- the DM content of cabbage is 14%</p> <p>- the residues taken for turnips are the residues detected for potatoes (was this intended?)</p> <p>- Rape forage is not a diet for dairy ruminants, should be replaced by grass</p> <p>- The contribution of turnips can account for 30% in maximum in the diet of cattle (60% was assumed in the DAR)</p> <p>- the maximum contribution of grass and other forages can account up to 100% Please correct table accordingly (see values in <b>bold</b> and <i>italics</i>).</p> <p>BCS would favour the calculation as described under (4).</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th colspan="11"><b>Poultry</b></th> </tr> <tr> <th>Crop</th> <th>T R</th> <th>a. s.</th> <th>D F A</th> <th>% D M</th> <th>m g/ k g</th> <th>D M in ta k e</th> <th>m g/ kg b w/ da y</th> <th>m g/ kg dr y fe ed</th> <th></th> <th></th> </tr> </thead> <tbody> <tr> <td>Tu</td> <td>0</td> <td>0.</td> <td></td> <td>1</td> <td>0</td> <td>2</td> <td>0.</td> <td>0.</td> <td></td> <td></td> </tr> </tbody> </table>				<b>Poultry</b>											Crop	T R	a. s.	D F A	% D M	m g/ k g	D M in ta k e	m g/ kg b w/ da y	m g/ kg dr y fe ed			Tu	0	0.		1	0	2	0.	0.			<ul style="list-style-type: none"> <li>- Agreed</li> <li>- Typo. Calculation was done with 14%</li> <li>- This was intended, see 3(55)</li> <li>- Cattle in the table refers to the worst case intake, calculated for meat cattle, used</li> <li>- 60% intake was derived from the EFSA dietary burden calculator.</li> <li>- The EFSA dietary burden calculator calculates the worst case intake, using variable contribution. Therefore, the intake of grass was not considered as 100% diet.</li> </ul>			
<b>Poultry</b>																																										
Crop	T R	a. s.	D F A	% D M	m g/ k g	D M in ta k e	m g/ kg b w/ da y	m g/ kg dr y fe ed																																		
Tu	0	0.		1	0	2	0.	0.																																		

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)											
No.	Column 1 Reference to DAR (vol., point, page)	Comments from Member States or applicant								Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	rni ps	.	0		0	.	0	00	02		
	2	2	1		1	0	1	1	0		
	7				0						
	W	0	0.		8	0	4	<0	0.		
	he	.	0		6	.	5	.0	00		
	at	6	1		0	0	01	01	5		
	gr	5			1	0					
	ai				1						
	n				4						
	Pe	2	0.		8	0	3	<0	0.		
	as	.	0		6	.	0	.0	00		
	(dr	3	1		0	0	01	01	3		
	y)				1	0					
	Ca	0	0.		4	.	5	0.	02		
	bb	.	0		4	5	7	00	9		
	ag	2	8		4	5	7	2	9		
	e										
	<i>Subtotal</i> <i>BYI 02</i> <i>960:</i>		0.					0.	0.		
		1	2					00	05		
								3	7		
	Tu	0		0.	1	2	2	0.	0.		
	rni	.	2	2	0	.	0	03	50		
	ps	2	7	5	5	0	0	2	0		
	W	0		0.	8	0	4	0.	0.		
	he	.		3	6	.	5	01	17		

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)										
No.	Column 1 Reference to DAR (vol., point, page)	Comments from Member States or applicant							Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	at gr ai n	6 5		3		3 8		1	3	
	Pe as (dr y)	2 .3		1. 6	8 6	0 .1 9	3 0	0. 03 5	0. 55 8	
	Ca bb ag e	0 .2		0. 1 2	1 4	0 .8 6	5	0. 00 3	0. 04 3	
	<i>Subtot al DFA:</i>			2. 3 8				0. 08 1	1. 27 4	
	<i>Totals:</i>						1 0 0	0. 08 4	1. 33 1	
	<b>Cattle</b>									
	Tu rn i p	0 .2 7	0. 0 1		1 0	0 .1 0	3 0	0. 00 1	0. 03 0	
	Gr as s	0 .4	0. 0 2		2 0	0 .1	5 0	0. 00 2	0. 05 0	

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)											
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant								Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		(fr es h)	1			0					
		Pe a (dr y)	2 .3	0. 1	8 6	0 0 1	2 0	<0 .0 01	0. 00 2		
		<i>Subtot al BYI 02 960:</i>	0. 0 3					0. 00 3	0. 08 2		
		Tu rn ip	0 .2 7	0. 2 5	1 0	2 .5 0	3 0	0. 02 7	0. 75 0		
		Gr as s (fr es h)	0 .4 1	0. 3 7	2 0	1 .8 5	5 0	0. 03 4	0. 92 5		
		Pe a (dr y)	2 .3	1. 6	1 8 6	1 .8 6	2 0	0. 01 4	0. 37 2		
		<i>Subtot al DFA:</i>		2. 8 0				0. 07 5	2. 04 7		

## **Reporting table, flupyradifurone**

24.06.2014

158/311

### section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)										
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant						Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant		Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<i>Totals:</i>	0. 0 3	2. 8 0			1 0 0	0. 07 8	2. 12 9	
		<b>Pigs</b>								
	Rape for age	0. 0 4 1	0. 2		1 4	0. 1 4	1 5	0. 00 1	0. 02 1	
	Turkey ps	0. 0 2 7	0. 1		1 0	0. 1 0	6 0	0. 00 2	0. 06 0	
	Pearls (dry)	2. 0 3	0. 1		8 6	0. 0 1	2 5	<0 .0 01	0. 00 3	
	<i>Subtotal BYI 02 960:</i>	0. 0 4					0. 00 3	0. 08 4		
	Rape for	0. 0 4 1	0. 3 7	1 4	2 6 4	1 5	0. 01 6	0. 39 6		

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																																											
No.	Column 1 Reference to DAR (vol., point, page)	Comments from Member States or applicant								Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																																
		<table border="1"> <tr> <td>age</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr> <tr> <td>Turnips</td><td>0. · 2 7</td><td></td><td>0. 2 5</td><td>1 0</td><td>2 · 5</td><td>6 0</td><td>0. 06 0</td><td>1. 50 0</td><td></td><td></td></tr> <tr> <td>Pears (dry)</td><td>1. · 6</td><td></td><td>1. 6</td><td>8 6</td><td>1. 8 6</td><td>2 5</td><td>0. 01 9</td><td>0. 46 5</td><td></td><td></td></tr> <tr> <td><i>Subtotal DFA:</i></td><td></td><td></td><td>5. 1 0</td><td></td><td></td><td></td><td>0. 09 5</td><td>2. 36 1</td><td></td><td></td></tr> <tr> <td><i>Totals:</i></td><td>0. 0 4</td><td>5. 1 0</td><td></td><td></td><td>1 0</td><td>0. 09 8</td><td>2. 44 5</td><td></td><td></td><td></td></tr> </table>	age											Turnips	0. · 2 7		0. 2 5	1 0	2 · 5	6 0	0. 06 0	1. 50 0			Pears (dry)	1. · 6		1. 6	8 6	1. 8 6	2 5	0. 01 9	0. 46 5			<i>Subtotal DFA:</i>			5. 1 0				0. 09 5	2. 36 1			<i>Totals:</i>	0. 0 4	5. 1 0			1 0	0. 09 8	2. 44 5					
age																																																											
Turnips	0. · 2 7		0. 2 5	1 0	2 · 5	6 0	0. 06 0	1. 50 0																																																			
Pears (dry)	1. · 6		1. 6	8 6	1. 8 6	2 5	0. 01 9	0. 46 5																																																			
<i>Subtotal DFA:</i>			5. 1 0				0. 09 5	2. 36 1																																																			
<i>Totals:</i>	0. 0 4	5. 1 0			1 0	0. 09 8	2. 44 5																																																				
3(57)	Vol. 3, B.7.12, proposed MRLs (animal matrices)	BCS (page 272, Table 7.12.2-5, estimation of residues in animal matrices according to RMS): Due to the different proposed contribution of the crops in the diet, the MRL proposals could be adapted.  <b>Table 7.12.2-5:</b> Theoretical residues resulting from feeding BYI 02960 and DFA to poultry and to dairy cows in a ratio relevant								NL (May 2014): proposed MRLs to be reconsidered taking into account the other comments, in particular 3(57)	See open point 3(56)																																																

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)										
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant						Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>		
		to the actual residues expected in feed commodities								
		Dietary burden (mg/kg bw/d) Matrix	T F *	Resuling residue (mg/kg) T F *	Dietary burden (mg/kg bw/d) T F *	Resuling residue (mg/kg) T F *	Sum of BYI 02960 and DFA (mg/kg)			
		<b>chicken</b>								
		<b>BYI 02960</b>			<b>DFA</b>					
		eg g · 5 7	0 · 0 1	<0 · 0 1	0. 08 1	1 · 4 7	0. 12	<b>0.1 3</b>		
	0.0 03 †	m us cl e · 9 3	0 · 0 1	<0 · 0 1	0. 08 1	2 · 5 9	0. 21	<b>0.2 2</b>		
		fat	0 · .	<0 · 0		0 · .	0. 07	<b>0.0 8</b>		

## **Reporting table, flupyradifurone**

24.06.2014

161/311

### section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)											
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant						Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant			Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			3 9	1		9 1					
		liv er	1 .1 4	<0 .0 1		3 .2 5	0. 26	<b>0.2</b> 7			
		<b>cattle</b>									
		<i>BYI 02960</i>			<i>DFA</i>						
		mi lk	0 .2 4	<0 .0 1		0 .7 7	0. 06	<b>0.0</b> 7			
		mus cl e	0 .3 5	<0 .0 1		2 .4 9	0. 19	<b>0.2</b> 0			
	0.0 03 †	fat	0 .2 3	<0 .0 1		0. 1 1	0. 16	<b>0.1</b> 7			
		liv er	0 .9 2	<0 .0 1		2 .3 0	0. 17	<b>0.1</b> 8			
		ki dn ey	0 .9 8	<0 .0 1		3 .2 6	0. 24	<b>0.2</b> 5			

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																																																
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant						Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																							
		<b>pigs</b> <table border="1"> <thead> <tr> <th colspan="4">BYI 02960</th> <th colspan="4">DFA</th> </tr> <tr> <th></th> <th>m us cl e</th> <th>0 .3 5</th> <th>&lt;0 .0 1</th> <th></th> <th>2 .4 9</th> <th>0. 24</th> <th><b>0.2 5</b></th> </tr> </thead> <tbody> <tr> <td>0.0 03 †</td> <td>fat</td> <td>0 .2 3</td> <td>&lt;0 .0 1</td> <td>0.09</td> <td>2 .1 1</td> <td>0. 20</td> <td><b>0.2 1</b></td> </tr> <tr> <td></td> <td>liv er</td> <td>0 .9 2</td> <td>&lt;0 .0 1</td> <td>5</td> <td>2 .3 0</td> <td>0. 22</td> <td><b>0.2 3</b></td> </tr> <tr> <td></td> <td>ki dn ey</td> <td>0 .9 8</td> <td>&lt;0 .0 1</td> <td></td> <td>3 .2 6</td> <td>0. 31</td> <td><b>0.3 2</b></td> </tr> </tbody> </table> <p>⇒ The estimated residues in all animal matrices are all covered by the MRLs proposed by the RMS</p>							BYI 02960				DFA					m us cl e	0 .3 5	<0 .0 1		2 .4 9	0. 24	<b>0.2 5</b>	0.0 03 †	fat	0 .2 3	<0 .0 1	0.09	2 .1 1	0. 20	<b>0.2 1</b>		liv er	0 .9 2	<0 .0 1	5	2 .3 0	0. 22	<b>0.2 3</b>		ki dn ey	0 .9 8	<0 .0 1		3 .2 6	0. 31	<b>0.3 2</b>
BYI 02960				DFA																																												
	m us cl e	0 .3 5	<0 .0 1		2 .4 9	0. 24	<b>0.2 5</b>																																									
0.0 03 †	fat	0 .2 3	<0 .0 1	0.09	2 .1 1	0. 20	<b>0.2 1</b>																																									
	liv er	0 .9 2	<0 .0 1	5	2 .3 0	0. 22	<b>0.2 3</b>																																									
	ki dn ey	0 .9 8	<0 .0 1		3 .2 6	0. 31	<b>0.3 2</b>																																									
3(58)	Vol. 3, B.7.15, consumer risk assessment	BCS (page 277, Table 7.15.2-1, input values for the consumer risk assessment: <u>Chronic risk assessment:</u> - the proposed IT-MTLs for poultry liver and milk were mixed up poultry liver: <b>1.0 mg/kg</b> (instead of 0.3)						Open point RMS to reconsider in a revised DAR , the consumer risk assessment considering the conclusions of the expert meetings on residue definitions (3(8), 3(13), 3(26), the comments on																																								

## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		mg/kg) <u>cattle milk: 0.3 mg/kg</u> (instead of 1.0 mg/kg) - the MRL for <u>goat and sheep milk</u> should be the <b>0.08 mg/kg</b> (instead of 0.15 mg/kg)  <u>Acute risk assessment:</u> - proposed MRLs for milk has to be corrected <u>cattle milk: 0.08 mg/kg</u> (instead of 0.15 mg/kg) <u>goat and sheep milk: 0.08 mg/kg</u> (instead of 0.15 mg/kg) - MRLs used for cattle muscle, fat liver kidney should be in line with the values proposed in Table 7.12.2-6 cattle muscle: <b>0.3 mg/kg</b> (instead of 0.5 mg/kg) cattle fat: <b>0.3 mg/kg</b> (instead of 0.4 mg/kg) cattle liver: <b>0.3 mg/kg</b> (instead of 0.4 mg/kg) cattle kidney: <b>0.4 mg/kg</b> (instead of 0.6 mg/kg) - what is the reason to use MRL values instead of IT-MRLs?		plant and animal MRL proposals 3(20), 3(22), 3(24), 3(25), 3(47), 3(55) and 3(56).  See also comments 3(60), 3(62) and 3(63)
3(59)	Vol. 3, B.7.15, consumer risk assessment (chronic)	BCS (page 277, Table 7.15.2-2, TMDI calculation: Using the corrected input values the TMDI values will slightly change (decrease)  Table 7.15.2-02 Worst-case results of the		See open point 3(60)

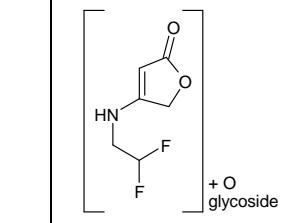
## section 3 – Residues (B.7)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)																
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)												
		<u>TMDI calculation in PRIMo model rev. 2</u> <table border="1"> <tr> <td><b>Highest calculated TMDI values in % of ADI</b></td><td><b>MS Diet</b></td></tr> <tr> <td>76.3</td><td>WHO Cluster diet B</td></tr> <tr> <td>62.8</td><td>NL child</td></tr> <tr> <td>61.7</td><td>DE child</td></tr> <tr> <td>55.9</td><td>UK Toddler</td></tr> <tr> <td>50.4</td><td>IE adult</td></tr> </table>	<b>Highest calculated TMDI values in % of ADI</b>	<b>MS Diet</b>	76.3	WHO Cluster diet B	62.8	NL child	61.7	DE child	55.9	UK Toddler	50.4	IE adult		
<b>Highest calculated TMDI values in % of ADI</b>	<b>MS Diet</b>															
76.3	WHO Cluster diet B															
62.8	NL child															
61.7	DE child															
55.9	UK Toddler															
50.4	IE adult															
3(60)	Vol. 3, B.7.15, consumer risk assessment (chronic)	BCS (page 278, typo in 1 <sup>st</sup> sentence): Two groundwater metabolites were identified, DFA and <b>6-CNA</b> ...	NL (May 2014): to be amended	Open point RMS, Typo in sentence page 278 to be corrected												
3(61)	Vol. 3, B.7.15, consumer risk assessment (acute)	BCS (page 280, acute consumer intake calculations; NESTI of imported crops citrus and celery use more of the ARfD compared with lettuce): The NESTI uses maximally 69.2% of the ARfD for the German child for lettuce. <b>Only the imported crops citrus and celery use more of the ARfD (83.4 and 80.0% of the ARfD, respectively).</b>	NL (May 2014): since the MRLs are dealt with in the ER, the specific NESTI values for celery and citrus were not reported, since they can be derived from figure 7.15.3-1	See open point 3(60)												
3(62)	Vol. 3, B.7.15, consumer risk assessment	BCS (page 279 and 281, chronic and acute consumer intake calculations): Please replace figure if different input values are used	NL (May 2014): agreed	See open point 3(60)												

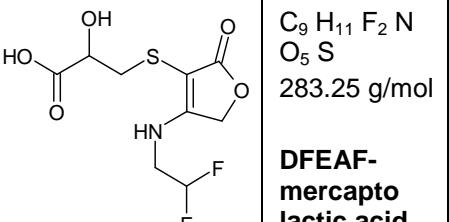
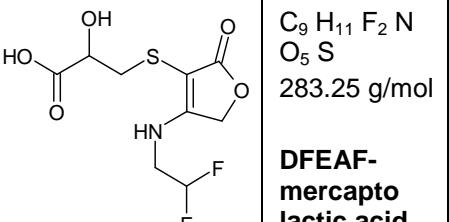
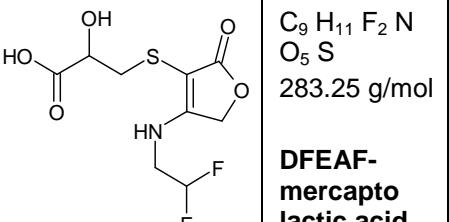
## section 3 – Residues (B.7)

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(63)	Vol. 3, B.7.16, Summary and Evaluation	BCS (page 291, summary livestock feeding): Please add an explaining sentence at the end of the 2 <sup>nd</sup> paragraph that the special study design allowed to calculate a transfer factor of DFA despite feeding BYI 02960, only.  Example: The feeding studies were designed to allow "material balancing" in order to evaluate levels and calculate transfer factors for both the total residue (parent BYI 02960 and DFA) and DFA, despite feeding parent compound only.	NL (may 2014): agreed, to be amended in revised DAR	Open point RMS to amend the summary section B.7.16 considering the overall conclusion of the expert meeting consultations and the comments in 3(65), 3(66), 3(67)
3(64)	Vol. 3, B.7.16, Summary and Evaluation	BCS (page 291, consumer risk assessment): Please explain that the listed MRLs are based on EU data only.  Example: Based on the supervised residue trials, [...] the following <b>EU MRLs</b> are proposed (using EU data only).	NL (may 2014): agreed, to be amended in revised DAR	See open point 3(64)
3(65)	Vol. 3, B.7.16, Summary and Evaluation	BCS (page 291, consumer risk assessment): The MRL for rotational root vegetables is identical with the MRL for rotational tuber vegetables indicating that the residue results from potatoes were used for the calculation. Why not using the residues detected in rotational carrots and turnips for rotational root vegetables as done in the MRL Evaluation Report?  Total BYI 02960 residues	NL (May 2014): see 3(55) since the carrot trials were performed with 1x 200 g/ha whilst the potato trials were performed at 2x 225 g as/ha, RMS considers that the potato trials represent the cGAP better. Hence, the MRL for rotational tuber vegetables needs to be increased in the ER, not decreased in the DAR.	See open point 3(64)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<ul style="list-style-type: none"> <li>• Carrots &amp; turnips (PBI = 25-30 days): 0.05, 0.07; 0.08; 0.14 mg/kg =&gt; MRL proposal: 0.3 mg/kg</li> <li>• Potatoes (PBI = 25-33 days): 0.048; 0.056; 0.21; 0.27 mg/kg =&gt; MRL proposal: 0.6 mg/kg</li> </ul>		
3(66)	Vol. 3, B.7.16, Summary and Evaluation	BCS (page 292, consumer risk assessment): The last paragraph is a bit misleading – only for citrus and celery, the HR instead of the MRL was used.	NL (May 2014): since all MRLs were used in the consumer risk assessment, not only the ones supported for Approval, the ARfD was exceeded but only for celery and citrus. Hence, for these crops, the acute intake calculation was refined by using the HR. Since the ARfD was not exceeded with any other crop, refinement was not necessary.	See open point 3(64)
3(67)	Vol. 3, B.7, Annex I, List of metabolites	BCS (page 312, name of metabolite 35): Please add the name DFEAF-OH-glyc as additional name as it was used by the RMS M3 5 BYI 02960-difluoroethyl-amino-furanone-OH-glyc  C <sub>12</sub> H <sub>17</sub> F <sub>2</sub> N O <sub>8</sub> 341.27 g/mol DFEAF-OH-glyc in the DAR	NL (may 2014): to be amended in revised DAR	Open point RMS; point to be amended in a revised DAR according BCS comment in column 2.
3(68)	Vol. 3, B.7, Annex I, List	BCS (page 313, name of metabolite 41):	NL (may 2014): to be amended in revised	Open point

## section 3 – Residues (B.7)

Other comments												
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)								
	of metabolites	<p>Please add the name DFEAF-mercaptopo-lactic acid as additional name as it was used</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <tr> <td style="padding: 2px;">M4</td> <td style="padding: 2px;"><b>BYI 02960-mercaptopo-lactic acid</b></td> </tr> <tr> <td style="padding: 2px;">1</td> <td style="padding: 2px;"></td> </tr> <tr> <td style="padding: 2px;"></td> <td style="text-align: center; padding: 2px;">  <p><b>DFEAF-mercaptopo-lactic acid</b></p> </td> </tr> <tr> <td style="padding: 2px;"></td> <td style="padding: 2px;">C<sub>9</sub>H<sub>11</sub>F<sub>2</sub>N O<sub>5</sub>S 283.25 g/mol</td> </tr> </table> <p>by the RMS in the DAR</p>	M4	<b>BYI 02960-mercaptopo-lactic acid</b>	1			 <p><b>DFEAF-mercaptopo-lactic acid</b></p>		C <sub>9</sub> H <sub>11</sub> F <sub>2</sub> N O <sub>5</sub> S 283.25 g/mol	DAR	RMS; point to be amended in a revised DAR according BCS comment in column 2.
M4	<b>BYI 02960-mercaptopo-lactic acid</b>											
1												
	 <p><b>DFEAF-mercaptopo-lactic acid</b></p>											
	C <sub>9</sub> H <sub>11</sub> F <sub>2</sub> N O <sub>5</sub> S 283.25 g/mol											
3(69)	MRL Evaluation Report, proposed MRLs	BCS (page 3, proposed MRLs): Peanut should be mentioned under oilseeds (not under nuts)	NL (may 2014): noted	Open point RMS, to amend the evaluation report related to peanut.								
3(70)	MRL Evaluation Report, proposed MRLs	BCS (page 3, proposed MRLs): Since root and tuber vegetables as well as bulb vegetables are exported from North America to Europe, an IT-MRL should be set based on rotational crop data	NL (may 2014): noted, to be amended. However, see 3(24)	Open point RMS to reconsider in a revised DAR/ER, the MRL proposals considering the conclusions of the expert meetings on residue definitions 3(8), 3(13), 3(26), the comment on Import tolerance setting 3(25) and the comments on plant and animal MRL proposals 3(20), 3(22), 3(24), 3(47), 3(55) and 3(56) and the additional BCS comments (72), 3(73), 3(79),								

## section 3 – Residues (B.7)

Other comments						
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant			Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Commodity	Existing EC MRL (mg/kg)	Proposed EC MRL (mg/kg)	Proposed IT (mg/kg)	
		0210000 Root & tuber except potatoes	0.01	0.6	<b>1.5</b>	
		0220000 Bulb vegetables	0.01	0.4	<b>0.8</b>	
3(71)	MRL Evaluation Report, proposed MRLs	BCS (page 3, proposed MRLs): - The IT-MRL of tomato (3 mg/kg) should also apply for eggplant. The proposed EC MRL should be based on the more critical rotational use (determined for the fruiting crop cucumber). - The IT-MRL for chili pepper should also apply for pepper			NL (may 2014): agreed, to be amended. However, see 3(24)	See open point 3(71)

## section 3 – Residues (B.7)

<b>Other comments</b>						
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant			<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		Commodity	Existing EC MRL (mg/kg)	Proposed EC MRL (mg/kg)	Proposed IT (mg/kg)	
		Tomato	0.01	<b>0.9</b>	3	
		Egg plant	0.01	<b>0.9</b>	<b>3</b>	
		pepper	0.01	1.0	<b>3</b>	
		Chili pepper	<b>0.01</b>	<b>1.0</b>	3	
3(72)	MRL Evaluation Report, proposed MRLs	BCS (page 4, proposed MRLs): - According to the DAR is the proposed EC MRL for brassicaceae and other leaf vegetables & fresh herbs is 0.04 mg/kg - MRL for stem vegetables (0270000) does not apply for celery - MRL for oilseeds does not apply for peanuts and soybean seeds - cereals include field corn			NL (may 2014): to be reviewed and amended.	See open point 3(71)

## section 3 – Residues (B.7)

<b>Other comments</b>					
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant		Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<b>Commodity</b>	<b>Existin g EC MRL (mg/kg)</b>	<b>Prop osed EC MRL</b>	<b>Pro pos ed IT</b>
	Brassicacea	0.01	<b>0.4</b>		
	All others of 0250000 Leaf veg. & fresh herbs	0.01	<b>0.4</b>		
	Stem vegetables, <b>except celery</b>	0.01	0.5		
	Peanut	0.01		0.15	
	Soy bean seed	0.01		4	
	<b>Oilseeds, except for peanuts and soybean seeds</b>	0.01	0.4	0.9	
	Barley, sorghum and wheat grain	0.01	<b>1.5</b>	4	
	<b>Cereals (including field corn), except barley, sorghum and wheat grain</b>	0.01	1.5		

## section 3 – Residues (B.7)

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(73)	MRL Evaluation Report, 1.1. Enforcement methods	BCS (page 7, Enforcement methods for residues in food of plant origin): => Enforcement methods used are method 01330 and <b>its modification M001 for oilseeds</b> (see also C.1.1.1)	NL (May 2014): to be reviewed and amended.	Open point, RMS to consider BCS comment on the analytical method in a revised ER. See also comment 3(75) and 3(76)
3(74)	MRL Evaluation Report, 1.1 Enforcement methods	BCS (page 7, Enforcement methods for residues in food of plant): - The LOQ in the box refers only to BYI 02960, the LOQ for DFA is 0.10 mg/kg for hops and 0.02 mg/kg for all other crops as stated in the text	NL (May 2014): The box was copied from the List of Endpoints from the DAR. If the information here is insufficient, this point should be referred to section2 of the reporting table.	See open point 3(74)
3(75)	MRL Evaluation Report, 1.2 Enforcement methods	BCS (page 7, Enforcement methods for residues in food of animal origin): - The LOQ in the box refers only to DFA, the LOQ for parent BYI 02960 is 0.01 mg/kg	NL (May 2014): The box was copied from the List of Endpoints from the DAR. If the information here is insufficient, this point should be referred to section2 of the reporting table.	See open point 3(74)
3(76)	MRL Evaluation Report, 3. Residues	BCS (page 10, Header of Figure 3.1.1.1-01): The header could be misleading => New proposal: Overview on analytical targets analysed for in the supervised residue trials. 6-CNA was determined for information only since it is a known metabolite of other insecticides bearing this moiety.	NL (May 2014): Agreed, the header can lead to unnecessary concern. Header to be rephrased	See open point 3(74)
3(77)	MRL Evaluation Report, 3. Residues	BCS (page 11, Supervised Residue trials): The text concerning 6-CNA is a bit misleading; 6-CNA was not included in the residue definition since	NL (May 2014): Agreed, the text can lead to unnecessary concern. to be rephrased	Open point RMS, to amend in a revised ER the text related to the metabolite 6-CAN

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<ul style="list-style-type: none"> <li>- only small residues were detected in most field crops</li> <li>- there is no toxicological concern</li> </ul> <p>1) 6-CNA was included in the <u>data collection method</u> to determine the residue of this metabolite under realistic conditions in field residues (other insecticides bearing the 6-CNA moiety can lead to rather high residues of 6-CNA in crops).</p> <p>2) The residue trials showed that 6-CNA represents only a minor part of the residue, if at all.</p> <p>3) 6-CNA was detected in the ADME studies, thus the metabolite constitute substantially to the tox effects of the parent and is therefore covered by the tox studies conducted with the parent compound.</p> <p>6-CNA should <b>not</b> be included in the residue definition</p>		according to BCS comments in column 2.
3(78)	MRL Evaluation Report, 3. Residues	<b>BCS (general remark):</b> - Calculation of MRL could be based on <b>total residue (BYI 02960, DFA and DFEAF)</b> as done in the Annex II dossier (DFEAF residues were always not significant and have thus no influence on the MRL) - Re-calculation of the combined residues of BYI 02960 and DFA can result in mistakes and will not result in different MRLs.	NL (May 2014): <ul style="list-style-type: none"> <li>- agreed. However, when DFEAF is excluded from residue definition, MRLs should reflect parent and DFA alone</li> <li>- agreed</li> </ul>	See open point 3(71)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<ul style="list-style-type: none"> <li>- in the DAR STMR and HR were based on the residue definition for RA, whereas the MRL was based on the residue definition for monitoring. In the MRL Evaluation Report STMR, HR and MRL are based on the residue definition for monitoring. This is not conclusive - however the values are nearly identical.</li> <li>- Ranges of residues (BYI 0296, DFA or total residue) should be given for the <b>peak residue</b></li> <li>- several trials show increasing residues after the PHI, however due to prolonged sampling intervals it was shown that at least a residue plateau was reached and thus that the trials are valid for MRL setting – this information is no longer given in the MRL Evaluation Report</li> </ul>	<ul style="list-style-type: none"> <li>- STMR and HR should be based on the residue definition for monitoring, since a CF will be applied in the RA. Hence, a double correction would be applied. To be amended.</li> <li>- Agreed, to be amended where this was not concluded correctly</li> <li>- To be considered</li> </ul>	
3(79)	MRL Evaluation Report, 3. Residues	BCS (page 14, Residue trials in grapes): <ul style="list-style-type: none"> <li>- For MRL calculation, residues in bunch of grapes should be used since residue peak was often detected <b>after</b> the PHI. Berries were only collected at the PHI. Although the berries showed slightly higher residues, the residues were comparable with those of bunch of grapes (same data set).</li> <li>- Calculation of MRL <b>could</b> be based on <b>total residue (BYI 02960, DFA and DFEAF)</b> as done in the Annex II dossier (DFEAF</li> </ul>	NL (May 2014): To be considered during revision of the ER. NL (May 2014): MRL in grapes was based on peak residues of bunches. See tables C.3.1.2.1-1 to -4 and table 3-1.  MRL for SEU grapes should be 0.6 mg/kg STMR: 0.16, HR: 0.34 Mean +4SD: 0.538 CF x 3Mean: 0.533	See open point 3(20) and 3(71)

## section 3 – Residues (B.7)

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<p>residues were always not significant and have thus no influence on the MRL)  - Re-calculation of the combined residues of BYI 02960 and DFA results often in mistakes and will not result in different MRLs.</p> <p><b>N-EU (peak residues in grapes):</b></p> <p>BYI 02960: 0.42; 0.38; 0.15; 0.11; 0.16; 0.22; 0.42; 0.18; 0.21</p> <p>DFA: 0.06; 0.07; 0.11; 0.06; 0.03; 0.15; 0.08; 0.05; 0.03</p> <p>DFEAF: always &lt;0.01</p> <p>Total (a.s.+ DFA): 0.17; 0.19; 0.23; 0.24; 0.26; 0.37; 0.45; 0.48; 0.50</p> <p>STMR: 0.26 mg/kg</p> <p>HR: 0.50 mg/kg</p> <p>⇒ MRL = 1.0 mg/kg</p> <p><b>S-EU (peak residues in grapes):</b></p> <p>BYI 02960: 0.22; 0.11; 0.09; 0.05; 0.08; 0.05; 0.07; 0.10</p> <p>DFA: 0.05; 0.08; 0.06; &lt;0.02; 0.25; .05; 0.11; 0.06</p> <p>DFEAF: always &lt;0.01</p> <p>Total (a.s.+DFA): 0.07; 0.10; 0.15; 0.16; 0.18; 0.19; 0.27; 0.33</p> <p>STMR: 0.17 mg/kg</p> <p>HR: 0.33 mg/kg</p> <p>MRL = 0.6 mg/kg</p>	To be considered during revision of the ER.	
3(80)	MRL Evaluation Report,	BCS (page 14, Residue trials in grapes):	NL (May 2014): To be considered during	See open point 3(20) and 3(71)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	3. Residues	<p>Please correct text in 2<sup>nd</sup> and 3<sup>rd</sup> paragraph.  <b>Peak residues</b> ranged from <b>0.05-0.42 mg/kg</b> for BYI 02960, from <b>&lt;0.02-0.25 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in all samples.</p> <p>Residue data from Northern European trials were <b>more critical</b> (STMR = <b>0.26 mg/kg</b>, HR = <b>0.50 mg/kg</b>) compared to Southern European trials (STMR = <b>0.17 mg/kg</b>, HR = <b>0.33 mg/kg</b>).</p>	revision of the ER. See also 3(80)	
3(81)	MRL Evaluation Report, 3. Residues	<p>BCS (page 14, Residue trials in pepper): Please correct text in paragraph 5, and paragraphs 10-12.</p> <p>Eight residue decline trials have been performed in Southern Europe in the seasons 2010 and 2011 and 8 residue decline trials indoor in the season 2011. A 200 g/L SL formulation was applied two times. The dose <b>rate (per application)</b> in the outdoor trials was 113-133 g a.i./ha (15.1-25 g a.i./hL), interval 14-15d and PHI 3d which is in line with the intended cGAP (<b>2 x 112.5 g a.i./ha</b>). The dose rate in the indoor trials <b>was adapted to the crop height</b> and accounted for 135-215 g a.i./ha (13.4-15.5 g a.i./hL, first application up to 22.5 g a.i./hL), interval 10-13d and PHI 3d which is in line with the critical GAP (<b>2 x 112.5 g a.i./ha</b>).</p> <p><b>Peak residues</b> ranged from <b>0.02-0.22 mg/kg</b></p>	NL (May 2014): To be considered during revision of the ER.	See open point 3(71)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<p>for BYI 02960, from &lt;0.02-<b>0.12</b> mg/kg for DFA and were &lt;0.01-0.015 mg/kg for DFEAF in outdoor sweet pepper.</p> <p><b>Peak residues</b> ranged from <b>0.09-0.55</b> mg/kg for BYI 02960, from &lt;0.02-<b>0.16</b> mg/kg for DFA and were &lt;0.01-0.022 mg/kg for DFEAF in indoor sweet pepper.</p> <p>Selected residue data for monitoring from the indoor trials were worst case (STMR = 0.26 mg/kg, HR = 0.60 mg/kg) compared to Southern European outdoor trials (STMR = <b>0.16 mg/kg</b>, HR = 0.24 mg/kg).</p>		
3(82)	MRL Evaluation Report, 3. Residues	<p>BCS (page 15, Residue trials in cucumber/gherkins): Please correct text in paragraphs 6-8.</p> <p>Four residue decline trials have been performed in Southern Europe in the season 2010 in cucumber. A 200 g/L SL formulation was applied two times. The dose rate <b>per application</b> was 125 g a.i./ha (15.6-25 g a.i./hL) and the interval was 14d and PHI 3d which is in line with the cGAP (2 x 112.5 g a.i./ha).</p> <p><b>Peak residues</b> ranged from &lt;0.01-0.06 mg/kg for BYI 02960, from <b>0.07</b>-0.20 mg/kg for DFA and were &lt;0.01 mg/kg for DFEAF in outdoor cucumber.</p> <p><i>Gherkin outdoor</i></p>	<p>NL (May 2014): To be considered during revision of the ER.</p>	See open point 3(71)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>Four residue decline trials have been performed in Southern Europe in the season 2011 in gherkin outdoor. A 200 g/L SL formulation was applied two times at <b>112.5 g a.i./ha</b> (18.8-22.6 g a.i./hL) with interval 14-15d and PHI 3d which is in line with the cGAP (2 x 112.5 g a.i./ha).</p> <p><b>Peak residues</b> ranged from <b>&lt;0.01-0.27 mg/kg</b> for BYI 02960, from <b>0.09-0.66 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in outdoor gherkin.</p> <p><i>Cucumber indoor</i></p> <p>Eight residue decline trials have been performed in cucumber in greenhouses in Northern and Southern Europe in the seasons 2010. A 200 g/L SL formulation was applied two times. The dose rate in the trials was adopted to the crop height and accounted for 113-250 g ai./ha per application (15.1-16.7 g a.i./hL), interval 9-14d and PHI 3d which is in line with the cGAP (2 x 112.5 g a.i./haxm)).</p> <p><b>Peak residues</b> ranged from <b>0.04-0.19 mg/kg</b> for BYI 02960, from <b>0.08-0.47 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in indoor cucumber.</p>		
3(83)	MRL Evaluation Report, 3. Residues	<p>BCS (page 15, Residue trials in cucumber/gherkins):</p> <p>Please delete the first paragraph under "Selected worst case residue data for MRL</p>	NL (May 2014): Agrees, to be amended, since indoor trials were considered as one data set it is incorrect to conclude this.	See open point 3(71)

## section 3 – Residues (B.7)

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<i>setting")</i> – this paragraph is misleading		
3(84)	MRL Evaluation Report, 3. Residues	<p>BCS (page 17, Residue trials in melon):            - Please correct the sentences in the paragraph 1,3 and 6</p> <p>Residues of 6-chloronicotinic acid have also been determined in melon. <b>No residues were detected in 13 of 18 trials (&lt;0.005 mg/kg); in 5 trials residues were detected ranging from 0.008 – 0.02 mg/kg (in pulp).</b></p> <p><i>Watermelon outdoor</i></p> <p><b>Peak residues</b> ranged from &lt;0.01-<b>0.05 mg/kg</b> for BYI 02960, from <b>0.03-0.21 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in whole fruits.</p> <p><i>Watermelon indoor</i></p> <p><b>Peak residues</b> ranged from &lt;0.01-<b>0.12 mg/kg</b> for BYI 02960, from <b>0.06-0.28 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in whole fruits.</p>	<p>NL (May 2014): considers that the sentences are not incorrect, but that BCS' proposal is more detailed.</p> <p>Results to be reviewed and amended where needed</p>	See open point 3(71)
3(85)	MRL Evaluation Report, 3. Residues	BCS (page 17, Residue trials in melon): The P-factor increased from day 3 to day 7, but <u>decreased thereafter</u> . This indicates that the residue peak was approx. 7 days after application. Thus, DFA residues increased with time, but at least a residue plateau was reached at the end of the trials.	NL (May 2014): To be considered during revision of the ER.	See open point 3(71)
3(86)	MRL Evaluation Report,	BCS (page 17, selected data for watermelon	NL (May 2014): Agrees, to be amended,	See open points 3(22) and 3(71)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	3. Residues	<p>MRL): BCS proposes to define the greenhouse as the "critical region" and an <b>MRL of 0.6 mg/kg</b> based on the greenhouse trials.</p> <p>MRL proposal outdoor (S-EU):            Total residue (a.s. + DFA):            0.04; 0.05; 0.09; 0.10; 0.12; 0.14; 0.15; 0.18;            0.25 mg/kg    <b>MRL = 0.4 mg/kg</b></p> <p>MRL proposal indoor:            Total residue (a.s. + DFA):            0.09; 0.12; 0.13; 0.15; 0.16; 0.18; 0.26; 0.29;            0.30 mg/kg    <b>MRL = 0.6 mg/kg</b></p>	since indoor and outdoor trials were considered as one data set which is incorrect.	
3(87)	MRL Evaluation Report, 3. Residues	<p>BCS (page 18, Residue trials in tomato):            - Please correct the sentences in the paragraph <i>Tomato outdoor</i>, <i>Tomato indoor</i> and <i>Selected data for MRL setting Tomato outdoor</i></p> <p><b>Peak residues</b> ranged from &lt;0.01-<b>0.08</b> mg/kg for BYI 02960, from &lt;0.02-<b>0.029</b> mg/kg for DFA and were &lt;0.01 mg/kg for DFEAF in whole fruits.</p> <p><i>Tomato indoor</i></p> <p><b>Peak residues</b> ranged from <b>0.06</b>-0.36 mg/kg for BYI 02960, from &lt;0.02-0.11 mg/kg for DFA and from &lt;0.01-0.029 mg/kg for DFEAF in whole fruits.</p>	NL (May 2014): To be considered during revision of the ER.	See open point 3(71)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<p><i>Selected data for MRL setting</i></p> <p>Selected residue data for monitoring from the indoor Northern European trials were worst case (<b>STMR = 0.13 mg/kg, HR = 0.47 mg/kg</b>)</p>		
3(88)	MRL Evaluation Report, 3. Residues	<p>BCS (page 19, Residue trials in apple): - Please correct the sentences in the paragraph <i>Apple NEU</i> and <i>Apple SEU</i> <i>Apple NEU</i></p> <p><b>Peak residues</b> ranged from <b>0.05-0.32 mg/kg</b> for BYI 02960, from &lt;0.02-<b>0.03 mg/kg</b> for DFA and were &lt;0.01 mg/kg for DFEAF in whole fruits.</p> <p><i>Apple SEU</i></p> <p><b>Peak residues</b> ranged from <b>0.01-0.09 mg/kg</b> for BYI 02960, from &lt;0.02-<b>0.036 mg/kg</b> for DFA and from &lt;0.01 mg/kg for DFEAF in whole fruits</p>	NL (May 2014): To be considered during revision of the ER.	To be amended in revised ER
3(89)	MRL Evaluation Report, 3. Residues	<p>BCS (page 21, Table 3-1, Overview of available supervised residue trials):</p> <p>Please note that the residue values mentioned for <u>orange</u> are the values calculated according to the residue definition for risk assessment and not for enforcement.</p>	NL (May 2014): see 3(91)	<p>Open point</p> <p>RMS to reconsider in a revised DAR/ER the overview residue trial table 3-1, taking also into account the conclusion of the expert meetings requested under 3(8), 3(13), 3(26), the comment on import tolerance 3(25)</p>

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<p>The conversion factor for censoring (CF) has to be <b>multiplied</b> with 3 mean</p> <p><b>Enforcement:</b></p> <p>NAFTA region</p> <p>Dilute spray</p> <p>0.07; 0.087; 0.12; 0.14; 0.14; 0.16; 0.17; 0.2; 0.21; 0.27; 0.29; 0.29; 0.31; 0.53; 0.72; 1.5</p> <p>STMR = 0.21</p> <p>HR = 1.5</p> <p><b>OECD</b></p> <p>Mean + 4xSD = 1.738</p> <p><b>CF x 3xmean = 0.974</b></p> <p>Concentrated spray:</p> <p>0.05; 0.10; 0.22; 0.24; 0.26; 0.26; 0.37; 0.66; 0.92; 1.3; 2.2</p> <p>STMR = 0.25</p> <p>HR = 2.2</p> <p><b>OECD</b></p> <p>Mean + 4xSD = 3.082</p> <p><b>CF x 3xmean = 1.680</b></p> <p>Brazil:</p> <p>1 soil drench + 2 foliar</p> <p>0.20; 0.35; 0.40; 0.48; 0.52</p> <p>STMR = 0.40</p> <p>HR = 0.52</p>		<p>and the open point 3(71). See also comments 3(91), 3(92) and 3(93)</p> <p><b>EFSA note:</b> There is no need to report OECD calculation details (mean + 4xSD, CFx 3mean...). Unrounded and rounded OECD values are sufficient.</p>

## section 3 – Residues (B.7)

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<u>OECD</u> Mean + 4xSD = 0.901 <b>CF x 3xmean = 1.200</b>  2 foliar 0.15; 0.22; 0.27; 0.28; 0.39 STMR = 0.27 HR = 0.39 <u>OECD</u> Mean + 4xSD = 0.891 <b>CF x 3xmean = 1.170</b>		
3(90)	MRL Evaluation Report, 3. Residues	BCS (page 21 ff, Table 3-1, Overview of available supervised residue trials): Please note that the non-EU residue values (including STMR and HR) mentioned for <u>grapefruit, lemon, mandarin, tree nuts, grape, blueberry, prickly pear, apple, pear, celery, tomato, pepper, chili pepper, sweet corn, pulses, soybean, hops, coffee, barley, sorghum, wheat, corn, cotton and peanuts</u> are the values calculated according to the residue definition <b>for risk assessment</b> and not for enforcement.  The conversion factor for censoring (CF) has to be <b>multiplied</b> with 3 mean Corrected Table can be sent on request.	NL (May 2014): residue values for non-EU studies were copied from the GJR report by USEPA/Health Canada. They did not report the residue levels in accordance with the residue definition for enforcement.  RMS would like to receive the corrected table from BCS so the ER can be amended, even though the ITs might not be taken into account by EFSA	See open point 3(90)
3(91)	MRL Evaluation Report, 3. Residues	BCS (page 22-23, Table 3-1, Overview of available supervised residue trials):	NL (May 2014): see 3(80). To be considered during revision of the ER.	See open point 3(90)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<p>Please note that the re-calculated values for grapes (according to residue definition for enforcement) are not always correct</p> <p><b>Enforcement:</b></p> <p><b>Grape (N-EU)</b></p> <p>0.17; 0.19; 0.23; 0.24; 0.26; 0.37; 0.45; 0.48; 0.50 STMR: 0.26 mg/kg HR: 0.50 mg/kg</p> <p><b>OECD</b></p> <p>Mean + 4xSD = 0.841 CF x 3xmean = 0.963 MRL = 1 mg/kg</p> <p><b>Grape (S-EU)</b></p> <p>0.07; 0.10; 0.15; 0.16; 0.18; 0.19; 0.27; 0.33 STMR: 0.17 mg/kg HR: 0.33 mg/kg</p> <p><b>OECD</b></p> <p>Mean + 4xSD = 0.521 CF x 3xmean = 0.544 MRL = 0.5 mg/kg</p>		
3(92)	MRL Evaluation Report, 3. Residues	<p>BCS (page 24 ff, Table 3-1, Overview of available supervised residue trials):</p> <p>Please note that the re-calculated values (EU trials) for <u>pepper, cucumber, tomato, lettuce</u> (according to residue definition for enforcement and the residue definition for RA) are not always correct</p>	<p>NL (May 2014): To be considered during revision of the ER RMS would like to receive the corrected table from BCS so the ER can be amended.</p>	See open point 3(93)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Corrected Table can be sent on request		
3(93)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (page 32-33, processing): The last sentence on page 32 and the first sentence of page 33 are a bit confusing: new proposals, The respective LOQs for BYI 02960 and its metabolites DFA and DFEAF were 0.01, 0.02, and 0.01 mg/kg (all in parent equivalents) yielding a calculated LOQ of 0.03* mg/kg for monitoring ( <b>since only BYI 02960 and DFA are considered</b> ). Only for one barley processing fraction higher LOQs were <b>needed</b> : LOQs were 0.1 mg/kg for BYI 02960 and DFEAF in hops draff and 0.2 mg/kg for DFA in hops draff (see study C.3.2.2.1).	NL (May 2014): To be considered during revision of the ER	Open point RMS, to amend sentences related to LOQ according BCS comment in colum 2.
3(94)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (page 32-33, processing factors and correction factors for barley): The residue for risk assessment was calculated by summing up the residues of BYI 02960, DFA and DFEAF. After summation the value was rounded to two <u>significant numbers</u> – this value was reported in the report When re-calculating the residue for monitoring by the RMS, the residues of BYI 02960 and DFA were added and rounded to <u>two decimal places</u> . When calculating the CF the same rounding	NL (May 2014): To be considered during revision of the ER	Open point RMS, to reconsider in a revised ER the processing and conversion (correction?) factors taking into account the conclusion of the expert meeting 3(8), 3(13), 3(26), on the residue definitions. See also comments 3(96), 3(97), 3(98) and 3(99)

## section 3 – Residues (B.7)

Other comments																																						
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																		
		<p>rules should be applied. However, the rounding differences are minimal and considering that the conversion factor will be set to 1, no re-calculation is needed.</p> <p>Example calculation (rounding to two significant numbers):</p> <p style="text-align: center;"><b>Table 3-2. Overview of the available processing studies with barley</b></p> <table border="1"> <thead> <tr> <th>Processed commodity</th> <th>N o</th> <th>Med ian PF <sup>(a)</sup> Mo</th> <th>Med ian PF<sup>(b)</sup> RA</th> <th>Med ian CF <sup>(c)</sup></th> </tr> </thead> <tbody> <tr> <td>Malt sprouts</td> <td>2</td> <td>0.77</td> <td>0.91</td> <td><b>1.18</b></td> </tr> <tr> <td>Brewer's malt</td> <td>2</td> <td>0.49</td> <td>0.52</td> <td><b>1.05</b></td> </tr> <tr> <td>Brewer's grain</td> <td>2</td> <td>0.07</td> <td>0.08</td> <td><b>1.10</b></td> </tr> <tr> <td>Hops draft</td> <td>2</td> <td><b>0.35</b></td> <td>0.44</td> <td><b>1.23</b></td> </tr> <tr> <td>Brewer's yeast</td> <td>2</td> <td>0.10</td> <td>0.11</td> <td><b>1.08</b></td> </tr> <tr> <td>Beer</td> <td>2</td> <td>0.08</td> <td>0.08</td> <td><b>1.10</b></td> </tr> </tbody> </table>	Processed commodity	N o	Med ian PF <sup>(a)</sup> Mo	Med ian PF <sup>(b)</sup> RA	Med ian CF <sup>(c)</sup>	Malt sprouts	2	0.77	0.91	<b>1.18</b>	Brewer's malt	2	0.49	0.52	<b>1.05</b>	Brewer's grain	2	0.07	0.08	<b>1.10</b>	Hops draft	2	<b>0.35</b>	0.44	<b>1.23</b>	Brewer's yeast	2	0.10	0.11	<b>1.08</b>	Beer	2	0.08	0.08	<b>1.10</b>	
Processed commodity	N o	Med ian PF <sup>(a)</sup> Mo	Med ian PF <sup>(b)</sup> RA	Med ian CF <sup>(c)</sup>																																		
Malt sprouts	2	0.77	0.91	<b>1.18</b>																																		
Brewer's malt	2	0.49	0.52	<b>1.05</b>																																		
Brewer's grain	2	0.07	0.08	<b>1.10</b>																																		
Hops draft	2	<b>0.35</b>	0.44	<b>1.23</b>																																		
Brewer's yeast	2	0.10	0.11	<b>1.08</b>																																		
Beer	2	0.08	0.08	<b>1.10</b>																																		

## section 3 – Residues (B.7)

Other comments																	
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant			Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)											
		<table border="1"> <tr> <td>Pearl barley rub</td><td>2</td><td><b>2.93</b></td><td>2.87</td><td><b>0.99</b></td><td></td></tr> <tr> <td>Pearl barley</td><td>2</td><td><b>0.12</b></td><td>0.13</td><td><b>1.10</b></td><td></td></tr> </table> <p>(a):The median processing factor is obtained by calculating the median of the individual processing factors of each processing study. The processing factor has to be applied to the sum of BYI 02960 and DFA (i.e. to be applied to the measured residue according to the residue definition for monitoring corrected with the correction factor CF to include <b>DFEAF</b>).  (b):The median processing factor is obtained by calculating the median of the individual processing factors of each processing study. The processing factor has to be applied to the sum of BYI 02960, DFA and <b>DFEAF</b> (residue definition for risk assessment).  (c): CF = correction factor to convert the residue for monitoring into the residue for risk assessment. The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.</p>			Pearl barley rub	2	<b>2.93</b>	2.87	<b>0.99</b>		Pearl barley	2	<b>0.12</b>	0.13	<b>1.10</b>		
Pearl barley rub	2	<b>2.93</b>	2.87	<b>0.99</b>													
Pearl barley	2	<b>0.12</b>	0.13	<b>1.10</b>													
3(95)	MRL Evaluation Report,	BCS (page 34, processing factors and			NL (May 2014): To be considered during	See open point 3(95)											

## section 3 – Residues (B.7)

Other comments																																							
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																			
	3.1.1.3 Effect of industrial processing...	<p>correction factors for wheat):</p> <ul style="list-style-type: none"> <li>- Conversion factors have to be estimated on same calculation basis for monitoring and risk assessment method (see above)</li> <li>- please correct value for white flour (0.33 instead of 0.36)</li> </ul> <p>=&gt; please consider that due to different rounding, slightly different values will occur for some of the conversion factors. However all CF are approx. 1 and the conclusion is that no conversion factor is needed.</p> <table border="1"> <thead> <tr> <th>Processed commodity</th> <th>No Mo</th> <th>Med ian PF (a) RO</th> <th>Med ian PF (b) RO</th> <th>Med ian CF (c)</th> </tr> </thead> <tbody> <tr> <td>Semolina bran</td> <td>2</td> <td>5.17</td> <td>4.99</td> <td>0.97</td> </tr> <tr> <td>Semolina</td> <td>2</td> <td>0.95</td> <td>0.98</td> <td>1.03</td> </tr> <tr> <td>White flour bran</td> <td>2</td> <td>6.63</td> <td>6.35</td> <td>0.96</td> </tr> <tr> <td>White flour</td> <td>2</td> <td><b>0.33</b></td> <td>0.36</td> <td>1.10</td> </tr> <tr> <td>white bread</td> <td>2</td> <td>0.27</td> <td>0.30</td> <td>1.14</td> </tr> <tr> <td>Whole meal</td> <td>2</td> <td>1.50</td> <td>1.48</td> <td>0.98</td> </tr> </tbody> </table>	Processed commodity	No Mo	Med ian PF (a) RO	Med ian PF (b) RO	Med ian CF (c)	Semolina bran	2	5.17	4.99	0.97	Semolina	2	0.95	0.98	1.03	White flour bran	2	6.63	6.35	0.96	White flour	2	<b>0.33</b>	0.36	1.10	white bread	2	0.27	0.30	1.14	Whole meal	2	1.50	1.48	0.98	revision of the ER	
Processed commodity	No Mo	Med ian PF (a) RO	Med ian PF (b) RO	Med ian CF (c)																																			
Semolina bran	2	5.17	4.99	0.97																																			
Semolina	2	0.95	0.98	1.03																																			
White flour bran	2	6.63	6.35	0.96																																			
White flour	2	<b>0.33</b>	0.36	1.10																																			
white bread	2	0.27	0.30	1.14																																			
Whole meal	2	1.50	1.48	0.98																																			

## section 3 – Residues (B.7)

Other comments						
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant			Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Whole meal bread	2	0.92	0.92	1.00
		Wheat germ	2	1.07	1.07	1.00
3(96)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (page 34, Table 3-3b, wheat): - Please correct header: Overview of the available processing studies with <b>wheat (USA)</b>			NL (May 2014): To be amended in revised ER	See open point 3(95)
3(97)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (page 34, Table 3-3b, wheat): - Was the processing factor in the USEPA evaluation really calculated on the basis of the residue definition for monitoring? (In the dossier submitted by BCS, the residue definition for risk assessment was the basis). - it is not conclusive that for IT crops no conversion factor is calculated, but for the EU crops => however if the conclusion from the EU trials is that no CF is needed, it is okay -the conclusion that the conversion factor monitoring/risk assessment will be set to 1 is missing – please add this in the conclusions			NL (May 2014): To be considered during revision of the ER.	See open point 3(95)
3(98)	MRL Evaluation Report, 3.1.1.3 Effect of industrial processing...	BCS (general remark): - No processing factors were described for lettuce, hops, peach, potato and sugar cane (these data were provided in the Annex II dossier)				See open point 3(95)
3(99)	MRL Evaluation Report,	BCS (page 41, 3.1.2.1 Preliminary			NL (May 2014): agreed, to be reviewed and	Open point

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	3.1.2 Rotational crops	considerations): Oilseed rape was also tested in a rotational crop study. To further substantiate residues in representative succeeding crops, rotational crop field studies performed <b>with-after</b> application of 2x125 g flupyradifurone/ha to bare soil and short plant back intervals in potatoes, leeks, cucumbers, onion, French beans, <b>and</b> peas and <b>oilseed rape</b> which are evaluated in this Evaluation Report.	amended.	RMS to amend in a revised ER the sections 3.1.2.1, 3.1.2.2 and 3.1.2.3 on rotational crops, taking into account the BCS comments 3(101), 3(102), 3(103), 3(104), 3(105) and 3(106). Conclusion of the expert meeting on residue definitions 3(8), 3(13), 3(26), and rotational crops 3(40) should be considered indeed.
3(100)	MRL Evaluation Report, 3.1.2 Rotational crops	BCS (page 41, 3.1.2.1 <i>Validation of the analytical method</i> ): - Typo in last paragraph - please add that method was also validated for crops with high oil content Flupyradifurone residues in the rotational crop field studies were determined using method 01304. The method was validated for the determination of parent BYI 02960 and its metabolites difluoroacetic acid (DFA) and BYI 02960-difluoroethyl-amino furanone ( <b>DFEAF</b> ) in crops <b>with high water and high acid content, in dry-starch crops and in crops with high oil content</b> .	NL (May 2014): agreed, to be reviewed and amended.	See open point 3(100)
3(101)	MRL Evaluation Report, 3.1.2 Rotational crops	BCS (page 41, 3.1.2.1 <i>Validation of the analytical method</i> ): - This paragraph refers only to the rotational field study conducted with three rotations ("main study"), however a lot of additional	NL (May 2014): - Agreed	See open point 3(100)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>rotational field studies were conducted with a 30-day plant-back interval  =&gt; Please adapt the paragraph  - Please correct the LOQ information</p> <p>The limit of quantitation (LOQ) for BYI 02960 and DFEAF, defined as the lowest validated fortification level, was 0.01 mg/kg in all matrices tested. All metabolite levels are expressed in parent equivalents. For DFA, the LOQ was 0.02 mg/kg in crop matrices high in acid and water content (e.g. oranges, tomatoes) or 0.05 mg/kg in dry/protein-rich matrices, fodder materials, and soybeans.</p> <p>⇒ Total calculated LOQ for crop matrices with high in acid and water content: 0.04 mg/kg</p> <p>⇒ Total calculated LOQ for dry/protein-rich matrices, fodder materials, and soybeans 0.07 mg/kg</p>	<ul style="list-style-type: none"> <li>- Agreed</li> </ul> <p>To be amended in revised ER</p>	
3(102)	MRL Evaluation Report, 3.1.2.2 Nature of residues	<p>BCS (page 42, 3.1.2.2 Nature of residues):</p> <p>- BYI 02960-difluoroethyl-aminofuranone (DFEAF) was only detected in higher amounts in the matrices of Swiss chard in the confined rotational crop studies (all rotations); in primary crops it was generally a minor metabolite.</p> <p>Since DFEAF was not observed in the rat and the metabolism studies indicated that no</p>	NL (may 2014): noted, to be amended.	See open point 3(100)

## section 3 – Residues (B.7)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		<p>other appropriate marker compound was present in rotational crops, BCS proposed to include this metabolite in the residue definition for risk assessment.</p> <p>Due to the results of the confined rotational crop studies, DFEAF was included in the residue definition for risk assessment.</p> <p>However, the only residues of BYI 02960 that were consistently observed at significant levels across all primary and succeeding crops in <u>field studies</u> were the parent compound BYI 02960 and DFA, both of which are specific to BYI 02960 use.</p>		
3(103)	MRL Evaluation Report, 3.1.2.3 Magnitude of residues	BCS (page 43, 3.1.2.2 Magnitude of residues, Table 3.1.2.3-01): - harvest interval for carrot: 95-114 days	NL (May 2014): to be amended.	See open point 3(100)
3(104)	MRL Evaluation Report, 3.1.2.3 Magnitude of residues	BCS (page 43-44, 3.1.2.2 Magnitude of residues, Table 3.1.2.3-03): - the residues given in the table are the sum of parent compound, DFA <b>and</b> DFEAF (all expressed in parent eq.) - how were the mean values (mean of NEU and SEU) calculated? - how was the CF calculated? Based on mean values calculated according to the different residue definitions (monitoring/RA)?	NL (May 2014): - agreed, to be amended - Table 3.1.2.3-02: the mean values were calculated with the OECD MRL with the values for calculator RA. To be amended. - The CF was calculayted by deviding the	See open point 3(100)

## section 3 – Residues (B.7)

Other comments																												
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																								
		<ul style="list-style-type: none"> <li>- cucumber DAT: <b>69-83</b></li> <li>- French bean: Residues in NEU: <b>0.59-1.1</b> Residues in SEU: <b>0.28-0.40</b></li> <li>- field pea DAT: <b>100-144</b></li> </ul>	<p>total residues with the RD for RA by the residues with the RD for enforcement. The median was calculated from the three or four CFs.</p> <ul style="list-style-type: none"> <li>- To be reviewed and amended</li> </ul>																									
3(105)	MRL Evaluation Report, 3.1.2.3 Magnitude of residues	<p>BCS (page 44, 3.1.2.2 Magnitude of residues, Table 3.1.2.3-03):</p> <ul style="list-style-type: none"> <li>- the residues given in the table are the sum of parent compound, DFA <b>and DFEAF</b> (all expressed in parent equivalents) – at least for the first line...</li> <li>- how was the CF calculated?</li> <li>- a separate MRL for root vegetables could be calculated based on the residues in rotational carrots and turnips</li> </ul> <table border="1" style="margin-top: 5px;"> <thead> <tr> <th colspan="4"><b>Total residue (BYI 02960 + DFA + DFEAF, expressed as BYI 02960) in mg/kg</b></th> </tr> <tr> <th>Crop</th> <th>STMR</th> <th>H R</th> <th>MR L</th> </tr> </thead> <tbody> <tr> <td>Root/Tuber veget.</td> <td>0.13</td> <td>0.2 7</td> <td><b>0.6</b></td> </tr> <tr> <td>Stem vegetables</td> <td><b>0.08</b></td> <td>0.2 5</td> <td><b>0.5</b></td> </tr> <tr> <td>Bulb vegetables</td> <td><b>0.08</b></td> <td>0.1 8</td> <td><b>0.3</b></td> </tr> <tr> <td>Fruiting vegetables</td> <td><b>0.32</b></td> <td>0.4 3</td> <td><b>0.9</b></td> </tr> </tbody> </table>	<b>Total residue (BYI 02960 + DFA + DFEAF, expressed as BYI 02960) in mg/kg</b>				Crop	STMR	H R	MR L	Root/Tuber veget.	0.13	0.2 7	<b>0.6</b>	Stem vegetables	<b>0.08</b>	0.2 5	<b>0.5</b>	Bulb vegetables	<b>0.08</b>	0.1 8	<b>0.3</b>	Fruiting vegetables	<b>0.32</b>	0.4 3	<b>0.9</b>	<p>NL (May 2014):</p> <ul style="list-style-type: none"> <li>- agreed, to be amended</li> <li>- The CF was calculated by dividing the total residues with the RD for RA by the residues with the RD for enforcement. The median was calculated from the three or four CFs</li> <li>- See 3(66)</li> </ul>	See open point 3(100)
<b>Total residue (BYI 02960 + DFA + DFEAF, expressed as BYI 02960) in mg/kg</b>																												
Crop	STMR	H R	MR L																									
Root/Tuber veget.	0.13	0.2 7	<b>0.6</b>																									
Stem vegetables	<b>0.08</b>	0.2 5	<b>0.5</b>																									
Bulb vegetables	<b>0.08</b>	0.1 8	<b>0.3</b>																									
Fruiting vegetables	<b>0.32</b>	0.4 3	<b>0.9</b>																									

## section 3 – Residues (B.7)

<b>Other comments</b>					
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant		Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Sweet corn	0.35	0.6 5	1.5
		legumes	0.50	1.1	2.0
		Leafy vegetables	0.08	0.2 1	0.4
		pulses	1.6	2.3	5
		oilseeds	0.10	0.1 7	0.3
		Cereal grains	0.35	0.6 5	1.5
3(106)	MRL Evaluation Report, 3.2 Nature of the magnitude of residues in livestock	BCS (page 45ff, 3.2 Nature of the magnitude of residues in livestock) - Please refer to the remarks made for the DAR - Please align tables in the DAR and the MRL Evaluation Report		NL (May 2014): agreed. DAR and ER to be aligned.	Open point RMS to align in the DAR and ER the sections related to residues in livestock
3(107)	MRL Evaluation Report, 4. Consumer risk assessment	BCS (page 60-62, Table 4-1 Input values for consumer risk assessment) - What is the reason for not using the IT- MRLs for the highly traded commodities: root & tuber vegetables; bulb vegetables; cattle and poultry matrices, except for milk and eggs?		NL (May 2014): in table 4-1, for the crops BCS mentions, IT MRLs are reported as input values.	Addressed Import tolerance values will be considered once the documentation requested under open point 3(25) provided.

## section 4 – Environmental fate and behaviour (B.8)

## 4. Environmental fate and behaviour

<b>Route and rate of degradation in soil (B.8.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(1)	Vol. 3, B.8.1.2.2, Field studies, page 135 and B.8.1.3 Summary route and rate of degradation in soil pages 138 and 140.	EFSA: It is not clear to us that the conclusion that the field dissipation observed for flupyradifurone and metabolite DFA was comparable to that found within the standardised laboratory studies is appropriate. Looking at the DT50 and DT90 endpoints for parent flupyradifurone, it could be that the compound is more persistent under field conditions than is indicated by the available lab incubations. It is difficult to do this comparison when the field studies have not been normalised to reference conditions. A further consideration of the field dissipation behaviour in comparison to that which was apparent from laboratory incubations would appear appropriate.	<b>APPL (04/2014) : The field data is not different from the laboratory data in that it does not result in longer DT50 values on average. A normalization may be conducted, however as the values are not required for modelling there seems no necessity.</b>  RMS (05/2014): The RMS agrees with the notifier. The conclusion could eventually be extended by an analysis according to the recent published EFSA guidance on DegT50	Addressed  RMS to consider providing the explanation in column 3 in a corrigendum or amended DAR.
4(2)	Vol. 3, B.8.1.2.2, Field studies, Kinetic analysis	DK: We acknowledge that drafting the DAR is a balance between giving important information and not to provide too bulky DAR's. However, we would have like to get more details on kinetic fitting of the field degradation studies (e.g. k1, k2, g), as the results are used later in the fate section.	RMS (05/2014): See 4(1). The results of the kinetic fits are not included in the DAR since these are not used for any further modelling except the maximum DT50 was used for the PECsoil calculations. The selection parameters for the fits visual and Chi2 error are given. For all field studies DFOP gave the best results and k values will be included in the revised assessment. In the summary of the PECsoil calculations the k1, k2 and g value is given that is been used for the calculations.	Open point  RMS to add the k1, k2 and g values for each DFOP fit for the field degradation studies for the DFOP fits to the list of endpoints.

## section 4 – Environmental fate and behaviour (B.8)

<b>Route and rate of degradation in soil (B.8.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(3)	Vol. 3,B 8.1, rate of degradation (Study IIA, 7.2.3/01)	DE: A table with soil characteristics and a table with the measured residues of the metabolite in the samples should be added to the summary of the study Lowden et al (1997).	RMS (05/2014): Agree, as described in the introduction of 6-CNA the study has been used for the review report of acetemiprid. Details on soil types can be found in this dossier. As the DAR for flupyradifurone should be read as a standalone document the information has to be included. The details will be included in a revised assessment report.	Addressed RMS to consider providing a table with soil characteristics and a table with the measured residues of the metabolite 6-CNA in the samples for the study Lowden et al (1997) in a corrigendum or amended DAR, i.e. the values included for this study in the peer review report of acetemiprid.
4(4)	Vol 1, Appendix 3, List of Endpoints, chapter 2.5	DE: Please add the soil names additionally to the soil types to the tables on degradation rate in soil, this will allow an easier attribution of the DT <sub>50</sub> and DT <sub>90</sub> values to the respective study summaries in Vol 3, B 8.	RMS (05/2014): The names are included in the assessment report. However the template of the LoEP foresees only soil types to be included. It will be checked if the relation with the soils in the studies is clear .	Addressed
4(5)	Vol 1, Appendix 3, List of Endpoints, chapter 2.5	DE: Since the DFOP kinetics evaluation of the active substance's degradation data are used later on for higher tier groundwater modelling and for PEC <sub>soil</sub> calculations, the parameters k <sub>1</sub> , k <sub>2</sub> and g of the kinetics should be added to the table on degradation and dissipation rates of flupyradifurone in the laboratory and in the field.	<b>APPL (04/2014): it may be of help to also show the corresponding DFOP parameters. However, the APPL would recommend an additional table in order to avoid confusing and overloaded table. The DFOP parameters used in the exposure assessments (PEC<sub>soil</sub> and PEC<sub>gw</sub>) are given in their respective section. Additionally, footnotes to the table "Rate of degradation in soil" indicate where the slow rate of the DFOP model fits were used to represent the degradation of flupyradifurone in soil.</b>  RMS (05/2014): See 4(2). The RMS agrees with the applicant. Such a table will be presented in an updated DAR.	Open point RMS to add the k <sub>1</sub> , k <sub>2</sub> and g values for each DFOP fit for the lab degradation studies for the DFOP fits as a minimum for the (AX) and (HN) soils to the list of endpoints. (i.e. the soils where for modelling the SFO DT50 was not selected).  See also open point at comment 4(2).  It is essential that this information is included in the list of agreed endpoints in the rate of degradation in soil section.

## section 4 – Environmental fate and behaviour (B.8)

<b>Route and rate of degradation in soil (B.8.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
				It would be appreciated if the RMS could also present the information as offered in a corrigendum or amended DAR.
4(6)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies	<b>Igor Kondzielski – IEP-NRI, Warsaw,</b> Poland: In the introductory paragraph to this whole section RMS declared that the kinetic analysis was performed using KinGUI tool. Could RMS specified which version of the tool – KingGUI 1 or KinGUI 2 was used? It might be of minor relevance, but while the KinGUI 1 offers only one fit option – OLS, the KinGUI 2 gives s possibility of choice between 3 – OLS, IRLS and MCMC, what may be considered as an additional refinement step. It might be useful, in case KinGUI 2 was used, to list the fit option selected as well.	APPL (04/2014), The APPL supports including the information regarding the KinGUI version in the introduction. The information is available in the individual methods sections already. However, the choice of a different solver for finding the global minimum in curve fitting exercises should not be regarded as a refinement step. It is rather an improved method to derive robust parameters for complex systems of degradation data. In the present case the data are not complex and were fitted with the PLS methods in KingGUI version 1.  RMS (05/2014): Agrees with notifier.	Addressed RMS to consider providing the clarification in column 3 in a corrigendum or amended DAR.
4(7)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies	<b>Igor Kondzielski – IEP-NRI, Warsaw:</b> There seems to be inconsistency In approach regarding to the selection of best fit made by the RMS. While in the first study – II A 7.2.1/01 (Menke U, 2011) the proposed by the Applicant selection of DFOP as best fit for AH and DD soil was rejected by the RMS and FOMC identified as returning the best fit, for the following studies such Applicant's approach was accepted by	RMS (05/2014): Agrees with the Igor Kondzielski, there seems to be an inconsistency. Initially the RMS states to use FOMC instead of DFOP. However, at the end of the evaluation 7.2.1/01 the RMS advises as the trigger endpoint to use DFOP as proposed by the applicant since the difference in DT50s are negligible.  For the other kinetic evaluation of soil	Addressed RMS to consider providing the clarification in column 3 in a corrigendum or amended DAR.

## section 4 – Environmental fate and behaviour (B.8)

<b>Route and rate of degradation in soil (B.8.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		the RMS. Moreover in the latter cases the exactly same justification for selecting DFOP above FOMC even though the latter returned statistically better fit, was accepted, while for the first study it was rejected. This looks like an inconsistent approach. Could RMS explain this?	degradation studies where DFOP was proposed instead of FOMC as best fit the difference between was DT50 regarded as negligible and the evaluation was not included.	
4(8)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies	<b>Igor Kondzielski – IEP-NRI, Warsaw:</b> the criteria of selection of the modelling endpoints for the parent compound seems to be not very clear. When examining the best-fit kinetics RMS declared that DFOP should be selected as returning the modeling endpoints and the slow phase should be used for this purpose. Were it so, why, for the same studies, in case of some soils this changed to SFO? This looks like inconsistent and confusing approach. Maybe it would be better to use the identified best-fit model to derive modeling endpoints instead of looking once again for them? Would RMs be so kind and explain this?	RMS (05/2014): The applicant followed the rules according the FOCUS Kinetics for endpoints as trigger and for modelling. The RMS accepted the approach used by the notifier.	Addressed
4(9)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies – rate of degradation of metabolite 6CNA	<b>Igor Kondzielski – IEP-NRI, Warsaw:</b> study by Lowden, Oddy and Jones (1997) is very briefly summarised with no information on soils used in examination, nor the experimental results. Probably more extent summary of this study can be found in the original (old) DAR for Flupyradifuron, never	RMS (05/2014): See 4(3).	See comment 4(3).

## section 4 – Environmental fate and behaviour (B.8)

<b>Route and rate of degradation in soil (B.8.1)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		the less it might be a good idea to transfer them into this document.		
4(10)	Vol. 3, B.8.1.2.1 – Rate of degradation in soil, Laboratory studies – rate of degradation of metabolite 6CNA	<p><i>Igor Kondzielski – IEP-NRI, Warsaw:</i> could RMS comment on such a huge difference of DT<sub>50</sub> values (8-10 fold) for 6-CAN obtained in studies II A 7.2.3/03 (Sur Dorn 2012) and IIA 7.2.3/04 (Shepherd, 2011). The results of one of them may not be fully reliable.</p> <p>Additionally, could RMS comment on why the results for 6-CNA in the study by Sur and Dorn (2012) were kinetically examined at all? These are very low levels of the compound detected, so the uncertainty related to so determined kinetic endpoints may be significant.</p>	<p>APPL (04/2014): The difference for DT50 values of 6-CNA is indeed quite large when considering the factor between the individual values. However, in general the data describes 6-CNA as a fast degrading compound with a range of DT50 values from 2.2 – 22.4 days representing a variability which is not uncommon.</p> <p>6-CNA has been identified as a major metabolite and thus it is mandatory to evaluate all relevant data and to respect the information in the exposure assessments. The low residue levels seemingly imply uncertain kinetic parameters, however, the results presented in Table B.8.1.2.1-35 show that the rate constant was well determined (t-prob &lt; 0.001).</p> <p>RMS (05/2014): Agrees with notifier.</p>	Addressed

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(11)	Vol. 3, B.8.2.1, batch	EFSA: We note that the batch adsorption 1/n	APPL (04/2014): The procedure to assume	Expert consultation

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	adsorption, pages 142 146 and 156. And B.8.2.4 summary adsorption, desorption and mobility in soil page 168.	values for the 4 European soils are used in the tier 2b groundwater modelling in combination with the adsorption parameters from the time dependent adsorption experiment for 4 European soils with the same names. Though the soils have the same names they are from different batches and have slightly different measured properties. In particular the organic carbon contents are somewhat different. (Table B.8.1.1-01 page 4 and Table B.8.2.1-02 page 142). This puts in question and adds uncertainty to the use of the time dependent sorption (TDS) approach in the tier 2b groundwater modelling. This also means the statement on page 168 'arithmetic mean of the 1/n of the four soils used from the batch adsorption and identical as the soils used for TDS' is inaccurate / misleading.	<p>1/n values from the paired batch equilibrium sorption study is a recommendation from Beulke and van Beinum (2012) in order to avoid over-parameterization of the TDS model fitted to the experimental results.</p> <p>Investigating the 1/n values from the batch sorption study it becomes clear that their coefficient of variation is very small accounting for only 1% for the four soils investigated. Comparing that to the coefficient of variation of the OC content of the soils accounting for &gt;350%. Thus it can be concluded that the nonlinearity of the Freundlich sorption is likely not dependent on the OC content of the soils. Therefore the use of the 1/n values in the TDS evaluation is justified and does not add uncertainty.</p> <p>RMS (05/2014): The TDS performed for the flupyradifurone was performed according to the latest guidelines Beulke and van Beinum (2012). The batch degradation study according to OECD 307 sample are initially extracted with <math>\text{CaCl}_2</math> solution in order to desorb active substance present in the soils. Afterwards other extraction methods were performed to extract additional active substance and/or possible metabolites. From the amount desorbed with the <math>\text{CaCl}_2</math></p>	Member state experts to discuss the time dependent sorption dataset and the appropriateness of the tier 2b groundwater modelling approach used, including the consideration of the RMS assessment of what is provided in response to the data requirement at reporting table comment 4(12). Experts to conclude if the available tier 2b simulations should be relied upon. Experts to discuss the issue of parameter correlation and discuss if averaging of simulation results for each soil rather than averaging input parameters from different soils is justified or whether the results from both approaches should be considered for decision making. <p>See reporting table comments 4(11), 4(12), 4(13), 4(16), 4(17), 4(31), 4(32) and 4(37).</p>

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>treatment at different time points the Rtds and other parameters are determined and modelled via the PEARLneq model. In order to obtain a 1/n for the estimated TDS parameters a batch adsorption with the same soils is advised. The soils were taken from the same locations but the soils were not from the same batch these therefore differ slightly. As explained there is no 1/n dependence with the %OC and using the 1/n doesn't add further uncertainty.</p> <p>The RMS has the opinion, after external scientific advice, that the TDS describes the fate and behaviour taken both degradation and aged sorption into account.</p>	
4(12)	Vol. 3, B.8.2.1, batch adsorption, page 157.	EFSA: We would find it helpful if the fitting of the time dependent sorption parameters could present results where the quality measures identified as being important in Beulke and van Beinum (2012) and earlier drafts, (that the RMS indicated were not done) have been completed. (I.e. plotting apparent adsorption with time and optimising using different starting parameters / transparently reporting all these optimisations).	<p><b>APPL (04/2014): The <math>R_{TDS}</math> values representing the apparent sorption overtime are given in form of a table (B.8.2.1-15) and are found to be equally good to assess the dynamics in time as it would be from a figure. The influence of starting values has not been reported as the parameter estimates showed robust predictions. The corresponding RSE values in Table B.8.2.1.17 indicate a very high level of parameter estimates. At the time of evaluating the TDS data the current revised guidance has not been available yet and the recommendation for different parameter starting values for <math>k_{des}</math> and <math>f_{ne}</math> was</b></p>	<p>Data requirement Applicant to submit reports of fitting of aged sorption experimental results, where a range of different starting parameters are investigated, with all these optimisations being transparently reported as outlined in the draft UK guidance Beulke and van Beinum (2012). Once applicant is confident that they have demonstrated that they have robust fitted parameters for each soil, applicant to rerun tier 2b simulations both averaging the input parameters from each available soil</p>

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>formulated more vaguely in the previous version. Given the excellent optimization results a test of the starting values was not conducted as the optimization results were expected to be independent.</p> <p>RMS (05/2014): Agree with notifier. In the evaluation the current criteria from the TDS guidance are evaluated and met.</p>	<p>and running simulation using results for each soil as input separately and then averaging the simulation results, as outlined in the draft UK guidance Beulke and van Beinum (2012).</p> <p>Note there are no' current criteria from the TDS guidance' as there is no agreed TDS guidance.</p>
4(13)	Vol. 3, B.8.2.4 summary adsorption, desorption and mobility in soil page 168.	EFSA: We do not agree that 'For BYI 02960 a fitted mean Koc,eq of 80.2 L/kg (Kom,eq of 46.5 L/kg) and the Freundlich exponent 1/n of 0.8605 can be used in higher tier simulation runs' Neither the associated geometric mean DT50_eq or K_des derived from the TDS study. This is because these factors are all expected to be correlated and soil property dependent so averaging them before input into a leaching model is considered by the regulatory community to be questionable. (This was identified by Beulke and van Beinum (2012) and earlier drafts). The draft guidance indicates that simulations should be done using the substance properties for each investigated soil separately and then taking a median value of the 80th percentile leaching concentration. When this approach gives a higher value than the approach presented in the DAR then the draft guidance	<p>APPL (04/2014): The TDS option is considered in the leaching models currently used in European regulation as a natural characteristic of pesticide behaviour. The nature of the TDS process description by differential equations comprising the 4 parameters also to be optimized in an evaluation inevitably leads to parameter correlations for the individual data sets. However, using individual parameter sets to derive separate PECgw values contradicts the principles laid out in FOCUS (2009) to use average fate parameters to describe the compounds behaviour. Moreover, averaging concentration without respecting the individual leachate volume may lead to wrong results. Furthermore it is stated that the information on PECgw from individual parameter sets should not be used for decision making.</p>	See expert consultation at comment 4(11) and data requirement at comment 4(12).

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		recommends that this value be compared to the regulatory trigger.	<p>The TDS parameters for Flupyradifurone show a high level of consistency among the four investigated soils. The coefficient of variation account for 20, 27, 5, and 27% for the parameters <math>K_{om,eq}</math>, <math>DT50_{eq}</math>, <math>k_{des}</math>, and <math>f_{ne}</math>, respectively. Which is in the range of the batch <math>K_{om}</math> (18%) and clearly lower than for the laboratory <math>DT50</math> (56%). Thus the TDS parameters seem to describe the behaviour of Flupyradifurone in soil more concisely. Therefore, the calculation for individual parameter sets appears not to be justified.</p> <p>RMS (05/2014): The point made by the EFSA is clear. On page 28 and 29 of the draft guidance on TDS (Beulk and Van Beinum, 2012) both methods are proposed assessing the individual parameters and averaging the PEC values or averaging the parameters and use them for leaching assessment. In the guidance it is stated that there is often a good agreement between the two options and that these should be compared. As pointed out by the notifier the coefficient of variation of the parameters for the four soils is small and it is expected that averaging the individual calculations of the PECgw will result in a similar result.</p>	
4(14)	B.8.2 Adsorption, desorption and mobility	FR : For flupyradifurone, Koc values were derived from soil which pH range is narrow	<b>APPL (04/2014): Flupyradifurone does no dissociates in aqueous solutions in the pH-</b>	Addressed RMS to consider providing the

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	in soil (IIA 7.1.2, 7.1.3, IIIA 9.1.2)  B.8.2.1 Batch sorption STUDY IIA, 7.4.1/03	(i.e. from 5.3 to 7.2). Please note that Koc values seem to decrease with higher pH values.  Then alkaline conditions may not be covered by this narrow pH range and risk assessment may not cover such conditions.  Further explanation: Alkaline conditions may have been investigated using the San Juan Bautista soil (used only for metabolite 6-chloronicotinic acid) having a soil pH value of 8.3.	range 1< pH <12) and hence there is no reason to expect a pH dependence of the sorption.  The range of tested pH values is about two units and reflects typical agricultural soils. Indeed, the Kom values seem to decrease with higher pH values, however, a statistical significant correlation could not be determined (e.g. by the Kendall test included in the German input decision tool). Moreover the coefficient of variation for the resulting Kom values accounts for 20 % and indicates a very good determination of this parameter. Looking at the Kf dependence on pH it becomes also clear that the magnitude of sorption is not dependent on pH.  RMS (05/2014): Agree with notifier.	clarification in column 3 in a corrigendum or amended DAR.
4(15)	B.8.2 Adsorption, desorption and mobility in soil (IIA 7.1.2, 7.1.3, IIIA 9.1.2)  B.8.2.1 Batch sorption STUDY IIA, 7.4.1/03	FR : Koc values for both 6-chloronicotinic acid and BYI 02960-DFA were derived using soil which pH (H <sub>2</sub> O) range is narrow (respectively from 6.2 to 8.3 and 5.8 to 7.4).	APPL (04/2014): For both metabolites the pH range of the soils is within the typical range of agricultural soils and there is no indication of a pH dependence of the sorption. This is not unexpected as the pKa of 6-CNA (3.28) and DFA (1.57) both indicate full ionisation above pH 5 and hence no influence of the pH of the soil would be expected  RMS (05/2014): Agree with the applicant, the	Addressed  RMS to consider providing the clarification in column 3 in a corrigendum or amended DAR.

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			pH range is 2 units difference which should be considered enough.	
4(16)	B.8.2 Adsorption, desorption and mobility in soil (IIA 7.1.2, 7.1.3, IIIA 9.1.2)  B.8.2.1 Batch sorption STUDY IIA, 7.4.1/03	<p>FR: FR agrees that time dependent sorption may be requested to adequately address pesticides leaching in soils as demonstrated in literature.</p> <p>The background information reviewed by RMS in its DAR would certainly be of interest for illustrating practical cases.</p> <p>Back to regulatory world, FR also agrees that no peer-review guidance on TDS have been adopted in Europe.</p> <p>Since there is no EU guidance on TDS, and for consistency with current risk assessment performed for PPP at EU level, TDS studies and following refinements based on TDS should be included as informative information only.</p> <p>Further explanation: If refinements may be proposed at EU level using TDS, one may acknowledge that for consistency at EU level and following national decisions a common agreement should be achieved on how implementing TDS in PPP risk assessment.</p>	<p><b>APPL (04/2014): We agree that refinement options presented at EU level should also be evaluated. In addition to the Tier 1 a higher Tier approach respecting a scientifically validated behavior, i.e. time dependent sorption which is included in standard leaching models should also be evaluated.</b></p> <p><b>The citation is misleading as the RMS clearly points out that the UK draft guidance has been recognized in that case. c.f: DAR_06_Volume_3_B-8.2.4 page 168, 3<sup>rd</sup> paragraph) also in the latter case. There the RMS refers to the UK draft TDS guidance to point out that at Tier 1 the Kom,eq values had been ignored.</b></p> <p>RMS (05/2014): For current assessment of active substances FOCUS 2009 is in place. Though only first tier was officially noted by the commission the use of higher Tier on a case by case base should be considered according to the latest scientific knowledge. The TDS studied for flupyradifurone is a perfect example where the parameters obtained can be used for higher tier leaching assessment. The uncertainty in the obtained parameters is small. The behavior of the</p>	See expert consultation at comment 4(11) and data requirement at comment 4(12).

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		Please note that in the DAR the “ UK guidance” is from time to time taken as reference : <i>“The RMS concludes that the study has been well conducted and that its results (i.e. decline curves of BYI 02960) are in line with the draft guidance on time dependent sorption and are suitable to be used in a kinetic analysis to calculate time dependent sorption parameters”</i> ; and sometimes not : <i>“The RMS was aware that in the guidance on how aged sorption studies for pesticides should be conducted, analysed and used in regulatory assessments () a different opinion is presented, i.e. not to combine the TDS and batch adsorption/desorption data »</i> .	active substance was studied in a soil batch degradation TDS experiment and a batch adsorption test with similar soils in order to obtain the 1/n. The results were also evaluated by external scientific experts and they indicated that the data are acceptable for higher tier risk assessment. There was a discussion with the external scientific experts on using the Kom,eq for the first Tier. The RMS decided not to use the Kom,eq for the first Tier. The RMS has the opinion that the obtained parameters are acceptable for higher tier groundwater risk assessment and should therefore be used and included in the risk assessment and in the list of endpoints.	
4(17)	B.8.2 Adsorption, desorption and mobility in soil (IIA 7.1.2, 7.1.3, IIIA 9.1.2)  B.8.2.1 Batch sorption STUDY IIA, 7.4.1/03	FR: The material and method to define accurate TDS parameters may not be accurate. For instance, the extraction performed may not accurately account for true available fraction. It may lead to underestimate the amount of available active substance and to overestimate adsorption. This may influence all the derived parameters and following calculations. TDS studies and following refinements based on TDS should be included as informative information only.  Further explanation:	<b>APPL (04/2014): The applicant agrees that an EU confirmed study definition may help to more accurately evaluate TDS parameters. Nevertheless, the extraction procedure employing CaCl<sub>2</sub> (0.01M) solution is widely accepted as being representative for soil solution and is also used in the standard batch sorption study. In case the adsorption is overestimated this would hold true for all batch sorption data as well.</b>  <b>RMS (05/2014): Agree with notifier, a 24 hours extraction employing CaCl<sub>2</sub> (0.01 M) is also proposed in the draft TDS guidance.</b>	See expert consultation at comment 4(11) and data requirement at comment 4(12).

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>																									
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																					
		If refinements may be proposed at EU level for future PPP risk assessment using TDS, definition and agreement on a material and method to define accurate TDS parameters would be of importance.																							
4(18)	Vol. 3, B 8.2, adsorption in soil (Study IIA, 7.1.2/01)	DE: A table with soil characteristics and a table with the concentration of the metabolite in the solid and liquid phase should be added to the summary of the study Lui (1997).	<p><b>APPL (04/2014), In the study of "Liu" (there is an error in the bibliographic data) the following pH of the soils are.</b></p> <table border="1"> <thead> <tr> <th>Soil type</th> <th>OC [%]</th> <th>pH</th> </tr> </thead> <tbody> <tr> <td>Loamy Sand I *</td> <td>0.25</td> <td>4.4</td> </tr> <tr> <td>Loamy Sand II</td> <td>1.5</td> <td>6.2</td> </tr> <tr> <td>Silt Loam</td> <td>0.44</td> <td>6.6</td> </tr> <tr> <td>Clay</td> <td>1.2</td> <td>7.5</td> </tr> <tr> <td>Clay Loam</td> <td>0.82</td> <td>8.3</td> </tr> <tr> <td>Pond sediment (Sandy Loam) **</td> <td>2.5</td> <td>5.6</td> </tr> </tbody> </table> <p>The remaining information is included in the report but does not add anything to the summary or understanding of the sorption characteristics.</p> <p>RMS (05/2014): agrees with the applicant,</p>	Soil type	OC [%]	pH	Loamy Sand I *	0.25	4.4	Loamy Sand II	1.5	6.2	Silt Loam	0.44	6.6	Clay	1.2	7.5	Clay Loam	0.82	8.3	Pond sediment (Sandy Loam) **	2.5	5.6	Addressed RMS to consider providing the clarification in column 3 in a corrigendum or amended DAR.
Soil type	OC [%]	pH																							
Loamy Sand I *	0.25	4.4																							
Loamy Sand II	1.5	6.2																							
Silt Loam	0.44	6.6																							
Clay	1.2	7.5																							
Clay Loam	0.82	8.3																							
Pond sediment (Sandy Loam) **	2.5	5.6																							

## section 4 – Environmental fate and behaviour (B.8)

<b>Adsorption, desorption and mobility in soil (B.8.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			for additional information the pH of the soils will be included in a revised assessment report.	
4(19)	Vol 1, Appendix 3, List of Endpoints, chapter 2.5	DE: Please add the soil names additionally to the soil types to the tables on the adsorption parameters in soil, this will allow an easier attribution of the parameters to the respective study summaries in Vol 3, B 8.	RMS (05/2014): LoEP template does not fore see in adding names.	Addressed
4(20)	Vol.3, B.8.2.1- Batch sorption, the adsorption/desorption of metabolite 6-CNA	<b>Igor Kondzielski – IEP-NRI, Warsaw:</b> The summary of the study by Lui (1997) reports the results of the examination of batch soil sorption of 6-CNA. However, in the table B.8.2.1-18 summarising the key results of this study one crucial soil property – soil pH is missing. This may be of particular importance for 6-CNA, which is a difluoroanalogue of acetic acid – one of the stronger organic acids, therefore prone to ionisation at favourable pH. For this reason the pH-dependence of the adsorption of this compound onto soil cannot be excluded and hence should be examined, what may be not possible without the information of soil pH. Could RMS insert these data into the indicated table?	<p><b>APPL (04/2014):</b> The study of Liu (1997) (there is a typo in the author name) refers to 6-CNA which is the chloronicotinic acid and not DFA (difluoroacetic acid)</p> <p>Further information on the soil pH is of course available and could be added to the table. However the study has already been evaluated at EU level and it was concluded that there was no pH dependence of the sorption behaviour. Considering the pKa of 6-CNA is 3.28 the conclusion of no pH dependence at relevant soil pHs is not unexpected.</p> <p>RMS (05/2014): agree with notifier, for additional information the pH of the soils will be included in the revised assessment report.</p>	Addressed RMS to consider providing the clarification in column 3 in a corrigendum or amended DAR.

## section 4 – Environmental fate and behaviour (B.8)

<b>PEC in soil (B.8.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(21)	Vol. 3, B.8.3, PEC soil, page 173  And Vol. 1, List of endpoints, PEC soil, page 208	EFSA: Are the PEC calculated for the metabolites correct? Have they accounted for the accumulated concentration of parent flupyradifurone precursor from use over repeated years? If they have then the metabolite DT50 must have been accounted for in the calculations. If this was the case then the information as reported in the DAR is insufficient to understand exactly how the concentrations were calculated.	APPL (04/2014) : The approach to calculate PEC <sub>soil</sub> values for metabolites was to use the maximum occurrence together with a molar correction in relation to the PEC <sub>soil, initial</sub> for the parent. The parent accumulation was not considered. When the parent accumulation is considered the PEC <sub>soil</sub> for metabolites should be calculated by a pathway approach but this is not currently part of the guidance for soil exposure calculations.  RMS (05/2014): Agrees with the applicant.	Data requirement  Applicant to provide PEC soil for metabolites that represent and include the situation that accumulated concentrations of the precursor active substance from repeated use over the years can occur. (worst case DT values to be used in calculations).
4(22)	Vol. 1, List of endpoints, PEC soil, page 207	EFSA: The PEC soil values for parent flupyradifurone in the list of endpoints are not consequent with the accumulated values calculated and presented in Table B.8.3-04 of Vol. 3 page 172. They should be. When updating this anomaly in the list of endpoints, further details / explanation is also required regarding mixing depths and depth assumed for the applications in the final year for the two crops.	RMS (05/2014): Agree with EFSA the RMS has forgotten to include the PECAccumulation in the list of endpoints. These will be included in a revised LoEP.	Open point  RMS to correct the PEC soil values in the list of endpoints for parent flupyradifurone so they are consequent to what is presented in Table B.8.3-04 of Vol. 3 page 172, further details / explanation to be included regarding mixing depths and depth assumed for the applications in the final year for the two crops.
4(23)	Vol. 3, B.8.3, Estimation of PECsoil, Parent	DK: RMS accept PECsoil calculation for a.s. We are not sure if the calculation is correct, as we get a different result. It would be easier to check to check the calculation, if the formula and the parameters were all present in the DAR. We agree that DFOP from worst case field study (UK) should be used, but in accordance with FOCUS	APPL (04/2014): The PECsoil calculation is done employing the worst case non-referenced DT50 in soil. As the corresponding data (i.e. Great Chishill, UK) were evaluated with a DFOP as the best fit it is justified and common practice to use the whole DFOP parameters in forward predictions for PECsoil calculations. The	Addressed  See also open point at comment 4(22).

## section 4 – Environmental fate and behaviour (B.8)

<b>PEC in soil (B.8.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		kinetics report, it is the slow phase DT50 that should be used (this can't be checked as it is not mentioned in the DAR).	<p>RMS may include the formula for calculating PECsoil and PECsoil accumulation when DFOP is assumed to illustrate the way of calculation.</p> <p>RMS (05/2014): Agree with the applicant. Opposite to what DK commented to our knowledge the current practice in calculating PECsoil is to use the worst case non normalised best fit DT50 value and this is in line with FOCUS kinetics. The use of slow phase is recommended for simulation modelling. The formula may be included in the revised DAR.</p>	

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(24)	Vol. 3, B.8.5, Impact on water treatment procedures, page 247.	EFSA: Article 4 (approval criteria for active substances) 3. (b) of Regulation (EC) No 1107/2009 requires that 'it shall have no immediate or delayed harmful effects on human health, including that of vulnerable groups, or animal health, ....through drinking water (taking into account substances resulting from water treatment)'. Information	<p>APPL (04/2014) : BCS does not have additional information or data on the issue. There is no current data requirement, nor is there any study guideline or risk assessment available.</p> <p>There are different disinfection processes available which water works apply as</p>	<p>Data Requirement</p> <p>Applicant to address the effect of water treatment processes on the nature of residues present in surface and groundwater, when surface water or groundwater are abstracted for drinking water. Probably in the first instance, a consideration of the</p>

## section 4 – Environmental fate and behaviour (B.8)

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		on the effect of water treatment processes on the nature of residues when surface water is abstracted for drinking water has not been presented or discussed in the DAR?	<p>needed, in different intensity and in different sequences. It is difficult to predict the effects of these disinfection treatments on residues of pesticides in the raw water, in particular since such effects will also depend on the highly variable chemical characteristics of the raw water. There are very few documented cases that disinfection treatment resulted in the formation of harmful by-products of pesticides. In addition, the formation of potentially harmful substances from treatment processes such as chlorination, ozonation or UV illumination can be related to any organic chemical in raw water, and is not a specific problem of pesticides. Water works that apply such treatments are well aware of the issue and take care that their treatments are set up in a way to minimize the risk (e.g. by minimizing treatment and treatment intensity, or by additional filtration steps after treatment).</p> <p>It is highly unlikely that Flupyradifurone or metabolites will be present in raw drinking water in relevant concentrations considering the surface water limitations and the groundwater legal limits.</p> <p>RMS (05/2014): Agree with the notifier with regard to the absence of clear guidance or</p>	processes of ozonation and chlorination would appear appropriate. If an argumentation is made that concentrations at the point of extraction for drinking water purposes will be low, this argumentation should cover metabolites predicted to be in groundwater and surface water, as well as the active substance. Should this consideration indicate novel compounds might be expected to be formed from water treatment, the risk to human or animal health through the consumption of drinking water containing them should be addressed.

## section 4 – Environmental fate and behaviour (B.8)

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>requirement for the effects of purification techniques in drinking water production sites. NL assesses whether drinking thresholds for active substances are exceeded at drinking water abstraction points. This approach is based on untreated water and does not consider any formation of byproducts.</p> <p>Different methods are in place in different MS. It is nearly impossible to cover all methodology in place over the EU with studies in the risk assessment. As flupyridifurone is not expected to reach the raw drinking water at relevant concentrations the potential risk of seems to be low. RMS would like to pinpoint to EFSA that not only the use of surface water is concerned but also groundwater.</p> <p>Further addressing this point in the regulation for the approval of substances should be taken to a general level and urgently asks for general guidance. RMS would kindly ask EFSA to take up this task</p>	
4(25)	Vol. 8.5, Impact on water treatment procedures	<p><b>Igor Kondzierski – IEP-NRI, Warsaw:</b> Only the potential impact of the residues of the Flupyradifuron on the wastewater treatment procedures was addressed. There is however no mention what could be a possible influence of the residues of this compound, itself or its degradation products on the processes of the abstraction of</p>	<p>APPL (04/2014), The respective EU requirement is just related to the relevant residue, and that is parent only in case of Flupyradifurone.</p> <p>Nor is there any study guideline or risk assessment scheme to address different disinfection processes available which water works apply as needed, in different intensity</p>	See data requirement at comment 4(24)

## section 4 – Environmental fate and behaviour (B.8)

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		drinking water. It was demonstrated that the aqueous photolysis may be a relevant process of transformation of the active substance in water, therefore it may become important if the residues of the parent reach the disinfection stage of drinking water purification. Would RMS be so kind and address the issue?	<p>and in different sequences. It is difficult to predict the effects of these disinfection treatments on residues of pesticides in the raw water, in particular since such effects will also depend on the highly variable chemical characteristics of the raw water. There are very few documented cases that disinfection treatment resulted in the formation of harmful by-products of pesticides. In addition, the formation of potentially harmful substances from treatment processes such as chlorination, ozonation or UV illumination can be related to any organic chemical in raw water, and is not a specific problem of pesticides. Water works that apply such treatments are well aware of the issue and take care that their treatments are set up in a way to minimize the risk (e.g. by minimizing treatment and treatment intensity, or by additional filtration steps after treatment).</p> <p>It is highly unlikely that Flupyradifurone or metabolites will be present in raw drinking water in relevant concentrations considering</p> <p>RMS (05/2014): See 4(24)</p>	

## section 4 – Environmental fate and behaviour (B.8)

<b>Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(26)	Vol. 3, B 8.4.3.2, degradation in water-sediment systems (Study IIA, 7.8.3/04)	DE: Has it been tested during or before the study, if the active substance does not adsorb to the plastic foil used to line the ponds? Were the residues in the biota (e.g. the lentils) analyzed? If yes, could this information please be added to the summary? Such studies might be used at some point to decide on the fulfilment of the P-criteria for PBT substances, this information is therefore important to evaluate if the dissipation of the active substance is actually mainly degradation.	APPL (04/2014), The fate-o-cosm was performed in an enclosure set-up. The concentration pattern of Flupyradifurone was investigated under realistic exposure conditions in a semi-field pond system. There is no risk that adsorption to the plastic foil played a role as there is no direct contact to the plastic foil. The enclosures used are set up within a pond in such a way that they are embedded in the sediment layer which covers the plastic foil. Therefore a direct interaction between the test item and the foil can be excluded. The adsorption to the material of the enclosures does not play a role as before the test item is applied there is already a biofilm (e.g.algae) growing on the enclosure surface. Therefore the system simulates a field situation without a negative impact of the materials used on the availability of the test item.  RMS (05/2014): Agree with notifier.	Addressed  RMS to consider providing the clarification in column 3 in a corrigendum or amended DAR.
4(27)	Vol. 3, B 8.4.3.2, degradation in water-sediment systems (Study IIA, 7.8.3/04)	DE: The column headers in Table B.8.4.3.2-38 are mixed up and need to be corrected.	APPL (04/2014), This is correct, the columns have been confused the table should read as follows  RMS (05/2014): Agree with notifier, table header will be updated in the revised risk assessment.	Addressed  RMS to consider providing the clarification in column 3 in a corrigendum or amended DAR.

## section 4 – Environmental fate and behaviour (B.8)

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)										
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant						Column 4 Data requirement or Open point (if data point not addressed or fulfilled)	
			Study Day	Control (1)	10 µg a.i./L (1)	100 µg a.i./L (1)				
			2010	(2)	µg BYI 02960 /kg dry weight	% of applied BYI 02960	µg BYI 02960 /kg dry weight	% of applied BYI 02960		
			03.06	n.d. 1	n.d.	n.d.	n.d.	n.d.	n.d.	
			09.06	< LQ	3.6 3.0 .3	5.4 .3 .4	1.2 8.7 .9	1.1 1.2 1.9		
			16.4	< L	3.8 3.0 .3	5.4 .4 .4	1.2 2.4 .4	2.2 3.6		

## **Reporting table, flupyradifurone**

24.06.2014

215/311

## section 4 – Environmental fate and behaviour (B.8)

## section 4 – Environmental fate and behaviour (B.8)

<b>PEC in surface water and in ground water (B.8.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(28)	Vol. 3, B.8.6.1, PEC in surface water, page 248.	EFSA: The statement 'There are currently no agreed European guidelines for the assessment of exposure of surface water from the use in glasshouses' is not accurate. FOCUS air guidance recommends that 0.2% emission from glasshouses to surface water is an exposure assumption that can be used. EFSA can however accept the approach taken of the assumption 'that the use in glasshouses on lettuce is covered by the outdoor field use even considering the different use pattern.', provided that the RMS can confirm that the mitigation considered for the field uses would mean that the exposure of surface water would be > than would occur assuming 0.2% emission from glasshouses (the currently noted EU guidance).	<p><b>APPL (04/2014): At the date of submission of the dossier, and even today, there is no common agreement on the assessment of exposure from greenhouse uses. This can only be addressed at member state level when the products are evaluated.</b></p> <p>RMS (05/2014): The generally accepted Dutch approach of 0.1 % emission is used in many other DARs for greenhouse applications. The 0.2 % emission from FOCUS air is generally used for more volatile compounds for ultralow volume spraying. If the 0.1% is applied the greenhouse use the proposed field uses cover the greenhouse use.</p>	Open point EFSA to indicate in its conclusion that the surface water exposure assessment for the field uses covers exposure from the assessed glasshouse uses provided that ultra low volume application techniques are not used in the glasshouses and that this application technique has not been assessed / may not be covered in the available assessment.
4(29)	Vol. 3, B.8.6.1, PEC in surface water, pages 251-255.  Vol. 1, List of endpoints, PEC surface water and sediment, pages 212-216 and TER step 4 pages 231-232 and 236-238.	EFSA: Some of the FOCUS step 4 calculations presented that combine no spray buffer distances with drift reducing nozzles do not respect the upper limit on total drift reduction in FOCUS landscape and mitigation guidance that is a maximum drift reduction of 95%. PEC and TER where drift is mitigated by more than 95% should not have been presented in the DAR or list of endpoints.	<p><b>APPL (04/2014): The presented values show a comprehensive summary of combinations of drift reductions by distance and the application of drift reducing technologies. On some occasions these combinations may exceed 95% drift reduction; however, the majority of case do not exceed this value.</b></p> <p>RMS (05/2014): All mitigation measures are presented for completeness. Agree that RMS could have made a comment in the</p>	Open point RMS to remove from the list of endpoints all PECsw and TER values derived from situations where spray drift has been mitigated by > 95%.

## section 4 – Environmental fate and behaviour (B.8)

<b>PEC in surface water and in ground water (B.8.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			remarks. This will be included in the revised assessment report.	
4(30)	Vol. 3, B.8.6.1, PEC in groundwater, page 260.  Vol. 1, List of endpoints, PEC groundwater, pages 219-220	EFSA: Footnotes indicate 'Data provided to justify that the plant uptake factor for the active substance and metabolites is 0.5'. What were these data? Where are they evaluated?	<b>APPL (04/2014): The parent compound is systemic and thus a PUF of 0.5 is justified. Additionally, the ECPA paper by Schriever et al (2013) was cited where PUF values for broad range of substances were shown to account for 1.0. Thus the use of the default 0.5 was selected.</b>  <b>RMS (05/2014): The data is available. A footnote with the reference to the paper was not included. This will be included in the revised assessment report an evaluation will be included if required.</b>	Open point RMS to provide an evaluation of the evidence that the use of a TSCF in FOCUS modelling of 0.5 for the active substance and its metabolites was justified.
4(31)	Vol. 3, B.8.6.1, PEC in groundwater, page 259-269.  Vol. 1, List of endpoints, PEC groundwater, pages 218-223	EFSA: We would not consider it appropriate to accept the tier 2b groundwater simulations regarding the parent flupyradifurone that are currently presented without further clarifications. Further to the EFSA comments above in the section 'Adsorption, desorption and mobility in soil (B.8.2)' EFSA would need further information from the applicant regarding the uncertainty created by the fact that the soils used in the batch aged adsorption experiments (from which 1/n was derived) are not 'identical' to those used in the TDS experiment, in particular OC content. We would also wish to have further detail / reassurance on the way that the	<b>APPL (04/2014): The procedure to assume 1/n values from the paired batch equilibrium sorption study is a recommendation from Beulke and van Beinum (2012) in order to avoid over-parameterization of the TDS model fitted to the experimental results.</b>  <b>Investigating the 1/n values from the batch sorption study it becomes clear that their coefficient of variation is very small accounting for only 1% for the four soils investigated. Comparing that to the coefficient of variation of the OC content of the soils accounting for &gt;350%. Thus it can be concluded that the nonlinearity of the</b>	See expert consultation at comment 4(11) and data requirement at comment 4(12).

## section 4 – Environmental fate and behaviour (B.8)

<b>PEC in surface water and in ground water (B.8.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		pertinent parameters were fitted from the results of the TDS experiments on each of the soils. Finally we would also wish to see groundwater simulations at tier 2b where the results are expressed as a median of the 80 <sup>th</sup> percentile values with separate sets of simulations completed for each of the 4 soils, in addition to the current approach where averages of the substance input parameters from the 4 soils have been input to the model.	<p>Freundlich sorption is likely not dependent on the OC content of the soils. Therefore the use of the 1/n values in the TDs evaluation is justified does not add uncertainty.</p> <p>RMS (05/2014): See 4(11) and agree with the notifier.</p>	
4(32)	B.8.6 Predicted environmental concentrations in surface water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3)  B.8.6.3 Predicted concentrations in groundwater (Annex IIIA 9.2.1)	FR: Since there is no EU guidance on TDS, and for consistency with current risk assessment at EU level, TDS studies and following PEC gw refinements based on TDS should be included as informative information only and deleted from the LoEP.	<p>APPL (04/2014): We agree that refinement options presented at EU level should also be evaluated. The higher Tier approach respecting a scientifically validated behavior, i.e. time dependent sorption which is included in standard leaching models should also be evaluated. While MS may apply their own parameter requirements at national product evaluation and the listing of the TDS parameters in the LoEP should remain as it describes a realistic behavior of Flupyradifurone in soil and will facilitate the harmonization of approach at MS level.</p> <p>RMS (05/2014): See 4(16) and RMS agrees with notifier.</p>	See expert consultation at comment 4(11) and data requirement at comment 4(12).
4(33)	B.8.6 Predicted environmental concentrations in surface	FR: It should be confirmed and indicated in the DAR that the mitigation factors used for runoff are according to FOCUS L&M.	<p>APPL (04/2014) FS: We agree that mitigation options should be referenced to the L&amp;M factors. The corresponding</p>	Addressed RMS to consider providing the clarification in column 3 in a

## section 4 – Environmental fate and behaviour (B.8)

PEC in surface water and in ground water (B.8.6)																																																																																								
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)																																																																																				
	water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3)  B.8.6.1 Predicted concentrations in surface water (Annex IIIA 9.2.3)	It's not obvious which mitigations values were used for 10; 15 and 20 m vegetative buffer strips, please clarify.	<p>information was provided to the RMS and may be included in the DAR.</p> <p>RMS (05/2014): agrees with notifier and the information will include the revised assessment report .</p> <table border="1"> <thead> <tr> <th>Crop</th><th>Fractional reduction in:</th><th>10m</th><th>15m</th><th>20m</th></tr> </thead> <tbody> <tr> <td rowspan="4">Lettuce 1</td><td>Runoff:</td><td>Volume</td><td>0.6</td><td>0.8</td></tr> <tr><td></td><td>Flux</td><td>0.6</td><td>0.8</td></tr> <tr><td>Erosion:</td><td>Mass</td><td>0.85</td><td>0.95</td></tr> <tr><td></td><td>Flux</td><td>0.85</td><td>0.95</td></tr> <tr> <td colspan="5"><hr/></td></tr> <tr> <td colspan="5"><hr/></td></tr> <tr> <td rowspan="4">Lettuce 2</td><td>Fractional reduction in:</td><td>10m</td><td>15m</td><td>20m</td></tr> <tr><td>Runoff:</td><td>Volume</td><td>0.6</td><td>0.6</td></tr> <tr><td></td><td>Flux</td><td>0.6</td><td>0.6</td></tr> <tr><td>Erosion:</td><td>Mass</td><td>0.85</td><td>0.85</td></tr> <tr><td></td><td>Flux</td><td>0.85</td><td>0.85</td></tr> <tr> <td colspan="5"><hr/></td></tr> <tr> <td colspan="5"><hr/></td></tr> <tr> <td rowspan="4">Hops</td><td>Fractional reduction in:</td><td>10m</td><td>15m</td><td>20m</td></tr> <tr><td>Runoff:</td><td>Volume</td><td>0.6</td><td>0.8</td></tr> <tr><td></td><td>Flux</td><td>0.6</td><td>0.8</td></tr> <tr><td>Erosion:</td><td>Mass</td><td>0.85</td><td>0.95</td></tr> <tr><td></td><td>Flux</td><td>0.85</td><td>0.95</td></tr> </tbody> </table>	Crop	Fractional reduction in:	10m	15m	20m	Lettuce 1	Runoff:	Volume	0.6	0.8		Flux	0.6	0.8	Erosion:	Mass	0.85	0.95		Flux	0.85	0.95	<hr/>					<hr/>					Lettuce 2	Fractional reduction in:	10m	15m	20m	Runoff:	Volume	0.6	0.6		Flux	0.6	0.6	Erosion:	Mass	0.85	0.85		Flux	0.85	0.85	<hr/>					<hr/>					Hops	Fractional reduction in:	10m	15m	20m	Runoff:	Volume	0.6	0.8		Flux	0.6	0.8	Erosion:	Mass	0.85	0.95		Flux	0.85	0.95	corrigendum or amended DAR.
Crop	Fractional reduction in:	10m	15m	20m																																																																																				
Lettuce 1	Runoff:	Volume	0.6	0.8																																																																																				
		Flux	0.6	0.8																																																																																				
	Erosion:	Mass	0.85	0.95																																																																																				
		Flux	0.85	0.95																																																																																				
<hr/>																																																																																								
<hr/>																																																																																								
Lettuce 2	Fractional reduction in:	10m	15m	20m																																																																																				
	Runoff:	Volume	0.6	0.6																																																																																				
		Flux	0.6	0.6																																																																																				
	Erosion:	Mass	0.85	0.85																																																																																				
	Flux	0.85	0.85																																																																																					
<hr/>																																																																																								
<hr/>																																																																																								
Hops	Fractional reduction in:	10m	15m	20m																																																																																				
	Runoff:	Volume	0.6	0.8																																																																																				
		Flux	0.6	0.8																																																																																				
	Erosion:	Mass	0.85	0.95																																																																																				
	Flux	0.85	0.95																																																																																					
4(34)	B.8.6 Predicted environmental concentrations in surface water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3)  B.8.6.1 Predicted	<p>FR: PECsw and sed provided for hops include at minimum a nozzle drift reduction of 25 %. Please provide additional values including no drift reduction for relevant uses.</p> <p>In FR, mitigation measures based on nozzle drift reduction can not be proposed (only untreated and vegetated buffer zones can be).</p>	<p>APPL (04/2014) : This refers to specific French requirements and therefore does not need to be addressed for the Active Substance registration but only in the national submissions, the use of drift reducing nozzles as a mitigation measure is well established and encouraged.</p>	See open point at comment 4(29).																																																																																				

## section 4 – Environmental fate and behaviour (B.8)

<b>PEC in surface water and in ground water (B.8.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	concentrations in surface water (Annex IIIA 9.2.3)		RMS (05/2014): agrees with notifier	
4(35)	B.8.6 Predicted environmental concentrations in surface water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3) B.8.6.1 Predicted concentrations in surface water (Annex IIIA 9.2.3)	FR: Please confirm that no PECsed accumulation are needed for the intended uses (see ecotox section).	<p><b>APPL (04/2014): It was stated that comparison to the PECsw values is the appropriate risk assessment, hence no PECsed accumulation is required (additionally there is no agreed method to calculate such PECs).</b></p> <p>RMS (05/2014): agree with notifier.</p>	Addressed For these representative uses where only a single application per year or every two years is requested (excepting glass house uses where there are two applications but 0.1-0.2 % emission are usually assumed) for a substance with a Koc of 98.4mL/g, flow in the water bodies (including ponds) and desorption from sediment are expected to mean that accumulation in sediment from use in successive years is unlikely for flupyraifurone (even though the half life assumed in modelling is long at 228 days (ascribed to water but is a whole system value) and 1000 days in sediment). Consequently completing the risk assessment to chironomous using the max PECsw and water concentration from a water spiked test as an endpoint can be accepted in this case. However for outdoor uses with multiple applications in the same year PEC sediment would have to be used in the risk assessment to address the risk to sediment dwellers. See also reporting table comment

## section 4 – Environmental fate and behaviour (B.8)

<b>PEC in surface water and in ground water (B.8.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(36)	Vol. 3, B.8.6.3, PECgw, conversion of SFo to DFOP, pp 259	DK: Is it reasonable to estimate that 'g' by default is 0.5 for all soils were no 'g' value has been calculated.	<b>APPL (04/2014) FS:</b> For soils where the most appropriate kinetics were SFO it is reasonable to assume an equal distribution (i.e. g=0.5) if pseudo-DFOP is imposed. In case of SFO the whole mass degrades at the same rate whereas in case of DFOP two parallel rates degrade the mass splitted by the "g". By recognizing the pseudo-DFOP as well the average of the faster first rate decreases slightly (i.e. degradation takes longer) and the corresponding mass-fraction is slightly higher (i.e. g increased)  RMS (05/2014): agree with notifier	5(21).  Addressed The argument can be accepted in this case for this data set. Consideration might be different with other datasets where the distribution of g values from different soils was different.
4(37)	Vol. 3, B.8.6.3, PECgw, Tier 2b, Time dependent sorption, hops and lettuce	DK: We have difficulties with this the use of time dependent sorption (tda) as a mean of refinement before harmonised guidelines for the derivation, use and assessment of tda has been agreed by EFSA (which to our knowledge is not the case). This is in line with the decision at the fate expert meeting at EFSA in September 2013. The gw assessment should be changed accordingly.	<b>APPL (04/2014) FS:</b> There is substantial guidance presented by Beulke and van Beinum since 2012 and before that has been discussed on an European level, it is noted that this has not yet been agreed by EFSA. Nevertheless, the presented case includes TDS data at a very high level of integrity that fulfils all the requirements on the experimental enforcement and parameter estimation and clearly shows that Flupyradifurone exhibits TDS behavior in soil. The tiered approach is also fully in-line with the guidance documents on groundwater risk assessment.	See expert consultation at comment 4(11) and data requirement at comment 4(12)

## section 4 – Environmental fate and behaviour (B.8)

<b>PEC in surface water and in ground water (B.8.6)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			RMS (05/2014): The substance where the TDS was not accepted showed besides aged sorption also pH dependent sorption. At the expert meeting this was considered to many uncertainties to accept the refinement. As indicated in the reporting table for flupyradifurone the obtained parameters are reliable and the studies are externally evaluated by TDS experts. Therefore, RMS considers these data acceptable for higher tier purposes.	
4(38)	Vol. 3, B.8.6.3, PECgw, metabolites	DK: We are of the opinion, that all metabolites are relevant and refined gw-modelling should be pursued until the concentration for all soils (at least in one zone for zonal approach or majority for inter-zonal approach) are under 0.1 ug/L. The gw assessment should be changed accordingly.	<b>APPL (04/2014): This is a national specific comment valid only for Danish registration, for the registration of the active substance the relevance of any metabolites in groundwater is assessed according to the valid European Regulation : Sanco/221/2000 –rev.10- final 25 February 2003</b> <b>The comment on zonal or inter-zonal approaches is also irrelevant to the registration of the active substance.</b>  RMS (05/2014): agree with notifier	Addressed
4(39)	Vol. 3, B 8.6.3, predicted concentrations in groundwater	DE: An application of a PPP only every 2 <sup>nd</sup> year to a permanent crop like hops will be very difficult for risk management to implement and to control; we thus suggest to delete this refinement option here and to generally only apply it to non-permanent crops that are generally cultivated in crop	<b>APPL (04/2014), Biennial applications are not unusual in permanent crops. Specifically in delicate crops such as hops, a biennial application is an important tool for resistance management and common practice. The environmental risk assessment covers this use.</b>	Open point RMS to update the list of endpoints GAP table row for hops to indicate that biennial (and not biannual) application is the representative use. The GAP table in the DAR from the

## section 4 – Environmental fate and behaviour (B.8)

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		rotations.	This is not presented as a refinement option but represents the actual intended use of the product.  RMS (05/2014): agree with notifier	beginning has indicated the representative use on hops is only every other year. Therefore this is the representative use that has been assessed.
4(40)	Vol. 3, B 8.6.3, predicted concentrations in groundwater	DE: No tier 2A and 2B groundwater modelling was performed for the metabolite 6-CNA; however refinement modelling for the metabolite DFA shows that the simulated decrease in groundwater concentration for the active substance is correlated with an increase in groundwater concentration for the metabolites. Since the tier 2A and 2B groundwater modelling is considered more realistic it should also be performed for 6-CNA to ensure that the concentrations of this metabolite remain <0.1 µg/L.	APPL (04/2014),: The correlation of the DFA groundwater concentration with the decreasing concentration of the active suggested by the MS is not given statistically.  The presentation of additional groundwater values for 6-CNA would not change the conclusion that the concentration is << 0.1 µg/L (maximum 0.012 µg/L).  RMS (05/2014): agree with notifier	Addressed
4(41)	Vol. 8.6.1, Predicted Environmental Concentrations in SW – calculations for the parent compound	<b>Igor Kondzieski – IEP-NRI, Warsaw:</b> The calculations were performed at Steps 1-4 using a standard set of FOCUS tools plus SWAN 1.1.4 for Step 4 calculations. At Step 4 one of the mitigation measures was the application of 15-meter buffer zone for spray drift and runoff in case of lettuce (e.g table B.8.6.1-11). Could RMS explain what reduction factors were used for runoff for 15-metres buffer zone and how this possibly complies with the recommendations given by FOCUS L&M Guidelines?	APPL (04/2014): The information from the corresponding modelling report is available and can be added by the RMS if required.  RMS (05/2014): See 4(33)	See comment 4(33).

## section 4 – Environmental fate and behaviour (B.8)

<b>Fate and behaviour in air and PEC in air (B.8.7-8.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)

<b>Definition of the residues (B.8.9)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
4(42)	General	EFSA: A search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, being conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) does not appear to be available. Searches	APPL (04/2014) A literature review was performed and included in Doc. N. No relevant literature was identified.  RMS (05/2014) The conclusions and evaluation of the literature review will be included in the revised draft assessment	Open point  RMS to present an evaluation of the literature review completed by the applicant in an addendum.  Data requirement  Applicant to provide a search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within

## section 4 – Environmental fate and behaviour (B.8)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		need to have been done and consider both the active substance and identified metabolites.		the last 10 years before the date of submission of dossier, being conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) for the aqueous photolysis metabolites BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide that do not appear to have been included in the available literature review.
4(43)	Vol1; LoEP	FR: Since there is no EU guidance on TDS, and for consistency with current risk assessment of AS at EU level, TDS studies and following PEC gw refinements should be deleted from the LoEP	<b>APPL (04/2014): The higher Tier approach respecting a scientifically validated behavior, i.e. time dependent sorption which is included in standard leaching models should also be evaluated. MS may apply their own parameter requirements at national product evaluation and the listing of the TDS parameters in the LoEP should remain as it describes a realistic behavior of Flupyradifurone in soil and will facilitate the harmonization of approach at MS level.</b>  <b>RMS (05/2014): See 4(16) and RMS agrees with the applicant.</b>	See expert consultation at comment 4(11) and data requirement at comment 4(12).
4(44)	B.8.3 Predicted environmental	FR: FR agrees with RMS that there are currently no agreed European guidelines for	<b>APPL (04/2014) : As there is no agreed scheme for the risk assessment an</b>	Addressed RMS to consider providing the

## section 4 – Environmental fate and behaviour (B.8)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	concentrations in soil (PECs) (Annex IIIA, 9.1.3) B.8.6 Predicted environmental concentrations in surface water, in sediment and in groundwater (PECsw, PECsed, PECgw) (Annex IIIA 9.2.1, 9.2.3)	the assessment of exposure from the use in glasshouses the pragmatic approach assuming that the use in glasshouses is covered by the outdoor field use. Still, when checking the approach in the different compartments, the approach followed is not the same: For soil it is assumed that the use in glasshouses is covered by the outdoor field use (no PEC and no reference of the different use pattern); for GW, calculations were provided using specific GAP for indoor use (2 applications); and for SW it is was assumed that the use in glasshouses is covered by the outdoor field use even considering of the different use pattern. Please clarify.	<b>additional calculations would not add to the risk assessment.</b>  RMS (05/2014): For soil bound glasshouse applications the soil exposure is not assessed. Soils in glasshouses are treated before growth of the crop new and natural population is not expected (Dutch approach). Therefore these soils are not assessed. Emissions to the surface water is set at 0.1 %. This is the generally EU accepted Dutch approach and used in other DAR for greenhouse application. The outdoor applications cover the glasshouse in this case. For groundwater the a spring scenarios is assessed and included in the assessment report.	clarification in column 3 in a corrigendum or amended DAR. Also see open point for EFSA at comment 4(28) in respect of the surface water exposure assessment and ultra low volume application methods.
4(45)	Vol. 1, Level 3, proposed decision on POP, PBT, vPvB, candidate for substitution	DE: An evaluation as to the question whether the active substance has POP, vPvB or PBT properties and whether it should be regarded as a candidate for substitution is missing. This evaluation should be included to Volume 1, Level 3 according to Guidance Document SANCO/12592/2012 –rev. 0 November 2012 (Template to be used for Assessment Reports); please also include short explanatory notes how the decisions were derived and which data were used to decide on the separate criteria.	RMS (05/2014): For this dossier this is not a data requirement is not applicable.	Open point RMS to provide in an addendum to volume 1, Level 3 their assessment against the annex II approval criteria; please also include short explanatory notes how the decisions were derived and which data were used to decide on the separate criteria.. It is suggested to follow Guidance Document SANCO/12592/2012 –rev. 0 November 2012 (Template to be used for Assessment Reports). The substance is assessed / will be

## section 4 – Environmental fate and behaviour (B.8)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
				approved under Regulation (EC) No 1107/2009, therefore a conclusion against these criteria is a responsibility of the RMS.

## section 5 – Ecotoxicology (B.9)

## 5. Ecotoxicology

<b>Birds and mammals (B.9.1 and B.9.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(1)	Vol. B.9.1, General	EFSA: It is noted that the short-term endpoints are considerably higher than the acute endpoints (mainly from encapsulated studies), which is a rather strange pattern. Is there any explanation for that?	APP (April/2014): contrary to the EFSA statement, lower toxicity after dietary exposure (even if repeated) than in single oral gavage or capsule dosing studies is in the opinion of the APP very typically observed, not only in avian toxicology studies but also in toxicology. The main reasons for lower toxicity in dietary are typically (a) repeated uptake occurs over time, involving metabolism and/or excretion to reduce the body burden before the next exposure, and (b) the much lower concentration of substance in the diet mix than in the oral dose, influencing the absorption rate. Therefore acute oral dosing studies have been often considered as unrealistic worst case for use in dietary exposure scenarios for animals that cannot ingest a lethal dose in one meal (feeding bout).  NL (May 2014): Agree with applicant.	Addressed.
5(2)	Vol. B.9.1.3, Long-term study on mallard	EFSA: EFSA shares the original concerns of the RMS regarding several reproductive parameters in the medium doses and considers that the further assessments (including considerations for outliers) were necessary for the conclusion and endpoint	APP (April/2014): we still consider the endpoint conclusions for this study as overly conservative since no impact on overall reproductive performance was observed at the test level assigned as the LOEC by the RMS, just statistical significance of a small	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		setting.	difference at a single one of the many steps along the “egg to 14-d survivor pathway”, not resulting in a lower number of chicks per egg set.  NL (May 2014): Noted.	
5(3)	Vol. B.9.1.3, Long-term study on quail	EFSA: It is just noted that it seems to be strange that for the parameter of eggs set/eggs laid (%) the higher difference in the lower concentration was not statistically different, while the lower average difference in the higher concentration was. It is assumed that the standard deviation of the data was significantly different.	APP (April/2014): the relative standard deviation (coefficient of variation CoV) around the means for “eggs set of eggs laid” is rather low for all test levels:  Control: 88.7 +/- 7.5 (CoV 8.5%) low concentration 111 ppm: 86.3 +/- 5.3 (CoV 6.1%) mid concentration 333 ppm: 87.1 +/- 3.5 (CoV 4.0%) top concentration 1000 ppm: 85.5 +/- 3.1 (CoV 3.6%)  NL (May 2014): Noted	Addressed.  RMS to consider updating , the standard deviations for long-term study on quail presented in column 3, in an amended DAR.
5(4)	Vol 3, B.9.3 Effects on terrestrial vertebrates	FR: We agreed with RMS proposal to consider the NOEL of 34 mg/kg bw/d derived from the toxicological studies (B.6) for screening and tier 1 calculations.	APP (April/2014): we also agree with the assessment of the RMS  NL (May 2014): Noted.	Addressed.
5(5)	Vol 3, B.9.3 Effects on terrestrial vertebrates  Residue decline and 21d-Ftwa proposal	FR: The mean 21d-Ftwa approach proposed for lettuce and hops uses should be discussed in expert meeting as the approach is quite new and need agreement to facilitate the assessment at national and zonal level.	APP (April/2014): we agree that the use of DFOP kinetics for calculation of maximum residue concentrations and 21-d TWA concentrations for bird and mammal risk assessment is novel for many applicants or	Expert consultation  The residue decline data was not used because based on the NOEAL of 34 mg/kg bw/d, a refined risk assessment is not necessary. However if the 1-

## section 5 – Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	Vol. 1 2.6.1.2 Effects on mammals	Therefore, the appropriateness of this approach should be discussed for single and multiple applications, e.g. case where moving "TWA x MAF" are required.  In addition, we agree with the RMS that due to the experimental conditions for the 17 trials carried out on lettuce further justifications are needed to consider that the trials also cover early application stages.	<p>evaluators, and technical agreement would therefore be beneficial.</p> <p>Calculation of residue decline kinetics with DFOP kinetics is not much more complex than calculation of SFO kinetics, and provides in many cases a much better fit to the data.</p> <p>Corresponding calculation tools (MS Excel spreadsheets) and training can be provided in case of interest. See also response to comment (4) from EFSA</p> <p>With regard to the last paragraph in comment (2) from France (lettuce growth stage at application) The data show no systematic difference, or larger variability, between DT50 generated in the same trial at different growth stages and between DT50 generated at the same growth stage between different trials.. Additionally it should be considered that the residue decline kinetics of BYI0296 in the lettuce trials are in good agreement with the residue decline kinetics of the compound in young cereals, and thus unlikely to be grossly misleading. Hence the same value can be used for all application stages.</p> <p>NL (May 2014): The mean 21-d ftwa approach can be discussed in an expert meeting if it is considered necessary. Please</p>	year dog study is considered to be relevant, a refined risk assessment may be needed. Depending on the outcome of the expert consultation 5(8), the experts may need to discuss if the 21-d ftwa approached proposed for lettuce and hops can be considered acceptable. <p>In all trials residue were determined after the second treatment, but for four trials residues were also determined after the first application and DT50 values were estimated for each decline interval. Some of the DT50 values were calculated with DFOP (both kfast and kslow was used). For most of the sites in lettuce only 5 sampling points were available. A geometric mean 21-day fTWA is proposed for the refined long-term exposure assessment. There are some uncertainties for lettuce whether the residue values is applicable to the full application period. Only one of the four doubly analysed trials was performed at a relatively early BBCH stage in lettuce.</p>

## section 5 – Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			note that in the risk assessment as it stands in the DAR, no risk is identified in the first tier and the refinement is therefore not used.	
5(6)	B.9.3.2, decline data from the lettuce residue trials	EFSA: It was considered that it is not possible to derive an overall average first order DT50 value, since the best fits were obtained from different models. However it would be possible just considering the slow phase DT50s from the DFOP kinetics.	<p><b>APP (April/2014): the use of only the slow phase is not appropriate in the context of the bird and mammal risk assessment, where particularly the residue decline from the peak below 50% (fast phase) is decisive in the risk assessment, whilst the decline over the slow phase is typically anyway below residue levels of any concern even without refinement.</b></p> <p>However, we have proposed in our submission a more appropriate approach: The 2 main objectives for employing residue decline kinetics in bird and mammal risk assessment are calculation of (a) the peak residue level and (b) 21-d TWA residues. When an overall SFO DT50 value can be generated, then this SFO DT50 is translated into (a) peak residue = AR x MAF and (b) 21-d TWA residues = AR x MAF x 21d fTWA. Fully equivalent is direct calculation of the peak residue concentration and the 21-d time weighted average concentration with DFOP kinetics. However, with DFOP, the peak residues and 21-d TWA concentrations are first calculated per replicate and afterwards expressed as the 90<sup>th</sup> peak concentration (for acute risk assessment)</p>	See expert consultation 5(5).

## section 5 – Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>and the mean 21-d TWA concentration (for reproductive risk assessment).</p> <p>See also response to comment (2) from France</p> <p>NL (May 2014): See response applicant. We believe that we have used the data in the most appropriate way.</p>	
5(7)	B.9.3.2, Generic field monitoring	EFSA: EFSA agrees that this is a good quality study, and note the remarks of the RMS especially the note regarding the possible effects of the surrounding habitat in the species composition in a crop.	<p>APP (April/2014): we also agree with the assessment of the RMS and the need to consider the surroundings was expressively discussed and addressed in the design of the study and the conclusions, so that the results of that study can be considered and applied without undue uncertainty in risk assessment.</p> <p>NL (May 2014): Noted.</p>	<p>Open point (EFSA)</p> <p>EFSA to make it clear in the conclusion that there is possible effects of the surrounding habitat in the species composition in a crop.</p>
5(8)	B.9.3.3, Endpoints for mammals	EFSA: EFSA welcomes the thorough assessments for the choice of the reproductive endpoint. However, EFSA is still wondering why the lower endpoint of 7.8 mg/kg bw can be omitted in the Tier 2 assessment as this endpoint is based on effects on offspring (as indicated in Table B.9.3.3-1), which should be considered as relevant effects for these risk assessments. It is further noted (already noted by the RMS) that this lower endpoint is not included in the mammalian tox. part of the LoEP	<p>APP (April/2014): we agree with the assessment of the RMS that the relevant end-point should be in agreement with that identified in the mammalian toxicology section..</p> <p>NL (May 2014): As EFSA also indicates, the lower endpoint from the rat study is not included in the mammalian toxicology part of the LoEP. One-year dog studies are to our knowledge never considered for ecotoxicological risk assessment. The EFSA</p>	<p>Expert consultation</p> <p>Should the 1-year dog study, with an endpoint of 7.8 mg/kg bw, be considered relevant in the risk assessment of other terrestrial vertebrates, mammals?</p>

## section 5 – Ecotoxicology (B.9)

<b>Birds and mammals (B.9.1 and B.9.3)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		under the rat 2 generation study. However and endpoint of 7.8 mg/kg bw is included for a 1-year dog study.	GD for birds and mammals of 2009 does not include this study in the list of mammalian tests relevant for the reproductive risk assessment. In conclusion we still consider the endpoint of 34 mg/kg bw/d the relevant endpoint for the ecotox assessment.	
5(9)		DE: no comment		Addressed.

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(10)	Vol. 3, Table B.9.2.4.02, p. 55/56 Vol. 1, Point 2.6.2 “Effects on Aquatic species” and Vol. 1, Appendix 3, chapter 2.6	DE: Typing error: The duration of the acute test with the test substance 6-CNA on <i>Chironomus tentans</i> according to the ASTM and EPA guidelines took 96 hours. Please correct time-scale in table B.9.2.3.02 of Vol. 3 (last line on page 80) and write 96 h instead of 48 h.	APPL (04/2014): Agreed the correct time should be 96 hours.  NL (May 2014): This will be corrected in the LoEP, and also in the DAR if a corrected version has to be made.	Open point. RMS to correct the timescale of the acute study with 6-CAN on <i>Chironomus tentans</i> to 96 h in the LoEP.
5(11)	Vol. 3, IIA, 8.3.2.2/01, Chronic endpoint for <i>C. riparius</i> . Comment also relevant for IIIA, 10.2.6.2/01, chronic chironomus	SE: We would hesitate to use the nominal concentrations to derive a NOEC since the mean measured concentrations in the test system is only 41% after 28 days. Especially since there is no information regarding fate of the study compound in the study	APPL (04/2014): According to guideline (OECD 219) the endpoint of chronic chironomus study (spiked water) should be based on initial measured concentration.  OECD 219: point 43. Effect concentrations expressed as concentrations in the	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	endpoint for the formulation.	summary, i.e. concentrations in the sediment.  Analytical measurements in the overlying water, pore water and sediment is listed as a minimum requirement in the OECD 219. Measurements should be performed at the start and at the end of the test in at least a higher and a lower concentration.	<p><i>overlying water, are calculated preferably based on measured concentrations at the beginning of the test (see paragraph 38).</i></p> <p><b>Test Item Analysis:</b> During the study, the measured concentrations of the test item in the overlying and pore water were analysed three times on days 0, 7 and 28 at all test concentrations and also in the control(s). Additional analyses in the sediment were considered to be not necessary because the partitioning of the active ingredient between water and sediment is known from water/sediment studies done under comparable conditions.</p> <p><b>Analytical Findings:</b> Chemical analysis of overlying water and pore water over time reflect expected aquatic fate data with high recoveries of 85 % to 110 % (mean 99 %) at the beginning of the exposure period in the overlying water of all test concentrations. Therefore, initial nominal concentrations were used for reporting and evaluation of the results.</p> <p>The fate of the test item in sediment can be evaluated based on the existing water sediment studies (see Flupyradifurone DAR Volume 3 Annex B.8.4.3.2 studies IIA,</p>	

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<b>7.8.3/01 and 7.8.3/02)</b>  NL (May 2014): The endpoint was derived according to the OECD guideline (see applicant's reference to the guideline above). The initial measured concentrations were in the range of 85-110% (mean 99%). Therefore it is acceptable to use the nominal concentration.	
5(12)	B.9.2.1.2, Study by Bowers L.M. & Lam C.V. (1998) and general for tests on AO	EFSA: It is noted that no analytical confirmation was done for the test water in this study. However, EFSA agrees that read across from other studies with the same metabolite is possible. It can generally be concluded that the a.s. and the metabolites indicated a good stability in the test waters of all the aquatic studies. Is this statement agreed?	<b>APPL (04/2014): BCS agrees that in acute exposure studies the a.s. and the metabolites generally indicated good stability.</b>  NL (May 2014): Agreed.	Addressed.  It was agreed that the a.s. and the metabolites generally indicated a good stability in the test waters of all the aquatic studies.
5(13)	B.9.2.2.1, Study by Matlock D. & Lam C.V. (2011)	EFSA: Please confirm that the larval survival of 88.8% at the 4.41 mg/L test concentration versus the control results of 93.8% is not considered as biologically relevant.	<b>APPL (04/2014): The observed effects correlate well with the outcome of the statistical analysis. None of the survival rates seen at the concentration range of 0.619 mg/L to 4.41 mg/L is consecutively below the control on at least 2 occasions. The next higher concentration (i.e. 8.4 mg/L) is the first concentration causing consecutively decreased survival rate. Thus 4.41 mg/L is the NOEC and 8.4 mg/L is the LOEC.</b>  Control: 93.8% 0.619 mg/L: 86.3%	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>1.11 mg/L: 95.0%</p> <p>2.05 mg/L: 97.5%</p> <p>4.41 mg/L: 88.8%</p> <p>8.40 mg/L: 87.5 %</p> <p>At the highest concentration an effect of 6.7% compared to the controls was observed.</p> <p>The observed survival in all tested levels was exceeding the validity criteria of the underlying guideline for the controls. The respective table taken from Annex 2 of the TG (OECD 210) is presented below.</p> <p>The table has been moved to the end of this section.</p> <p>Therefore the statistically observed LOEC can be taken as a worst case effect level. The 88.8 % survival observed at 4.41 mg/l can clearly be considered as not biologically relevant. The difference to the controls is 5.3 % only. The lowest survival rate of 85% observed for a single replicate at 4.41 mg/L is identical to the lowest replicate survivals in the controls and solvent controls. This survival is still clearly exceeding the validity criteria of 75% for controls as given in the underlying guideline.</p>	

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			NL (May 2014): We confirm that we do not consider this observation biologically relevant.	
5(14)	B.9.2.2.1, Study by Riebschläger T. (2012)	EFSA: Although a clear concentration-effect relationship can be seen, all biological parameters were worse in all of the treated concentrations than the results from the control. Please comment whether at least the results for the number of offsprings are or are not considered as biologically relevant.	<p>APPL (04/2014): No statistically or biologically relevant effect on the total living offspring per surviving parental female could be observed as visualized in the figure below:</p> <p>The table has bee moved to the end of this section.</p> <p>The observed differences are within the known variations of the test system. The test concentrations of 43.3 mg/L resulted in 6.1 % difference to the controls only. No clear dose response was observed up to and including the highest test item concentration. At 100 mg/L a difference of 13.6% to the controls was observed. The validity criteria for controls with respect to the number of offspring were clearly fulfilled in all tested concentrations. It can therefore be stated that the observed differences in comparison to the controls are not biologically relevant.</p> <p>NL (May 2014): Presumably EFSA means 'although NO clear concentration effect can</p>	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			be seen? We agree with the statement of the applicant and do not consider the results for the number of offspring as biologically relevant.	
5(15)	B.9.2.2.1, Study by Claude M.B. et al. (2011)	EFSA: EFSA welcomes the further analysis and careful control of the assessments on the results of these studies by the RMS. However EFSA still considers that ~30% difference on average from the control might be considered as biologically relevant. If it is believed that no robust endpoint can be derived from this study than it maybe considered to repeat the test.	<p>APPL (04/2014): According to the current data requirements (1107/2009) two invertebrate standard species have to be tested in case of insecticides:</p> <p>1<sup>st</sup> species: <i>Daphnia magna</i></p> <p>2<sup>nd</sup> species: <i>Chironomus riparius</i> or <i>Americanysis bahia</i></p> <p>As for flupyradifurone both, Daphnia and Chironomus data are available current data requirements are fulfilled and no new mysid study is considered necessary for registration purposes. The mysid study has been conducted in order to fulfil EPA requirements and was submitted for completeness reasons. The chronic mysid study is a study which frequently fails. The standard variation observed in controls over several years is known to be about 30% (please see BCS position paper M-452374-01-1 including control data). Based on this enormous variability a difference of 30 % is not a clear sign for an effect.</p> <p>NL (May 2014): Agree with applicant. We consider that the 30% effect observed is not biologically relevant based on the detailed</p>	Open point RMS to put a footnote in the LoEP:s that clarifies that the NOEC has some uncertainties and that a ~30% difference on average from the control was seen in the study.

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			discussion in the DAR, and that a new study is not necessary nor required.	
5(16)	Vol. 3, B.9.2.5.5, Refined RA aquatic invertebrates	DK: For the acute RA to invertebrates from use in lettuce, not enough scenarios show TER values above the trigger. In our view, furthered refinements are required in order to address the risk to aquatic invertebrates, e.g. mesocosm study	<p><b>APPL (04/2014):</b>  <b>A safe use has been shown for the scenario R1 (pond) in both hops and lettuce with no risk mitigation. Additionally by applying mitigation measures an acceptable use can be shown for scenario D3 with no buffer zone and drift reducing nozzles, and for scenarios R1 stream, R2 stream and R3 stream considering different buffer zones (and or vegetated filter strips).</b>  <b>As risk can be addressed with risk mitigation measures, higher tier studies are no requirement.</b></p> <p>NL (May 2014): Agree with applicant. To our knowledge, it has not been defined how many scenarios should meet the trigger to conclude on a safe use; did we miss something? See also next comment.</p>	Addressed.
5(17)	B.9.2.5, RA for AO	EFSA: Please note that when a FOCUS scenario has more than one water body, EFSA considers this scenario as 'safe' only if a low risk was proven for all the linked water bodies.	<p><b>APPL (April 2014): This criterion is fulfilled either at Step 3 or Step 4 for both safe use crops</b></p> <p>NL (May 2014): We do not know this term but assume that EFSA means all water bodies within a scenario, e.g. D4 pond and D4 stream. To our knowledge, it has not</p>	Addressed.

## Reporting table, flupyradifurone

24.06.2014

240/311

### section 5 – Ecotoxicology (B.9)

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			<p>been defined what a 'safe use' is. Based on this EFSA criterion, both uses have safe scenario's. Below, it is shown which scenario's show a safe use, i.e. all water bodies within the scenario show acceptable risk based on the critical endpoint (acute invertebrates) and mitigation measures, and which do not or only partly.</p> <p><u>hops:</u> For the only relevant scenario, the trigger is met: R1 (pond and stream)</p> <p><u>lettuce:</u> For three complete scenario's the trigger is met: D3 (ditch 1<sup>st</sup> and 2<sup>nd</sup>), R1 (pond 1<sup>st</sup> and 2<sup>nd</sup>, ditch 1<sup>st</sup> and 2<sup>nd</sup>) and R2 (stream 1<sup>st</sup> and 2<sup>nd</sup>) For two scenario's, the trigger is partly met: R3 (stream 1<sup>st</sup> is met, stream 2<sup>nd</sup> is not) and R4 (stream 1<sup>st</sup> is met, stream 2<sup>nd</sup> is not) For two scenario's, the trigger is not met: D4 (pond 1st and stream 1st ), D6 (ditch 1st )</p>	
5(18)	Vol. 3, B.9.2.5, Risk assessment on aquatic insects	DE: Even if the butenolide flupyradifurone (nicotinic acetylcholine receptor (nAChR) agonist) is not as toxic to <i>Chironomides</i> as the closely related neonicotinoids, such as imidacloprid, the concerns about possible effects on mayflies (Ephemeroptera) should	<p><b>APPL (04/2014): Test on mayflies is not a data requirement.</b></p> <p><b>Differences in species sensitivity should be covered by the used Assessment (Safety-) factors. The publication of Brock &amp; Wijngarden (<i>Acute toxicity tests with</i></b></p>	<p>Expert meeting Experts to discuss if a test on mayflies should be considered needed in the aquatic risk assessment.</p> <p>Reporting table comment 5(18);</p>

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		be investigated and discussed further because mayflies show higher sensitivity to neonicotinoids compared to <i>Chironomides</i> . The aquatic risk could be well addressed exploring sensitivity of mayflies to the a.s.  -	<p><i>Daphnia magna, Americamysis bahia, Chironomus riparius and Gammarus pulex and implications of new EU requirements for the aquatic effect assessment of insecticides</i>; Environ Sci Pollut Res (2012) 19:3610–3618) evaluated the protectiveness of the aquatic risk assessment for insecticides. For cases where daphnia and chironomid data were available it was demonstrated that the risk assessment is protective.</p> <p>Therefore the current data set should assure a protective aquatic risk assessment for invertebrates including Ephemeropteran species. As the submitted aquatic risk assessment is passing the tier 1 risk assessment in some scenarios no additional data are required.</p> <p>Hence, for Annex I listing of flupyradifurone all data requirements according to 1107/2009 are fulfilled.</p> <p>NL (May 2014): Agree with applicant that all data requirements are fulfilled and that based on the Brock &amp; Wijngaarden paper, no additional data would be needed. However, recent developments regarding imidacloprid and ephemeropterans are not taken into account in this paper yet. We propose that</p>	<p>“Even if the butenolide flupyradifurone (nicotinic acetylcholine receptor (nAChR) agonist) is not as toxic to Chironomides as the closely related neonicotinoids, such as imidacloprid, the concerns about possible effects on mayflies (Ephemeroptera) should be investigated and discussed further because mayflies show higher sensitivity to neonicotinoids compared to Chironomides. The aquatic risk could be well addressed exploring sensitivity of mayflies to the a.s.”</p> <p>Data requirement:</p> <p>To support the discussions in the expert meeting the Applicant should submit any information available, which might even be a position paper or an argumentation.</p>

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			the need for additional data is discussed in an expert meeting; the outcome of the discussion of the peer review meeting on the aquatic risk assessment of imidacloprid of June 2014 can then be taken into account.	
5(19)	Vol 3, B.9.2 Effects on aquatic organisms  Vol. 1 2.6.2 Effects on aquatic organisms	FR: FR: There are some uncertainties regarding the term biannual associated with intended uses on lettuce. Could RMS precise if the term biannual in the DAR refers to two applications per year or one application every two years. In the last case biannual is wrongly used and the term biennial should be used.  Due to these uncertainties could RMS clarify whether PECsw Step 2 for use in lettuce two application per year or one application every two years? In addition, could you, please, also indicate the frequency of applications used for the estimation of the PECsw in Step 3 and Step 4. If the TER are based on one application every two years, then annual application could not be considered covered and the risk assessment could have to be revised.	<b>APPL (April, 2014):</b> In all cases the term <b>biannual or biennial</b> is used to indicate a use once every 2 years.  <b>FOCUSsw</b> does not consider multiple years of usage but the usage in one specific year, although a “carry-over” assumption is part of the simulation, the model assumes that the application is every year. The question of usage every second year is therefore not relevant and the simulations cover all use patterns (annual or biennial uses).  <b>NL (May 2014):</b> Indeed, the use of the term biannual refers to one application every two years. We apologise for the confusion. This will be revised in later versions of the DAR and LoEP (also in the fate section).  The PECsw Step 2 for use in lettuce are based on one application of 0.125 kg as/ha per two years with low interception (from BBCH 12). This covers the other field use in lettuce with one application of 0.125 kg as/ha per year, but with high interception (from BBCH 41).	Open point  RMS to clarify in the LoEP:s and a revised DAR that the application on hops is biennial and not biannual.

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			No PECs were presented for the glasshouse use in lettuce with two applications of 0.125 kg a.s./ha per year with low interception (from BBCH 12). It would indeed be possible that exposure to surface water from this use is higher than that of the field uses, especially considering that extensive drift reduction is necessary to achieve acceptable TER values for aquatic invertebrates. This issue was considered by the fate section (see fate reporting table) and it was concluded that the glasshouse uses are in fact covered by the assessment for the field uses. With a PECsw of 0.0788 µg a.s./L, the triggers for all aquatic organisms are met.	
5(20)	Vol 3, B.9.2 Effects on aquatic organisms	FR: In line with the e-fate comment regarding PECsw, could it be possible to add TER calculation with buffer zone (drift + run-off) only for uses in hops?	<b>APPL (April, 2014): This is a French specific requirement and should be taken into account at national level and is not part of the active substance assessment.</b>  NL (May 2014): This would indeed be part of a national assessment.	See comment 4(34) and open point of comment 4(29).
5(21)	Vol 3, B.9.2 Effects on aquatic organisms	FR: In line with the e-fate comment regarding PECsed, please confirm that no risk assessment for sediment dwelling organisms is needed?	<b>APPL (04/2014): The used standard species for a risk assessment covering sediment dwelling organisms is Chironomus. The current aquatic guidance document focuses on exposure via the water phase. No specific guidance for a sediment risk assessment is currently available.</b>	Addressed  A sediment dweller risk assessment is needed. A Chironomus NOEC based on a nominal water concentration can be accepted in this case for this

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>Therefore a spiked water test for <i>Chironomus</i> has been performed and the risk assessment is based on PECsw calculated with FOCUS (water bodies) as it is appropriate for EU registration purposes.</p> <p>NL (May 2014): Agree with the applicant.</p>	<p>purpose, as for outdoor uses there is only a single application per year in the representative uses, so a water spiked study and max PECsw approach is defensible, see also reporting table comment 4(35) for further discussion on exposure aspects.</p>
5(22)	Vol. 3, B.9.2.5, Risk assessment Invertebrates and Point 2.6.2 “Effects on Aquatic species”	DE: We acknowledge that the more sensitive species of the tested aquatic invertebrates is <i>Chironomus</i> . Accordingly, please use <i>Chironomus</i> data for the acute and chronic TER calculations for the 4 relevant metabolites (DFA, 6-CNA, BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide). Nevertheless, metabolites are less toxic to aquatic invertebrates compared to the active substance.	<p>APPL (04/2014): TER calculations for the metabolites were presented based on <i>Daphnia magna</i> data as <i>Daphnia</i> seems to be more sensitive to most of the metabolites than <i>Chironomus</i> (due to the use of limit tests for most studies).</p> <p>The available <i>Chironomus</i> data for the metabolites are shown below. As for the metabolite DFA the chronic <i>Chironomus</i> endpoint is 100 mg /L it can be concluded that the acute endpoint would be &gt; 100 mg/L. None of the metabolites are acutely more toxic than the parent compound. Thus no chronic testing of the metabolites is required. Nonetheless chronic toxicity values are available for 6-CNA and DFA.</p> <p>Available <i>Chironomus</i> data for metabolites:</p> <p><u>Acute</u></p> <p>6-CNA : EC<sub>50</sub> &gt; 1 mg/L</p> <p>BYI 02960-succinamide : EC<sub>50</sub> &gt; 100 mg/L</p>	<p>Open point</p> <p>RMS to update the LoEP:s with acute and chronic TER calculations for <i>Chironomus</i> and the 4 relevant metabolites (DFA, 6-CNA, BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide).</p>

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>BYI 02960-azabicyclosuccinamide : EC<sub>50</sub> &gt; 100 mg/L</p> <p><u>Chronic</u></p> <p>6-CNA : NOEC 100 mg/L</p> <p>DFA : NOEC 100 mg/L</p> <p>NL (May 2014): Indeed the toxicity values for <i>Chironomus</i>, where available, should have been included in the TER calculations of the metabolites. Based on the high endpoints and the low PEC values it is clear that the risk will be low. Revised TER values can be included in a revised version of the LoEP, if considered necessary.</p>	
5(23)	B.9.2.5, RA for AO	EFSA: Please clarify that when 'R' is indicated for a buffer type in a table of this chapter, whether it indicates runoff mitigation or runoff mitigation and spray drift mitigation. Please also clarify how to understand the mitigation regime in Table B.9.2.5.5-12 (buffer zone + nozzle for D scenarios and nozzle + VFS for R scenarios without spray drift buffer zone??)	<p>APPL (04/2014):</p> <p>Table B 9.2.5.5-06 (p. 89): S = spray drift only; R = spray drift + VFS</p> <p>Table B 9.2.5.5-07 (p. 90): S = spray drift only; R = spray drift + VFS</p> <p>Table B 9.2.5.5-12 (p. 94):</p> <p>D scenarios: 20 m buffer (spray drift only) + drift reduction (nozzles)</p> <p>R scenarios: 20 m buffer (spray drift + VFS) + drift reduction (nozzles)</p> <p>NL (May 2014): The meaning of 'R' (spray</p>	<p>Open point</p> <p>RMS to clarify in the LoEP:s which mitigation measures that are assumed in the higher tiers.</p>

## section 5 – Ecotoxicology (B.9)

<b>Aquatic organisms (B. 9.2)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			drift + VFS) and the mitigation regimes of table 9.2.5.5-12 will be clarified in an updated LoEP.	

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(24)	B.9.4. Effects on bees	Nature et Progrès Be  Bees are a livestock and should be considered in the framework of assessment of risks to animal health, that is to say: residues studies, sublethal effects studies leading to the definition of ARfD, definition of LMRs in pollen and nectar.	APPL (APR/2014): The current European legislation requires the applicant to assess the risk to bees within the ecotoxicology section according to the principles as outlined in Regulation (EC) No 1107/2009. This provision has been followed by the applicant.  NL (May 2014): See applicant's response.	Addressed  Notes: Indeed, risk to bees (not necessarily restricted to honey bees) are addressed within the ecotoxicology section according to the pertinent legislation and practice.
5(25)	B.9.4. Effects on bees	Nature et Progrès Be  Chronic toxicity tests were performed as well as larvae tests. This is a great improvement of assessment of the risk to bees!	NL (May 2014): Noted.	Noted  EFSA also agrees that this is a great improvement.
5(26)	B.9.4.1.3. Chronic toxicity of the active substance and metabolites	Nature et Progrès Be  Behavioural effects are present in some trials; there is no dose-response pattern (in	APPL (APR/2014): Nature et Progrès Be refers to a study (as summarised under 8.16.1/01) which has not shown adverse effects on mortality up to and including the	See point for expert consultation in 5(36), below.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>Kling 2011). Absence of dose-response patterns should lead assessors to consider with caution the idea that a substance has no harmful effects below a dose for which no effects appeared; effects can appear when insects are exposed to lower doses. Absence of dose-response patterns is described in peer-review studies for bees and other arthropods:</p> <ul style="list-style-type: none"> <li>- Charpentier G, Louat F et al. 2014: Lethal and sublethal effects of imidacloprid, after chronic exposure, on the insect model <i>Drosophila melanogaster</i>, Environ. Sci. Technol., Just Accepted Manuscript • DOI: 10.1021/es405331c</li> <li>- Suchail S, Guez D and Belzunces LP, 2000: Characteristics of Imidacloprid toxicity in two <i>Apis mellifera</i> subspecies, Environmental Toxicology and Chemistry: 19(7): 1901–1905</li> <li>- Suchail, S., Guez, D., and Belzunces, L.P., 2001: Discrepancy between acute and chronic toxicity induced by Imidacloprid and its metabolites in <i>Apis mellifera</i>, Environmental Toxicology and Chemistry 20, 2482 – 2486</li> </ul>	<p>highest concentration tested (10 ppm). This result does not mean that there is something like a “compound-inherent absence of a dose-response-relationship”, it simply means that even the highest concentration tested had no effect on honey bees (NOEC <math>\geq</math>10 ppm).</p> <p>This conclusion has been verified three years later where the same study has been repeated by including elevated treatment levels into the test design, in order to determine additionally to a NOEC/NOED also a LC50/LDD50 (study summarised under 8.16.1/09). The results of this repeat 10 day chronic adult feeding study with flupyradifurone confirmed the results of the already existing study and showed a distinct dose-response relationship (due to the elevated treatment levels).</p> <p>NL (May 2014): The study to which Nature et Progres Be refers was not accepted for risk assessment, mainly because of the high control mortality but another reason was the uncertainty about the sublethal effects which showed no dose-response pattern. See also the applicant's response to the next comment on the difficulties in performing this study. A new study was requested which achieved low control mortality; furthermore in</p>	<p>Notes: The main aim of the lab. studies are to find the lethal doses/concentrations. Sub-lethal effects seen in these kind of studies are usually linked with the strong (but not necessarily lethal) intoxication. NOEC/NOED values derived from these studies cannot directly be considered as ‘field’ NOEC/NOED (e.g. what would cover any kind of potential behavioural effects or effects on navigation for example). In future risk assessments (which will based on the new EFSA GD) the median lethal levels will be in the focus and when more specific ‘field’ NOEC/NOED levels will be necessary, this will need to be investigated in more realistic conditions.</p> <p>However, in agreement with the commenter, overly EFSA considers that the information on sub-lethal effects needed to be considered in the related risk assessments (rather as qualitative information). In this case, EFSA does not see a</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			the new study a clear dose-response pattern was seen both for lethal and sublethal effects. We therefore see no reason to believe that there is no dose-response pattern for this particular substance; in our opinion there is no concern for effects at exposure to lower doses.	particular concern from these data.  See also open points and comment in 5(31).  See also comment in 5(44).
5(27)	Vol 3, B.9.4.1.3.1  Chronic toxicity on adult honeybees, B.9.4.1.3.1  Chronic toxicity on adult honeybees, STUDY IIA, 8.16.1/01	DK: We agree with RMS conclusion regarding control mortality. We would have liked a reference substance (toxic standard) in the study, but as this is not the case, we would like a statement in the study summary regarding previous exposure of bees to other pesticides.	<b>APPL (APR/2014): There is even to date no agreed testing guideline, ring-testing will start this year (2014) and by today, there are globally only very few scientists in individual laboratories who have experience with the chronic laboratory feeding test in adult honey bees. The submitted study as summarised under KIIA 8.16.1/01 was amongst the very few studies which had up to that date been conducted and clearly showed, although the control mortality exceeded slightly the proposed value of 15%, no adverse effects of flupyradifurone at levels of up to and including the highest tested concentration, i.e. the NOEC was determined to be <math>\geq 10000</math> ppb (<math>\geq 10</math> ppm). A toxic standard evaluation is part of initiated the this year's (2014) starting ring-testing activities, and neither a defined toxic standard nor a defined reference performance of a toxic standard is available by today.</b>  <b>In the meantime, three years after the study as summarised under 8.16.1/01, the bee</b>	See open point in 5(28).  Notes: A more robust newer study is available. Currently no agreed reference performance is available for any potential toxic standard.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>testing community in Europe had gained significantly more experience with this test system and as consequence, control mortalities are nowadays generally lower than during these very first study (and were already lower at the time when the metabolites were tested (KIIA 8.16.1/02 - 06), based on the experienced gained in-between).</p> <p>In the light of this methodological progress, the study as summarised under KIIA 8.16.1/01 was repeated recently by including elevated treatment levels into the test design, in order to determine additionally to a NOEC/NOED also a LC50/LDD50 (see study summarised under 8.16.1/09). The results of this repeat (2<sup>nd</sup>) 10 day chronic adult feeding study with a control mortality considerably below the proposed validity criterion of &lt;15%, fully confirmed the results and the conclusions of the 1<sup>st</sup> 10 day chronic adult feeding study (KIIA 8.16.1/01) and corroborated that flupyradifurone does not induce chronic/delayed toxicity.</p> <p>The honey bees for testing chronic toxicity in adult honey bees were derived for all studies (KIIA 8.16.1/01 - 06 and KIIA 8.16.1/09) from bee colonies located directly on the premises of the respective testing facility. The honey bees are as such exposed to natural</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<b>environmental conditions.</b>  NL (May 2014): See applicant's response.	
5(28)	Vol 3, B.9.4.1.3.1 Chronic toxicity on adult honeybees, B.9.4.1.3.1 Chronic toxicity on adult honeybees, Study IIA 8.16.1/09, Study IIA 8.16.1 /02, Study IIA 8.16.1/03, Study IIA 8.16.1 /04, Study IIA 8.16.1 /05 and Study IIA 8.16.1 /06	DK: We would have liked at reference substance (toxic standard) in the study, but as this is not the case, we would like a statement in the study summary regarding previous exposure of bees to other pesticides.	APPL (april 2014) See above  NL (May 2014): See applicant's response. We believe that the applicant have done their utmost to perform these studies in the best possible way. A statement on previous exposure of the test bees cannot be given; this would probably be impossible for any adult bee test. We believe that this does not invalidate the tests and that they can be used for risk assessment.	Open point  RMS to indicate in the LoEP (e.g. via a footnote) that there are some uncertainties of the results of the chronic lab. studies arising from the lack of toxic standard and the lack of information on the history of the used bees. The lack of experience of conducting these kind of tests and the lack of experience for the interpretation of these tests might also be mentioned.  Notes: Currently no agreed reference performance is available for any potential toxic standard. EFSA considers the current period as an interim period, when there is some room for some flexibility with this new type of studies, when the design and the results (including the control mortality) were reasonable.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
				See also open points in 5(29) and 5(31).
5(29)	B.9.4.1.3.1. Chronic toxicity on honeybee larvae	Nature et Progrès Be  Since no statistically significant effects are reported, it is concluded from the larvae test that both NOEC and LOEC are > 10 000 microg/bee (the highest concentration used in the trial). However, from raw data (Table 9.4.1.3-09 p. 176) it appears that mortality was generally higher in the treated items than in control items even for the lowest concentration (150 microg/bee). Even when the Abbott-corrected mortality reaches 25% this additional mortality is not statistically significant. What is the statistical power of this test? Which level of additional mortality is it able to discriminate?	APPL (APR/2014): The study was conducted according to the provisions of INRA and the ICPBR-organised ring test group (Aupinel et al, 2009), and exceeded in both, in the exposure design (repeated exposure) and in the duration of the study (until hatch at day 22) the currently existing, ring-tested and adopted OECD 237 guideline requirement. Nature et Progrès Be refers to test runs which have not fulfilled the validity criteria and which were consequently not considered for the derivation of a NOEC.  The data of these non-valid test runs have been displayed for reasons of completeness and transparency.  All three valid test runs show a consistent picture with mortality rates similar to control mortality and a NOEC always in excess of 10 ppm, which clearly revealed that immature honey bee life stages are not more susceptible to flupyradifurone than adult bees, which is also consistent to the mode of action of flupyradifurone and the findings in the higher tier honey bee brood study.	Open point  RMS to indicate in the LoEP (e.g. via a footnote) that there are some uncertainties of the results of the larval test arising from the lack of experience of conducting and the interpretation these kind of tests.  Notes: EFSA agrees that some uncertainties exist around this NOEC value. In some (valid) test runs the mortality in the treated groups was consistently higher than in the controls. On the other hand at least test run No.4 indicated a lack of effects up to 10 ppm and the performance of the reference item clearly indicated the sensitivity of larvae to chemical stress in all runs.  See also open points in 5(28) and 5(34).

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL (May 2014): See applicant's response.	
5(30)	Vol. 3, B.9.4.1.3.1, Chronic adult tests and larval test	EFSA: EFSA welcomes to have these 'new type' of tests in the dossier. EFSA also considers that the way of the evaluations of these studies by the RMS, in general, was very good. However, please consider the following related comments.	NL (May 2014): Noted, thank you.	Addressed
5(31)	Vol. 3, B.9.4.1.3.1, Chronic adult tests and Vol. 1, LoEP	EFSA: As general remark, the control mortality should always be clearly reported, especially if it was used for correction, what is not particularly supported by relevant EFSA documents. In relation to that EFSA is unsure on the statistically derived (here from corrected mortality data) NOEC values (i.e. NOEC is established where there were some mortalities, sometimes even higher than in the control). As in the future the LC50 will be used, EFSA is of the opinion that it is enough to include only the LC50 values in the LoEP (also expressed in ug/bee/day). The results on the analytical findings were not always reported. Were the test items stable in the feed items?	<p>APPL (APR/2014): In all chronic adult study reports (5 metabolites and 2 times parent flupyradifurone) and in all summaries prepared by the RMS, both, the observed cumulative mortality and the corrected cumulative mortality (exception: control mortality = 0%), were reported.</p> <p>The NOECs were always derived by a direct statistical comparison of the findings as obtained in the treatment group(s) with the findings in the corresponding control group.</p> <p>The comparison of the acute and chronic NOEC of flupyradifurone shows that there is no indication of any delayed or particularly chronic effects in honey bees; moreover, the comparison of the NOECs of the chronic laboratory toxicity studies of the flupyradifurone metabolites with the corresponding chronic NOEC(s) of the chronic toxicity study/studies with parent flupyradifurone reveals that the flupyradifurone metabolites are not of any</p>	Open point  RMS to make clear the control mortality and the analytical findings for the test item stability for all chronic adult tests in an addendum.  Open point  RMS to remove the NOEC values from the LoEP.  Notes: EFSA just noted that there are some uncertainties around some NOEC values if a read-across for all the available data (including also the acute oral test) is done. This is might be partly due to the correction procedure (the

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>higher toxicity regarding potentially delayed or chronic effects than the parent compound. Thus, the NOECs from the chronic studies significantly contribute to the understanding of the intrinsic properties of flupyradifurone and its metabolites in honey bees.</p> <p>In the 2<sup>nd</sup> chronic toxicity study with parent flupyradifurone, elevated test levels were included which allowed for the derivation of and LC50 [mg a.s./kg diet] and the corresponding, dose-related LDD50 [<math>\mu</math>g a.s./bee/day].</p> <p>The results of the chemical analysis of the feeding solutions revealed that the actual concentrations were always well in line with the nominal concentrations.</p> <p>NL (May 2014): If not explicitly mentioned, control mortality was 0. There is still no harmonised guideline for this type of study. We believe that the data have been analysed according to normal procedures (i.e. with control-corrected mortality data); could EFSA provide more information on what kind of alternative analysis they consider more relevant?</p> <p>We agree with the applicant that the NOEC values are important for the understanding of the working of flupyradifurone in honeybees. However, if a new LoEP format becomes</p>	<p>alternative would be do not apply the correction and consider the NOEC where actually 0 % effect was seen). It does not mean that the information on the likely no effect levels is ignored. EFSA agrees that the available data suggest rather a lack of potential for accumulative effect at least for the a.s., which should be taken into consideration.</p> <p>It is likely that the new template for LoEP will ask only the LC50 (LDD50) as this will be used in the follow up risk assessments in the future.</p> <p>See also comments in 5(26), 5(27), 5(28) and in 5(44).</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			available in which the NOEC is not included, we are willing to follow that.	
5(32)	Vol. 3, B.9.4.1.3.1, Chronic adult tests	EFSA: It is noted that the first study was invalidated due to relatively high control mortality. It is further noted that the temperature used in this test was lower than in the second test (considered as valid).	<p>APPL (APR/2014): The 1<sup>st</sup> study showed, although the control mortality exceeded slightly the (now) proposed value of 15%, no adverse effects of flupyradifurone at levels of up to and including the highest tested concentration, i.e. the NOEC was determined to be ≥10000 ppb (≥10 ppm). The findings and conclusions from this 1<sup>st</sup> study were fully confirmed by the findings of the 2<sup>nd</sup> study, which included also elevated treatment levels.</p> <p>There is even to date no harmonised and ring tested test guideline (first ring test activities in spring/summer 2014), the 1<sup>st</sup> study was conducted in 2010, the 2<sup>nd</sup> test was conducted in 2013 and considered a temperature regime as recently recommended by EFSA. As indicated above, the results of both studies are fully in line.</p> <p>NL (May 2014): Noted.</p>	Addressed
5(33)	Vol. 3, B.9.4.1.3.1, Chronic adult tests	EFSA: It is noted that the chronic endpoint on adults for the a.s. is higher than the acute, which is a rather surprising result. Provided that this conclusion is valid, it might indicate that no accumulative effects is expected for this a.s.  Some uncertainty on the used test item in the acute test is noted.	<p>APPL (APR/2014): Considering the mode of action of flupyradifurone, comprising a reversible receptor binding, the results of the chronic study are not surprising.</p> <p>When comparing the acute and chronic data in adult honey bees as obtained with technical flupyradifurone, the NOED (oral) accounts to 0.7 (bolus application, acute)</p>	Open point  RMS to confirm (if possible) that the question regarding the identity of the test item used in the acute test (first study under B.9.4.1.1) is resolved and indeed technical

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>and to 0.8 (continuous feeding for 10 consecutive days) µg a.s./bee(/day), the acute LD(D)50 accounts to 1.2 (bolus application, acute) and to 1.8 (continuous feeding for 10 consecutive days) µg a.s./bee(/day).</p> <p>These findings are, when considering the typical variability of biological test systems, virtually identical and confirm that even repeated/continuous exposure to flupyradifurone does not result in delayed, accumulative or chronic effects in honey bees. This has been consistently confirmed by all higher tier studies.</p> <p>The question regarding the test item is resolved. There is no remaining uncertainty regarding the test item in the acute test (conducted with technical flupyradifurone).</p> <p>NL (May 2014): We do not agree with EFSA that the chronic endpoint is higher than the acute. The acute and chronic studies actually show very similar results. See further the applicant's response above.</p>	<p>flupyradifurone was used with comparable profile with other studies and the specification.</p> <p>Note: EFSA do not disagree that the acute and chronic studies indicated similar results, but numerically the chronic endpoint is higher than the acute one. Since the difference is rather small, this does not trigger a particular concern provided that the test items used in these tests are comparable.</p>
5(34)	Vol. 3, B.9.4.1.3.1 (B.9.4.1.3.2 ?), larval test Vol. 1, LoEP	EFSA: It is noted that the exposure of the larvae was only between days 3 and 6 in the test. The young larvae did not feed on the treated food in the first 2 days, therefore this part of the exposure is not covered by this test. It is acknowledged that this design is	<p>APPL (APR/2014): The conducted <i>in-vitro</i> larval test followed the available outlines at the time of study conduct, i.e. the provisions of INRA and the ICPBR-organised ring test group (Aupinel <i>et al</i>, 2009), and exceeded in both, in the exposure design (repeated</p>	<p>Open point</p> <p>RMS to include the endpoint for honeybee larvae expressed in mass of the total intake of</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>indeed in line with the latest developments from OECD.</p> <p>Please express the endpoint in mass/larvae (accumulated test item intake/larvae) and include this value in the LoEP. The unit of the existing value in the LoEP needs also an amendment.</p> <p>Additionally, it would be interesting to see, what was the mortality in the larval phase (e.g. by day 7). Were the discarded runs valid considering only the larval phase?</p>	<p>exposure between days 3 and 6) and in the duration of the study (until hatch at day 22) the currently existing, ring-tested and adopted OECD 237 guideline requirement (i.e. 1 day exposure, study ends at day 7).</p> <p>Moreover, the OECD <i>in-vitro</i> larval ring test group is currently investigating whether the extremely challenging prolongation of the study until hatch at day 22 is at all feasible under routine testing conditions; the currently ring-tested feeding regime is identical to the one employed in the submitted study, and as such, the submitted study already complied with requirements which are currently investigated for potential feasibility of future regulatory testing.</p> <p>NL (May 2014): Table 5 of the study report contains the nominal feeding rates of the larvae in µg a.s./larvae. From this table it can be calculated that the NOEC level of 10.000 µg a.s./kg diet corresponds to an accumulated test item intake of 1.32 µg a.s./larvae (nominal). This value will be included in the LoEP.</p> <p>Table 9 to 13 of the study report contain the results of the individual test runs both for day+7 and day+22. The INRA/ring test validity criteria of mortality in the control</p>	a.i./larvae throughout the exposure period in LoEP (e.g. ug/larvae over 3 days). If only nominal values are available than please indicate clearly that these values are nominal and it cannot be excluded that the real test item intake was lower. If more than one value are available than the range from the valid test runs could be indicated.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			group ≤15% and in the reference group ≥50% until day +7 are met for all five test runs. Two of the five test runs were not considered valid based on a self-set validity criterion from the study author of control mortality of ≤30% at day+22 (end of the test); this was probably done because the guidelines existing at the time only considered a test duration until day +7 and therefore did not include a validity criterion for adult emergence. It is noted that this criterion is now included in the OECD draft guidance document for repeated larval exposure (revision of 25 November 2013) ; the value of 30% will be checked within the ring test. As already said in the DAR, the study author states for the two discarded test runs that “as the self-set validity criterion was not met, no detailed statistical evaluation is presented; however, when subjecting the data to statistical analysis, there is no statistical significance up to and included 10000 µg a.s./kg diet; Chi <sup>2</sup> Test [Bonferroni-Holms corrected, one-sided, α = 0.02”. This means that even if the two discarded test runs would be included, which is not in accordance with the state-of-the-art guidance, the NOEC would not change.	
5(35)	Vol. 3, B.9.4.1.4. Foliage residue trial	EFSA: RMS has indicated that it is unclear how this study can be used in the risk assessment, therefore it was not evaluated.	<b>APPL (APR/2014): The results of the honey bee foliage residue toxicity study revealed no treatment-related adverse effects on</b>	Addressed

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		This type of study might be useful to see persistence of effects and if some risk mitigation measure is needed to be established (e.g. restriction to evening application).	<p>behaviour and on survival of honey bees when the bees were exposed for 24 hours to alfalfa foliage, collected after 3, 8 and 24 hours after treatment with flupyradifurone at a rate corresponding to 205 g a.s./ha. As such, the findings of the honey bee foliage residue toxicity study are fully in line to the results of the semi-field and field studies, which revealed no adverse effects following applications of up to 205 g a.s./ha, applied during honey bees actively foraging on highly bee attractive crops at full bloom.</p> <p>NL (May 2014): We doubt that one laboratory trial on residue ageing can give sufficient information to determine a reliable waiting period for field situations.</p>	Notes: As a package of higher tier studies is available and this test did not indicate more adverse effects, the detailed evaluation of this study might not be essential. However EFSA notes that this study could have been used, at least, as supporting information. Moreover, as a general rule, all information included in the dossier should be evaluated and taken into account.
5(36)	Vol. 3, B.9.4.2, Semi-field studies	<p>EFSA: It is noted that significant food store (not contaminated) was available for the colonies at the start of the tests. It is further noted that 2 of these studies had no GLP certificate.</p> <p>RMS has indicated that the EFSA opinion concluded that the main exposure route for bee brood is via pollen. Indeed, in general, pollen samples had higher residue levels than nectar samples (on the basis of the data that were available). However honey bee larvae are fed with significantly more nectar than pollen.</p>	<p><b>APPL (APR/2014): All tunnel studies comprised at least one honey bee brood cycle and consistently revealed that after a peak exposure following application during honey bees actively foraging at full bloom has not resulted in adverse effects on honey bees and honey bee colonies.</b></p> <p><b>In the colony feeding study (summarised under 8.16.2/03), bee colonies were exposed for a duration of 6 consecutive weeks exclusively to flupyradifurone-treated carbohydrate and pollen-diet and this exposure scenario has not resulted in any</b></p>	<p>Expert consultation</p> <p>Experts from Member States to discuss the design and the results of the available higher tier studies for bees. Experts from Member States to discuss the risk assessment and conclude the risk to bees for the representative uses. Beside the available higher tier effect studies, the experts should/may pay attention to the</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		As general remarks, the EFSA opinion on bees noted that the semi-field trials are suitable to observe immediate effects (e.g. large acute contact effects), but have only limited usefulness to study long-term effects. The foraging area thus the potentially collected and stored food is limited. This was also observed in these studies. The fate of the colonies were monitored for cca. one month, but not followed until overwintering. It is noted that the RMS has captured these notes in Vol. 3. B.9.4.4.	long-term effects, including bee-health and overwintering performance. The same results were obtained from two independent field studies (no long-term effects, no bee-health impairments, no effects on overwintering).  The non-GLP status of the two tunnel studies of Schnorbach (2012a,b) was indicated throughout the study reports and the non-GLP status is typical for early research activities. The results were summarised and submitted for reasons of completeness and transparency.  NL (May 2014): Noted.	-available laboratory endpoints -available residue data -off-field risk assessment -sub-lethal effects observed in laboratory studies -repellent effects seen in some higher tier studies -risk via honeydew -risk to wild pollinators  See also comments in 5(26), from 5(37) to 5(45), from 5(47) to 5(50) and from 5(52) to 5(55). In some of these points some open points were set for further information to ease the discussion.
5(37)	Vol. 3, B.9.4.2, Semi-field studies	EFSA: It is not clear from all summaries whether there were or not significant rainfalls after the application(s) and if so whether these could influence the exposure. Could you please indicate this?	APPL (APR/2014): Except for one of the six tunnel studies, there was no significant rainfall during at least the first three days of confined exposure following application during full bloom. In one study , 6.5 mm rainfall occurred on the day following application, in another study, absolutely no rainfall occurred at all throughout the entire 12 d lasting exposure period of the bees). Since all of the tunnels studies revealed consistent findings, it can be concluded that	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>rainfall - when not occurring immediately after application - does not have a significant influence on the study results. This fact has been acknowledged by the latest edition of the EPPO 170(4)-guideline of 2010, which stated that "...there should not be any rainfall before directly sprayed applications have dried, e.g. for about 2 h after application..." .</p> <p>NL (May 2014): See applicant's response.</p>	
5(38)	Vol. 3, B.9.4.2, Semi-field studies, Study by Schnorbach, H. (2012a)	EFSA: It is agreed that no apparent (i.e. no large, no medium) effects on the bee colonies were observed in this trial. EFSA however not sure that slight effects was not indicated e.g. for brood, adult abundance and hive weight in the 150 g/ha group.	<p>APPL (APR/2014): Abundance of total brood was at any point in time almost identical in the 150 g/ha-flupyradifurone treatment group when compared to the control group, at some assessment days slightly lower, on other assessment days slightly higher. As such, there is no adverse effect on honey bee brood development.</p> <p>The same holds true for the abundance of adult bees: at any point in time there were almost identical numbers of adult bees in the 150 g/ha-flupyradifurone treatment group when compared to the control group, at some assessment days slightly lower, on other assessment days slightly higher. As such, there is no adverse effect on colony strength.</p> <p>Regarding hive weight, there were also only tiny differences when comparing the hive weights of the 150 g/ha-flupyradifurone</p>	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			treatment group with the control group: Until end of confinement, i.e. during the period when all the colonies have the identical foraging area, the weights were practically identical in both groups, after the end of confinement, i.e. when the colonies were allowed to forage freely, the control colonies had an average weight at the end of the study of 7812 g compared to 7707 g in the 150 g/ha-flupyradifurone treatment group (=98.7% of control).  Overall, the study did not reveal any adverse effects on brood-, colony (=adult abundance)- and weight development.  NL (May 2014): See applicant's response.	
5(39)	Vol. 3, B.9.4.2, Semi-field studies, Study by Schnorbach, H. (2012b)	EFSA: EFSA does not share the RMS's view on this study. Some effects on forager mortality (supported by the fact of short-lived reduced foraging activity) seem to be apparent (on the basis of the provided averages). Please provide more detailed information on the forager mortality from this trial.  Some slight effects also cannot be excluded on the larvae on the basis of day 14 data (Figure 9.4.2-13) and that the reference group of Insegar also did not indicated any apparent effect.	APPL (APR/2014): During the 12 days lasting exposure period following application during bee flight at full-flowering, the sum of the total average mortality in the control (C), the bee-brood-toxic reference group (BR), the flupyradifurone treatment group (T) and in the overall-bee-toxic reference group (OR), accounted to 16(C), 19(BR), 30(T) and 1907(OR) dead bees, respectively. As such, there is no adverse effect on mortality.  The application in this study resulted only in a very slightly reduced foraging activity which recovered fully during 1-2 hours after treatment, so that when considering the	Open point  RMS to provide more detailed data (i.e. for each repetition for each day) at least for adult and larvae/pupa mortality in an addendum from the study by Schnorbach, 2012b. Table and/or graphical presentations are preferred.  Note: this information will be used

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>average foraging activity on the day of application, after application, there were on average 23.6 flower visits/m<sup>2</sup> in C and 20.7 flower visits/m<sup>2</sup> in T; at the following day, the values were 14.8 flower visits/m<sup>2</sup> in C and 15.3 flower visits/m<sup>2</sup> in T.</p> <p>In the flupyradifurone treatment group (T) there was no effect on bee brood at any point in time. On day 14, the control group slightly outperformed the flupyradifurone treatment group in the number of larvae, however, at the same day, the flupyradifurone treatment group outperformed the control group in the number of eggs and pupae; as the brood stages continuously develop, the slight differences at a given assessment day do not indicate effects on brood. This becomes obvious when comparing the total abundance of brood (=eggs+larvae+pupae) amongst the treatment groups: At any point in time after application, there was a higher abundance of total brood in the flupyradifurone treatment group when compared to control.</p> <p>The effects of the bee-brood-toxic reference (BR) Insegar became apparent at the brood assessments following application: Whereas the number of larvae and pupae in the BR-group was almost on the same level (slightly</p>	<p>for the expert discussion (see in 5(36)).</p> <p>See also point for expert consultation in 5(36), above.</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>higher) as in the control group before application, comb coverage with larvae and pupae decreased distinctly until day 14 after application in the BR-group when compared to control. Moreover, the effects of the bee-brood-toxic reference (BR) Insegar became further apparent in the number of dead pupae collected in front of the hive: elevated numbers of dead pupae become apparent from day 9 after application onwards, which is the typical time of the onset of effects of Insegar; the sum of the total average number of dead pupae found in front of the hives following application until the end of the study (day 28) in the control (C), the bee-brood-toxic reference group (BR), the flupyradifurone treatment group (T) and in the overall-bee-toxic reference group (OR), accounted to 2(C), 190(BR), 1(T) and 7(OR) dead pupae, respectively. As such, there was a distinct effect of the bee-brood-toxic reference Insegar.</p> <p>Overall, the study did not reveal any adverse effects on mortality, foraging activity as well as on brood-, food- and colony development.</p> <p>NL (May 2014): We agree with the applicant's response and would like to add the following. The mortality numbers in the applicant's response are derived from Table</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			20 in the study report and are the numbers of dead worker bees in front of the bee hives (average value for 2 hives). (Table 35 in the study report contains the values for the individual hives.) Admittedly, the number of dead worker bees in the first twelve days after application is twice as high in the test item as in the control, but it is ~60x as low as the toxic standard. Therefore we do not think there really is an effect on mortality.	
5(40)	Vol. 3, B.9.4.2, Semi-field studies, Study by Rentschler,S. (2012a)	EFSA: It is agreed that some effects on mortality and on foraging activity was indicated in this study. However, Figure 9.4.2-17 includes larvae and pupa mortality. Would the picture be similar if only the forager mortality were presented? Also, on the basis of Figure 9.4.2-20 some effects on larvae cannot be excluded. Please provide more detailed information at least on the larval abundance.	<b>APPL (APR/2014): From the set-up of the colonies inside their respective tunnel until the 2<sup>nd</sup> application during bee flight at full flowering of the crop (day-6 until day 0-before application), the average mortality in the control group (C) accounted to 9.2 dead bees/day and in the flupyradifurone treatment group (T) to 11.4 dead bees/day. From the 2<sup>nd</sup> application until the end of the confined exposure period (day 0-after application until day 11), the average mortality in the control group (C) accounted to 10.4 dead bees/day and in the flupyradifurone treatment group (T) to 14.3 dead bees/day. During the same time period (day 0-after application until day 11), the mean foraging activity in the control group (C) accounted to 15.7 bees/m<sup>2</sup> and in the flupyradifurone treatment group (T) to 15.3 dead bees/day.</b>	Open point  RMS to provide more detailed data for adult and larvae/pupa mortality or abundance separately in an addendum from the study by Rentschler, 2012a. Table and/or graphical presentations are preferred.  Note: The more formal format (i.e. addendum) is needed for transparency reason and because this information will be used for the expert discussion (see in 5(36)).  See also point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p><b>As such, the study did not reveal any adverse effects on mortality and foraging activity.</b></p> <p>Regarding forager mortality versus pupal mortality in front of the hive: based on flupyradifurone's mode of action, the total mortality (sum of laervae, pupae and adults) is almost exclusively composed of adult bees (same as in control). This is confirmed by the results of the two semi-field studies of Schnorbach (2012a,b), which have shown that there are almost no dead pupae in front of the hive following an application of 150 g flupyradifurone a.s./ha during bee flight at full-flowering (see also comment to No. (22)) as well as by the results of the semi-field brood study (Rentschler, S., 2012b), which revealed after an application of 200 g flupyradifurone a.s./ha during bee flight at full-flowering a sum of dead pupae, dead young bees, dead malformed bees and dead malformed pupae inside the dead bee traps to be 18 dead individuals in the control group and to be 4 dead individuals in the 200 g flupyradifurone a.s./ha treatment group.</p> <p>In all semi-field studies there were virtually no dead pupae, dead young bees, dead malformed bees and dead malformed pupae. Moreover, there were also no adverse effects on immature honey bee life stages in</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>the study (Rentschler, S., 2012a): The mean abundance of brood (sum of cells containing eggs, larvae, and pupae) assessed before set-up of the hives (first colony assessment) was 10933 cells/hive for C, 13267 cells/hive for T and 10733 cells/hive for R. At the second colony assessment, during the confined exposure period, 7 days after application (DAA7), the mean abundance of brood in C and T decreased slightly, but synchronously (9000 cells/hive for C and 10133 cells/hive for T), whereas the mean abundance of brood in R decreased strongly to 3200 cells/hive. After one honey bee brood cycle, i.e. 3 weeks after the 2<sup>nd</sup> test item application (fourth colony assessment, DAA21), the mean abundance of brood in C and T was almost identical (10799 cells/hive for C and 10400 cells/hive for T), the same holds true for the last colony assessment (fifth colony assessment, DAA29: 12733 cells/hive for C and 14000 cells/hive for T). Overall, the brood development was comparable between the control and the test item treatment colonies, the differences were within the range of natural variation. No test item related adverse effects on brood development were observed.</p> <p>NL (May 2014): As indicated in the DAR, in</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>the remarks by the RMS to this study, we do not think that the study shows an adverse effect on mortality. Though on DAA1 there is a slight increase of mortality in the treatment group, there is no significant difference in the total post application period and we consider the effect, if there at all, negligible.</p> <p>Flight activity was reduced only on the day of the second application and the two following days.</p> <p>EFSA requested more information on the number of larvae. This was (numbers taken from Tables 20-22 of the study report), on the five subsequent colony assessment days: 2267, 2267, 3000, 3333, 1333 in the control; 3067, 2200, 1733, 3067, 1933 in the treatment; and 1867, 467 in the reference group. Presumably EFSA worries about the lower number of larvae on the third assessment? Standard deviations on this day were as follows: 1733 with STD 1102 in the treatment vs. 3000 with STD 529 in the control.</p> <p>The applicant does not mention the total number of brood cells on the third colony assessment day (DAA13, thirteen days after the second application). On this day, the mean abundance of brood in C and T was 9000 cells/hive for C with STD 917 and 7600</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			cells/hive with STD 4303 for T. Based on these numbers and because on the first, second, fourth and fifth colony assessment day, there is clearly no effect on total number of brood cells as can be seen in the applicant's response above (numbers either equal or higher in T), we consider that there is no adverse effect on brood development.	
5(41)	Vol. 3, B.9.4.2, Semi-field studies, Study by Pröbsting, A. (2012a)	EFSA: EFSA shares the concerns of the RMS regarding this study. It is noted that pollen and nectar samples for residue analysis were taken from the combs, therefore dilution from uncontaminated stored food cannot be excluded.	<b>APPL (APR/2014): We agree with the RMS that the study of Pröbsting, A. (2012a) suffers from a non-ideal colony size allocation. However, when accounting for this short-coming, nothing adverse or alerting can be concluded when evaluating the data in-depth. This conclusion is further corroborated by the results of the three other tunnel studies.</b>  NL (May 2014): The presented residue levels are clearly separated between those from bees and those from the hive.	Addressed  See also point for expert consultation in 5(36), above.
5(42)	Vol. 3, B.9.4.2, Semi-field studies. ( <i>RMS: probably: Study by Pröbsting, A. (2012b)</i> )	EFSA: Some slight, temporary effects on forager mortality cannot absolutely be excluded. The number of bees was slightly lower at the second hive assessment in the treated group (similarly to the reference). Repellent effects were apparent in this study. At the second hive assessment practically	<b>APPL (APR/2014): In the study of Pröbsting, A. (2012b), from the set-up of the colonies inside their respective tunnel until the 3<sup>rd</sup> application during bee flight at full flowering of the crop (day-4 until day 0-before application), the average mortality in the control group (C) accounted to 77.6 dead</b>	Open point  RMS to provide more detailed data for adult mortality and adult and brood abundance in an addendum from the study by Pröbsting, 2012b.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>there was no larvae in the treated groups. These might be due to the shortage of pollen, but can also be indication of toxic effects (or the combination of them).</p> <p>Please provide more detailed information at least on the forager mortality.</p> <p>Was the crop in good condition in this trial?</p>	<p>bees/day and in the flupyradifurone treatment group (T) to 37.6 dead bees/day. From the 3<sup>rd</sup> application until the end of the confined exposure period (day 0-after application until day 7), the average mortality in the control group (C) accounted to 74.4 dead bees/day and in the flupyradifurone treatment group (T) to 49.2 dead bees/day. At the day of the 3<sup>rd</sup> application (day 0-after application), the average mortality in the control group (C) accounted to 26.0 dead bees/day and in the flupyradifurone treatment group (T) to 31.3 dead bees/day. Thus, the applications of flupyradifurone have not resulted in adverse effects on mortality.</p> <p>From the set-up of the colonies inside their respective tunnel until the 3<sup>rd</sup> application during bee flight at full flowering of the crop (day-4 until day 0-before application), the average foraging activity in the control group (C) accounted to 7.4 bees/m<sup>2</sup> and in the flupyradifurone treatment group (T) to 8.0 bees/m<sup>2</sup>. From the 3<sup>rd</sup> application until the end of the confined exposure period (day 0-after application until day 7), the average foraging activity in the control group (C) accounted to 10.3 bees/m<sup>2</sup> and in the flupyradifurone treatment group (T) to 7.8 bees/m<sup>2</sup>.</p>	<p>Table and/or graphical presentations are preferred.</p> <p>Note: this information will be used for the expert discussion (see in 5(36)).</p> <p>See also point for expert consultation in 5(36), above.</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>Thus, the applications of flupyradifurone have not resulted in adverse effects on foraging activity.</p> <p>Colony strength up to the last colony assessment (28 days after the 3<sup>rd</sup> flupyradifurone application) was comparable between C and T with fluctuations which are typical for this endpoint. Fluctuations in colony strength during the confinement period can be well explained by the unavoidable difference in colony strength of individual colonies. Overall, no test-item related adverse effects on colony strength were observed.</p> <p>The observed reduction in the number of larvae occurred concurrently in both the control and the flupyradifurone treatment group, and can be attributed to the severe exposure conditions during the confinement period. During the entire course of the study, brood development was always comparable between the control and the test item treatment colonies, with differences being within the range of natural variation. No test item related effects on brood development were observed.</p> <p>Care was taken throughout the course of the study, from planting until the confined exposure period that the crop was in good condition.</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			NL (May 2014): In addition to the above information, we note that the forager mortality was statistically analysed. No significant differences were detected throughout the entire assessment period.	
5(43)	Vol. 3, B.9.4.2, Semi-field studies , Study by Rentschler,S. (2012b)	EFSA: The mortality was practically continuously higher in the treated group than in the control, with continuously less flower visits in the treated tunnels. This is a clear indication of (at least a slight) potential effect of the a.s. Please clarify if pupae mortality was indeed combined with forager mortality in Figure 9.4.2-29 and if so, how important was this. Also some sublethal intoxication symptoms were noted.  It is just noted that the colonies originates from 2 beekeepers. The pollen and nectar samples for residue analysis were taken from the combs, therefore dilution from uncontaminated stored food cannot be excluded.  Please clarify the used Guideline.	<b>APPL (APR/2014):</b> In the study Rentschler, S. (2012b), from the set-up of the colonies inside their respective tunnel until the 2 <sup>nd</sup> application during bee flight at full flowering of the crop (day-4 until day 0-before application), the average mortality in the control group (C) accounted to 50.5 dead bees/day and in the flupyradifurone treatment group (T) to 86.8 dead bees/day. From the 2 <sup>nd</sup> application until the end of the confined exposure period (day 0-after application until day 7), the average mortality in the control group (C) accounted to 71.0 dead bees/day and in the flupyradifurone treatment group (T) to 91.0 dead bees/day. At the day of the 2 <sup>nd</sup> application (day 0-after application), the average mortality in the control group (C) accounted to 46.3 dead bees/day and in the flupyradifurone treatment group (T) to 91.3 dead bees/day. Thus, mortality in the flupyradifurone treatment group (T) after the 2 <sup>nd</sup> application during full bloom has not changed when compared to the time period before the full	Open point  RMS to provide more detailed data for adult and larvae/pupa mortality separately in an addendum from the study by Rentschler, 2012b. Table and/or graphical presentations are preferred. As an alternative solution, clearly confirm that the contribution of pupae mortality was negligible throughout the study and this does not disturb the interpretation of the adult mortality from the DAR (i.e. the overall picture suggested by Figure 9.4.2-29 would be the same for adult mortality).  Note: The more formal format (i.e. addendum) is needed for transparency reason and because

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>bloom application. This is also expressed by the calculated <math>Q_M(DAA0aa)</math>-values of 0.9 (C) and 1.1 (T) as well as by the <math>Q_M(DAA0aa</math> to 7)-values of 1.4 (C) and 1.0 (T), respectively.</p> <p>As such, there is no indication that the treatment with flupyradifurone resulted in any increase of mortality.</p> <p>Although there was a slight repellent in the flupyradifurone treatment group, foraging activity was overall still on a high level. The daily flight intensity during the confined exposure period following the application of flupyradifurone during fully bloom, accounted to 0 - 27.7 forager bees/m<sup>2</sup> in C and to 0.0 - 25.9 in T, the mean daily flight intensity was recorded during the same time period to be 15.1 and 11.8 in C and T, respectively. As such, the treatment with flupyradifurone resulted under the forced (confined) exposure conditions of this study in a slight repellent effect, however, this slight repellent effect is in its extent neither apiculturally nor ecologically adverse.</p> <p>Regarding pupae (immature life stage) mortality, the sum of dead pupae, dead young bees, dead malformed bees and dead malformed pupae found inside the dead bee traps in front of the hives was lowest in the flupyradifurone treatment (T), when</p>	<p>this information will be used for the expert discussion (see in 5(36)).</p> <p>See also point for expert consultation in 5(36), above.</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>compared to the control group (C) (18 individuals in C, 4 individuals in T). As such, pupae mortality in front of the hive did not substantially contribute to the observed overall mortality.</p> <p>The bee colonies were obtained from two beekeepers, but were distributed equally among the replicates in order to guarantee uniform bee material in all treatments.</p> <p>The study followed the provisions of the OECD Guidance Document No. 75 (2007).</p> <p>NL (May 2014): We agree with the applicant's response. Please note that the presented residue levels are clearly separated between those from bees and those from the hive. Apologies for the mistake in the reported guideline; this can be corrected if a revised version of the DAR is made.</p>	
5(44)	B.9.4.2. Semi-field studies, Rixer 2013 p. 239 and following studies	<p>Nature et Progrès Be</p> <p>Residues levels as high as 3 mg/kg and 70 mg/kg (70 ppm) are present in nectar and pollen from forager bees, respectively.</p> <p>Since behavioural effects exist without dose-response pattern the innocuousness of the substance for pollinators is not proved.</p>	<p>APPL (APR/2014): Nature et Progrès Be refers to a residue study in Phacelia which shared the same flupyradifurone exposure scenario as employed in a series of honey bee tunnel effect studies in Phacelia. The study was conducted to reveal the typical concentrations in nectar and pollen after an application scenario that has been repeatedly tested without adverse effects on honey bees and honey bee colonies.</p>	<p>See point for expert consultation in 5(36), above.</p> <p>Note: EFSA agrees with the commenter that the innocuousness of the substance for pollinators is not proved merely by the available laboratory studies. The concern is further justified by the fact of high</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>All honey bee laboratory studies with flupyradifurone which aimed to derive an LD50/LDD50 showed a distinct dose-response pattern, in honey bee tunnel studies repeatedly the highest envisaged application rate(s) of flupyradifurone in agronomically relevant crops were tested (consistently without adverse effects).</p> <p>NL (May 2014): We agree with the applicant's response.</p>	<p>potential of mobility of the a.s. in plants. However the available higher tier studies help to assess the potential effects of flupyradifurone in more realistic conditions. These studies include exposure to contaminated pollen and nectar.</p> <p>See also open points and comment in 5(31) and comment in 5(26).</p>
5(45)	Vol. 3, KIIIA 10.4.5/01 and KIIIA 10.4.5/02, Honey bee field studies.	<p>SE: It is noted that the flight intensity was quite low in the field trials, 0-2 bees /m<sup>2</sup> throughout the majority of the study. The low flight intensity was observed both in the controls and the treated fields.</p>	<p><b>APPL (APR/2014): The flight intensity is typical for winter OSR in early springtime, when this crop is flowering; winter OSR can be considered to be the most important agricultural honey crop in Central Europe.</b></p> <p>NL (May 2014): As the applicant states, this flight intensity is indeed typical for WOSR, it has been seen in other bee field studies with this crop as well.</p> <p>We speculate that the relatively low flight intensity could have something to do with the lower numbers of bees per ha.</p> <p>The requirement in EPPO is 2-3 bees/m<sup>2</sup> for rape for a 1 ha plot. Per plot it is said to use at least four colonies of at least 10.000 bees,</p>	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>but to relate this to plot size and attractiveness of the crop. If the guideline numbers are used, this gives 40,000 bees/ha.</p> <p>The first field study in the DAR (in DE) was done on 4-5 ha fields, used 8 colonies with on average 9000 bees per field, thus 18,000-14,400 bees/ha. This study had a flying intensity at flowering stage of 1.0 bees/m<sup>2</sup>/day.</p> <p>The second field study (in FR) was done on 4 to 4.5 ha test fields, used 8 colonies with on average 12,000 bees per field, thus 24,000 – 21,333 bees/ha. This study had a flying intensity at flowering stage of 1.5-1.8 bees/m<sup>2</sup>/day.</p> <p>It should be noted that care was taken in the study design not to have nearby flowering crops. Pollen analysis was done as another way to estimate exposure. As said in the DAR, we believe that these trials are useful for the risk assessment. The field studies are to be seen together with the semi-field studies and the spiked diet study to get an overall picture.</p>	
5(46)	Vol. 3, B.9.4.2, Residue trials	EFSA: EFSA welcomes the residue data on pollen and nectar. Could you please clarify how exactly the foragers were sampled (e.g.	<b>APPL (APR/2014): At each sampling, the hive entrances of the colonies were sealed before the sampling and the forager bees</b>	Addressed

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		collected in front of the hive, in the hive, in the crop) in the study Rexer 2013. The trials with drenching and non EU representative crops – although also welcomed – are less relevant for the current assessments.	were subsequently collected as they returned to the hive by suction into a box filled with dry ice, using modified hoovers ("bee vac"). After sampling, the hives were re-opened.  NL (May 2014): See above. We agree with EFSA as to the usefulness of the non EU and drenching trials; we say so already in the DAR.	Note: the sampling method as described in Column 3 is in line with the recommendation of the new EFSA GD.
5(47)	Vol. 3, B.9.4.3, Field studies, Study by Rexer 2012a	EFSA: EFSA agrees that some increase in forager mortality is apparent for a few days after the 3 <sup>rd</sup> application (day 13 data might be statistically different). Also some sublethal intoxication symptoms were noted. Also agreed that the average hive weight was somewhat lower for the treated hives after the 2 <sup>nd</sup> and 3 <sup>rd</sup> spray applications, while this parameter was very similar before this period.  An important element that the surroundings of the fields were checked and major flowering crops were not present within 2 kms of the treated fields. However attractive wild trees and shrubs were foraged as indicated by the pollen analysis. In general, EFSA agrees with the assessments of the RMS ('Remarks by the evaluator'). Please confirm that the 2 <sup>nd</sup> application was	APPL (APR/2014): The 2 <sup>nd</sup> spray application at immediate pre-flowering/early bloom occurred on April 26, which is DAS6 (= 6 days after set-up of the colonies), the 3 <sup>rd</sup> spray application at full bloom occurred on May 02, which is DAS12. There were no significant rain events throughout the entire field exposure phase.  The daily mean mortality (dead bees/colony) during DAS7 to DAS12 (= after 2 <sup>nd</sup> before 3 <sup>rd</sup> application) accounted to 11.2 in the control group (C) and to 7.6 in the flupyradifurone treatment group (T); the daily mean mortality (dead bees/colony) during DAS13 to DAS24 (= after 3 <sup>rd</sup> application until end of flowering/relocation of the colonies) accounted to 9.4 in the control group (C) and to 8.8 in the flupyradifurone treatment group (T). The "perceived higher mortality" in T is more than "overcompensated" 2-3 days later	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>on Day 6 and the 3<sup>rd</sup> on Day 12. Please also clarify if there was any significant rain after the 2<sup>nd</sup> and 3<sup>rd</sup> spray applications in the fields.</p> <p>It is acknowledge that in terms of a.s. treatments (4 different treatments), the study can be considered as worst case. However the severity of the study in terms of residue dilution of the collected food from the surroundings is unknown (might be typical but likely not worst case). Also, the impact of the comb(s) removal is unknown.</p>	<p>by the same, slightly higher mortality in C, and as such, the recorded mortality values in both, C and T, display the natural variability of this endpoint under field conditions. This conclusion is confirmed by the average values following the respective flupyradifurone treatments (see figures above), which are on the same (actually even on a slightly lower) level in T when compared to C.</p> <p><b>As such, the flupyradifurone treatments have not resulted in increased mortality.</b></p> <p>Concerning hive weight, the study showed an absolute hive weight development of the colonies which was very similar between the flupyradifurone treatment group and the control group. Whilst hive weights during the honey bee foraging season were slightly lower in the flupyradifurone treatment in the study of Rexer, 2012a, hive weights were higher during the honey bee foraging season in the flupyradifurone treatment group when compared to control group in the second study (Rexer, 2012b; identical study design as of Rexer, 2012a). Actually, weight development was always very similar between treatment and control and the observed small differences display the natural variation between colonies.</p> <p><b>There were no flupyradifurone-related</b></p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p><b>adverse effects on hive weight development.</b></p> <p>Regarding other flowering crops in the surrounding of the fields under investigation, it is not the aim of a field study to fully exclude any potential foraging outside the treatment area - this scenario is investigated via the set of the provided tunnel studies - but to study honey bee colonies in a realistic worst-case environment, under non-forced but prolonged exposure conditions, and as such, by also avoiding potential artefacts resulting from the confinement in gauze tunnels. In both field studies, however, particular care was taken to minimize foraging outside the treatment area by selecting isolated field plots with little alternative forage in the vicinity and as such to set-up a realistic-worst case field condition (e.g. the colonies were placed inside the treated field and not at the field boundary, at least a distance of 2 km distance was kept to other potentially flowering crops, care was taken that no mass flowering wild flowers are present, etc.).</p> <p>The palynological analysis of the collected pollen revealed that the oil-seed rape crop was a significant foraging area of the honey bee colonies under investigation.</p> <p>Regarding comb removal, this is an</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>apiculturally necessary operation to prevent swarming in field studies when conducted at that period of time in the year in a highly bee attractive crop, which offers the colonies nectar and pollen in abundance. Without this necessary operation, there is a high risk of technical failure; moreover, this operation fully reflects routine apicultural practice.</p> <p>NL (May 2014): See applicant's response for confirmation of days and rain events. In the DAR, we concluded the following based on this study: No clear effects on mortality, flight intensity, brood and food storage area, and colony development were detected. Some possible short-term effects on mortality, flight intensity, behaviour and colony weight might have occurred after the 3rd application. There was however, a clear recovery from these effects. No effects on the capacity of the colony to overwinter are expected. Given the agricultural landscape in Germany, there is not a better set-up of a field study possible. Higher exposure to flupyradifurone in the treated field is difficult to realize and exposure to pesticides in general in the control cannot be avoided.</p>	
5(48)	Vol. 3, B.9.4.3, Field studies, Study by Rexer	EFSA: It is noted (already noted by the RMS) that the average forager mortality was	<b>APPL (APR/2014): The 2<sup>nd</sup> spray application at immediate pre-flowering/early bloom</b>	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
	2012b	<p>continuously slightly higher in the treated field in the last period of the exposure, however this phenomenon was not observed shortly after the applications.</p> <p>Some decrease in brood (queen loss ?) of one treated hive was observed in late of the season.</p> <p>One control pollen sample contained the a.s. (this was not noted on page 279 only on page 289).</p> <p>Again, in general, EFSA agrees with the assessments of the RMS ('Remarks by the evaluator') including the noted uncertainties. Please confirm that the 2<sup>nd</sup> application was on Day 1 and the 3<sup>rd</sup> on Day 10. Please also clarify if there was any significant rain after the 2<sup>nd</sup> and 3<sup>rd</sup> spray applications in the fields.</p>	<p>occurred on April 09, which is DAS1 (= 1 days after set-up of the colonies), the 3<sup>rd</sup> spray application at full bloom occurred on April 18, which is DAS10. There were no significant rain events throughout the entire field exposure phase (the only significant rain event occurred at the day of relocation back to monitoring site on May 11), after flowering was completed and the last assessments on the study fields have been made (at May 09).</p> <p>Regarding average forager mortality being slightly higher in the flupyradifurone treatment group during the last period of the exposure phase, it should be considered that forager mortality was almost continuously higher in the untreated control group compared to the flupyradifurone treatment group: The daily mean mortality (dead bees/colony) during DAS1 to DAS10 (= after 2<sup>nd</sup> before 3<sup>rd</sup> application) accounted to 22.5 in the control group (C) and to 18.7 in the flupyradifurone treatment group (T); the daily mean mortality (dead bees/colony) during DAS11 to DAS31 (= after 3<sup>rd</sup> application until end of flowering/relocation of the colonies) accounted to 14.5 in the control group (C) and to 11.8 in the flupyradifurone treatment group (T).</p> <p>As such, the recorded mortality values in</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>both, C and T, display the natural variability of this endpoint under field conditions.</p> <p>Regarding decrease in the number of brood cells, almost all colonies of the study showed all brood stages at all assessment dates during the observation period except in late summer and autumn, when the natural period of breeding activity of the colonies ended. Where exceptions were noticed (e.g. short-term loss of an egg-laying queen), both, control and test item treatment group, were equally affected. There were no test item-related adverse effects on brood development, including queen survival and overwintering performance.</p> <p>All residue findings in the control group (flowers, pollen from comb, nectar from comb, pollen from forager bees and nectar from forager bees, comprising in total more than 100 samples which have been collected during the period from April until beginning of October showed - except for one single sample collected by middle of September - no quantifiable residues. As this single sample was collected several months after the end of the field exposure period with no residue detects before and after, contamination is a likely explanation. The body of residue data in the control group demonstrated that the control colonies were</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>not exposed to flupyradifurone due to a sufficient isolation of the test fields.</p> <p>NL (May 2014): See applicant's response for confirmation of days and rain events. In the DAR, we concluded the following based on this study: No clear effects on mortality, flight intensity, brood and food storage area, colony development, behaviour and colony weight were detected. Some possible short-term effects on mortality and flight intensity might have occurred after the 3rd application. If so, these did not result in effects on colony development before and after overwintering.</p>	
5(49)	Vol. 3, B.9.4.3, Field studies, Study by Nikolakis, Krieg et al. 2012	<p>EFSA: Again, EFSA agrees with the assessments of the RMS ('Remarks by the evaluator') including the noted uncertainties. Please confirm also whether the food supplements placed inside the hive in periods when honey bees did not sufficiently forage were also spiked. It is noted that no reference treatment was used in this study. The adult mortality in T1 was definitely higher than in the other groups, what most likely originates from the elevated mortality of one colony (No. 8 in tunnel 13). It was also argued (page 294) that this colony had disease-like symptoms. Could you please clarify that it is believed that this elevated</p>	<p>APPL (APR/2014): The food supplements placed inside the hive in periods when honey bees did not sufficiently forage were treatment-related, i.e. treatment-specifically spiked in the respective flupyradifurone treatment groups and untreated in the control group.</p> <p>Total worker bee mortality of the flupyradifurone -T1 - colony 8 in tunnel 13 was much higher than the mortality range of the other four colonies at the same treatment level. Mortality of colony 8 in tunnel 13 (T1) increased primarily towards the end of the confined exposure period, starting in the 4<sup>th</sup> week of exposure, with bees showing</p>	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>mortality was not linked with the a.s. consumption.</p> <p>Reading across of some parameters, but mainly considering the average data on colony strength, some delayed effects in group T3 cannot be excluded. A same trend (lower abundance from September) can be observed also for T1 and T2. The colony strength after overwintering was clearly lower in all treated groups than in the control (22-33%).</p> <p>It is acknowledged that this special feeding study represents quite severe conditions in terms of oral exposure of a honey bee colony (up to 10 mg/kg a.s. in pollen and nectar).</p>	<p>concurrently disease-like symptoms and sometimes increased motility, which finally resulted in the non-continuation of the colony. The higher mortality level of this colony is not considered to be treatment related, as neither the four other T1 – colonies revealed a comparable mortality level, nor did any of the other colonies in the higher test item treatment levels showed this dimension of worker bee mortality. However, in a conservative approach to assess potential effects of flupyradifurone on mortality, colony 8 in tunnel 13 was still included in the applied statistical models and thus contributes to the statistical evaluation of the treatment group T1. Statistical comparisons of the mortality assessments (i.e. for worker bees, drones, immature life stages – in front of the hive and at the tunnel walls) summed-up for each tunnel for the entire study period revealed no statistically significant results between control and test item treatments, except for worker bee mortality at the tunnel walls, which was found to be significantly lower in exposure T1 compared to control.</p> <p>All measured effect-parameters (honey bee mortality in front of the hive and at the tunnel walls during confinement, foraging activity (flight activity) during confinement, colony strength, colony brood status/brood</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>development, nectar/honey stores, pollen stores, honey bee disease and virus analysis, mite-drop assessment via <i>Varroa</i> boards, behaviour of the bees and overwintering-performance) were carefully evaluated and whenever the data qualified for statistical analysis, the data were thoroughly statistically evaluated.</p> <p>These analyses revealed no adverse acute, short-term or long-term effects of a 6 weeks lasting exclusive and continuous exposure of honey bee colonies to flupyradifurone treatment levels of up to and including 10 ppm.</p> <p>The findings of this colony feeding study are further fully in line to the acute and chronic laboratory data in adult honey bees and honey bee larvae.</p> <p>There is no indication of any delayed effects in the colony feeding study.</p> <p>Colonies behaved very uniformly during the confined and as such controlled semi-field exposure period, and showed the typical variability once released from confinement (field conditions).</p> <p>NL (May 2014): In the DAR, we concluded the following based on this study: under the specific circumstances of this study, the</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			different treatments of the test substance do not lead to an adverse effect in one of the observed parameters (or the combination of adverse effects of the different parameters) to such an extent, that it led to the collapse of one or more colonies.	
5(50)	B.9.4.5.5. p. 340: <i>Repellence of flupyradifurone leads to decreased flight intensity. In that way bees will minimize exposure of the hive to flupyradifurone.</i>	Nature et Progrès Be  Reduction of flight intensity is not always due to repellence. Knock-down effects may lead to a reduction in flight intensity too. These two situations are different since in the first case bees are not intoxicated; in the second one they are intoxicated and other effects may appear.  When pyrethroids are usually considered to be repellent, scientific studies have shown that the stopping of foraging was actually due to a knock-down effect. Effects on temperature regulation may lead to bees' mortality depending on temperature of the place where the bee has to overnight.  Cox RL and Wilson WT, 1984: Effects of permethrin on the behavior of individually tagged honey bees, <i>Apis mellifera L</i> (Hymenoptera : Apidae), <i>Environ. Entomol.</i> 13: 375-378  Rieth JP, 1986 : The repellent effect of pyrethrinoids insecticides on honey bees, <i>Physiological Entomology</i> 13(2): 213–218	<b>APPL (APR/2014): The slightly reduced flight intensity observed after the application of flupyradifurone under forced (confined) exposure conditions has neither resulted in mortality nor in adverse effects on the colony level (brood-, food- and colony strength development). The set up of the tunnel studies pay also particular attention on potential secondary ("other") effects – which were, however, consistently not observed.</b>  NL (May 2014): Agree with the applicant.	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(51)	Vol. 1 and Vol 3 B.9.4, Effects on bees	FR: The data and risk assessment for bees is well-built, clear and agreed.	NL (May 2014): Noted, thank you.	Addressed.
5(52)	Vol. 3, B.9.4.4, RA for bees	EFSA: In general, EFSA agrees with the conclusions of the RMS and welcomes the overview tables for the higher tier studies. However please consider specific comments above, and in line with those, please consider to amend the entries in the LoEP (especially for the higher tier studies). EFSA notes that a kind of calculation method for the oral exposure for lower tier RAs (which allow to use the endpoints from the laboratory data) was used for the RA for the neonicodinoids (published in January 2013 by EFSA). These maybe used if needed.	NL (May 2014): See our answers to your comments above. At the moment we do not see the need to amend the LoEP. The higher tier effect studies could be discussed in an expert meeting so that we can reach agreement on their interpretation. We note the availability of the calculation method in the 2013 EFSA publication. Because this method was not officially established in guidance ánd did not have trigger values, we did not use it. We propose to wait with calculations on oral exposure until there is a harmonised method available to calculate exposure levels and especially the corresponding risk. For the (nót bee- attractive!) representative uses of the DAR, there is no need for first tier calculations because there is a large number of higher tier effect studies available.	See point for expert consultation in 5(36), above.
5(53)	Vol 1, Risk assessment for honey bees, Exposure via honeydew.	SE: At applications at later growth stages there is a possibility that build-up of honeydew has occurred before spraying with flupyradifurone, hence honey bees may be exposed to honey dew.	<b>APPL (APR/2014): High aphid infestation levels and associated formation of honeydew is not in compliance with Good Agricultural Practice, since it poses the risk of secondary fungal, bacterial or viral infections which impacts yield and/or quality. Accordingly, advisory use recommendations aim for product applications at infestation levels at which honeydew formation does not attain</b>	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>levels which attract honey bees. Nonetheless, it can be concluded from the extensive semi-field and field honey bee data package, comprising application rates to highly bee attractive, flowering crops of up to and including 200 g a.s./ha that honey bees are not at risk even if honey dew would be present.</p> <p>NL (May 2014): We note that there currently is no agreed risk assessment method for this exposure route. We agree with the applicant that, based on the higher tier effect studies in highly attractive flowering crops, the risk via honeydew is probably low.</p>	
5(54)	Vol. 3, B.9.4.4.1	AT: The calculation of in-field and off-field HQ values for bees is not foreseen in the guidance document. The calculation of off-field HQs indicates that there might be no risk for bees in the off-field and hence a higher tier risk assessment is not required. Please clarify the purpose of the calculation of off-field HQ values.	<p>APPL (APR/2014): Although “off-field” HQs are not common in the honey bee section, the off-field HQs as calculated by the RMS - similarly to the specific approach routinely employed for non-target arthropods - simply complete the risk assessment picture for the use pattern of a non-bee attractive crop: When considering realistic worst-case drift rates in such a non-bee attractive crop, the validated HQ of 50 is not breached, even if honey bees are assumed to exclusively forage in a highly bee attractive crop directly adjacent to the treated, non-bee attractive area (i.e. the so-called “in-field” area). As</p>	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			such, the calculated off-field HQs simply illustrate this situation.  NL (May 2014): See applicant's response.	
5(55)	Vol. 3, B.9.4., Effects on wild pollinators	DE: Even if the butenolide flupyradifurone (nicotinic acetylcholine receptor (nAChR) agonist) is not as toxic as the closely related neonicotinoids, such as imidacloprid, the concerns about possible sublethal effects on wild pollinators such as bumble bees and wild bees (e.g. due to persistence, potency, systemic properties, bioavailability, mobility and findings in pollen of succeeding crops) should be investigated and discussed further. Concerns about long term sublethal effects on brood development or queen production cannot be excluded per se and possible effects could cause unacceptable damage for the population of wild pollinators. For the risk assessment of wild pollinators only ecotoxicological studies with honey bees are available (except for one bumble bee study for pollen collection). Thus, there is insufficient data provided for the risk assessment of wild bees and solitary bees. The risk assessment for wild bees should be discussed.	APPL (APR/2014): There are to date no harmonised test guidelines on how to reproducibly test non- <i>Apis</i> bees for risk assessment purposes, however, the international bee testing community under the auspices of ICPPR and OECD are currently developing these test systems (laboratory and higher tier) with first activities in 2014.  From the envisaged non- <i>Apis</i> test systems, the acute bumble bee contact laboratory toxicity test is most progressed, and for flupyradifurone, tested via Flupyradifurone SL 200, no intrinsic sensitivity differences were found between <i>Bombus</i> ( $LD_{50} > 100 \mu\text{g a.s./bee}$ ; Vergé, 2012; KIIA 8.7.1/07) and <i>Apis</i> ( $LD_{50} = 15.7 \mu\text{g a.s./bee}$ ; Schmitzer, 2009; KIIIA 10.4.2.1 /01); in the <i>Bombus</i> laboratory study (Vergé, 2012; KIIA 8.7.1/07), no behavioural abnormalities or sub-lethal effects were recorded throughout the entire test period.  The butenolide insecticide flupyradifurone is about three orders of magnitude less toxic to honey bees compared to nitro-substituted neonicotinoid insecticides. Overall,	See point for expert consultation in 5(36), above.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>flupyradifurone reveals a much more favourable risk profile to honey bees than the majority of insecticides currently registered in the EU; therefore, flupyradifurone will substantially contribute to a more bee-pollinator-friendly insecticide portfolio in the EU agricultural system.</p> <p>NL (May 2014): We note that there was no harmonised risk assessment scheme for wild pollinators available at the time of writing the DAR (nor is there one at this moment, in May 2014). We also note the much lower toxicity to honeybees as compared to e.g. imidacloprid and the low toxicity found in the bumblebee contact study. Nevertheless, the wild bee risk assessment can be discussed in an expert meeting.</p>	
5(56)	Vol. 3, B.9.5.1, Aged residue studies on NTAs	<p>EFSA: The aging processes were conducted in semi-natural conditions in both trials. It seems that the temperature was very high (at least occasionally). Was not the degradation accelerated too much in these conditions?</p> <p>It is noted that the effects on the reproduction on 42DAT2 is considerable higher than on day 28DAT2.</p>	<p>APPL (04/2014): Mean temperature between the 1<sup>st</sup> application and the start of the last bioassay of the <i>Aphidius</i> aged residue study was 19.4 °C which is high but considered acceptable. For the <i>Orius</i> aged residue study the mean temperature between the 1<sup>st</sup> application and the start of the last bioassay was with 20.0 °C in the same range.</p> <p>The mortality data of the <i>Orius</i> study showed a constant decrease of mortality from the 1<sup>st</sup> to the 4<sup>th</sup> bioassay. The slight increased effect on fecundity from 23% on 28DAT2 to</p>	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>34.7% on 42DAT2 is within the natural variability of the reproduction assessment in this test system and below the ESCORT 2 trigger of less than 50% effect there is no quantitative difference in the interpretation of the values. The aged residue study with the more sensitive species <i>Aphidius</i> showed a constant decline of mortality and of the effects on reproduction.</p> <p>NL (May 2014): The ageing of the residues on potted maize plants or apple trees in the two studies in the DAR (10.5.1/01 and 10.5.3/02) took place under natural semi-field conditions with rain protection (Plexiglass, UV permeable). Temperatures ranged from 5.2 to 39.3 and 7 to 37 °C, with means of 19.4 and 20 °C. To our knowledge, there are no validity criteria or indeed guideline recommendations for the ageing conditions of plant residues in semi-field environment in NTA testing. It seems logical that if these studies are used in risk assessment, it should be considered if their conditions are relevant. In this case, the temperature may be high but the plants were protected from rain, so for both parameters field conditions are not exactly matched. We consider these studies useful to indicate that recovery can occur after a certain amount of time, without</p>	

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>deriving exact recovery dates from the studies.</p> <p>With regard to the comment of EFSA on the Orius study (effect on reproduction on 42DAT2 35% and on 28DAT2 23%) we agree with the applicant that this is within the range of natural variation and not an indication of a delayed effect.</p>	
5(57)	Vol. 3, B.9.5.2, Field studies for NTAs	<p>EFSA: It is noted that the checkerboard design could be favourable for the re-colonisation of the test plots.</p> <p>A relatively undisturbed habitat (grassland) with little agricultural impact may have not represent well a typical NTA communities of typical agricultural habitats. Although it is acknowledged that the study sites were surrounded by agricultural fields.</p>	<p><b>APPL (04/2014):</b> The study design follows (as recommended by ESCORT 3) the design of the case study as presented in the Dutch Guidance document (de Jong et al. 2010, Guidance for summarizing and evaluating field studies with non-target arthropods, RIVM report 601712006/2010. Bilthoven, NL). The short duration of only a few weeks limits the re-colonization of the treated area. Grassland was chosen as habitat for this study since off-crop habitats along fields are often covered by grass and represents a homogenous test system allowing for meaningful statistical comparisons and the use of standardized sampling techniques. The selection of an area with little agricultural impact ensures that there is no preselection in favor of less sensitive species due to exposure to plant protection products, which was one of the major criticisms of using NTA in-field studies for the NTA off-field risk assessment.</p>	See expert consultation 5(60).

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			<p>Both studies assessed a large number of non-target arthropod species which do occur in off-field habitats.</p> <p>NL (May 2014): Agree with applicant. In the study summaries (results/arthropod species composition and abundance) it is discussed why we consider the studies sufficiently representative for the off-field environment.</p>	
5(58)	Vol. 3, B.9.5.2	AT: The table B.9.5.2-02 (p. 367) is not readable; please change the table.	<p><b>APPL (04/2014): A table with improved graphical quality could be provided to the RMS as necessary,</b></p> <p>NL (May 2014): Our apologies. If the applicant sends us the table with improved graphical quality, we will include it in a revised DAR or addendum.</p>	<p>Data requirement Applicant to submit more comprehensive study summary of the two studies Aldershof S. &amp; Bakker F. (2012). Furthermore the present table B.9.5.2-02 should be presented in a readable version. More detailed information will be necessary to understand the visualised results and especially the data standing behind it (e.g. validity criterion).</p> <p>See also expert consultation 5(60).</p>
5(59)	Vol. 3, B.9.5.3, RA for NTAs	EFSA: It is noted that a correction factor of 5 was used in the Tier 2 HQ off-field calculations; however a factor of 10 is recommended in ESCORT 2. It is also noted that for hops, risk mitigation (i.e. 20 ms buffer zone) measures are	<b>APPL (04/2014): The DAR presents in line with the recommendations of ESCORT 2 the HQ only for the Tier 1 NTA risk assessment. For the Tier 2 off-field risk assessment the DAR uses in line with ESCORT 2 a correction factor of 5 for the exposure</b>	See expert consultation 5(61).

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		recommended to manage the off-field risk.	<p>assessment (see ESCORT 2, page 19-20, footnote "e" to equation 4).</p> <p>NL (May 2014): See applicant's response. In addition, the default correction factor of 5 in higher tier HQ calculations is mentioned in the terrestrial guidance document SANCO/10329/2002) on page 22.</p>	
5(59) a	Vol. 3, B.9.5.3, Refined off-field risk assessment	<p>DE: The two non-target arthropod field studies (off-crop) from the authors Aldershof S. and Bakker, F. (2012) are quite comprehensive and a summary of it is obviously labour-intensive.</p> <p>Nevertheless, in the study summary more readable (e.g. Table on page 367) as well as more detailed information will be necessary to understand the visualised results and especially the data standing behind it (e.g. validity criterion). It will also be helpful to provide more information within the summary to avoid misinterpretation of the results.</p> <p>Furthermore, there are some shortcomings of the studies that question the applicability for the refinement in off-crop risk assessment as well as the reliability of the selected endpoints:</p> <p>In an off-crop field study suitable for the</p>	<p><b>APPL (04/2014): A more readable version of the table could be provided. The two study summaries follow the recommendations of the Dutch Guidance document (de Jong et al. 2010, Guidance for summarizing and evaluating field studies with non-target arthropods, RIVM report 601712006/2010. Bilthoven, NL) and have an extent of 13 to 15 pages each and are considered appropriate. Furthermore we do not agree with the comments provided by Germany (DE) listed under (1) to (4):</b></p> <p><b>The study design follows the case study as presented in the Dutch Guidance document (de Jong et al. 2010, Guidance for summarizing and evaluating field studies with non-target arthropods, RIVM report 601712006/2010. Bilthoven, NL) and was recommended by the ECORT 3</b></p>	<p>Expert consultation</p> <p>Experts to discuss the two non-target arthropod field studies (off-crop) from the authors Aldershof S. and Bakker F. (2012). Can they be considered acceptable to be used in the risk assessment?</p> <p>See reporting table comment 5(60). "DE: The two non-target arthropod field studies (off-crop) from the authors Aldershof S. and Bakker, F. (2012) are quite comprehensive and a summary of it is obviously labour-intensive. Nevertheless, in the study summary more readable (e.g. Table on page 367) as well as more detailed information will be necessary to understand the visualised results and especially</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>refinement of the off-field risk assessment it has to be shown that toxic effects are not overlaid by re-colonisation, but the studies were conducted to show NOER/NOEAER by recovery, thus the focus was different influencing the design and outcome of the study. In the two conducted (off-crop) field studies the plots were established in a checkerboard design with open (uncovered) plots, which makes it difficult to conclude on the reliability of the study results on toxic effects. Furthermore, arthropods were sampled one, two, four and eight weeks after treatment. Thus, overlaying of toxic effects by re-colonisation cannot be excluded, and a clear separation of NTA-communities between treated and non-treated plots in the off-field is missed.</p> <p>The off-crop field studies were performed only on grassland and are, therefore, insufficient as surrogate for the variability of possible off-field habitats around arable land. The study is not representative for 100% of existing worst case landscape. Standing alone, these field studies are insufficient for the</p>	<p>workshop (2010) for higher tier study design for the NTA off-field risk assessments. We consider in line with the RMS that the chosen off-crop field study design is suitable for the refinement of the off-field risk assessment. The study follows a dose response design and plot size is sufficient considering the short study duration. The short sampling intervals at the beginning of the studies allow an appropriate detection of initial effects and an assessment of recovery in the following weeks. The checkerboard design ensures that plots are not affected by spray drift from neighbouring plots which is an essential factor when considering the performance of the untreated control plots in the studies. No surrogate habitat can cover 100% of a worst case landscape. Grassland is never the less a suitable surrogate for off-crop habitats, since many off-crop habitats are covered by a meadow like vegetation. Both studies assessed the effects on more than 70 arthropod species that do occur in off-crop habitats and cover the taxa that should be</p>	<p>the data standing behind it (e.g. validity criterion). It will also be helpful to provide more information within the summary to avoid misinterpretation of the results. Furthermore, there are some shortcomings of the studies that question the applicability for the refinement in off-crop risk assessment as well as the reliability of the selected endpoints:</p> <p>In an off-crop field study suitable for the refinement of the off-field risk assessment it has to be shown that toxic effects are not overlaid by re-colonisation, but the studies were conducted to show NOER/NOEAER by recovery, thus the focus was different influencing the design and outcome of the study. In the two conducted (off-crop) field studies the plots were established in a checkerboard design with open (uncovered) plots, which makes it difficult to conclude on the reliability of the study results on toxic effects. Furthermore, arthropods were sampled one, two,</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		<p>refinement of the NTA off-crop risk assessment (please see DE comment 3, below “reduction of the correction factor”).</p> <p>The study design is not suitable to show time and concentration related trends of toxic effects. Therefore, reliability of population related endpoints, such as NOER an NOEAER is questionable and conclusions on recovery and dose effect relationships are not reliable</p> <p>Information on the mode of action as well as physical-chemical properties of the test substance flupyradifurone and the reference substance lambda-cyhalothrin should be used to underline and interpret the results in observations of treated plots.</p>	<p>considered in off-crop field studies according to the Dutch Guidance document (de Jong et al. 2010). Using habitats with a higher variability would reduce the likelihood of detecting potential effects in the treatment groups.</p> <p>The study design follows a dose response design with 4 test rates and repeated assessments up to 8 weeks. It is therefore appropriate to assess dose response effects and short term recovery.</p> <p>The mode of action and physico-chemical properties are given in the appropriate chapters, however the comment does not indicate how such information is relevant.</p> <p>NL (May 2014): We agree with the applicant's response. As we obviously have different opinions on what is required from an off-field study on NTA, we propose that this issue is discussed in an expert meeting.</p>	<p>four and eight weeks after treatment. Thus, overlaying of toxic effects by re-colonisation cannot be excluded, and a clear separation of NTA-communities between treated and non-treated plots in the off-field is missed.</p> <p>The off-crop field studies were performed only on grassland and are, therefore, insufficient as surrogate for the variability of possible off-field habitats around arable land. The study is not representative for 100% of existing worst case landscape. Standing alone, these field studies are insufficient for the refinement of the NTA off-crop risk assessment (please see DE comment 3, below “reduction of the correction factor”).</p> <p>The study design is not suitable to show time and concentration related trends of toxic effects.</p> <p>Therefore, reliability of population related endpoints, such as NOER an NOEAER is questionable and conclusions on recovery and dose effect relationships are not reliable</p>

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
				Information on the mode of action as well as physical-chemical properties of the test substance flupyradifurone and the reference substance lambda-cyhalothrin should be used to underline and interpret the results in observations of treated plots. „
5(60)	Vol. 3, B.9.5.3, Refined potential exposure, Table 2.6.3.2-08	DE: Reduction of the correction factor for the off-field PEC calculations from 5 to 1 is not acceptable, considering the shortcomings of the available off-crop field studies (please see DE comment (1) above). The uncertainty concerning the sensitivity of off-field arthropod species cannot be clarified. A correction factor of 5 will clearly result in a risk for off-crop NTAs. A study design for the refinement with a correction factor of 1 for the off-crop community requires a clear separation of toxic effects, recovery and re-colonisation as well as a 100% covering of a existing worst case landscape. The refined risk assessment for off-field arthropods should be discussed.	<b>APPL (04/2014): Please see response given above to the comment from Germany (DE) on "Vol. 3, B.9.5.3, Refined off-field risk assessment".</b>  NL (May 2014): In the DAR, the relevant table is B.9.5.3-08. We believe that the data package (with two field studies in off-field environment) is sufficient to address the off-field risk to non-target arthropods and that the correction factor can be set to 1. We agree that the risk assessment for off-field arthropods can be discussed in an expert meeting.	Expert consultation Experts to discuss the off-field arthropod risk assessment. Can the refined risk assessment for off-field arthropods be accepted?  See reporting table comment 5(61). “Reduction of the correction factor for the off-field PEC calculations from 5 to 1 is not acceptable, considering the shortcomings of the available off-crop field studies (please see DE comment (1) above). The uncertainty concerning the sensitivity of off-field arthropod species cannot be clarified. A correction factor of 5 will clearly result in a risk for off-crop NTAs. A study design for the refinement with a correction factor of 1 for the off-crop community requires a clear separation of toxic effects, recovery and re-

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
				colonisation as well as a 100% covering of a existing worst case landscape. The refined risk assessment for off-field arthropods should be discussed.“
5(61)	Vol. 3, B.9.5.3, Refined off-field risk assessment, Reference product, page 365  Aldershof, S. and Bakker, F. Date: 17.2.2012 Study No.: <b>B154FFN</b> ; Figure A8-1, page 123	DE: “ <i>The validity criterion for the reference treatment was clearly met (at least 50% effect on at least one sample date for at least 10% of the taxa evaluated; De Jong et al., 2010)</i> ”  In the summary, more detailed information was missed to be able to follow the conclusion on the validity of the study. The study report (B154FFN) was available and the following results were found: 16.2%, 47.8%, 40.6%, 47.3% and 16.9% at the analysed sample dates (week -1, 1, 2, 4 and 8, respectively). Accordingly, the validity criterion 50% has not been reached in this field study from 2012. Thus, the validity of the study should be discussed.	<b>APPL (04/2014):</b> The validity criterion met according to De Jong et al (2010) requires that at least a proportion of 10% of the assessed taxa show on at least one sample date an effect of ≥50%. On the first post application assessment a proportion of 47.8% of the assessed taxa in the toxic reference group showed an Abbott effect of >50%, clearly exceeding the required proportion of 10%. Therefore, is the validity criterion for this off-crop field study clearly met and this is stated in the study summary in the DAR.  <b>NL (May 2014):</b> FYI The corresponding number in the DAR is study IIIA 10.5.4/01.  There appears to be a misunderstanding on the meaning of Figure A8-1 in the study report. The numbers presented by DE (16.2-...-16.9) are not overall effect percentages. They represent the proportion of taxa for which an effect >50% was seen. Thus, almost half of the taxa showed an effect of at	See data requirement 5(58) and expert consultation 5(60).

## section 5 – Ecotoxicology (B.9)

<b>Bees and non-target arthropods (B. 9.4 and B.9.5)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
			least 50% on the first three sampling dates after application of the reference substance. The validity criterion is clearly met.	

<b>Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(62)	Vol. 3, B.9.6.1, General	EFSA: It is noted that in some studies the results of the reference item (2-chloroacetamide) was out of the range of the recommendation LC50 being between 20-80 mg/kg soil by the very similar ISO test guideline.	<p><b>APPL (04/2014):</b> Noted.</p> <p>NL (May 2014): The guideline used in the acute earthworm studies, OECD 207, has only validity criterion: no more than 10% mortality in the control. This criterion was met in all studies.</p> <p>It is furthermore noted that in the two studies (with the a.s. and the DFA metabolite) in which the criterion of the ISO guideline was not met, the LC50 of the reference substance was below the required range of 20-80 (13.2 mg/kg). This indicates, if anything at all, possible higher sensitivity of the test organisms, which would lead to worst case endpoints.</p>	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(63)	Vol. 3, B.9.6.1, Study by Leicher T. (2010a)	EFSA: There were two test run in this study, but results only for one control were reported. Please confirm that a control was used for both runs and they performance were sufficiently comparable to each other.	<b>APPL (04/2014): Both test runs were performed with 4 replicates in the control and for overall statistical evaluation both controls were pooled (in sum: n=8). In both controls no mortality was observed and results on biomass were very similar.</b>  <b>NL (May 2014): See applicant's response.</b>	Addressed.
5(64)	Vol. 3, B.9.6.2, Lab. sublethal studies on earthworms	EFSA: Please confirm that the differences in reproductive parameters seen at the established NOECs compared to the control are not considered as biologically relevant. It is noted that these differences expressed in % using the average data were ~ 6.7% in the formulation study and for the metabolites > 13%.	<b>APPL (04/2014): At the NOECs in the mentioned studies no biologically relevant effects took place. The studies fulfil all validity criteria in the OECD 222 guideline. Additionally, the chronic earthworm risk assessment for the formulation and the metabolites provide sufficient margin of safety and a risk for earthworms can be excluded.</b>  <b>NL (May 2014): See applicant's response.</b>	Expert consultation Experts to discuss the chronic risk assessment for earthworms.  Experts to discuss the sublethal studies on earthworms, Leicher T. (2010c) and Leicher (2010d). Are the differences in reproductive parameters seen at the established NOECs compared to the control considered as biologically relevant? It is noted that these differences expressed in % using the average data were ~ 6.7% in the formulation study and for the metabolites > 13%.  Experts also to discuss if the earthworm field study by Menke, U. (2012, report number NMU/RG-F-8/12) is considered acceptable to be

## section 5 – Ecotoxicology (B.9)

<b>Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
				used in the refined chronic risk assessment. Is the timing of the substance application considered to be acceptable? Do the experts consider the endpoint correctly derived from the study? Should the effects seen on the number and the biomass of juveniles of <i>Lumbricus terrestris</i> considered to be relevant?
5(65)	Vol. 3, B.9.6.4, Earthworm field study, Menke,U. (2012), p. 407	DE: The field study from Menke, U. (2012, report number NMU/RG-F-8/12) shows some shortcomings that question the acceptability for the refined chronic risk assessment. (1) Possibly inappropriate timing of substance application. The 25 <sup>th</sup> of May 2010 might have been too late for the study performance. The results gained 4 weeks after application (end of June) are less representative because there are few earthworms present. The recorded mean (!) temp. of 18°C was higher than long term recording and mean precipitation of 12.3 mm far less compared to long term precipitation of 77.5 mm. Thus, reliability of the results 4 weeks after treatment is questionable. (2) The effects of the test substance on the number and the biomass of juveniles of <i>Lumbricus terrestris</i> are significant and constant over the test period of 11 months	APPL (04/2014): 1) The results of the study can be regarded as representative and reliable, because the toxic reference shows a clear effect of > or = 50% lasting until 5 months after application (48% effect at 5 months sampling), when endogeic and anecic earthworms were found in high abundances (anecics: 5.4 individuals per 0.25 m <sup>2</sup> and endogeics: 30.25 ind. per 0.25 m <sup>2</sup> ). So, sensitivity and validity of this study is clearly given, despite dry weather conditions in June. 1) There is no significant effect of the test item (not even initially) on juvenile <i>L. terrestris</i> at 300 g ai/ha. The results for juvenile <i>L. terrestris</i> cannot be reliably predicted one year after application based on this study, due to low abundances. However, the results show that the abundance and biomass of total <i>L. terrestris</i> is clearly not impacted up to 1500 g ai/ha	See expert consultation 5(65).

## section 5 – Ecotoxicology (B.9)

<b>Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		showing a concentration dependent trend. No recovery is shown during the whole test for <i>L. terrestris</i> juveniles at 300, 600 and 1500 g ai/ha. We do not support the conclusion stating that no effects are present at the end of the study. A NOER of 300 g ai/ha (0.271 µg ai/kg soil) for <i>L. terrestris</i> juvenile survival/ <i>L. terrestris</i> reproduction can be derived from the study.	<p style="color: red;"><b>one year after application and there is no dose response relationship. Thus, no unacceptable risk can be concluded up to 1500 g ai/ha.</b></p> <p>NL (May 2014): Agree with the applicant's response. See also the DAR for our reasoning as to why the NOER can be set at the highest test dose. The earthworm field study could be discussed in an expert meeting so that we can reach agreement on the interpretation.</p>	
5(66)	Vol. 3, B.9.6.4 (3?), Study by Menke, 2012	EFSA: It is noted that although reductions in abundance/biomass of some categories even after 11 month were observed with the available data, these differences were not considered as biologically relevant. The main reasons for these were the relative low abundance within those categories (even in the control), the lack of dose-effect relationship and the natural variation.	NL (May 2014): See previous comment.	See expert consultation 5(65).
5(67)	Vol. 3, B.9.6.4.1-04, TER <sub>long-term</sub> calculations for earthworms	DE: Based on the available earthworm field study from Menke, U. (2012), page 407 ff., the new relevant value for the chronic risk assessment is the NOER of 300 g ai/ha (corresponding to 0.271 mg a.i/kg soil) for the endpoints <i>L. terrestris</i> survival of juveniles and <i>L. terrestris</i> reproduction, (please see comment (1) above). Regarding	<p style="color: red;"><b>APPL (04/2014): The field study showed that there is no unacceptable risk for earthworm populations up to a rate of 1500 g ai/ha (1.23 mg/kg, measured at 0-10 cm). The presented risk assessment clearly does not indicate an unacceptable chronic risk considering both the Tier 1 risk assessment and the field study.</b></p>	See expert consultation 5(65).

## section 5 – Ecotoxicology (B.9)

<b>Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / response from the Notifier/applicant	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		the chronic risk assessment for earthworms, we preliminarily calculate a TER long-term of 1.7 (Trigger = 5). Thus, the chronic risk assessment for earthworms should be discussed.	NL (May 2014): See previous comment.	
5(68)	Vol. 3, B.9.6.4, Earthworms field studies, IIIA 10.6.4/01, reference: Menke, U. (2012), “Remarks”, p. 421	DE: “...low numbers of anecic earthworms ( <i>L. terrestris</i> ) is considered to be a feature of the test plots...” and “...low residues of the a.s. were found in the control plots...”: Please provide more information about the aim of the study as well as the study design in the study summary, to avoid misinterpretation of the results.	APPL (04/2014): With a concentration of 5.2 µg/kg this cross-contamination is very slightly above the LOQ (5 µg/kg) and represents 0.4 % of the exposure in the highest test item treatment group, where no unacceptable effects on earthworms were seen. So, the impact of the residues found can be regarded as negligible.  NL (May 2014): See applicant's response. We discuss the study aim and design in the DAR and explain why we do not consider the control contamination relevant. What other information would you like to have?	See expert consultation 5(65).
5(69)	Vol. 1 Vol. 3 B.9.6, B.9.7 and B.9.8  Effects on soil organisms	FR: To our understanding for glasshouse “soil bound” indicates that this structure could be set up on natural soils. If it the case, the risk assessment on lettuce for biannual applications (two applications per year) in glasshouse with soil bound may be performed as the GAP for field uses do not cover this intended use. New PEC accumulations calculations could be needed in case two applications per year have not	APPL (04/2014): There is no agreement on assessing exposure in greenhouse (irrespective of the nature of the soil). However BCS considers that the soil risk assessment for glasshouse use is considered being covered by the field use even considering the use of 2 applications in the glasshouse. A glasshouse represents an artificial environment for non-target organisms including soil organisms, so the	See reporting table 4(44).  Open point (EFSA) EFSA to make clear in the conclusion that the risk to soil dwelling organisms from glasshouse uses was not assessed.

## section 5 – Ecotoxicology (B.9)

<b>Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		been already considered.	<p>risk for soil organisms is covered since after conversion of the glasshouse area to arable field a recovery of the communities in the area is possible. Given the plateau PECsoil values reported this is considered possible and a real risk can be excluded.</p> <p>NL (May 2014): We consider that management practice for glasshouse uses includes regular sterilisation of the soil, which prevents the formation of a natural soil organism community within (under) glasshouses. However, theoretically the soil can be used for other purposes in the long term and therefore, for persistent substances a risk assessment could be performed based on the PECplateau. In the fate section, no calculations were performed for the glasshouse use in lettuce as there is currently no guidance on calculation of PECsoil for greenhouse crops. Based on the highest PECplateau for the field uses in lettuce (0.016 mg a.s./kg, see Table B.8.3-04 in B.8 of the DAR) and the most critical endpoint for soil organisms (Collembola 1.44 mg a.s./kg) the TER is 90. We do not expect that a twofold application per year would lead to a PEC so much higher that a risk would be indicated.</p>	

## section 5 – Ecotoxicology (B.9)

<b>Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(70)	Vol. 3, B.9.6.4, RA for earthworms	EFSA: EFSA is wondering, why it is justified to calculate the PECs for lettuce for 20 cm.	APPL (04/2014): Perhaps EFSA has misunderstood the calculation as the simulation follows the current guidance whereby, for non-permanent crops, the plateau is calculated over a 20cm depth reflecting regular soil management practices. The concentration in the final year is calculated over a 5cm depth.  NL (May 2014): See applicant's response.	Addressed. See also open point 4(22).

<b>Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(71)		DE: no comment		Addressed.
5(72)	Vol. 3, B.9.9.2	EFSA: It is noted that a study (although non GLP) was available that indicated that difluoroacetic acid has no insecticidal efficacy compared to parent. This kind of information should be available for all metabolites which has high potential to leaching to GW (i.e. PECgw > 0.1 ug/L).	APPL (April 2014): DFA is the only metabolite which exceeds the groundwater trigger and hence requires a relevance assessment and the requirement is fulfilled.  NL (May 2014): See applicant's response.	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
5(73)		DE: no comment		Addressed.
5(74)	Vol. 1 (page 183) Vol 3 B.3 Table 3.3.1 Vol 3 B.9 Intended uses in Hops	FR: For uses in hops, only one application per year was assessed in B.9 while biannual application ( <i>i.e.</i> two applications per year) is reported in the last column of the summary of intended uses (Vol. 1 and Vol.3, B.3, Table 3.3.1). Could RMS clarify?  If two applications in hops are possible, then the complete risk assessment should be revised.  If the remark means one application every two years, then the term “biennial” should be used (or application every two year).	Appl (April 2014): The use referred to should be 1 use every 2 years and not 2 uses/year.  NL (May 2014): See applicant's response. In revised DAR and LoEP the correct term biennial will be used. This is already an open point (see 5(19)).	See open point 5(19).
5(75)	Vol. 1, 2.6	FR: We have an editorial remark for Vol1. We are favourable to limit the detailed assessment to Vol 3 B.9 and to focus on validated assessment in Vol 1. This allows an easier reading of the Vol. 1.  For example, all the justifications regarding the choice of the mammalian endpoint or the description of the method used to estimate a mean 21-d FTWA could have not been inserted in Vol 1. As this comment would not impact the conclusions, an update of the current Vol. 1 is not considered necessary.	NL (May 2014): Noted. We will try to do this in next dossiers.	Addressed.
5(76)	Vol. 3, B.9, General	EFSA: It is noted that many of the study summaries are rather short (especially for the aquatic organisms). A very detailed test description is indeed not necessary for the	NL (May 2014): Yes. If there were major deviations we would have mentioned them.	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		highly standardised laboratory tests if there are no deviations from the test guideline. Deviations or the lack of deviations from the test guidelines however were not indicated by the RMS. Can the indication of 'acceptable' be considered as there were no major deviations from the TGs?		
5(77)	Vol. 3, B.9, General	EFSA: Could you please confirm that the batches used in the ecotoxicological studies are equivalent with the technical specification?	NL (May 2014): Information on the batches used in ecotoxicological testing can be found in Vol.4, Table C.1.4-01. We did not receive further information from the applicant. If more information is necessary, this should be requested from the applicant so that it can be checked by the RMS.	Data requirement Applicant to submit further information on the technical specification of the batches of the test material used in the ecotoxicity studies.
5(78)	Vol. 3, B.9 and Vol.1, General	EFSA: It is noted that no detailed discussion/assessment was available on the approval criterion (cut-off criterion) including potential for endocrine activity. However it is noted that some potential effects on the endocrine system was indicated in the mammalian toxicology section (e.g. on thyroid). Specific assessment on this issue in B.9 was not available.	NL (May 2014): As soon as harmonised guidance becomes available with the criteria for evaluating whether a substance has potential for endocrine activity, we can include such an assessment.	Data requirement: The Applicant may wish to submit further information on the potential endocrine disruption properties, or for the lack of them, to the RMS.
5(79)	Vol. 3, B.9, General	EFSA: A search of the scientific peer-reviewed open literature relevant to the scope of the application for amendment to the conditions of approval, dealing with side-effects on health, the environment and non-target species and published within the last	<b>APPL (April/2014)</b> <b>A literature research of the scientific peer-reviewed open literature relevant to the scope of the application according to Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092). has been</b>	Open point RMS to present an evaluation of the literature review completed by the applicant in an addendum.  Data requirement

## section 5 – Ecotoxicology (B.9)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		10 years before the date of submission of dossier, to be conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092).	<p>conducted and can be found in the Annex II Dossier under Document N.</p> <p>NL (May 2014): See applicant's response. Note that this literature research has not been evaluated by the RMS.</p>	Applicant to provide a search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, being conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) for the aqueous photolysis metabolites BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide that do not appear to have been included in the available literature review.
5(80)	Vol. 1, LoEP, General	EFSA: Please include always the correct name of the test item in the LoEP, i.e. 'G' is usually missing from the end of the name of the formulation (compared to the name indicated in B.9).	NL (May 2014): We will check this in a revised version of the LoEP.	Open point RMS to amend the LoEP:s with the correct name of the formulation.
5(81)	Vol. 1, LoEP, box for birds	EFSA: The included long-term endpoint from the mallard study is based on the measured food concentration, while for the quail study the nominal value is included. It might be considered to harmonise or clearly indicate	NL (May 2014): A clarification can be added to the LoEP.	Open point RMS to amend the LoEP:s to clarify for long-term bird endpoints whether they are based on nominal or measured concentrations.

## section 5 – Ecotoxicology (B.9)

<b>Other comments</b>				
No.	<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
		the bases of each endpoint.		
5(82)	Vol. 1, LoEP, box for birds & mammals	EFSA: Please indicate everywhere the 'kind of endpoints' (e.g. LD50, NOEC) in this box.	NL (May 2014): Will be done.	Open point RMS to amend LoEP:s to clarify the type of endpoint for all bird and mammal endpoints.
5(83)	Vol. 1, LoEP, box for RA for birds	EFSA: The DDD and the TER values for the 'pigeon' scenario are not the same as reported in B.9. Please clarify this.	NL (May 2014): The DDD and TER values in the DAR are correct. The values in the LoEP will be amended.	Open point RMS to amend the LoEP:s, make sure that the DDD and TER value for the pigeon scenario corresponds with those from the DAR.
5(84)	Vol. 1, LoEP, box for AO	EFSA: Please consider to indicate all the data for <i>chironomus</i> under 'sediment dwelling organisms'. Please also indicate if the test used water spiking.	<b>APPL (April/2014): The study used water spiking.</b>  NL (May 2014): Will be done.	Open point RMS to amend the LoEP:s, include all Chironomus data under 'sediment dwelling organisms' and indicate if the tests used water spiking.
5(85)	Vol. 1, LoEP, box for bumble bee	EFSA: The name of the test item used in the text is not the same as indicated in B.9. Please correct it.	NL (May 2014): Will be done.	Open point RMS to amend the LoEP:s, insert the correct name for the test item.
5(86)	Vol. 3, B.9, General	EFSA: Generally, EFSA considers that the RMS did a comprehensive risk assessment even undertaking unusual, extra assessments where it was necessary.	NL (May 2014): Thank you!	Addressed.

## section 5 – Ecotoxicology (B.9)

<b>Efficacy (B.10)</b>			
<u>Column 1</u> Reference to DAR (vol., point, page)	<u>Column 2</u> Comments from Member States or applicant	<u>Column 3</u> Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur / <b>response from the Notifier/applicant</b>	<u>Column 4</u> Data requirement or Open point (if data point not addressed or fulfilled)
Vol. 3, B.10 Efficacy, General comment.	FR: The RMS presented a well written evaluation report. As a very minor remark, there is a repetition of text in page 8 – line 4 of the B.10.	NL: (May 2014) Typo confirmed.	Addressed

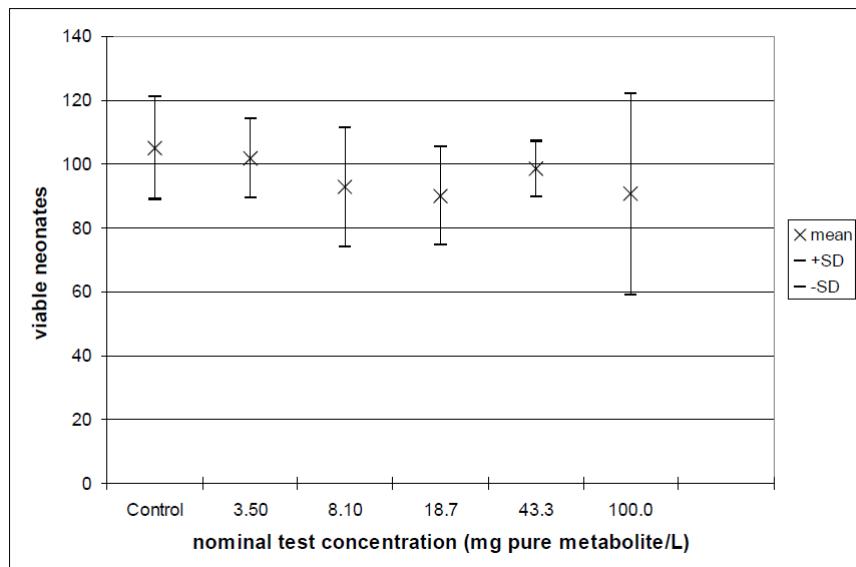
## section 5 – Ecotoxicology (B.9)

**Table form row 5(13):****TEST CONDITIONS, DURATION AND SURVIVAL CRITERIA FOR RECOMMENDED SPECIES**

SPECIES	TEST CONDITIONS			RECOMMENDED DURATION OF TEST	SURVIVAL OF CONTROLS (minimum)	
	Temperature (°C)	Salinity (‰)	Photoperiod (hrs)		Hatching success	Post-hatch success
<b>Freshwater:</b>						
<i>Oncorhynchus mykiss</i> Rainbow trout	10 ± 1.5 <sup>(2)</sup>		12 - 16 <sup>(3)</sup>	2 weeks after controls are free-feeding (or 60 days post-hatch)	40	75%
<i>Pimephales promelas</i> Fathead minnow	25 ± 1.5		16	32 days from start of test (or 28 days post-hatch)	18	70% 75%
<i>Danio rerio</i> Zebrafish	26 ± 1.5		12 - 16 <sup>(4)</sup>	30 days post-hatch	11	70% 75 %
<i>Oryzias latipes</i> Japanese Ricefish or Medaka	25 ± 2		12 - 16 <sup>(4)</sup>	30 days post-hatch	17	80% 80%
<b>Estuarine and Marine:</b>						
<i>Cyprinodon variegatus</i> Sheepshead minnow	25 ± 1.5	15.35 <sup>(5)</sup>	12 - 16 <sup>(4)</sup>	32 days from start of test (or 28 days post-hatch)	17	75% 80%
<i>Menidia</i> sp. Silverside	22 - 25	15.35 <sup>(5)</sup>	13	28 days	20	80% 60%

## Key:

- (1) Typical minimum mean total length is not a validity criterion but deviations below the figure indicated should be carefully examined in relation to the sensitivity of the test. The minimum mean total length is derived from a selection of data available at the current time.
- (2) The particular strain of rainbow trout tested may necessitate the use of other temperatures. Brood stock must be held at the same temperature as that to be used for the eggs. After receipt of eggs from a commercial breeder, a short adaptation (e.g. 1-2 h) to test temperature after arrival is necessary.
- (3) Darkness for larvae until one week after hatching except when they are being inspected, then subdued lighting throughout test (12-16 hour photoperiod)<sup>(4)</sup>.
- (4) For any given test conditions, light regime should be constant.
- (5) For any given test this shall be performed to ±2%.

**Table from row 5(14):**Figure 3: Total living offspring per surviving parental female

## TABLE OF CONTENTS

	<b>Document</b>
00	Cover page
01	Comments on the assessment report
02	Reporting table
<b>03</b>	<b>Pesticides peer review meeting reports</b>
04	Evaluation table
05	Comments on the additional information assessment
06	Comments on the draft EFSA conclusion

List of all reports from Pesticides Peer Review Meetings

Date		Section
18.11.2014	<a href="#"><u>Pesticides Peer Review expert meeting 122</u></a>	Mammalian Toxicology
20.11.2014	<a href="#"><u>Pesticides Peer Review expert meeting 121</u></a>	Environmental Fate and Behaviour
27.11.2017	<a href="#"><u>Pesticides Peer Review expert TC 107</u></a>	Residues
05.12.2014	<a href="#"><u>Pesticides Peer Review expert meeting 124</u></a>	Ecotoxicology

## REPORT OF PESTICIDES PEER REVIEW MEETING 122

### FLUPYRADIFURONE

Rapporteur Member State: NL

#### Specific comments on the active substance in the section

#### **2. Mammalian Toxicology**

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

##### 1. Comments submitted for this meeting:

None

##### 2. Documents submitted for meeting:

Date	Supplier	File Name
November 2014	NL	flupyradifurone evaluation table NAS section 2 November 2014.doc
November 2014	NL	flupyradifurone updated DAR volume 3 B6 November 2014.doc
24.06.2014	NL	flupyradifurone_reporting_table_2014-06-24.doc

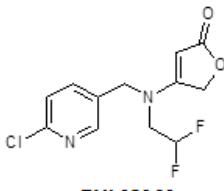
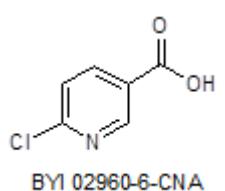
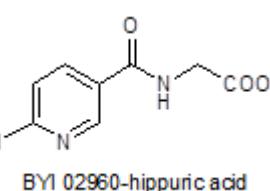
##### 3. Documents tabled at the meeting:

None

Appendix 1: Discussion table: FLUPYRADIFURONE

## Appendix 1: Discussion Table, Flupyradifurone

### 2. Mammalian Toxicology

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting																														
Expert consultation 2.1  MS to discuss whether the metabolite 6-CNA can be regarded as a major metabolite or not  See also 2(42)	<p><b>Background</b> See updated DAR (November 2014), pp. 4-5 and study 1, p. 12, table 6.1.1-06 (Klempner, 2012)</p> <div style="text-align: center;">  <p><b>BYI 02960</b></p>  <p><b>BYI 02960-6-CNA</b></p>  <p><b>BYI 02960-hippuric acid</b></p> </div> <p>The toxicity of 6-CNA is assumed to be covered by the endpoints derived for the parent compound since 6-CNA and its succeeding metabolite BYI 02960-hippuric acid - which can be formed from 6-CNA only – represent a prominent portion in the urine of male rats. The two metabolites, 6-CNA (0.4% to 6.0%) and BYI 02960-hippuric acid (1.1% to 10.4%) were detected in the urine of male and female rats after administration of [pyridinylmethyl-14C]BYI 02960 at dose levels of 2 and 200 mg/kg bw, as well as in male rats after i.v. administration (female rats were not tested). The two metabolites represented a prominent portion in male rats, however showed lower concentrations in female rats.</p>	Expert consultation fulfilled: 6-CNA is considered a major metabolite in male rat but not in females.																														
See reporting table 2(1)	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th colspan="6">Proportion of dose detected in urine (% of total dose administered)<sup>1</sup></th> </tr> <tr> <th>Compound</th> <th>Male, p.o. 2 mg/kg bw</th> <th>Female, p.o. 2 mg/kg bw</th> <th>Male, p.o. 200 mg/kg bw</th> <th>Female, p.o. 200 mg/kg bw</th> <th>Male, i.v. 2 mg/kg bw</th> </tr> </thead> <tbody> <tr> <td>6-CNA</td> <td>2.3</td> <td>0.4</td> <td>6.0</td> <td>1.3</td> <td>2.7</td> </tr> <tr> <td>BYI 02960- hippuric acid</td> <td>7.4</td> <td>1.1</td> <td>10.4</td> <td>2.2</td> <td>5.1</td> </tr> <tr> <td><b>Sum</b></td> <td><b>9.7</b></td> <td><b>1.5</b></td> <td><b>16.4</b></td> <td><b>3.5</b></td> <td><b>7.8</b></td> </tr> </tbody> </table>	Proportion of dose detected in urine (% of total dose administered) <sup>1</sup>						Compound	Male, p.o. 2 mg/kg bw	Female, p.o. 2 mg/kg bw	Male, p.o. 200 mg/kg bw	Female, p.o. 200 mg/kg bw	Male, i.v. 2 mg/kg bw	6-CNA	2.3	0.4	6.0	1.3	2.7	BYI 02960- hippuric acid	7.4	1.1	10.4	2.2	5.1	<b>Sum</b>	<b>9.7</b>	<b>1.5</b>	<b>16.4</b>	<b>3.5</b>	<b>7.8</b>	
Proportion of dose detected in urine (% of total dose administered) <sup>1</sup>																																
Compound	Male, p.o. 2 mg/kg bw	Female, p.o. 2 mg/kg bw	Male, p.o. 200 mg/kg bw	Female, p.o. 200 mg/kg bw	Male, i.v. 2 mg/kg bw																											
6-CNA	2.3	0.4	6.0	1.3	2.7																											
BYI 02960- hippuric acid	7.4	1.1	10.4	2.2	5.1																											
<b>Sum</b>	<b>9.7</b>	<b>1.5</b>	<b>16.4</b>	<b>3.5</b>	<b>7.8</b>																											

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p><sup>1</sup> Klempner, A.; 2012: [Pyridinylmethyl-<sup>14</sup>C]BYI 02960 – Absorption, Distribution, Excretion, and Metabolism in the Rat, Report No. MEF 11/747, Document No. M-422210-01-1</p> <p>In sum the metabolites represented 8% to 16% of the administered dose in male rats. Since BYI 02960-hippuric acid can be formed from 6-CNA only, the proportion of BYI 02960-hippuric acid can be added to the 6-CNA proportion to estimate the proportion of 6-CNA which was systemically available in the rat. When considering the two metabolites together, 6-CNA accounted for ≥ 10% of the dose administered dose in male rats after oral administration. Thus, 6-CNA was present in a sufficient concentration to contribute to the toxicological effects when testing the parent compound. Since the toxicological endpoints derived for parent compound were not dependent on the sex of the animals, it can be concluded that the different metabolic behaviour of male and female rats had no influence on the toxicological profile.</p> <p><b>Comments</b></p> <ul style="list-style-type: none"><li>• EFSA commented that 6-CNA cannot be regarded as a major metabolite in the rat studies as the level of 6.3% of the administered dose was obtained only in males treated with 200 mg/kg bw and was indiscriminately found in urine and faeces.</li><li>• The applicant responded that significant 6-CNA concentrations were detected in the organs/tissues of the laying hen (1.8% of the TRR in fat, 6.4% in liver, 7.2% in eggs and 8.8% in muscle) indicating that the metabolite has a certain retention time in the body of the animals and thus contributes to the overall toxicity of the parent compound.</li></ul> <p><b>Pesticides Peer Review Experts' Meeting</b></p> <p>6-CNA is mentioned as intermediate forming hippuric acid in the rat metabolic pathway. Adding hippuric acid to 6-CNA in the metabolism studies result in 6-CNA being a major rat metabolite in males, but not in females. It was agreed to sum up 6-CNA and hippuric acid for males and females. It was noted that in females both metabolites are not major rat metabolites, even when summing them up (at any dose level in the ADME studies). For 6-CNA, oral LD<sub>50</sub> &gt; 2000 mg/kg bw (less acutely toxic than the parent), no data are available for hippuric acid. This is not sufficient to conclude on the toxicity of the metabolites for the females, however for males, the experts agreed that the toxicity of the parent would cover</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>the toxicity exerted by the metabolite 6-CNA.</p> <p>Expert consultation fulfilled.</p>	
Expert consultation 2.2  MSs to discuss the possibility of waiving toxicokinetic study with repeated dosing.  See reporting table 2(2)	<p><b>Background</b></p> <p>All single dose experiments revealed no indication of a potential for retention, accumulation and/or persistence of the administered radioactivity in organs or tissues. This observation is supported by the low log <math>P_{OW}</math> of BYI 02960 of 1.2. Therefore, in line with paragraph 26 of the OECD Test Guideline 417 (July 22<sup>nd</sup>, 2010), a repeated dose study was not considered necessary</p> <p><b>Comments</b></p> <ul style="list-style-type: none"><li>EFSA commented that the data requirements state that repeated dose studies must be submitted, the OECD guideline also acknowledge that this test may be required by regulatory authorities and the test may provide more detailed information on bioaccumulation.</li></ul> <p>Considering the bi-phasic kinetic of flupyradifurone, low radioactive residues were still measured in almost all organ and tissues, day 7 (ref. study 4 – [REDACTED], 2011).</p> <p><b>Pesticides Peer Review Experts' Meeting</b></p> <p>The RMS considers that from a scientific point of view there is no need for a toxicokinetic study with repeated dosing.</p> <p>It was noted that after single dose, residual radioactivity was measured in fatty tissues/fat. Considering the radioactive labelling, it is expected that residues can also be related to metabolites.</p> <p>The biphasic kinetic was not evident in the different studies available.</p> <p>Considering all the information available, the experts agreed that there is no potential for bioaccumulation, flupyradifurone being completely absorbed and excreted according to a biphasic kinetic.</p> <p>The waiving of the repeat dose toxicokinetic study was agreed by the experts.</p>	Expert consultation fulfilled: Waiving of the repeated dose toxicokinetic study is considered acceptable.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	Expert consultation fulfilled.	
Expert consultation 2.3  MSs to discuss the NOAEL/LOAEL of the 28-day oral study in rat by gavage (study 1).  See reporting table 2(8)	<p><b>Background</b></p> <p><b>Rat, 28-day oral toxicity - study 1 (Capt, 2007)</b></p> <p>Groups of 5 rats/sex were orally dosed flupyradifurone by gavage at dose levels of 0, 75, 200 and 350 mg/kg bw per day for 28 days</p> <p>Two females treated with 350 mg/kg bw per day died day 6. BROWD activity (but not EROD) was induced at 350 mg/kg bw per day in both sexes and at 200 mg/kg bw per day in males, with no clear induction of PROD activity, BYI 02960 appears to be an inducer of the Cytochrome P-450 3 A family. The NOAEL was set at 75 mg/kg bw per day based on increased liver weight and liver histopathological findings.</p> <p><b>Comments</b></p> <ul style="list-style-type: none"><li>FR suggested setting a LOAEL of 75 mg/kg bw per day based on observed effects on liver and clinical chemistry. The applicant replied that the only statistically significant effect seen at the low dose level is decreased bilirubin and stated that this was due to one animal only. Liver findings at 75 mg/kg bw per day are limited to prominent liver lobulation in one male without associated microscopic findings or liver weight increase and would be considered incidental.</li></ul> <p><b>Pesticides Peer Review Experts' Meeting</b></p> <p>At 75 mg/kg bw per day, only decreased bilirubin in one animal was observed, liver findings did not include microscopic effects, only macroscopic observation (liver lobulation).</p> <p>The effect on bilirubin is observed in several studies (e.g. 90-day). The adversity of a decreased bilirubin level is less clear than for an increased bilirubin level.</p> <p>In this study, mortality was also observed at mid and high dose, whereas in other studies, mortality is not observed at the same dose levels. It was noted that this was a gavage study.</p> <p>The experts agreed on a NOAEL of 75 mg/kg bw per day, considering that the decreased bilirubin in one animal is not relevant for the derivation of the NOAEL.</p> <p>Expert consultation fulfilled.</p>	Expert consultation fulfilled: The NOAEL of the 28-day study in rat by gavage is 75 mg/kg bw per day based on mortality, increased liver weight and liver histopathological findings.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Expert consultation 2.4  MSs to discuss the NOAEL/LOAEL of the 28-day dietary study in rat (study 2).  See reporting table 2(9)	<p><b>Background</b></p> <p><b>Rat, 28-day oral toxicity - study 2 (Blanck, 2008)</b></p> <p>Groups of five males were treated with flupyradifurone via the diet for 28 days at concentrations of 0, 500 ppm (actual analysed dose level of 410 ppm, which equates to 33.6 mg/kg bw per day) and 5000 ppm (equivalent to 385 mg/kg bw per day). At the high dose level, mean body weight was reduced up to 19% during the first 3 weeks of the study; overall cumulative body weight was significantly reduced by 38% compared to controls. Mean food consumption was reduced up to 39% being more pronounced between days 1 to 8 of the study. Total bilirubin and glucose concentrations were significantly reduced and urea and total cholesterol were significantly increased at 5000 ppm. At the high dose level, thyroid, liver weight and TSH were increased while T4 decreased. The NOAEL was set at 500 ppm (33.6 mg/kg bw per day), based on clinical chemical findings, increased relative liver and thyroid weights and associated pathological findings.</p> <p><b>Comments</b></p> <ul style="list-style-type: none"><li>FR suggested setting a LOAEL of 500 ppm based on observed effects on liver and clinical chemistry. The applicant answered that there are no statistically significant effects seen at 500 ppm in any clinical chemistry parameters; 2/5 males showed prominent lobulation at 500 ppm but this was not associated with liver weight increase and not associated with microscopic findings.</li></ul> <p><b>Pesticides Peer Review Experts' Meeting</b></p> <p>One expert noted that with 5 animals by dose group, statistical analysis could not be relied on in this preliminary study. This was agreed.</p> <p>The experts agreed on a NOAEL of 500 ppm (33.6 mg/kg bw per day), based on clinical chemical findings, increased relative liver and thyroid weights and associated pathological findings.</p> <p>Expert consultation fulfilled.</p>	Expert consultation fulfilled:  The NOAEL of the dietary 28-day study in rats is 33.6 mg/kg bw per day based on clinical chemical findings, increased relative liver and thyroid weights and associated pathological findings.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Expert consultation 2.5  MSs to discuss the NOAEL of the 28-day study in an experts meeting.  See also 2(11), 2(12)  See reporting table 2(10)	<p><b>Background</b></p> <p><b>Mouse, 29-day oral toxicity - study 3 (Blanck, 2007)</b></p> <p>Flupyradifurone was administered via the diet to groups of 5 mice/sex for 28 days at concentrations of 0, 300, 600 and 1200 ppm (equating approximately to 0, 50, 98 and 207 mg/kg bw per day in males and 59, 122, 240 mg/kg bw per day in females).</p> <p>Overall cumulative mean body weight gain was reduced by 15% between Study Days 1 and 29. As the effect on body weight was slight and transient and in the absence of other findings, it was considered to be a non-adverse effect of treatment. Higher levels of alanine aminotransferase (+43%, p &lt;0.01) and alkaline phosphatase (+21%, p &lt;0.05) activities were observed in females at 1200 ppm. Lower epididymis weights were found in treated animals when compared to controls but this change was considered not to be relevant since it was not associated with relevant histological findings. Mean absolute and relative spleen weights were statistically significantly higher in males at 300 ppm when compared to controls, but this change was considered not to be relevant since it was not dose-related.</p> <p>The NOAEL was set at 1200 ppm based on the lack of adverse effects in males and females, given the instability of flupyradifurone in rodent diet the actual concentration was considered to be in the region of 960 to 1080 ppm (166 to 186 mg/kg bw per day for males and 192 to 216 mg/kg bw per day for the females, respectively).</p> <p><b>Comments</b></p> <ul style="list-style-type: none"><li>DK and FR commented that the statistically significant decrease in absolute and/or relative epididymis weights in all 3 dose groups should be considered relevant as found to be dose-related even if no relevant histological findings were observed. EFSA added that, further to the epididymides weight, the reduced body weight gain and clinical chemistry changes should be considered when setting the NOAEL. Applicant responded that the change in epididymides weight was not clearly dose-related and provided historical control data (see updated DAR, p. 74-75).</li></ul> <p><b>Pesticides Peer Review Experts' Meeting</b></p> <p>The RMS noted that the decreased epididymis weight was within background historical control data. Due to the low number of animals by dose group, the study has to be considered as supplementary.</p>	Expert consultation fulfilled:  The NOAEL of the 28-day mouse study is 98 mg/kg bw per day based on reduced body weight gain and clinical chemical chemistry changes.

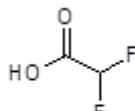
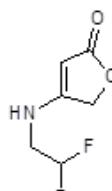
Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>Considering the reduction of body weight gain at the high dose (15%), this might be considered as a LOAEL. Additionally ALT was also increased at the high dose. Based on these effects the experts agreed on a NOAEL of 98 mg/kg bw per day.</p> <p>Expert consultation fulfilled.</p>	
<p>Expert consultation 2.6</p> <p>MSs to discuss the NOAEL of the 90-day study in rat (study 1) in an experts meeting. See also 2(14), 2(15)</p> <p>See reporting table 2(13)</p>	<p><b>Background</b></p> <p><b>Rat, 90-day oral toxicity - study 1 (Odin-Feurtet, 2009)</b></p> <p>Groups of 10 rats/sex were fed diets containing flupyradifurone at concentrations of 100, 500, 2500 ppm (corresponding to 0, 6.0, 30.2, 156 mg/kg bw per day in males and 0, 7.6, 38.3, 186 mg/kg bw per day in females) for 90 days. Additional satellite groups of 10 animals/sex were fed control or high dose test diet to assess the reversibility of effects after a recovery period of 28 days.</p> <p>At 2500 ppm, a lower body weight was observed in both sexes throughout the study (6-10%). At 500 ppm the overall mean body weight gain was 12% lower than the controls in females at the end of the treatment period. Haematological evaluation revealed a higher mean platelet count in high dose females when compared to the control group (+15%). In addition, mean total bilirubin and glucose concentrations were slightly lower in both sexes and mean total cholesterol and triglycerides concentrations were slightly higher when compared to the controls. Liver and thyroid weights were increased at 2500 ppm in association with histopathological findings.</p> <p>The NOAEL was set at 500 ppm (30.2 mg/kg bw per day for males and 38.3 mg/kg bw per day for females) based on the clinical chemical findings, the increased relative liver and thyroid weights and associated pathological findings.</p> <p><b>Comments</b></p> <ul style="list-style-type: none"> <li>EFSA commented that the 500 ppm dose level produced reduced bw gain (12%), increased relative and absolute thyroid weight by 20 and 17%, and should therefore be considered a LOAEL. DK and FR suggested a NOAEL of 100 ppm based on dose-related increase in relative thyroid weight and reduced body weight/bw gain respectively.</li> </ul> <p><b>Pesticides Peer Review Experts' Meeting</b></p>	<p>Expert consultation fulfilled: The NOAEL of the 90-day dietary study in rats is 6 mg/kg bw per day based on reduced thyroid weight and body weight gain.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>At 500 ppm the overall mean body weight gain was 12% lower than the controls in females at the end of the treatment period. The RMS noted that this was not accompanied by effects on body weight.</p> <p>With regard to the thyroid weight, the RMS highlighted that the effect was not observed in other studies, and only observed in males. Considering the severity of the effect (20% for the relative weight, statistically significant, and 17% for the absolute weight), the experts agreed that it had to be considered as adverse.</p> <p>Based on these findings, the agreed NOAEL is 100 ppm, corresponding to 6 mg/kg bw per day.</p> <p>Expert consultation fulfilled.</p>	
Expert consultation 2.7  MSs to discuss the NOAEL of the 2-year rat study in an experts meeting. See also 2(19), 2(20), 2(21)  See reporting table 2(18)	<p><b>Background</b></p> <p><b>Rat, long term toxicity and carcinogenicity – study 1 (████, 2012)</b></p> <p>Groups of 60 rats/sex were administered flupyradifurone via the diet during 104 weeks at dose levels of 0, 80, 400 and 2000 ppm corresponding to 0, 3.17, 15.8 and 80.9 mg/kg bw per day in males and 0, 4.48, 22.5 and 120 mg/kg bw per day in females at the end of the study. Satellite groups of 10 rats/sex treated at the same dose levels corresponding to 0, 3.57, 18.5 and 95.1 mg/kg bw per day in males and 0, 5.97, 25.3 and 136 mg/kg bw per day in females were sacrificed after 52 weeks of treatment.</p> <p>Overall mean cumulative body weight gain was decreased by 23% and mean bw was 13% lower in the high dose group compared to control animals. At 400 ppm, mean cumulative body weight gain was statistically significantly lower than in controls during the first week of treatment for males (-6%, p≤0.05) and females (-12%, p≤0.05) and was comparable to control thereafter. Mean body weight was not affected throughout the study. Lower plasma bilirubin and higher cholesterol concentrations were observed in high dose females.</p> <p>The NOAEL was set at 400 ppm corresponding to 15.8 and 22.5 mg/kg bw per day over 104 weeks based on liver, thyroid and lung effects in females.</p> <p><b>Comments</b></p> <ul style="list-style-type: none"><li>EFSA commented that some effects observed at 400 ppm appear to be first signs of substance-related adverse effects in the liver.</li></ul>	Expert consultation fulfilled: The NOAEL of the 2-year rat study was agreed by a small majority of the experts to be 15.8 mg/kg bw per day based on reduced body weight / body weight gain, liver, lung and thyroid toxicity.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<ul style="list-style-type: none"><li>• DK considered that the incidence of colloid alteration in the thyroid (38 and 40 in the 400 and 2000 ppm groups) should be considered further regarding its adversity.</li><li>• DE noted that tables B.6.5.1-4/5/6 that the control findings show erroneous statistical significance values. This was confirmed by RMS.</li><li>• FR suggest the setting of a NOAEL at 80 ppm based on the effects observed on the liver and thyroid in males: in the liver, an increase in incidence and severity of alteration eosinophilic focus of hepatocellular and a higher incidence of centrilobular hepatocellular hypertrophy was found in male at 400 ppm and 2000 ppm. In the thyroid, increased incidences of colloid alteration were noted in male at 400 ppm and 2000 ppm.</li><li>• The applicant responded that there was no increased incidence or severity in eosinophilic foci in the liver at 400 ppm, but an increased incidence in colloid alteration in the thyroid with no increased severity compared to control males. The findings observed in the males at 2000 ppm (liver histopathological findings and colloid alteration) were considered adverse because the hepatocellular hypertrophy was associated with pre-neoplastic findings (eosinophilic foci in the liver). Whereas the findings observed the liver at 400 ppm were considered adaptive: the hypertrophy was minimal, there was no liver weight effects, no pre-neoplastic or clinical chemistry changes. The thyroid effects which have been demonstrated to be secondary to liver induction were not considered adverse.  Further tabled results (bw and haematological findings) and historical control data are presented in the updated DAR.  <b>Pesticides Peer Review Experts' Meeting</b> Effects occurring at the mid dose were discussed: hepatocellular hypertrophy (statistically significant in males), and colloid alterations in the thyroid (males). The RMS noted that liver hypertrophy was minimal at 400 ppm, and should be considered as an adaptive response. No effects were observed in the clinical chemistry parameters or regarding liver weight. The experts agreed that the liver effect at 400 ppm may be considered as adaptive. For the thyroid effect, the RMS noted that it was slight/minimal, only accompanied by brown pigmentation (also minimal). The notifier claimed this effect was secondary to liver</li></ul>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>induction at 400 ppm (adaptive). At 2000 ppm (high dose), there is an increased incidence and severity of this alteration (colloid alterations in the thyroid), observed in both sexes, accompanied by thyroid hypertrophy, and considered adverse.</p> <p>Considering the lack of increased severity of the colloid alterations at 400 ppm, this effect would not be considered adverse.</p> <p>The majority of the experts (7 vs. 6) agreed on a NOAEL of 400 ppm, corresponding to 15.8 mg/kg bw per day.</p> <p>Expert consultation fulfilled.</p>	
<p>Expert consultation 2.8</p> <p>MSs to discuss the parental, reproductive and offspring NOAEL of the multigeneration study in an experts meeting and the potential for an endocrine-mediated MoA.</p> <p>See also 2(25), 2(27)</p> <p>See reporting table 2(24)</p>	<p><b>Background</b></p> <p><b>Rat two-generation reproductive toxicity – study 2 (████, 2011)</b></p> <p>See updated DAR pp. 137-162</p> <p>Groups of 30 rat/sex were administered via the diet flupyradifurone at dose levels of 0, 100, 500 and 1800 ppm corresponding to 0, 6.5, 32.3 and 119.8 mg/kg bw per day (mean premating values in males) throughout 2 generations.</p> <p>After the commenting period, the RMS proposed to set a lower the parental NOAEL than the one set in the first draft DAR at 100 ppm considering parental female body weight effects: a significant decrease in body weight, &lt;10% observed in the mid-dose of the F1 females and a non-significant decrease in body weight gain found in the parental animals (21% in females) and the F1 animals (16% in females).</p> <p>The reproductive NOAEL was set at 500 ppm based on decreased oestrous cycle number, litter size, and the number of implants observed in the F<sub>1</sub> generation at the highest dietary level tested.</p> <p>The offspring NOAEL was set at 500 ppm based on significant decrease in pup weight, but &lt;10% and physical development observed in the mid-dose of the F2 pups.</p> <p><b>Comments</b></p> <ul style="list-style-type: none"> <li>• The suggestion made by FR, (and also DK and EFSA) to set the parental systemic NOAEL and the offspring NOAEL at 100 ppm, based on decreased of body weight and body weight gain at 500 ppm and 1800 ppm in parental and F1 generation during premating, gestation and lactation and on offspring in F1 and F2 generation</li> </ul>	<p>Expert consultation fulfilled:</p> <p>Regarding the 2-generation reproductive toxicity study in rats, the parental and offspring NOAEL is 6.4 mg/kg bw per day based on reduced body weight/body weight gain and the reproductive NOAEL is 32 mg/kg bw per day based on reduced number of implantation sites and oestrus cycle, reduced litter size (reduced number of pups born and higher number of stillborn).</p> <p>Considering the effects observed on the reproduction, an endocrine-mediated MoA could not be ruled out and a data gap was identified for level 2 tests currently indicated in the OECD Conceptual Framework, noting that further tests might be necessary pending on the outcome.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>was accepted by the RMS.</p> <ul style="list-style-type: none"><li>DK considered the statistically significantly decreased body weight PND 14-21 and a reduced weight gain in F2 generation in the mid- and high dose group. In the F1 generation a significant decreased body weight week 10 of premating and during gestation and lactation in the mid – and high dose group was reported. The argument for not using this effect at 100 ppm is that the decrease is &lt; 10 % but there seems to be dose- response and the effect in the F1 generation is persistent.</li><li>EFSA further commented that it may be arguable whether all offspring/reproductive findings at the high dose level may be explained only by parental decrease in bw/bw gain (delay in preputial separation and vaginal patency; reduced brain, thymus and spleen weights; and reduced number of implantation sites). Or whether another MoA may be expected (endocrine mediated).</li><li>The applicant provided an assessment of the possible endocrine-mediated MoA of flupyradifurone and the information has been reported in the updated DAR.</li></ul> <p><b>Pesticides Peer Review Experts' Meeting</b></p> <p>With regard to the parental toxicity, the RMS proposed a revised NOAEL of 100 ppm (equivalent to 6.4 mg/kg bw per day), considering significant decrease in body weight (&lt;10% observed in the mid-dose of the F<sub>1</sub> females) and a non-significant decrease in body weight gain found in the parental animals (21% in females) and the F<sub>1</sub> animals (16% in females). This was agreed by the experts.</p> <p>The reproductive NOAEL was set at 500 ppm (equivalent to 32 mg/kg bw per day) based on decreased oestrous cycle number, litter size, and the number of implantation sites observed in the F<sub>1</sub> generation. This was agreed by the experts.</p> <p>The offspring NOAEL was set at 500 ppm based on significant decrease in pup weight in F<sub>1</sub> generation (21%). Considering the effect in the F<sub>2</sub> pups on body weight, the experts agreed on a NOAEL of 100 ppm for the pup development (reduced weight gain).</p> <p>Some findings could be considered as endocrine-mediated, even though the notifier claimed that they were within historical control data. It was noted that historical control data were not fully appropriate and more weight should be given to the concurrent control data.</p> <p>The experts agreed that there was not sufficient evidence demonstrating that the mode of action was not endocrine-mediated and set a data gap for level 2 studies according to OECD Conceptual Framework.</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	Expert consultation fulfilled.	
<p>Expert consultation 2.9</p> <p>Considering that the metabolite DFA is a major metabolite in rotational crops and in poultry, and is found above 0,75 µg/L in groundwater, MSs to discuss the reference values applicable to the metabolite in an expert meeting.</p> <p>See also 3(36), 2(37), 2(38), 2(39), 2(40), 2(43)</p> <p>See reporting table 2(34)</p>	<p><b>Background</b></p> <p>BYI 02960-DFA</p>  <p>BYI 02960-difluoroethyl-amino-furanone</p>  <p><b>Difluoroacetic acid (DFA, BCS-AA56716, M44)</b> is a major soil, water and plant metabolite of flupyradifurone.  It was found in the rat metabolism study according to the RMS around 6% recovered in urine. According to metabolism study 7 it was recovered as 1.7-1.9% in urine after 24 h, and at low levels in plasma, liver, kidney, muscle and fat.</p> <ul style="list-style-type: none"> <li>- Rat oral LD<sub>50</sub> of DFA is between 300-2000 mg/kg bw</li> <li>- Ames test, <i>in vitro</i> mammalian cells chromosome aberrations and gene mutation test were negative.</li> <li>- Rat, 14-day dietary study NOAEL is 500 ppm corresponding to 51 mg/kg bw per day based on clinical chemistry changes.</li> <li>- Rat, 90-day dietary study NOAEL is 200 ppm corresponding to 12.7 mg/kg bw per day based on reduced body weight and clinical chemistry changes.</li> </ul> <p><b>BYI 02960-difluoroethyl-amino-furanone (BCS-CC98193, BYI 02960-DFA, M34)</b>  Possibly included in the residue definition, recovered in the rat metabolism studies (study 6 and 7) around 3.6% in male and up to 1% in female urine.</p> <ul style="list-style-type: none"> <li>- Rat oral LD<sub>50</sub> &gt; 2000 mg/kg bw.</li> <li>- Negative Ames test and <i>in vitro</i> mammalian cells gene mutation test (CHO/HGPRT).</li> <li>- Positive <i>in vitro</i> mammalian cells cytogenetic assay: induced structural chromosome</li> </ul>	<p>Expert consultation fulfilled:  The reference values of the parent flupyradifurone are applicable to both metabolites DFA and DFEAF; the experts considered that there was sufficient evidence to conclude that DFEAF is unlikely to have genotoxic potential.</p> <p>Open point to residue section to take into consideration that the reference values of the parent are applicable to both metabolites, DFA and DFEAF.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>aberrations in V79 cells (Chinese hamster cell line) in the absence of metabolic activation at all tested concentrations.</p> <ul style="list-style-type: none"><li>- Negative micronucleus test, however FR pointed out an increased number of PCEs with micronuclei and the applicant presented HCD, see updated DAR, pp. 229-230.</li><li>- Negative UDS assay.</li><li>- Rat 14-day dietary study NOAEL 1280 ppm corresponding to 135 mg/kg bw per day based on reduced bw gain and lower blood glucose concentration in females.</li><li>- Rat 28-day dietary study NOAEL 3000 ppm corresponding to 243 mg/kg bw per day</li></ul> <p><b>Comments</b></p> <p><u>Difluoroacetic acid:</u></p> <ul style="list-style-type: none"><li>• FR suggested setting a LOAEL for the 14-day study with DFA (study 1) of 500 ppm or 48 mg/kg bw per day for male and 51 mg/kg bw per day for female, based on decreased of glucose concentration in both sexes at 500 ppm, 2000 ppm and 8000 ppm.</li><li>FR suggested setting a LOAEL for the 90-day study at 200 ppm or 12.7 mg/kg bw per day for male and 15.6 mg/kg bw per day for female, based on decreased of glucose concentration in both sexes at 200 ppm, 1000 ppm and 6000 ppm.</li><li>FR further commented that considering the LOAEL of 200 ppm, based on decreased of glucose concentration in both sexes at 200 ppm, 1000 ppm and 6000 ppm, setting in the 28 days study on difluoroacetic acid (DFA); the toxicity of this metabolite is not covered by the overall toxicological profile of the parent compound.</li><li>• The applicant considers that the toxicological profile of DFA is covered by the toxicological profile of the parent flupyradifurone as shown in a comparative assessment of the findings: metabolic changes observed with difluoroacetic acid were also observed with flupyradifurone in a 28-day rat study at 5000 ppm, where a marked decrease in total bilirubin and glucose and a significant increase in urea and total cholesterol compared to controls were observed at 5000 ppm.</li></ul> <p>Even if estimating an ADI for DFA based on 90-day rat study and considering that the low dose (200 ppm) is the LOAEL (and not the NOAEL), the estimated value is very close to the parent ADI, confirming that a separate risk assessment for DFA is not warranted.</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>In the scenario where the low dose of 200 ppm is not considered as a NOAEL in the 90-day rat study but as a LOAEL, the applicant is of the opinion that it is preferable to use the bench mark dose (BMD) approach instead of applying an additional uncertainty factor to the LOAEL, as recommended by EFSA (EFSA Scientific Committee, 2012). See 2(43)</p> <p><b><u>BYI 02960-difluoroethyl-amino-furanone</u></b></p> <ul style="list-style-type: none"><li>FR commented that the toxicity of the metabolite BYI 02960-difluoroethyl-amino-furanone (BYI 02960-DFA) is not covered by the overall toxicological profile of the parent compound.</li></ul> <p>FR suggested setting a LOAEL of 1280 ppm or 135 mg/kg bw per day for male and female, for the 14-day study based on decreased of glucose concentration at 1280 ppm, 3200 ppm, 8000 ppm and 20000 ppm.</p> <p>FR further suggested setting a NOAEL of 800 ppm or 68 mg/kg bw per day for male and 76 mg/kg bw per day for female for the 28-day study, based on decreased of body weight in both sexes at 3000 ppm and considered that its genotoxic potential should be discussed.</p> <p><b>Pesticides Peer Review Experts' Meeting</b></p> <p><u>For the metabolite DFA:</u></p> <p>The decreased glucose concentration was the only treatment-related effect at all doses in the <b>14-day study</b>. In the absence of other findings, the RMS considered this change as not adverse and proposed a NOAEL of 500 ppm based on effects on body weight (-12% in females). Bilirubin decrease (in females only) and increased urea were observed in all dose groups without dose response relationship or concurrent findings in organs. The experts agreed on a NOAEL of 500 ppm corresponding to 51 mg/kg bw per day.</p> <p>In the <b>90-day study</b>, bilirubin and glucose effects were observed in all dose groups. No dose-response relationship was observed in the clinical chemistry parameters. The RMS proposed a NOAEL of 200 ppm corresponding to 12.7 mg/kg bw per day based on reduced body weight gain. This was agreed by the experts.</p> <p>In the rat metabolism, DFA did not appear as a major metabolite.</p> <p>Comparison with the toxicity profile of the parent could not be concluded.</p> <p>The experts considered the use of the reference value of the parent or reference values</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>derived from specific data with the metabolite. The majority agreed to use the reference values of the parent.</p> <p><u>For the metabolite BYI 02960-difluoroethyl-amino-furanone:</u></p> <p>In the <b>14-day rat</b> dietary study, the proposed NOAEL is 1280 ppm corresponding to 135 mg/kg bw per day based on reduced bw gain and lower blood glucose concentration in females.</p> <p>In the <b>28-day rat</b> dietary study, the proposed NOAEL is 3000 ppm corresponding to 243 mg/kg bw per day.</p> <p>The experts agreed with the RMS conclusions.</p> <p>Historical control data were provided for the positive <i>in vitro</i> chromosome aberration test; negative results were obtained in a micronucleus test where exposure of the bone marrow was indirectly demonstrated by signs of general toxicity. In the absence of toxicokinetic data for the metabolite, this might not be considered as a direct sign of exposure of the bone marrow. An <i>in vivo</i> UDS test provided also negative results but might not be the most appropriate follow up (nowadays a Comet assay would be required).</p> <p>In the ADME studies of the parent, this metabolite has been found in urine, plasma, kidney, muscle.</p> <p>The experts agreed that negative results in micronucleus and UDS tests <i>in vivo</i> were sufficient to conclude on the absence of genotoxic potential for this metabolite.</p> <p>The RMS proposed that the reference values of the parent should be applied to this metabolite as well. This approach was agreed by the experts.</p> <p>Expert consultation fulfilled.</p> <p>Open point to residues:</p> <p>Residue section to take into consideration that the reference values of the parent are applicable to both metabolites, DFA and DFEAF.</p>	
Expert consultation 2.10	<p><b>Background</b></p> <p><u>ADI/AOEL</u></p> <p>Originally in the DAR, the RMS proposed to base both the ADI and AOEL on the NOAEL of</p>	<p>Expert consultation fulfilled:</p> <p>The ADI and AOEL are 0.064 mg/kg bw per day based on the parental</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>MSs to discuss the ADI and AOEL in an expert meeting. See also 2(16), 2(46), 2(47)</p> <p>See reporting table 2(45)</p>	<p>7.8 mg/kg bw per day from the 1-year dog study. Similar critical effects (myofiber degeneration, similar number of effected animals) were seen in the 90-day study with dog. It was therefore suggested to use both the 1-year and the 90-day dog studies to set the NOAEL of 12 mg/kg bw per day used as a starting point for the establishment of the ADI/AOEL, also taking into account the sufficient dose spacing between the 90-day dog NOAEL and the 1-year LOAEL. The resulting ADI/AOEL being 0.12 mg/kg bw per day.</p> <p>RMS revised the ADI/AOEL values in the updated DAR considering the comments received:</p> <p>The ADI and AOEL are 0.08 mg/kg bw per day, based on the NOAEL of 7.7 mg/kg bw per day from the multigeneration study in rats applying an uncertainty factor of 100 (no correction being necessary regarding oral absorption for the AOEL).</p> <p><b>ARfD</b></p> <p>The ARfD value has been revised in the updated DAR to 0.15 mg/kg bw, based on the maternal NOAEL of 15 mg/kg bw per day from the developmental toxicity study in rabbits and applying an uncertainty factor of 100.</p> <p><b>Comments</b></p> <ul style="list-style-type: none"> <li>• EFSA noted that as both the 90-day and 1-year studies in dogs are considered short term, only the most relevant one should be mentioned in the LoEP. It appears to be the 1-year, once a longer duration of exposure is tested (although considering dose spacing, the 12 mg/kg bw per day from the 90-day study may be discussed). Considering the comments regarding 90-day, 2-year and multigeneration rat NOAELs, these may have an impact on the setting of the ADI and/or AOEL.</li> <li>• FR commented that pending the discuss on the NOAEL in the 2 years rat study, France suggests setting an ADI of 0.032 mg/kg bw per day on the basis of NOAEL of 3.17 mg/kg bw per day, applying a standard assessment factor of 100.</li> </ul> <p>FR suggests setting an AOEL of 0.078 mg/kg bw per day on the basis of NOAEL of 7.8 mg/kg bw per day from the 1-year oral dog study, applying a standard assessment factor of 100.</p> <p>This AOEL can be supported by the NOAEL of 7.6 mg/kg bw per day from the 90-days oral rat study, the NOAEL of 7.8 mg/kg bw per day from the 2-generation rat</p>	<p>and offspring NOAEL of 6.4 mg/kg bw per day from the 2-generation reproductive toxicity study in rats applying an UF of 100, no correction regarding oral absorption being necessary in deriving the AOEL.</p> <p>The ARfD is 0.15 mg/kg bw based on the maternal NOAEL of 15 mg/kg bw per day from the developmental toxicity study in rabbits, 100 UF applied.</p> <p><b>Open point:</b> RMS to revise operator, worker, bystander and residential exposure risk assessment taking into consideration the new AOEL value set by the experts.</p> <p><b>Open point to Residue section to revise consumer assessment taking into consideration the revised reference values (ADI and ARfD) set by the experts.</b></p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>study and by the NOAEL of 12 mg/kg bw per day from the 90-days oral dog study.</p> <p><b>Pesticides Peer Review Experts' Meeting</b></p> <p>Considering the parental and offspring NOAEL in the multigeneration study, the experts agreed to set the ADI at 0.064 mg/kg bw per day, applying an uncertainty factor of 100. For the AOEL, the experts also agreed on a value of 0.064 mg/kg bw per day, applying an uncertainty factor of 100, no correction being necessary regarding oral absorption. The experts agreed that ARfD is 0.15 based on the maternal NOAEL in the rabbit developmental study (reduced body weight gain within the first days).</p> <p>Expert consultation fulfilled.</p> <p>Open point: RMS to revise operator, worker, bystander and residential exposure risk assessment taking into consideration the new AOEL value set by the experts.</p> <p>Open point to Residues: Residue section to revised consumer assessment taking into consideration the revised reference values (ADI and ARfD) set by the experts.</p>	

## REPORT OF PESTICIDES PEER REVIEW MEETING 121

### FLUPYRADIFURONE

Rapporteur Member State: NL

Specific comments on the active substance in the section

#### 4. Environmental Fate and Behaviour

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

##### 1. Comments submitted for this meeting:

Date	Supplier	File Name
none		

##### 2. Documents submitted for meeting:

Date	Supplier	File Name
November 2014	NL	flupyradifurone evaluation table NAS section 4 November 2014.doc
November 2014	NL	flupyradifurone updated DAR volume 3 B8 November 2014.doc
24.06.2014	NL	flupyradifurone_reporting_table_2014-06-24.doc
15.10.2014	NL	flupyradifurone_fate addendum for expert meeting.doc

##### 3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

Appendix 1: Discussion table: FLUPYRADIFURONE

## Appendix 1: Discussion Table, Flupyradifurone

### 4. Environmental Fate and Behaviour

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Expert consultation 4.1  Member state experts to discuss the time dependent sorption dataset and the appropriateness of the tier 2b groundwater modelling approach used, including the consideration of the RMS assessment of what is provided in response to the data requirement at reporting table comment 4(12). Experts to conclude if the available tier 2b simulations should be relied upon. Experts to discuss the issue of parameter correlation and discuss if averaging of simulation results for each soil rather than averaging input parameters from different soils is justified	<p><b>PEC GW calculations considering TDS (named Tier 2b in the DAR and RT).</b></p> <p>Draft guidance for TDS is currently under discussion by the PPR panel. The existing draft guidance is not an EFSA draft guidance but a guidance developed by FERA and Alterra and proposed for adoption at EU level. Experts considered the appropriateness of using a guidance that is not yet accepted and under discussion by the panel.</p> <p>Additional information requested in the evaluation table has been provided by the applicant but has not yet been included in the updated addendum. Overall results were presented to the meeting by the RMS in a presentation.</p> <p>An addendum has been presented to the meeting where open points to the RMS are addressed and the information presented by the applicant is listed but not yet evaluated.</p> <p>The experts agreed that the studies presented were done according the draft guidance developed by FERA and Alterra. The trigger is exceeded in the majority of the scenarios for hops.</p> <p>Specific issues.</p> <p>1/n on similar soils but not identical. RMS show that the 1/n range in the soils tested is narrow. Experts accept that in this case the slight differences in soil would not have significant effect on the 1/n.</p> <p>The experts agree that age adsorption is a real process but the impact on the risk assessment if the final implementation of TDS changes with respect to what is currently in</p>	<p>Open point</p> <p>RMS to remove tier 2b input parameters and results from the LoEP.</p> <p>RMS to present the results of the tier 2b in and addendum or updated DAR including results of the simulations performed with PELMO and PEARL in hops and lettuce considering geometric and mean input parameters (as appropriate) and median results of the separated soils simulations.</p> <p>RMS to add tier 1 and tier 2a PEC GW simulations for field lettuce to the LoEP.</p> <p>RMS to check and confirm and update the results for PELMO tier 1 and tier 2a in the updated DAR and the LoEP.</p> <p>For the metabolites the calculations presented should be performed</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>or whether the results from both approaches should be considered for decision making.</p> <p>See reporting table comments 4(11), 4(12), 4(13), 4(16), 4(17), 4(31), 4(32) and 4(37).</p>	<p>the draft guidance developed by FERA and Alterra needs to be considered.</p> <p>In previous dossiers, where the consideration of TDS was proposed no fundamental discussion was usually needed since the studies presented usually did not meet the minimum quality criteria.</p> <p>Current leaching models used for regulatory purposes contain options to consider TDS as refinement based on the “two site” model. The “two site” model description in PEARL and PELMO is slightly different but expected to be compatible.</p> <p>Experts consider that the model were calibrated without considering TDS and that the consideration of the TDS would need to perform a new calibration exercise in order to give the model predictive capacity needed for regulatory purposes in order to ensure that protection goals are not changed. Some experts indicated situations where the calibration of the parameters of TDS of a system may produce a very good improvement in the data fitting of the system that is parameterized but may translate very bad when the parameters are applied to another system.</p> <p>The experts consider that for regulatory purposes the implementation of the TDS based on laboratory experiments to determine the parameters would need to be harmonized (the draft guidance is in fact a proposal for this harmonization).</p> <p>A number of data sets would need to be independently tested in order to be able to understand how to use TDS input parameters derived from laboratory experiments and the impact on the regulatory framework. Current models were originally calibrated against a limited number of leaching experiments (eg. lysimeters).</p> <p>Current scheme is a framework that allows having a set of rules that allow ranking the substances based on their properties taking into consideration the intended uses and climatic conditions (not necessarily giving accurate predictions). By incorporating other individual processes the ranking capacity of the scheme is lost.</p> <p>In conclusion, the experts agreed that the kinetic sorption experiments were performed</p>	<p>assuming a plant uptake factor of 0.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>following the draft guidance developed by FERA and Alterra and the calculations of the model input parameters and the ground water modelling required were provided but still need to be included in an addendum or in an updated DAR. Since the experts have still doubts on the acceptability of the TDS scheme as in the draft guidance developed by FERA and Alterra due to uncertainties in the validation of the scheme against accepted (and not completely clear) protection goals, experts considered that at this stage the results of these simulations should not be included in the LoEP.</p> <p><b>Plant uptake</b></p> <p>Based on the ECPA paper on PUF (plant uptake factor, change in solution concentration) the applicant presented calculations using TSCF (transpiration stream concentration factors) of 0.5 for parent and metabolites. For the parent a TSCF of 0.5 for substances that uptake by root from soil is accepted here. In this case it can be accepted on basis of the following crop metabolism studies however evidence for the metabolites is not available (only generic data was provided and in it is not accepted). Therefore, calculations for metabolites need to be redone using a TSCF of 0.</p>	

## REPORT OF PESTICIDES PEER REVIEW MEETING TC 107

### FLUPYRADIFURONE

Rapporteur Member State: NL

#### Specific comments on the active substance in the section

#### 3. Residues

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

##### 1. Comments submitted for this meeting:

Date	Supplier	File Name
20/11/2014	EFSA	 Flupriradifurone  Flupyradifurone  Flupyradifurone  Flupyradifurone Residue trials %p.xls Animal metabolism.xls Plant metabolism.xls Rotational trials.xls
20/11/2014	EFSA	 Report Pesticides Peer Review 122_04

##### 2. Documents submitted for meeting:

Date	Supplier	File Name
November 2014	NL	flupyradifurone evaluation table NAS section 3 November 2014.doc
November 2014	NL	flupyradifurone updated DAR volume 1 November 2014.docx
November 2014	NL	flupyradifurone updated DAR volume 3 B7 November 2014.docx
24.06.2014	NL	flupyradifurone_reporting_table_2014-06-24.doc

##### 3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

Appendix 1: Discussion table: FLUPYRADIFURONE

## Appendix 1: Discussion Table, Flupyradifurone

### 3. Residues

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p><b>Expert consultation 3.1</b> The plant residue definition for enforcement and risk assessment should be discussed in a meeting of experts, considering the following points: - the conclusion of the review on the toxicological property of the DFA metabolite. - the DE comment on DFA to be specific to flupyradifuron only (contribution from tetriconazole unlikely)</p> <p>See also comments 3(9), 3(11), 3(12), See reporting table 3(8)</p>	<p>The meeting on toxicology concluded that the reference values for parent are applicable to the metabolite. DFEAF is present in only 6% of analysed samples and in low amounts, it does not need to be included in the RD for RA.</p> <p>For risk assessment, it is therefore proposed to define the residue definition for risk assessment as the sum of flupyradifurone and DFA, expressed as flupyradifurone.</p> <p>For monitoring, it is suggested that parent would be a sufficiently good marker for primary crops, but for risk based monitoring it will be appropriate to consider also DFA since:</p> <ul style="list-style-type: none"><li>- reliable conversion factors cannot be established for some plant commodities (i.e. ratio "(parent+DFA)/parent" 2.1 and 3.3 at 3 day PHI in cucurbits and melon respectively, while 10 and 11 at 14 day PHI),</li><li>- parent is almost not present in rotational crops (&lt;0.01 mg/kg), where DFA is the main component, observed in high levels resulting in some situations in higher residue levels than those observed in primary crops.</li></ul> <p>Based on the available data, it is noteworthy, that DFA is the marker of the residues in rotational crops, while flupyradifurone is the marker of the residues in primary crops.</p> <p>Therefore, it is considered appropriate to establish 2 separate residue definitions to be monitored,: 1) one as flupyradifurone based on the results in primary crops, and 2) DFA based on the findings in rotational crops.</p> <p>This approach acknowledges that DFA is not specific to flupyradifurone as it may occur as a metabolite of other active substances (however, the meeting is not certain if currently there is an authorisation of another active substance leading to significant DFA levels).</p> <p>A residue definition for monitoring defined as "sum of parent + DFA expressed as</p>	<p>The residue definition for <b>risk assessment</b> is set as the sum of flupyradifurone and DFA, expressed as flupyradifurone.</p> <p>Two separate residue definitions are proposed for <b>monitoring</b> as</p> <ol style="list-style-type: none"><li>1) flupyradifurone and</li><li>2) DFA, separately</li></ol> <p>Analytical method is available to analyse both components simultaneously.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>"parent" would result in default MRL values in rotational crops higher than the MRL proposals derived from the uses on primary crops.</p> <p>It was noted that a single method is available to analyse both compounds flupyradifurone and DFA together, but a multi-residue method seems currently not available for capturing both compounds simultaneously (no such method has been validated for DFA).</p> <p>There was a minority opinion, that the monitoring definition should be the same as for risk assessment. However, the majority opted for the approach of setting 2 different monitoring residue definitions as 1) flupyradifurone and 2) DFA, and for proposing 2 sets of MRLs, accordingly.</p>	
<p>New open point arisen from the meeting:</p> <p>To reconsider the MRL proposals, taking into account the plant residue definitions agreed during the TC 107 meeting, and to reconsider the consumer risk assessment taking into account the toxicological reference values concluded in the Peer review meeting 124 (ADI 0.064 mg/kg bw/d, ARfD: 0.15 mg/kg bw, reference values applicable to the metabolite DFA).</p>		
<p><b>Expert consultation 3.2</b></p> <p>Animal residue definitions should be discussed in a meeting of experts, considering the conclusion of the review on the toxicological property of the DFA metabolite.</p> <p>See reporting table 3(13)</p>	<p>DFA was not analysed in the animal metabolism studies since the active substance was not labelled on the ethyl group. However, the feeding studies give indication that significant residue levels of DFA appeared upon dosing with parent, and DFA seems to be a major metabolite in livestock.</p> <p>For monitoring, in terms of ruminant matrices, parent appeared to be a good marker, while in poultry it was DFA, but considering studies where animals were dosed with flupyradifurone only.</p> <p>It is suggested that, given the exposure pattern of livestock and the observations in the feeding study, the definition for risk assessment is set as the sum of flupyradifurone and DFA, expressed as flupyradifurone.</p> <p>Currently, the information regarding DFA residue levels in livestock is very limited, and the levels expected in animal matrices in terms of the representative uses</p>	<p>The animal residue definition for <b>risk assessment and for monitoring</b> is set as the sum of flupyradifurone and DFA, expressed as flupyradifurone.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>cannot be assessed with sufficient certainty.</p> <p>It has to be considered that the actual livestock burden will be composed mainly by DFA, and thus the picture in the study may be shifted to higher proportions and levels of DFA. DFA cannot be ignored as a relevant marker.</p> <p>Hence, the monitoring definition should be proposed as flupyradifurone and DFA, expressed as flupyradifurone</p>	
<b>Expert consultation 3.3</b> Member states to discuss the residue definitions for processed commodities, considering the conclusion on the toxicity of the DFA metabolite.  See reporting table 3(26)	<p>The residue definition for risk assessment for processed commodities is set in line with raw commodities as the sum of flupyradifurone and DFA, expressed as flupyradifurone, considering the stability of both compounds under processing conditions.</p> <p>Accordingly, the residue definition for monitoring should apply, i.e. 1) flupyradifurone and 2) DFA, separately.</p>	<p>For processed commodities, the residue definition for <b>risk assessment</b> is set as the sum of flupyradifurone and DFA, expressed as flupyradifurone.</p> <p>The residue definition for <b>monitoring</b> is proposed as 1) flupyradifurone and 2) DFA, separately</p>
New open point arisen from the meeting: Transfer factors for flupyradifurone and DFA, to be reconsidered according to the residue definitions proposed for primary crops and for processed commodities.		
Expert consultation 3.4  Member states to discussed whether the feeding studies conducted with the parent compound flupyradifurone are appropriate to estimate DFA residue levels in animal matrices. The approach to derived MRLs for products of animal	<p>The feeding study was conducted on animals dosed with the parent flupyradifurone only. Samples were analysed for parent, DFA and 2 other metabolites; M03 (flupyradifurone-OH) and M40 (flupyradifurone-acetyl-AMCP). The applicant proposed to estimate the animal exposure to DFA in the feeding studies, considering the ratio "DFA metabolite levels in all animal matrices /flupyradifurone feeding rates" (estimated to be 31% for poultry and only 2.9% for bovine). These estimated DFA exposure levels were used to calculated transfer (TF) factors for the different animal matrices. However, the way this factors was</p>	<p>For the time being, as an interim approach, the use of the transfer factors to estimate residues of DFA upon exposure flupyradifurone is considered to derive provisional MRLs. These</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>origin should be discussed indeed (use of transfer factors, ...). See comment in 3(55)</p> <p><b>EFSA Note:</b> RMS comment on OECD studies limited to the parent active substance is surprising, as it is clearly stated in the OECD guideline 503 on metabolism in livestock that "<i>If a plant metabolite comprises a major portion of the TRR on a feed item, a livestock metabolism study involving dosing with the plant metabolite may be needed</i>". Moreover, in the guideline 505 on residues in livestock it is mentioned "<i>Livestock are dosed with the representative component(s) of the residue as defined in the feed, which is derived from crop metabolism, confined rotational crop and processing studies. The residue definition of a pesticide might consist of parent compound plus one or more metabolites, or a single or several metabolites or degradation products</i>". In addition, it is also mentioned in the current EU guidance on livestock feeding studies 7031/VI/95 rev.4 "<i>The initial active substance is often the relevant part of the residue. In other instances, a metabolite or metabolite mix may also be used in the trial.</i>"</p> <p>See reporting table 3(28)</p>	<p>derived is considered not very transparent and further information has to be given to enhance the reliability of the results (e.g. toxicokinetics, rate of excretion, etc.) It was agreed that there is a high uncertainty with regard to this approach and with regard to the uncertainty in livestock exposure calculations to DFA (uncertainty in terms of actual residue levels in rotational crops). In order to avoid potential MRL exceedances or unnecessarily high MRLs and to lower uncertainty regarding expected residue levels in animal matrices (i.e. the basis for MRL proposals), a feeding study with DFA should be made available.</p> <p>It was noted that also metabolite M09 (flupyradifurone OH sulphate) was a major metabolite in hen matrices (fat, liver) in one study. It was not considered necessary to require any new metabolism study to elucidate the metabolic pathway. As for the structural similarity to M03 analysed in the feeding study (leading to negligible residues), and considering M09 was present in 2 matrices in 1 study only and that poultry will be mainly exposed to residues of DFA, it is not likely that significant levels of M09 will occur in hen liver and fat.</p> <p>For the time being, as an interim approach, the use of the transfer factors to estimate residues of DFA in animal matrices upon exposure flupyradifurone will be considered upon presentation of full details of the calculation. The provisional MRL proposals for animal matrices will have to be reviewed when DFA feeding studies and appropriate rotational crop studies are available. The feeding studies should be conducted with DFA. The requirement is in line with the OECD and EU guidelines (see comments in column 2).</p>	<p>provisional MRL proposals for animal matrices will have to be reviewed when DFA feeding studies and appropriate rotational crop studies are available. The requirement is in line with the OECD guidelines.</p> <p>Data gap: Feeding studies in hen and cow conducted with the DFA metabolite to be submitted.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>Expert consultation 3.5 Member states to discuss if the rotational crop studies conducted with a dose rate of 2x 125 g/ha and a PBI of 30 days, are appropriate to estimate the residue levels expected in food commodities and in the feed commodities used for the animal burden calculations.</p> <p>See also comment 3(5), 3(41) and 3(47) See reporting table 3(39)</p>	<p>It is acknowledged, that residue levels observed for DFA and thus, the MRL proposals, will be surrounded by a high uncertainty (higher than for parent in primary crop residue trials) since unsufficient data are currently available for rotational crops and the potential for long term accumulation of DFA following several years of consecutive applications is not addressed by the available data. It is unknown if the trials were conducted at rates reflecting the expected plateau level in soil since soil analysis was not provided in these rotational crop trials. Hence, it is not certain that the 30 day PBI does indeed cover the worst-case in terms of DFA residues expected in rotational crops. Moreover, for several all crops, a PBI of 30 days is unrealistic in practice (especially for cereals, oilseeds, potatoes...) and therefore, information at different PBI is necessary.</p> <p>To estimate the residues of DFA occurring in rotational crops with confidence, new rotational crop trials should be submitted, conducted at realistic-worst-case plant back intervals with regard to the following crop selected, and providing in addition soil analyses to enable comparison with the expected soil plateau concentrations. For the time being, MRL setting for DFA has to be done with caution and provisionally, considering the available data and pending the submission of additional data.</p> <p>Therefore, MRL proposals for rotational crops will be made considering the highest residues observed in the rotational crop trials currently available. The OECD MRL calculator results in overestimated MRLs, since it includes an uncertainty of small data sets and rounds up. However, it is acknowledged that these MRLs are provisional only.</p>	<p>Data gap: Rotational crop trials should be submitted, conducted at realistic-worst-case plant back intervals with regard to the following crop selected, and providing in addition soil analyses.</p> <p>Proposed MRLs for DFA for rotational crops are provisional, pending the availability of the new data.</p>

## REPORT OF PESTICIDES PEER REVIEW MEETING 124

### FLUPYRADIFURONE

Rapporteur Member State: NL

Specific comments on the active substance in the section

#### 5. Ecotoxicology

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name
None.		

2. Documents submitted for meeting:

Date	Supplier	File Name
November 2014	NL	flupyradifurone addendum 1 to volume 3 B9 November 2014.doc
November 2014	NL	flupyradifurone appendix 1 to addendum 1 to Volume 3 B9.pdf
November 2014	NL	flupyradifurone appendix 2 to addendum 1 to volume 3 B9.docx
November 2014	NL	flupyradifurone evaluation table NAS section 5 November 2014.doc
November 2014	NL	flupyradifurone updated DAR volume 3 B9 November 2014.docx
24.06.2014	NL	flupyradifurone_reporting_table_2014-06-24.doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
None.		

Appendix 1: Discussion table: FLUPYRADIFURONE

## Appendix 1: Discussion Table, Flupyradifurone

### 5. Ecotoxicology

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
Expert consultation 5.1  The residue decline data was not used because based on the NOAEL of 34 mg/kg bw/d, a refined risk assessment is not necessary. However if the 1-year dog study is considered to be relevant, a refined risk assessment may be needed. Depending on the outcome of the expert consultation 5(8), the experts may need to discuss if the 21-d ftwa approached proposed for lettuce and hops can be considered acceptable.  In all trials residue were determined after the second treatment, but for four trials residues	<p>Background:</p> <p>Ftwa might be used as refinement for the RA for B&amp;M (the need for the EU assessment on mammals is pending on Expert consultation 5.2). Four trials on cereals were summarised in the DAR (may be used as surrogate for hops). Additionally, a number of residue trials in lettuce heads were available from different MSs (N&amp;S). The trials not necessarily cover early crop stages. DT50 values were derived from trials where at least 5 measurements (time points) were available. The DT50s were obtained either from SFO or from DFOP fits (fast and slow phase). The RMS has carefully checked exercises for DT50 derivation from the lettuce trials and did amendments where it was necessary. The RMS considered that it is not possible to derive an overall average first order DT50 value, since the best fits were obtained from different models (this is for both crops). Therefore, ftwa values were calculated from each trial (from some trials 2 DT50s were derived, one after the first and one after the second application, but for the ftwa calculation only the DT50s from the 2nd applications were used). The average of these ftwa values were 0.15 for lettuce and 0.17 for cereals. Where DT50 from both the slow and the fast phases were available (DFOP fit), a combined ftwa was calculated.</p> <p>It was raised in the commenting phase that it would be possible just considering the slow phase DT50s from the DFOP kinetics and combine them with the SFO DT50s. This might be used when moving "TWA x MAF" are required.</p> <p>The NOT had another proposal for this kind of issues. The following is copied from the RT (5(6)):</p> <p>"The 2 main objectives for employing residue decline kinetics in bird and mammal risk assessment are calculation of (a) the peak residue level and (b) 21-d TWA residues. When an overall SFO DT50 value can be generated, then this SFO DT50 is translated into (a) peak residue = AR x MAF and (b) 21-d TWA residues = AR x MAF x 21d ftWA. Fully equivalent is direct calculation of the peak residue concentration and the 21-d time weighted average concentration with DFOP kinetics. However, with DFOP, the peak</p>	<p>Open point</p> <p>The RMS to include a refined risk assessment in an updated DAR and the LoEP taking account of the appropriate ftWA, in addition to the NOAEL of 100 ppm (see the open point on the experts- consultation 2).</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>were also determined after the first application and DT50 values were estimated for each decline interval. Some of the DT50 values were calculated with DFOP (both kfast and kslow was used). For most of the sites in lettuce only 5 sampling points were available. A geometric mean 21-day fTWA is proposed for the refined long-term exposure assessment. There are some uncertainties for lettuce whether the residue values is applicable to the full application period. Only one of the four doubly analysed trials was performed at a relatively early BBCH stage in lettuce.</p> <p>See reporting table 5(5)</p>	<p>residues and 21-d TWA concentrations are first calculated per replicate and afterwards expressed as the 90th peak concentration (for acute risk assessment) and the mean 21-d TWA concentration (for reproductive risk assessment).“</p> <p><b>Discussion:</b></p> <p>It was noted in the reporting table that there was an inconsistency in the GAP table where it was stated that applications were biannual (twice per year) or biennial (once every 2 years)? It was confirmed that only a single application will be made per year and the GAP table has been updated.</p> <p>It was noted that a fate assessment would take the slower phase DT50 when the DFOP degradation is observed. It was questioned whether the approach taken by the RMS was reasonable as a refinement. The studies performed on lettuce were questioned as food items could be weeds including monocots. The RMS highlighted that trials on cereals were also available and the difference in the fTWA was minor indicating not too dissimilar speed of degradation/dissipation. It was noted that 18 trials were available for lettuce and only 4 for cereals. It was discussed whether the scenarios in the GD cover mammals consuming the lettuce crop plants in addition to weeds. Experts noted that different FIR would be needed for a lettuce scenario. The experts agreed that, when refining the assessment, the food items taken by the focal species should be considered.</p> <p>The representativeness of the studies used was discussed noting that the studies were not performed at the correct growth stage. The trials were performed at BBCH 17 to 46 whereas the GAP is BBCH 12 to 49 (lettuce). The RMS considered this in the DAR and noted that the lettuce trials do not cover the entire GAP for lettuce. Furthermore, the RMS noted during the meeting that it could be at latter growth stages that the dissipation is slower due to slower growth. Some experts did not consider the BBCH stage of the crop to be an issue as the studies should represent weeds in addition to the crop. Furthermore, the DT50 in the two types of trials were not too dissimilar.</p> <p>The cereal trials were performed at BBCH 25 to 29 and therefore were at a growth stage palatable to birds and mammals. The RMS considered that this was reasonable to represent weeds. The fTWA from both trials were comparable regardless of the growth stage further supporting the use of the studies.</p> <p>Overall the experts agreed that the available studies were suitable to be used for the</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>refined assessment for the representative uses. It was discussed how the fTWA values should be used in the risk assessment (i.e. geometric mean, pooled, lower, two assessments). The geometric mean was questioned as it does not result in a worst case value but then the RMS noted that there were more than 10 values indicating that the geometric mean was reasonable (NL approach). The RMS also noted that the studies needed to cover the entire EU. Some studies were performed in NEU and SEU, no differences were noted. Overall, the experts considered that the data were sufficient for N and SEU. The RMS suggested that the data should be pooled and then the geometric mean from the pooled data used. The experts noted that pooling data should be done with care and therefore it is difficult to agree on the basis of the available raw data. It was agreed that the RMS should pool the data but check statistically significant differences between the two data sets (lettuce crop vs. cereals and N vs. SEU) whether the pooled data are ok. If so, then the geometric mean can be taken. If not, then the experts considered that separate risk assessments may be required.</p> <p>It was agreed that the data was suitable for all weed types and lettuce crop plants given that the data cover monocots and dicots and that the DT50 may not depend on the structure of the plant.</p> <p>On the basis of the above, the RMS needs to update the risk assessment using the appropriate fTWA. Open point.</p> <p>It was noted that the approach in which the 21-d fTWA is calculated from measurements which started at the last application (in trials with two applications) is acceptable for the current GAP, since this has only one application per year. It was discussed that it may not cover GAPs which have multiple applications, as the 21-d exposure window may be higher at an earlier stage. Therefore, for other GAPs it needs to be carefully considered how to use these data.</p>	
Expert consultation 5.2  Should the 1-year dog study, with an endpoint of 7.8 mg/kg bw, be considered relevant in the risk assessment of	Background: The 2 generation rat study and the 1-year dog study concluded an endpoint of 7.8 mg/kg bw (mammalian toxicity section, original DAR). This endpoint from the rat study has changed to 'parental' and 'offspring' NOAEL of 6.4 mg/kg bw per day (100 ppm) and reproductive NOAEL of 32 mg/kg bw per day (500 ppm) (paper meeting for mamtox). The RMS has used the endpoint of 34 mg/kg bw/day in the ecotoxicology risk assessment in the DAR, which is now the reproductive NOAEL of 32 mg/kg bw per day.	Open point RMS to provide a revised DAR or addendum and to update the LoEP with the revised long-term risk assessment based on the NOAEL of 100 ppm.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
other terrestrial vertebrates, mammals?  See reporting table 5(8)	<p>The 'parental' NOAEL of 6.4 mg/kg bw per day is based on significant decrease in body weight (&lt;10% observed in the mid-dose of the F<sub>1</sub> females) and a non-significant decrease in body weight gain found in the parental animals (21% in females) and the F<sub>1</sub> animals (16% in females). The 'offspring' NOAEL of 6.4 mg/kg bw per day is based on reduced body weight/body weight gain in the F<sub>2</sub> pups. These were agreed by the meeting of experts for mammalian toxicology (PESTICIDES PEER REVIEW MEETING 122).</p> <p><b>Discussion:</b></p> <p>The 1y-dog study was considered as not relevant for ecotox for reproductive risk assessment. Some observed effects (degeneration of skeleton muscle and other muscle degeneration) from this study might be considered as relevant but not for the reproduction. It was noted that in general such type of study is not considered robust by tox experts (few test individuals).</p> <p>The discussion was focused on the 2-generation rat study. 3 endpoints are available from this study, NOAEL of 500 ppm for reproduction and 100 ppm for offspring and parental toxicity. A dose response relationship was noted for the pup body weight decrease. At 500 ppm the decrease was statistically significant but &lt; 10%. It was questioned if this should be considered as biologically relevant. At 1800 ppm (the next higher dose) the decrease was &gt;10%. Some experts considered that the statistical significance in this case should not be disregarded considering also the dose response relationship and preferred the lowest NOAEL of 100 ppm.</p> <p>Overall, the majority of the experts considered that a NOAEL of 100 ppm should be used for risk assessment (6.4 mg a.s./kg bw/d).</p> <p>The RMS should revise the risk assessment accordingly i.e. with the NOAEL of 100 ppm.</p>	
Expert consultation 5.3  Experts to discuss if a test on mayflies should be considered needed in the aquatic risk assessment.  Reporting table	<p>Background:</p> <p>Aquatic invertebrates drive the RA for AO. The lowest endpoint that was considered in the higher tier RA was from an acute water-spiked <i>C. riparius</i> study that resulted in an EC50 of 61.7 ug/L (the lowest chronic NOEC for <i>C. riparius</i> was 10 ug/L).</p> <p>A comment from the commenting phase highlighted that the concerns about possible effects on mayflies (Ephemeroptera) should be investigated and discussed further because mayflies show higher sensitivity to neonicotinoids compared to Chironomides. It was pointed out that formally all data requirements are fulfilled and no additional data would be needed. Generally, the safety factor should cover such issues (sensitivity between</p>	Open point  RMS to amend the risk assessment to aquatic organisms in a revised DAR and in the LoEP by considering the endpoint for chironomus expressed as mean measured concentration in the water column.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>comment 5(18);      “Even if the butenolide flupyradifurone (nicotinic acetylcholine receptor (nAChR) agonist) is not as toxic to Chironomidae as the closely related neonicotinoids, such as imidacloprid, the concerns about possible effects on mayflies (Ephemeroptera) should be investigated and discussed further because mayflies show higher sensitivity to neonicotinoids compared to Chironomidae. The aquatic risk could be well addressed exploring sensitivity of mayflies to the a.s.”</p> <p>See reporting table 5(18)</p>	<p>species). On the other hand, recent concerns of imidacloprid for aquatic organisms raised in the open literature should not be omitted as it may underpin some concerns for insecticides.</p> <p>The applicant provided a position paper for this issue highlighting the official data requirement and standard RA scheme that includes a safety factor, arguing on the difference of the molecule structure of flupyradifurone and imidacloprid and on the uncertainties of testing mayfly.</p> <p><b>Discussion:</b></p> <p>EFSA clarified that for imidacloprid the data set available at the time of the first peer review already indicated some concerns as regards Ephemeroptera. The endpoint agreed for risk assessment was based on chironomus from a mesocosm study where Ephemeroptera were not enough abundant.</p> <p>The experts questioned whether potentially more sensitive insects should always be considered for insecticides. Some experts considered that the available data were not sufficient and it is needed to ask for more data because a higher sensitivity for ephemeropatra is expected for this substance. However, not enough data were available to support such a requirement.</p> <p>The experts discussed in deep the available data on chironomus. Some experts considered that the chironomus endpoint should be expressed in terms of mean measured concentration in the water column since the substance does not partition quickly to sediment. Likely the substance degrades relatively fast in water. The endpoint expressed in this way would be relevant also for other organisms living in the water.</p> <p>However, the concentration in the sediment was unknown; in the pore water it was relatively low. Therefore, some experts noted that there is not enough information to agree on the mean measured concentration in the whole test system (which could be more appropriate). However, for the water column the information was available therefore the experts agreed to express the chironomus endpoint based on mean measured concentration.</p> <p>The current TERs with the chironomus standard endpoint expressed in terms of nominal concentrations resulted below the trigger for many scenarios. With the endpoint expressed in terms of mean measured concentrations, likely the majority of scenarios will be below the trigger. Therefore, it is likely that higher tier studies should be performed to further address the risk to aquatic insects. In performing this higher tier assessment, potentially</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>more sensitive insects should also be considered.  The RMS should amend the risk assessment to aquatic organisms, accordingly.</p> <p><u>As general point</u>, it was agreed that the endpoints for chironomous should be expressed in terms of mean measured concentration in water column when the analytical measurement concentrations are outside of the range 80-120% and when concentrations in the sediment are not available. The endpoint in this case would be relevant for other insects living in water.</p>	
<p>Expert consultation 5.4</p> <p>Experts from Member States to discuss the design and the results of the available higher tier studies for bees.</p> <p>Experts from Member States to discuss the risk assessment and conclude the risk to bees for the representative uses.</p> <p>Beside the available higher tier effect studies, the experts should/may pay attention to the</p> <ul style="list-style-type: none"> <li>- available laboratory endpoints</li> <li>- available residue data</li> <li>- off-field risk assessment</li> </ul>	<p><b>Background:</b></p> <p>6 semi-field studies were available on <i>phacelia</i>. One of them was invalidated by the RMS. Some shortcomings and some – usually rather slight – indications of effects were noted by the RMS and/or during the commenting phase. In terms of the application regimes of the GAP, many of these studies can be considered as worst case.</p> <p>2 field studies on OSR were available. Some indications of effects were noted by the RMS and/or during the commenting phase. Again, in terms of the application regimes of the GAP, these studies are considered as worst case. On the other hand, considerable dilution of residues from the surroundings and food stock of the hives was obvious. Overwintering assessments were available from these studies.</p> <p>Additionally a feeding study (semi-field then field) was available. Some shortcomings and some indications of effects were noted by the RMS and/or during the commenting phase.</p> <p><b>Discussion:</b></p> <p>The RMS summarised the available data for honey bees. A chronic lab study was available with the parent and honey bee larvae. A further lab. study was available for bumble bees. The RMS noted that the metabolites were shown not to be particularly toxic, based on the lab. trials. The RMS also noted that the a.s. is toxic to bees, but compared to other active which have similar modes of action, it is less toxic.</p> <p>The RMS concluded a low risk to honey bees on the basis of the available data for the representative uses. Nevertheless the RMS noted that it is likely that authorisation for flowering crops will be requested.</p> <p>Generally, looking at the overall picture, the RMS concluded that at the dose rates tested it</p>	<p>Open point for EFSA  EFSA to reflect in the conclusion that the available assessment does not cover the risk to pollinators other than honey bees.</p> <p>Open point for the RMS  RMS to update the LoEP to ensure that the text is in line with the conclusions of the meeting.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<ul style="list-style-type: none"> <li>- sub-lethal effects observed in laboratory studies</li> <li>- repellent effects seen in some higher tier studies</li> <li>- risk via honeydew</li> <li>- risk to wild pollinators</li> </ul> <p>See also comments in 5(26), from 5(37) to 5(45), from 5(47) to 5(50) and from 5(52) to 5(55). In some of these points some open points were set for further information to ease the discussion.</p> <p>See reporting table 5(36)</p>	<p>cannot be concluded that there is a high risk to honey bees, i.e. a low risk is demonstrated.</p> <p>The experts agreed with the RMS that a low risk can be concluded for honey bees for the representative uses including the risk to honey bees foraging on flowering weeds.</p> <p>It was noted that the assessment of the higher tier studies in the DAR was comprehensive and the way that the evaluation was presented was useful. The experts were pleased with the available evaluation and it will be useful for future assessments. Some experts noted that they agree with the conclusion of the RMS regarding the outcome of the higher tier studies.</p> <p>It was noted that semi-field studies can be useful to investigate repellent effects (shown as a reduction in flight intensity) but may have limitations to understand other types of effects. The experts noted that extrapolation from semi-field to field for repellent effects could be slightly uncertain. Repellence (unless very strong and consistent) probably cannot be used as argumentation in risk assessment. It was discussed and noted that repellence in semi-field studies decreases the use of the study given that these types of effects may not be apparent in the field.</p> <p>In the available studies some small transient effects were noted but these were not consistent across all studies. The RMS had considered these in their evaluation. In some cases the effects may have been within natural variation. The RMS noted that for the brood effects is particularly difficult to understand whether effects are within natural variations. The RMS noted that they considered all of the studies as a whole when reaching their conclusion.</p> <p>It was noted that two semi-field studies were not performed to GLP. These studies are therefore only supportive. Care should be taken with the use of these studies in the overall risk assessment. If there were adverse effects then these must be accounted for.</p> <p><u>Post meeting EFSA notes:</u> In the following discussions on the individual tests the word 'effect' might be interpreted as different from the control (i.e. may or may not include effects from the treatment), pending on the context. The discussion on the first study by</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>Schnorbach 2012a includes general discussions on the design and usefulness of semi-field studies.</p> <p><u>Schnorbach 2012a (non-GLP) – Note:</u> The weight development of the bee hives in the treated groups was slightly lower at later sampling points. Similar picture in egg laying.</p> <p>Some experts considered that these studies were mostly well performed and useful (except for the non-GLP status). The size of frames were relatively small and the colonies were quite small &lt;3000 bees (noting that the EFSA GD recommends &gt;6000 bees). When young bees are primarily used, the biological variability can be large. The adaption of young bees may be an additional issue, there was 6 days between when the queen was added and the test substance was applied. This resulted in many stressful steps for the colony just prior to application.</p> <p>The conditions of a semi-field study are very artificial limiting their usefulness when comparing to the field i.e. the colony results are of limited use as there is not sufficient food so a downward trend will always be observed – limiting the ability of the study to detect treatment related effects on the colony. The large advantage is to ensure that there is no alternative foraging area other than the treated crop. The assessment methodology of the comb was discussed and the experts agreed that taking a digital image of the comb is less stressful for the bees and therefore is an advantage over making an assessment by eye.</p> <p>Overall, the experts agreed with the RMS's assessment of this study.</p> <p><u>Schnorbach 2012b (non-GLP)</u> Some possible effects on workers and larvae were observed. The second toxic reference (Insegar), normally used in bee brood studies, did not have consistent effect on the larvae in this study. This questions the results of the larvae assessments.</p> <p>The experts agreed that the toxic references are only for demonstrating that the conditions of the study were suitable to detect effects. The results of the test items should not be compared to the results of the toxic reference.</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>The possible effect on workers was discussed in detail given that the increase in mortality was very low and could be only the natural variation. However, it was stressed that any increase should be considered. The effects were only apparent only just after application and not at later time points. These apparent effects were only evident in front of the hive and not at the tunnel edge. The experts agreed that the level of effect on mortality was not of concern and did not affect the colony.</p> <p><u>Rentschler 2012a (GLP)</u></p> <p>The experts noted that the colony size at the study initiation was reasonable (approx. 7000 bees). Only visual inspections were used to assess the combs.</p> <p>Fewer larvae were observed in the treated groups on assessment day 3. Fig. B.4.2-20 (DAR). These effects could be within natural variation but effects of the test item could not be excluded also. In addition, there was also an increase in forager mortality, as noted by the RMS, just after application (day 1 and day 0).</p> <p>It was noted that it was difficult to interpret the results of the study from visual inspection of the figures alone. The actual numbers (in the tables) needs to be considered also.</p> <p>Overall, there was no disagreement with the RMS's assessment.</p> <p><u>Pröbsting 2012a (GLP)</u></p> <p>The RMS did not consider this study as valid for risk assessment. The reason for this was that the size of the control colonies differed from the test item colonies at the study initiation.</p> <p>The experts agreed with the assessment of the RMS.</p> <p><u>Pröbsting 2012b (GLP)</u></p> <p>Some effects on forager mortality could not be excluded. Furthermore, at the second assessment there were virtually no larvae in T2 (T2 = assessment day 2). This may have</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>been related to the shortage of pollen or test item related. It was noted that the larvae in the control also decreased indicating something affecting the colonies. However, the test item decreased to a greater extent. Due to the decreasing control it is difficult to be able to detect test-item related effects. It was considered that these types of effects were worth noting and then can be considered as a whole taking account the entire data set. The RMS noted that when they state that write that the numbers in the control and the test item were similar they mean the values were comparable (but not necessarily equal). Other experts consider that it is more useful for evaluation if it is stated that there is a difference and then the difference is not an issue. This is a minor point but helps when considering the data set as a whole i.e. looking for trends within the available data. In this case the experts agreed with the conclusion of the RMS.</p> <p>There was statistical analysis of the forager mortality performed and some statistical effects on the treatment groups were observed. The RMS noted that it is difficult to interpret results by comparison of numbers without taking account of the statistical analysis.</p> <p>Overall, the experts agreed with the RMS's assessment that the very slight increase on forager mortality were likely not due to the test item. This was because the level of effect was very slight and not statistically significant.</p> <p><u>Rentschler 2012b (GLP)</u></p> <p>The RMS considered that this study resulted in the greatest level of exposure. The experts noted that there was a clear indication of a potential, slight effect due to the test item. Some indications of sublethal intoxication were noted. The flower visits were also lower for the test item. These effects were noted by the RMS.</p> <p>Statistical analysis on forager mortality was performed. A statistically significant effect was only observed on a few times points. The level of mortality was not consistently statistically significant compared to the control. The experts noted that there was an application prior to the introduction of the hives. Therefore, it is not possible to compare with pre-application data.</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>The pooling of the dead adult bees and pupae was discussed. Ideally the data would be presented separately.</p> <p>There was no agreement on whether this study indicates a slight test item related effect under the exposure conditions in the study. This differs to the RMS who believes that the study indicates no clear effect on forager mortality. The majority of the experts agreed with the assessment of the RMS and did not consider that the results indicated a clear effect on mortality.</p> <p><u>Rexer 2012a, GLP field study conducted with flowering OSR</u></p> <p>The treatment regime was treated seed, soil spray and two foliar applications to the same crop. This study may be useful for the assessment for the risk to bees from residues in succeeding crops.</p> <p>The evaluation of the RMS was agreed. Some potential effects were noted including some sublethal effects. Overall there was a suggestion that the observed effects do indicate some test item related effect. The RMS reflected that the treatment hives showed a slower increase in weight compared with the control colonies. The RMS stated that the reason for this was unknown i.e. it could be due to difference in hive location. The RMS noted that this data was difficult to interpret and it was questionable as to whether this was due to natural variation or was treatment related.</p> <p>The study included an assessment of overwintering success. The final assessment was made in March the following year. There appeared to be no effects on the over wintering success.</p> <p>A concern was raised during the commenting of the low flight intensity observed. The RMS noted they have discussed foraging intensity with experts and they consider that the criteria in the EPPO (2 - 3 bees per m<sup>2</sup> for OSR) is very difficult to achieve.</p> <p>It was noted that the study included a statement to indicate that there were no major flowering crops within 2 km of the field. The new EFSA Guidance recommends that a</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>survey is performed and to minimise alternative foraging opportunities (i.e. also for weeds, trees, bushes). The RMS considered that the conditions of this study were reasonable and realistic. It was acknowledged that the requirements of the EFSA GD are difficult to adhere to but is there to maximise ‘worst-case conditions’. The question was raised as to whether multiple studies address the concern of replicating ‘worst-case conditions’. Multiple studies increase the probability that ‘worst-case conditions’ are achieved but it would still need to be demonstrated that this has been achieved.</p> <p>Overall, the experts in the meeting agreed with the RMS’s conclusions on this study.</p> <p><u>Rexer 2012b, GLP field study conducted with flowering OSR</u></p> <p>The treatment regime was treated seed, soil spray and two foliar applications to the same crop (performed in France).</p> <p>Some potential effects were observed on forager mortality and bee brood. The hive weight in the treated groups was consistently higher than the control. How worst case the conditions were, was also questioned with respect to the dilution of alternative food etc. There was 60% dilution in the treated group pollen being brought back to the hive. The nectar data (residues) also indicated dilution from non-contaminated food. It was noted that one pollen sample in the control contained residues of the test item indicating contamination. This was surprising because the treatment and control hives were 8 km apart. The RMS noted that this was only 1 sample out of 121 samples and therefore the RMS did not consider this to be an issue. It was suggested that it may have been due to a mistake in the residue analysis in the laboratory.</p> <p>Flight intensity was also noted to be low in relation to the criteria given in the EPPO 170 Test Guideline. The RMS reflected on this in the reporting table in the same way as for the field study above.</p> <p>The experts noted that, in general, the studies were well designed. The conclusion of the RMS on this field study was agreed.</p> <p><u>Nickolakis et al. 2012, tunnel study with feeders containing spiked food</u></p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>It was noted that this study design was novel and may be useful to address the uncertainties of field studies (discussed above and in the EFSA GD). The experts noted that this study ensure adequate exposure to the test item but may be unrealistic and too high. The use of this type of study could be problematic in risk assessment as the conditions are too severe to be considered as a field-type study. The study could be considered as an extended lab-type study.</p> <p>This study only covers oral exposure and not contact.</p> <p>The RMS noted that only 3 of the 5 control colonies survived making it not possible to detect all types of effects. The RMS considered that the study was sufficient to assess overwintering success. This was questioned since all three treatment groups were less in weight than the control (up to 33%). The RMS noted that this was explained in the study report and DAR. The apparent difference could be explained that one of the control colonies was abnormally high which was hypothesised may have been due to swarming bees coming in to the hive. This cannot be confirmed with the available data. This is problematic to consider and may affect the interpretation of the results. The RMS noted that their assessment concluded only that the treatment hives survived. No conclusion regarding the health of the treated hives could be reached given the insufficient number of controls.</p> <p>The experts agreed with the assessment of the RMS indicating that the study was useful for assessing overwintering success only.</p> <p><u>Overall conclusion of the available higher tier studies</u></p> <p>The RMS concluded that the data sets indicate that overall no adverse acute or long-term effects (including over-wintering evaluation) were indicated for a spray of 2 x 200 g a.s./ha on bee attractive crops during full flowering and active foraging (1 application prior to flowering and 1 application during flowering). The experts at the meeting agreed with the conclusion of the RMS noting that some slight transient treatment related effects may have been observed.</p> <p>It must be noted that these higher tier studies are not essential to conclude on the</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
	<p>representative uses. However, the studies were discussed in detail due to the comments received during the peer review of the DAR.</p> <p><u>Other issues</u></p> <p>It was discussed how the endpoints from the lab studies for larvae, the 10-day chronic honey bee and the acute bumble bee should be recorded in the LoEP as some uncertainties were highlighted during the peer review and that there is currently no standard protocol. It was agreed that the endpoints should be maintained in the LoEP with a footnote saying that they have been used as additional information only.</p> <p>A concern was raised as to whether the assessment would be sufficient to pollinators other than honey bees. There was an acute contact bumble bee study available indicating that acutely bumble bees were of similar sensitivity as honey bees, however, no information for the sensitivity of bumble bees via oral toxicity is available. Open point for EFSA to reflect in the conclusion that the available data and assessment may not sufficiently cover the risk to other pollinators.</p> <p>The RMS included a consideration of the risk via insect honey dew in the DAR. The RMS considers that the higher tier studies were sufficient to cover the risk to honey bees via this route of exposure. The experts agreed with the conclusions of the RMS that this route of exposure was addressed.</p> <p>The RMS also included an off-crop risk assessment for honey bees foraging in the field margin. The RMS concluded a low risk to honey bees for this route of exposure. No concerns were raised regarding the assessment included by the RMS in the DAR.</p>	
Expert consultation 5.5  Experts to discuss the two non-target arthropod field studies (off-crop) from the authors Aldershof S. and Bakker F. (2012).	Background:  Two comprehensive non-target arthropod field studies (NL, FR) focussing on off-crop habitats were available. During the commenting phase some shortcomings of the studies and therefore the reliability of the selected endpoints were noted. Due to the checkerboard design (22mX22m plots with treated and untreated plots alternating), even if an effect had happened, the populations could easily recover. Therefore toxic effects could be overlaid by re-colonisation. It was also questioned how these studies are representative for existing worst case landscapes as they were conducted on grasslands. The validity criterion for at	For any action points, see related discussion in point 5.6, below.

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>Can they be considered acceptable to be used in the risk assessment?</p> <p>See reporting table comment 5(60).</p> <p>“DE: The two non-target arthropod field studies (off-crop) from the authors Aldershof S. and Bakker, F. (2012) are quite comprehensive and a summary of it is obviously labour-intensive. Nevertheless, in the study summary more readable (e.g. Table on page 367) as well as more detailed information will be necessary to understand the visualised results and especially the data standing behind it (e.g. validity criterion). It will also be helpful to provide more information within the summary to avoid misinterpretation of the results.</p> <p>Furthermore, there are some shortcomings of</p>	<p>least 50% effect on at least one sample date for at least 10% of the taxa evaluated (De Jong et al., 2010) was also questioned.</p> <p>More readable detailed summaries were made available by the NOT and included in Annex 2 of the addendum.</p> <p><b>Discussion:</b></p> <p>The RMS derived an NOAER and an NOER derived from each of the studies. The RMS noted that the studies were evaluated in relation to the Dutch Guidance for summarising and evaluating NTA field studies (De Jong et al., 2010). The RMS noted that this GD is not official EU guidance but is very useful and therefore was used for evaluating the studies. This guidance has been incorporated and accepted by the NEU Zone guidance. The experts noted that De Jong et al., 2010 guidance included the checkerboard design.</p> <p>Both studies were performed in grassland and used checkerboard design. The treatments were over spraying with different rates and different types of sampling techniques were used. The design of the study was questioned given that there were areas of low dose and control which could serve as source of recolonisation for the populations. The RMS noted that it was impossible to have zero possibility for recolonisation of NTA populations but rather the question was whether there were too much possibility for recolonisation in these studies. Some experts considered that the design could have made further effort to reduce the possibility of recolonisation noting that these studies were to address the off-field environments i.e. the source of NTAs for in-field population recolonisation.</p> <p>The endpoints derived by the RMS meant to include or not a recovery; i.e. both NOAER and NOER were established.</p> <p>It was noted that the first sampling day was 7 days after application. The experts considered that it would have been beneficial to have an earlier sampling date such as 3 days after application. It was questioned whether day 0 sampling would be useful given that it may take some time for the test substance to effect.</p> <p>The experts noted that the goal of the study should be taken into account when considering the suitability of the checkerboard design. It was questioned whether recovery could be</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>the studies that question the applicability for the refinement in off-crop risk assessment as well as the reliability of the selected endpoints:</p> <p>In an off-crop field study suitable for the refinement of the off-field risk assessment it has to be shown that toxic effects are not overlaid by re-colonisation, but the studies were conducted to show NOER/NOEAER by recovery, thus the focus was different influencing the design and outcome of the study. In the two conducted (off-crop) field studies the plots were established in a checkerboard design with open (uncovered) plots, which makes it difficult to conclude on the reliability of the study results on toxic effects. Furthermore, arthropods were sampled one, two, four</p>	<p>accounted for an off-field assessment. It was noted that the plots were large compared to field margins. The RMS noted that smaller plots could have problems with statistical analysis. The RMS noted that it was good that the study was performed on grassland as there would be NTA species which are not adapted to continuous use of pesticide exposure. Some experts had difficulties with the basic concept of using field studies for off-field risk assessments and the representativeness of the study in respect to the landscape structure. This concern related to the possibility of recolonisation in the off-field and whether in reality there would be any source of NTAs for recolonisation. It was noted that recolonisation and recovery concepts were included in ESCORT 2 and 3.</p> <p>It was suggested that the NOER could be used from these studies as these do not (less likely) account for recovery/ recolonisation. NOER population level were 1.7 and 5.1 g a.s./ha (French and Dutch study respectively). The NOER for community levels were higher.</p> <p>A concern was raised in the reporting table regarding the validity criteria defined in the De Jong et al., 2010 guidance. This concern was addressed by the RMS in the reporting table.</p> <p>Overall the experts agreed that it was appropriate to only use the NOER values from these studies i.e. not accounting for recovery and recolonisation (however see also discussion in point 5.6, below).</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>and eight weeks after treatment. Thus, overlaying of toxic effects by re-colonisation cannot be excluded, and a clear separation of NTA-communities between treated and non-treated plots in the off-field is missed.</p> <p>The off-crop field studies were performed only on grassland and are, therefore, insufficient as surrogate for the variability of possible off-field habitats around arable land. The study is not representative for 100% of existing worst case landscape. Standing alone, these field studies are insufficient for the refinement of the NTA off-crop risk assessment (please see DE comment 3, below “reduction of the correction factor”).</p> <p>The study design is not suitable to show time and concentration related trends of toxic</p>		

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>effects. Therefore, reliability of population related endpoints, such as NOER and NOEAER is questionable and conclusions on recovery and dose effect relationships are not reliable</p> <p>Information on the mode of action as well as physical-chemical properties of the test substance flupyradifurone and the reference substance lambda-cyhalothrin should be used to underline and interpret the results in observations of treated plots. „</p> <p>See reporting table 5(59) a</p>		
<p>Expert consultation 5.6</p> <p>Experts to discuss the off-field arthropod risk assessment. Can the refined risk assessment for off-field arthropods be accepted?</p>	<p><b>Background:</b> An off-field RA was conducted using endpoints (NOER and NOEAER) derived from the field studies on NTAs. In these assessments the correction factor was lowered from 5 to 1 considering that a wide range of taxa had been studied in the field studies. However, the lowering of this factor was questioned in the light of the shortcomings identified for the studies (see point for Expert consultation 5.5, above).</p> <p><b>Discussion:</b> See above for discussion of the endpoints from the NTA off-field studies. The NOER</p>	<p>Open point for the RMS RMS to update the risk assessment (risk mitigation) considering the agreed NOER of 1.7 g/ha in the DAR and in the LoEP. As agreed no additional safety factor is needed.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>See reporting table comment 5(61).</p> <p>“Reduction of the correction factor for the off-field PEC calculations from 5 to 1 is not acceptable, considering the shortcomings of the available off-crop field studies (please see DE comment (1) above). The uncertainty concerning the sensitivity of off-field arthropod species cannot be clarified. A correction factor of 5 will clearly result in a risk for off-crop NTAs. A study design for the refinement with a correction factor of 1 for the off-crop community requires a clear separation of toxic effects, recovery and re-colonisation as well as a 100% covering of a existing worst case landscape.</p> <p>The refined risk assessment for off-field arthropods should be discussed.”</p>	<p>values were considered as appropriate: population level NOER = 1.7 and 5.1 g a.s./ha in French and Dutch studies respectively.</p> <p>The RMS noted that the correction factor according to ESCORT 2 used to calculate the PER values are for lab studies to take account of the few species tested in lower tiers. Some experts considered that the correction factor was not suitable for field studies as multiple species are tested. One expert noted that in their MS they considered that there are still uncertainties from field studies and therefore some form of safety factor should be applied. The RMS noted that they had evaluated the study and accounted for the representativeness of the species in the plots in the studies. The experts noted that they would apply a safety factor as to other field-type studies used in the ecotoxicology e.g. mesocosm. The RMS emphasised that they had carefully considered the representativeness of the taxa and species in relation to the De Jong et al., 2010 guidance and concluded that the studies were suitable.</p> <p>It was stated that this is not a NOER strictly as there was a 7 day period between application and first sampling. Some experts considered that there was a possibility of fast recovery/recolonisation within the 7 day period which therefore questions the design of the studies and as a consequence means that there is uncertainty which should be accounted for.</p> <p>The RMS stated that they consider that the study design and the way that a NOER was used in the risk assessment uncertainty was accounted for sufficiently.</p> <p>Safety factors are not usually applied to field studies but the frequency of the use of field studies for off-field assessments is not high. In a previous meeting it was agreed to use an NOAER (low effects) without a safety factor. In this case, there was a no effect rate from two in-field studies which the RMS considers sufficient.</p> <p>Overall, the majority of the experts agreed that no additional safety factor is required in this case given that the endpoint is a NOER and that two studies (accounting for the representativeness of the taxa) are available. Therefore, the risk assessment (and risk mitigation) should be updated using the NOER with no additional safety factor.</p>	

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
See reporting table 5(60)		
<p>Expert consultation 5.7</p> <p>Experts to discuss the chronic risk assessment for earthworms.</p> <p>Experts to discuss the sublethal studies on earthworms, Leicher T. (2010c) and Leicher (2010d). Are the differences in reproductive parameters seen at the established NOECs compared to the control considered as biologically relevant? It is noted that these differences expressed in % using the average data were ~ 6.7% in the formulation study and for the metabolites &gt; 13%.</p> <p>Experts also to discuss if the earthworm field study by Menke, U. (2012, report number</p>	<p><b>Background:</b></p> <ul style="list-style-type: none"> <li>- Lab. studies</li> </ul> <p>In the study by Leicher T. (2010c) a clear concentration-response effect on the No. of juveniles were seen. The proposed NOEC is from the lowest treatment group of 8.9 mg/kg, where the No. of juveniles were 6.7 % lower than in the control.</p> <p>The proposed NOEC from the study by Leicher T. (2010d) is 62 mg/kg test item (=59 mg/kg metabolite). At this level the No. of juveniles were 13 % lower than in the control.</p> <ul style="list-style-type: none"> <li>- Field study</li> </ul> <p>In the field study, 3 doses were used all above the PECsoil. A reduction in abundance/biomass of some worm categories even after 11 month were observed with the available data and data analysis. These differences however, were not considered as biologically relevant by the RMS. The main reasons for these were the relative low abundance within those categories (even in the control), the lack of dose-effect relationship and the natural variation. However it was noted in the commenting period that the timing of the study was not ideal and the weather looked too hot and dry. This may contributed in the low abundance in the first assessment (4 weeks after the treatment). Particularly, the effects of the test substance on the number and the biomass of juveniles of <i>Lumbricus terrestris</i> looked significant and constant over the test period of 11 months showing a concentration dependent trend without recovery. Overall, it was questioned whether any robust conclusion or a NOER can be drawn from this study. The RMS disagrees with this interpretation of the study and concludes a NOER for the highest dose.</p> <p>It is noted that low residues of the a.s. were found in the control plots (spray drift?). In general, the carbendazim treatment group (reference) indicated some effects.</p> <p><b>Discussion:</b></p> <p><u>Study by Leicher T. (2010c).</u> NOEC of 8.9 mg/kg.</p> <p>The difference on No. of juveniles at the NOEC (i.e. 6.7%) was not statistical significant. It was questioned whether the statistical method used was sensitive enough. The RMS confirmed that the Williams test was used that is the most appropriate against the study design and results.</p>	<p><b>Open point</b></p> <p>The RMS to remove the field study from the LoEP. A statement regarding the conclusion from the experts' meeting on this study should also be reported in a revised DAR.</p>

Subject	Discussion Pesticides Peer Review Meeting	Conclusions Pesticides Peer Review Meeting
<p>NMU/RG-F-8/12) is considered acceptable to be used in the refined chronic risk assessment. Is the timing of the substance application considered to be acceptable? Do the experts consider the endpoint correctly derived from the study? Should the effects seen on the number and the biomass of juveniles of <i>Lumbricus terrestris</i> considered to be relevant?</p> <p>See reporting table 5(64)</p>	<p><u>Study by Leicher T. (2010d)</u>. NOEC of 62 mg test item /kg (59 mg metabolite/kg). Also in this study the difference at the NOEC was not statistical significant. Also the Williams test was used.</p> <p>In previous meeting it was agreed that when there are effects (about 20%) at the NOEC the EC10 should be requested to be used.</p> <p>The experts considered that the not statistical differences at the NOECs in this case might be considered also as not biological relevant i.e. no clear dose-response relationship was observed in Leicher T. (2010d). In Leicher T. (2010c) the dose-response relationship was clear but the difference was only 6.7%.</p> <p>Overall, the experts agreed with the originally proposed endpoints for both cases.</p> <p><u>Field study</u></p> <p>Some experts suggest to set the NOER at lower level than proposed by the RMS because effects were noted in all the treatments on <i>lumbricus terrestris</i>.</p> <p>However, the number of <i>lumbricus terrestris</i> individuals was very low and this species was considered a difficult species to be tested. Therefore the RMS proposed to keep out of the analysis. It was noted that also the abundance of other species tested in the study was quite low. The results of sampling collected after 4 weeks were questioned due to too hot and dry conditions. However, it was noted that the abundance in general was sufficient at the beginning of the test. After 4 weeks, the abundance in the control (although individual groups had a low number which does not match with the recommendation) was higher than the treated plots.</p> <p>Additionally, it was noted that the effects of the test substance on the number and the biomass of juveniles of <i>Lumbricus terrestris</i> looked significant and constant over the test period of 11 months showing a concentration dependent trend without recovery. It was also noted that if the effects on <i>L. terrestris</i> are disregarded as proposed by the RMS, the effects on anecic (burrowing) earthworms cannot be estimated since <i>L. terrestris</i> was the only representative of this group.</p> <p>Overall, the experts considered the study as not reliable for risk assessment.</p> <p>The RMS should remove this study from the LoEP. This conclusion should also be reported in a revised DAR.</p>	

## TABLE OF CONTENTS

	<b>Document</b>
00	Cover page
01	Comments on the assessment report
02	Reporting table
03	Pesticides peer review meeting reports
<b>04</b>	<b>Evaluation table</b>
05	Comments on the additional information assessment
06	Comments on the draft EFSA conclusion

section 0 – General

**0. General**

No comments

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

### 1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point 1.1  RMS to update table B.2.1.1 with the report of the oxidising property in an addendum to Vol.3..  See reporting table 1(12)	NL (October 2014): Has been updated in revised Volume3.			Addressed: The oxidising property was updated in the revised Volume3.
Open point 1.2  RMS to include the information concerning the minimum and maximum use concentrations and the commercial packaging in an addendum to Vol.3...  See reporting table 1(13)	NL (October 2014): Noted.			Addressed.
Open point 1.3  RMS to include the summary of the results after storage in an addendum to Vol.3.	NL (October 2014): Summary has been included in revised Volume 3 B.2.			Addressed: The summary of the results after storage was included in the revised Volume 3 B2.

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 1(14)				
Data requirement 1.1  Applicant to submit the report M-402996-02-1, if not already submitted in the dossier.  See reporting table 1(14)	NL (October 2014): Report has been submitted by the applicant. Summary is included in revised Volume 3 B2.			Addressed: The summary of report M-402996-02-1 was included in the revised Volume 3 B2.
Open point 1.4  RMS to include the recovery results of method 01330/M001 submitted in November 2012 in the updated version of the Annex II dossier, presented in the col. 3 of the RT in an updated Vol.3. See also comment 1(68).  See reporting table 1(156)	NL (October 2014): The recovery results are included.			Addressed: The recovery results of method 01330/M001 were included in the revised Volume 3.
Open point 1.5	NL (October 2014): Note is included in revised			Addressed: The note in B.5.2 Residue

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
RMS to update the note in B.5.2 Residue methods for plants, method 01330 for BYI 02960 according to the entry in col. 3 of the RT in an updated Vol.3.  See reporting table 1(17)	Volume 3.			methods for plants, method 01330 for BYI 02960, was updated in the revised Volume 3
Open point 1.6  RMS to update the Vol. 3 with the information from col.3 of the RT concerning residue method 01330 for BYI 02960 and DFA  See reporting table 1(18)	NL (October 2014): Note is included in revised Volume 3.			Addressed: The residue method 01330 for BYI 02960 and DFA was updated in the revised Volume 3
Open point 1.7  RMS to include the information concerning the extraction efficiency of the methods for plants presented in col.3 of the RT in an updated Vol.3.	NL (October 2014): Information is included in revised Volume 3.			Addressed: The information concerning the extraction efficiency of the methods for plants was presented in the revised Volume 3

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See also comments 1(46), 1(49)  See reporting table 1(19)				
Open point 1.8  RMS to include the information concerning the extraction efficiency of the methods for animal matrices presented in col.3 of the RT in an updated Vol.3.  See also comment 1(49).  See reporting table 1(20)	NL (October 2014):  Information is included in revised Volume 3.			Addressed:  The information concerning the extraction efficiency of the methods for animal matrices was presented in the revised Volume 3
Open point 1.9  RMS to harmonise the residue definition for monitoring for water in the LoEP with the residue definition proposed.  See also comments	NL (October 2014):  Residue definition for the monitoring of water is harmonised in revised LoEP.			Addressed:  The residue definition for the monitoring in water is harmonised in the revised LoEP.

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
1(36), 1(40), 1(43), 1(59)  See reporting table 1(23)				
Open point 1.10  RMS to harmonise the residue definition for monitoring for food of plant and animal origin in the LoEP with the residue definition proposed.  See also comment 1(42)  See reporting table 1(25)	NL (October 2014): Residue definitions have been harmonised in revised LoEP.			Addressed: The residue definition for the monitoring in food of plant and animal origin is harmonised in the revised LoEP
Open point 1.11  RMS to include the complete chemical name of the metabolite DFA in an updated Vol.3  See reporting table 1(26)	NL (October 2014): Name has been included.			Addressed: the complete chemical name of the metabolite DFA has been included in the revised Volume 3
Open point 1.12  RMS to update the	NL (October 2014): LOQs have been updated in			Addressed: LOQs have been updated in the revised LoEP

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
LOQs for the analytical methods for food/feed of plant origin in the LoEP  See reporting table 1(44)	revised LoEP. See also open point 1.27.			
Open point 1.13  RMS to update the LOQs for the analytical methods for food/feed of animal origin in the LoEP.  See reporting table 1(45)	NL (October 2014): LOQs are amended in revised Volume 3.			Addressed: The LOQs for the analytical methods for food/feed of animal origin have been updated in the revised LoEP
Open point 1.14  RMS to include the information from the col.3 of the RT concerning B.5.2, studies 5and 6 in an updated Vol.3  See also comments 1(19), 1(28)  See reporting table 1(46)	NL (October 2014): Information is included in revised Volume 3. See response to open point 1.7			Addressed: The information concerning the extraction efficiency of the methods for plants was presented in the revised Volume 3

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point 1.15  RMS to describe the studies KIIA 4.3/10 (Schulte & Teubner, 2012) and KIIA 4.3/11 (Konrad, 2012) in an updated Vol.3..  See reporting table 1(47)	NL (October 2014): Noted.			Addressed.
Open point 1.16  RMS to update the Vol.3 with the information presented in col.3 of the RT concerning B.5.2, studies 7 and 8.  See reporting table 1(50)	NL (October 2014):  Additional information is included in revised Volume 3.			Addressed:  The additional information concerning B.5.2, studies 7 and 8 is included in the revised Volume 3
Open point 1.17  RMS to report the parent ion of the selected MRM transitions for B.5.3, study 9 in an updated Vol.3	NL (October 2014): Noted.			Addressed.

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 1(51)				
Open point 1.18  RMS to correct the typos concerning the units in an updated Vol.3.  See reporting table 1(52)	NL (October 2014): Typos have been corrected in revised Volume 3.			Addressed:  Typos have been corrected in the revised Volume 3
Open point 1.19  RMS to include the information from the col.3 of the RT concerning B.5.3, study 9 in an updated Vol.3..  See reporting table 1(54)	NL (October 2014): Additional information is included in revised Volume 3.			Addressed:  Additional information concerning B.5.3, study 9 was included in the revised Volume 3
Open point 1.20  RMS to update the Vol. 3 with the LC-MS/MS parameters of B.5.3 study 10  See reporting table 1(55)	NL (October 2014): Additional information is included in revised Volume 3.			Addressed:  Additional information concerning the LC-MS/MS parameters of B.5.3 study 10 was included in the revised Volume 3

rapporteur NL

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point 1.21  RMS to update the Vol.3 with the information presented in col.3 of the RT concerning B.5.3, study 10  See reporting table 1(57)	NL (October 2014):  Additional information is included in revised Volume 3.			Addressed:  Additional information concerning B.5.3 study 10 was included in the revised Volume 3
Open point 1.22  RMS to update the information concerning B.5.3, study 11 in an updated Vol.3.  See reporting table 1(61)	NL (October 2014): Noted.			Addressed.
Open point 1.23  RMS to update the word processing errors of the tables concerning B.5.3, study 11 in an updated Vol.3.  See reporting table 1(62)	NL (October 2014): Noted.			Addressed.
Open point 1.24	NL (October 2014):			Addressed:

rapporteur NL

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
RMS to update B.5.5, Evaluation and assessment with the information from col.3 of the RT in an updated Vol.3  See reporting table 1(64)	Information is included in revised Volume 3.			B.5.5, Evaluation and assessment was updated in the revised Volume 3
Data requirement 1.2  Applicant to submit the table for plant and animal matrices, if not already included in the dossier.  See reporting table 1(64)	NL (October 2014): Table is submitted by the applicant and included in revised Volume 3.			Addressed: the table for plant and animal matrices was submitted by the applicant and included in revised Volume 3
Open point 1.25  RMS to indicate in an updated Vol. 3 that methods RARVP013 & 01212 (plant) and method RV-004-AII-04 (animal) are data collection methods.	NL (October 2014): The requested indication is included in revised Volume 3.			Addressed: It was indicated in the updated Vol. 3 that methods RARVP013 & 01212 (plant) and method RV-004-AII-04 (animal) are data collection methods

section 1 – Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 1(70)				
Open point 1.26  RMS to correct the typo in the LoEP concerning the used wavelength.  See reporting table 1(72)	NL (October 2014): Typo has been corrected.			Addressed: The typo in the LoEP concerning the used wavelength has been corrected
Open point 1.27  RMS to update the LOQs for the analytical methods in the LoEP.  See reporting table 1(73)	NL (October 2014): LOQs have been updated accordingly in revised LoEP.			Addressed: LOQs have been updated in the revised LoEP

## section 2 – Mammalian toxicology

**2. Mammalian toxicology**

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Expert consultation 2.1  MS to discuss whether the metabolite 6-CAN can be regarded as a major metabolite or not  See reporting table 2(1)	RMS: To be discussed in a meeting of experts.	<u>Pesticides Peer Review expert meeting 122 (17 – 18 November 2014):</u>  6-CNA is considered a major metabolite in male rat but not in females.		Addressed: 6-CNA is considered a major metabolite in male rat but not in females
Data requirement 2.1  6-CNA cannot be regarded as a major metabolite in the rat studies (the level of 6.3% of the administered dose was obtained only in males treated with 200 mg/kg bw and was indiscriminately found in urine and faeces). Pending on the fate and behaviour section conclusion on 6-CNA calculated levels in groundwater, further toxicological data may be needed for this metabolite.	RMS: A new statement is provided in the revised DAR.	Not applicable.		Data requirement obsolete: Although insufficient data is available to assess the toxicological relevance of the metabolite in groundwater according to the respective guidance document, the assessment is not triggered according to fate and behaviour models in the environment (see section 4).

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 2(1)				
Expert consultation 2.2  MSs to discuss the possibility of waiving toxicokinetic study with repeated dosing.  See reporting table 2(2)	RMS: To be discussed in a meeting of experts	<u>Pesticides Peer Review expert meeting 122 (17 – 18 November 2014):</u>  Waiving of the repeated dose toxicokinetic study is considered acceptable.		Addressed: Waiving of the repeated dose toxicokinetic study is considered acceptable.
Open point 2.1  RMS to revise the LoEP adding some relevant information regarding toxicokinetics and metabolism of flupyradifurone.  See reporting table 2(4)	RMS: A revised LoEP is provided.	Not applicable.		Addressed: The LoEP has been revised.
Open point 2.2  RMS to revise the LoEP regarding the acute oral, acute inhalation and skin sensitisation endpoints. See also 2(5)  See reporting table 2(7)	RMS: A revised LoEP is provided.	Not applicable.		Addressed: The LoEP has been revised.
Expert consultation 2.3	RMS: To be discussed in a meeting of experts.	<u>Pesticides Peer Review expert meeting 122 (17 – 18</u>		Addressed: The NOAEL of the 28-day

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
MSs to discuss the NOAEL/LOAEL of the 28-day oral study in rat by gavage (study 1).  See reporting table 2(8)		<u>November 2014):</u>  The NOAEL of the 28-day study in rat by gavage is 75 mg/kg bw per day based on mortality, increased liver weight and liver histopathological findings.		study in rat by gavage is 75 mg/kg bw per day based on mortality, increased liver weight and liver histopathological findings.
Expert consultation 2.4  MSs to discuss the NOAEL/LOAEL of the 28-day dietary study in rat (study 2).  See reporting table 2(9)	RMS: To be discussed in a meeting of experts.	<u>Pesticides Peer Review expert meeting 122 (17 – 18 November 2014):</u>  The NOAEL of the dietary 28-day study in rats is 33.6 mg/kg bw per day based on clinical chemical findings, increased relative liver and thyroid weights and associated pathological findings.		Addressed:  The NOAEL of the dietary 28-day study in rats is 33.6 mg/kg bw per day based on clinical chemical findings, increased relative liver and thyroid weights and associated pathological findings.
Data requirement 2.2  Applicant to provide the historical control data regarding epididymis weights for the 28-day study in mice.  See reporting table 2(10)	RMS: Historical control data is provided in a revised DAR.	Not applicable.		Addressed:  The information was taken into consideration under expert consultation 2.5 below.
Expert consultation 2.5	RMS: To be discussed in a	<u>Pesticides Peer Review</u>		Addressed:

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
MSs to discuss the NOAEL of the 28-day study in an experts meeting.  See also 2(11), 2(12)  See reporting table 2(10)	meeting of experts.	<u>expert meeting 122 (17 – 18 November 2014):</u>  The NOAEL of the 28-day mouse study is 98 mg/kg bw per day based on reduced body weight gain and clinical chemical chemistry changes		The NOAEL of the 28-day mouse study is 98 mg/kg bw per day based on reduced body weight gain and clinical chemical chemistry changes.
Expert consultation 2.6  MSs to discuss the NOAEL of the 90-day study in rat (study 1) in an experts meeting.  See also 2(14), 2(15)  See reporting table 2(13)	RMS: To be discussed in a meeting of experts.	<u>Pesticides Peer Review expert meeting 122 (17 – 18 November 2014):</u>  The NOAEL of the 90-day dietary study in rats is 6 mg/kg bw per day based on reduced thyroid weight and body weight gain.		Addressed:  The NOAEL of the 90-day dietary study in rats is 6 mg/kg bw per day based on reduced thyroid weight and body weight gain.
Data requirement 2.3  Applicant to provide the tabled results of body weight/body weight gain and haematological findings of the 2-year rat study and relevant historical control data.  See reporting table 2(18)	RMS: New data is provided in the revised DAR.	Not applicable.		Addressed:  The information was taken into consideration under expert consultation 2.7 below.
Expert consultation 2.7	RMS: To be discussed in a	<u>Pesticides Peer Review</u>		Addressed:

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
MSs to discuss the NOAEL of the 2-year rat study in an experts meeting. See also 2(19), 2(20), 2(21)  See reporting table 2(18)	meeting of experts.	<u>expert meeting 122 (17 – 18 November 2014):</u>  The NOAEL of the 2-year rat study was agreed by a small majority of the experts to be 15.8 mg/kg bw per day based on reduced body weight / body weight gain, liver, lung and thyroid toxicity.		The NOAEL of the 2-year rat study was agreed by a small majority of the experts to be 15.8 mg/kg bw per day based on reduced body weight / body weight gain, liver, lung and thyroid toxicity.
Data requirement 2.4  Applicant to provide clarification on the possible endocrine-mediated MoA of flupyradifurone. The information embedded in column 3 of the reporting table should be included.  See reporting table 2(24)	RMS: Statement from the notifier including data from historical control is provided by the applicant. To be discussed in a meeting of experts.	Not applicable.		Addressed: The information was taken into consideration under expert consultation 2.8 below.
Expert consultation 2.8  MSs to discuss the parental, reproductive and offspring NOAEL of the multigeneration study in an experts meeting and the potential for an	RMS: To be discussed in a meeting of experts.	<u>Pesticides Peer Review expert meeting 122 (17 – 18 November 2014):</u>  Regarding the 2-generation reproductive toxicity study in rats, the parental and offspring NOAEL is 6.4		Data gap: Considering the effects observed on the reproduction, an endocrine-mediated MoA could not be ruled out and a data gap was identified for level 2 tests currently indicated in the OECD Conceptual

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
endocrine-mediated MoA. See also 2(25), 2(27)  See reporting table 2(24)		<p>mg/kg bw per day based on reduced body weight/body weight gain and the reproductive NOAEL is 32 mg/kg bw per day based on reduced number of implantation sites and oestrus cycle, reduced litter size (reduced number of pups born and higher number of stillborn).</p> <p>Considering the effects observed on the reproduction, an endocrine-mediated MoA could not be ruled out and a data gap was identified for level 2 tests currently indicated in the OECD Conceptual Framework, noting that further tests might be necessary pending on the outcome.</p>		<p>Framework, noting that further tests might be necessary pending on the outcome.</p> <p>Regarding the 2-generation reproductive toxicity study in rats, the parental and offspring NOAEL is 6.4 mg/kg bw per day based on reduced body weight/body weight gain and the reproductive NOAEL is 32 mg/kg bw per day based on reduced number of implantation sites and oestrus cycle, reduced litter size (reduced number of pups born and higher number of stillborn).</p>
Open point 2.3  RMS to revise tabled results of body weight and food consumption of the multigeneration study in rats in an addendum to the DAR.	RMS: New table is provided in the revised DAR.	Not applicable.		<p>Addressed: The information was taken into consideration under expert consultation 2.8 above.</p>

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 2(26)				
Open point 2.4  RMS to revise the LoEP regarding the relevant maternal NOAEL of the rabbit developmental study.  See reporting table 2(29)	RMS: LoEP is revised.	Not applicable.		Addressed: The LoEP has been revised.
Open point 2.5  RMS to add the systemic NOAEL of the neurotoxicity study and its basis in the LoEP.  See reporting table 2(31)	RMS: LoEP and Vol1&3 are amended.	Not applicable.		Addressed: The LoEP has been revised.
Open point 2.6  RMS to revise the LoEP clarifying maternal, developmental and developmental neurotoxicity NOAELs  See reporting table 2(32)	RMS: LoEP is amended.	Not applicable.		Addressed: The LoEP has been revised.
Open point 2.7	RMS: Evaluation of the literature search is	Not applicable.		Data gap: A literature search has been

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
RSM to include the assessment of the literature search performed by the applicant in an addendum to the DAR.  See reporting table 2(33)	available in the revised DAR.			performed according to the EFSA guidance document; however detailed assessment of the relevant papers has not been provided together to the actual submission of these.
Expert consultation 2.9  Considering that the metabolite DFA is a major metabolite in rotational crops and in poultry, and is found above 0,75 µg/L in groundwater, MSs to discuss the reference values applicable to the metabolite in an expert meeting.  See also 3(36), 2(37), 2(43)  See reporting table 2(34)	RMS: To be discussed in a meeting of experts.	<u>Pesticides Peer Review expert meeting 122 (17 – 18 November 2014):</u>  The reference values of the parent flupyradifurone are applicable to both metabolites DFA and DFEAF; the experts considered that there was sufficient evidence to conclude that DFEAF is unlikely to have genotoxic potential.  Open point to residue section to take into consideration that the reference values of the parent are applicable to both metabolites, DFA and DFEAF.		Addressed: The reference values of the parent flupyradifurone are applicable to both metabolites DFA and DFEAF; the experts considered that there was sufficient evidence to conclude that DFEAF is unlikely to have genotoxic potential.

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Data requirement 2.5  Applicant to provide historical control data for the in vivo micronucleus assay performed with BYI 02960-difluoroethyl-amino-furanone (study 4). See also 2(43)  See reporting table 2(38)	RMS: Data available in revised DAR.	Not applicable.		Addressed: The information has been taken into consideration under expert consultation 2.9 above.
Open point 2.8  EFSA to conclude on the NOAEL of the 28-day rat study with BYI 02960-difluoroethyl-amino-furanone.  See reporting table 2(40)	RMS: Noted.	Not applicable.		Addressed: Both the 28-day and 14-day studies were discussed under expert consultation 2.9 above. The experts confirmed both NOAELs as proposed in the DAR.  The 14-day NOAEL is 135 mg/kg bw per day based on reduced bw gain and lower glucose concentration in females.  The 28-day NOAEL is 243 mg/kg bw per day, the highest dose tested, as the bw effects were not clearly dose-related and reduced glucose levels were not seen as adverse as a single finding.

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Expert consultation 2.10  MSs to discuss the ADI and AOEL in an expert meeting. See also 2(16), 2(46), 2(47)  See reporting table 2(45)	RMS: To be discussed in a meeting of experts.	<p><u>Pesticides Peer Review expert meeting 122 (17 – 18 November 2014):</u></p> <p>The ADI and AOEL are 0.064 mg/kg bw per day based on the parental and offspring NOAEL of 6.4 mg/kg bw per day from the 2-generation reproductive toxicity study in rats applying an UF of 100, no correction regarding oral absorption being necessary in deriving the AOEL.</p> <p>The ARfD is 0.15 mg/kg bw based on the maternal NOAEL of 15 mg/kg bw per day from the developmental toxicity study in rabbits, 100 UF applied.</p> <p>New open points proposed</p> <p>Open point to Residue section to revise consumer assessment taking into consideration the revised reference values (ADI and ARfD) set by the experts.</p> <p>See evaluation table section</p>		Addressed: The ADI and AOEL are 0.064 mg/kg bw per day based on the parental and offspring NOAEL of 6.4 mg/kg bw per day from the 2-generation reproductive toxicity study in rats applying an UF of 100, no correction regarding oral absorption being necessary in deriving the AOEL. The ARfD is 0.15 mg/kg bw based on the maternal NOAEL of 15 mg/kg bw per day from the developmental toxicity study in rabbits, 100 UF applied.

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
		3: New open point 3.48		
New open point 2.10:  RMS to revise operator, worker, bystander and residential exposure risk assessment taking into consideration the new AOEL value set by the experts.				Addressed: Operator, worker, bystander and residential exposure estimates have been revised; the resulting values expressed as % of the AOEL are presented in the LoEP.
Open point 2.9  RMS to revise the LoEP regarding the dermal absorption for the highest dilution.  See reporting table 2(48)	RMS: LoEP is amended.	Not applicable.		Addressed: The LoEP has been revised.
Data requirement 2.6  Applicant to provide historical control data for the in vivo micronucleus assay performed with BYI 02960-difluoroethyl-amino-furanone (study 4).  See reporting table 2(54)	RMS: Data is provided in a revised DAR.	Not applicable.		Data gap: A typographical error has occurred in the transcription of the data requirement (this data requirement is repeated from the above 2.5). The original data requirement in reporting table comment 2(54) was for the applicant to assess the relevance of the individual impurities present in the technical specification in

## section 2 – Mammalian toxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
				comparison with the toxicological profile of the parent compound. As the issue has not been addressed, a data gap has been set.

## section 3 – Residues

**3. Residues**

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point 3.1  RMS, to amend the section B.7.6.4 on storage stability in a revised DAR (overall recoveries following storage under frozen conditions not corrected from procedural recoveries).  See reporting table 3(1)	Uncorrected recoveries were already reported in the tables, but not in the text.  The text under 'results' has been amended to represent the apparent (uncorrected) recoveries after a period of frozen storage.	Not applicable.		Addressed  Section B.7.6.4 on storage stability has been amended in the revised DAR of November 2014, considering the uncorrected recovery values.
Open point 3.2  RMS to mentioned in a revised DAR that study 10 on paddy rice was conducted following soil granule application (instead of seed dressing).  See reporting table 3(2)	In the characteristics tables of studies 10 and 11, metabolism in paddy rice, seed treatment was amended to granular treatment. In the study design, granular treatment was already reported.	Not applicable.		Addressed  Tables for study 10 and 11 have been corrected to "granule application".
Open point 3.3  Table 7.1.1.8 should be amended in a revised	For study 6, metabolism study in apples, the results in table 7.1.1-8 and text below 'Results' were amended to give the	Not applicable.		Addressed  Table 7.1.1-8 and corresponding text have been amended in the revised DAR

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
DAR considering BCS comment in column 2.  See reporting table 3(3)	correct results for the DFEAF (M34), BYI 02960-OH (M3) and BYI 02960 acetic acid (M15).			of December 2014
Open point 3.4  Table number in page 99 should be corrected (7.1.2-15 instead of 7.1.2-35)  See reporting table 3(4)	Corrected, table nr is amended accordingly	Not applicable.		Addressed Table number has been corrected
Open point 3.5  RMS: Tables 7.2-1, 7.2-2 and B.7.2-3 should be reconsidered in a revised DAR, taking into account the BCS comment in column 2 and the conclusion of the expert consultations 3(13), 3(29), 3(40) on residue definitions, feeding studies/transfer factors, rotational crops and the comment in open point 3(53).  See also comment in 3(7)	Tables with input values for dietary burden calculations were reconsidered, using the comments in the reporting table.  Following the discussions of the expert consultation on residue definition, transfer factors and rotational crops, input values might need to be reconsidered again.	Not applicable.		Addressed  Tables 7.2-1, 7.2-2 and B.7.2-3 have been reconsidered in the revised DAR of December 2014.

## section 3 – Residues

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
See reporting table 3(6)				
Expert consultation 3.1  The plant residue definition for enforcement and risk assessment should be discussed in a meeting of experts, considering the following points: - the conclusion of the review on the toxicological property of the DFA metabolite. - the DE comment on DFA to be specific to flupyradifurone only (contribution from tetriconazole unlikely)  See also comments 3(9), 3(11), 3(12)  See reporting table 3(8)	In Vol 3, B.6.9.1, toxicological studies with 6-DFA are summarised and evaluated.  Acute oral toxicity , genotoxicity and short-term toxicity studies are available. Applicant submitted a position paper on the metabolites (B.6.9.6).  DFA is formed in the rat metabolism.  Since DFA is found in supervised residue trials and is the most abundant residue component in field rotational crop studies, RMS is of the opinion that DFA should be included in the RD for RA.  In vol 3, B.5.2 it is reported "The European multi-residue methods <u>DFG S 19</u> and <u>QuEChERS</u> are unsuitable for the enforcement of this	<u>Pesticides Peer Review teleconference 107 (27 November 2014):</u>  The residue definition for <b>risk assessment</b> is set as the sum of flupyradifurone and DFA, expressed as flupyradifurone.  Two separate residue definitions are proposed for <b>monitoring</b> as 1) flupyradifurone and 2) DFA, separately  Analytical method is available to analyse both components simultaneously.  New open point proposed, see below.	The residue definition was amended according to the conclusions drawn during the expert meeting an as reported in Column C.  Residue levels for DFA, expressed as DFA were calculated from DFA, expressed as flupyradifurone.	Addressed  The Pesticides Peer Review teleconference 107 (27 November 2014) agreed on the following residue definitions for plants:  - <b>Monitoring:</b> Two separate residue definitions: 1) flupyradifurone and 2) DFA, separately - <b>Risk assessment:</b> Sum of flupyradifurone and DFA, expressed as flupyradifurone.  Analytical method is available to analyse both components simultaneously.

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
	<p>compound because the determination of the metabolite DFA is not possible – none of the extraction processes described in either of the methods would allow appropriate extraction of this molecule.“</p> <p>It would therefore be most practical to not include DFA in the RD for monitoring.</p>			
New open point 3.49: To reconsider the MRL proposals, taking into account the plant residue definitions agreed during the TC 107 meeting, and to reconsider the consumer risk assessment taking into account the toxicological reference values concluded in the Peer review meeting 124 (ADI 0.064 mg/kg bw/d, ARfD: 0.15 mg/kg bw, reference values applicable to the metabolite DFA).		Not applicable.		<p>Addressed</p> <p>MRL proposals related to the representative uses on lettuce and hops have been reconsidered by the RMS in the revised DAR of December 2014, considering the residue definitions agreed in the TC meeting 107.</p> <p>However, MRLs proposals related to the MRL application included in the DAR (apple, grape, tomato, pepper, cucumber and melon), have not been reconsidered by the RMS.</p> <p>Proposals for the crops</p>

## section 3 – Residues

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
				included in the MRL application have therefore been reconsidered by EFSA and included in the LoEP.
Expert consultation 3.2  Animal residue definitions should be discussed in a meeting of experts, considering the conclusion of the review on the toxicological property of the DFA metabolite.  See reporting table 3(13)	See expert consultation 3.1  Since DFA is the most abundant residue component in livestock feeding studies, RMS is of the opinion that DFA should be included in the RD for RA.	<u>Pesticides Peer Review teleconference 107 (27 November 2014):</u>  The animal residue definition for <b>risk assessment and for monitoring</b> is set as the sum of flupyradifurone and DFA, expressed as flupyradifurone.	After TC 107, it was discussed between RMS and EFSA to set the residue definition for animal products as the residue definition for plant products, hence:  The residue definition for <b>risk assessment</b> is set as the sum of flupyradifurone and DFA, expressed as flupyradifurone. Two separate residue definitions are proposed for <b>monitoring as</b> 1) flupyradifurone and 2) DFA, separately  The DAR was amended accordingly	Addressed  It was agreed during the Pesticides Peer Review teleconference 107 (27 November 2014) that both flupyradifurone and DFA, should be included in the residue definitions for monitoring and risk assessment. Therefore, the definition was proposed as sum of flupyradifurone and DFA, expressed as flupyradifurone  After the TC, The RMS and EFSA re-discussed this proposal and it was agreed that it would be more appropriate to express the residues for animal commodities as it was done for plant commodities:  - <b>Monitoring:</b> Two separate residue definitions: 1) flupyradifurone and

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
				2) DFA, separately <b>- Risk assessment:</b> Sum of flupyradifurone and DFA, expressed as flupyradifurone.
Open point 3.6  RMS to amend Table 7.4-1 in a revised DAR according BCS comment in column 2  See reporting table 3(14)	Framelines were added to table 7.4-1	Not applicable.		Addressed  Table B.7.4 has been corrected in the revised DAR of December 2014
Open point 3.7  RMS to amend Table 7.4-1 in a revised DAR according BCS comment in column 2. However, the following clarification is requested.  1 - BCS comment on "home and garden field use" does not result in a change to the cGAP, since the cGAP for lettuce was already defined in Table 7.5-1	1 – The GAP would be changed, since the Home and Garden use is a <u>field</u> use of 2x 125 g/ha, interval 10 d, PHI 3 d and maximum 2 uses per 12 months. The cGAP in lettuce reported in the current DAR is 2x 125 g/ha, interval 10 d, PHI 3 d and maximum 2 uses per 12 months in <u>glasshouse</u> or 1x 12.5 g/ha PHI 3 or 10d in the <u>field</u> .  Since this use was reported for the residues section only, but not for other sections, this home and garden use was not	Not applicable.		Addressed  Tables B.7.4.1 and B.7.5.1 have been amended in the revised DAR of December 2014  To avoid any misunderstanding, - wording "use" has been changed to "application" - "Home and garden use" is a "field use".

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>as 2x 125 g/ha, interval 10 d, PHI 3 d and maximum 2 uses per 12 months. Is EFSA understanding the correct one?</p> <p>2 – To avoid any misunderstanding, could the RMS confirm that "max. 2 uses/12 months" means "maximum 2 times 2 applications at 125 g/ha/yea = total 500 g/ha/year" (and not maximum 2 applications at 125 g/ha/year, total 250 g/ha/year)</p> <p>See reporting table 3(15)</p>	<p>included in the DAR, but is was included in the MRL dossier.</p> <p>2- with the term 'use', the number of applications is meant. Tables 7.4-1 and 7.5-1 were revised to include the term applications instead of use and to correspond with List of representative uses evaluated in Vol 1, List of Endpoints</p>			
<p>Open point 3.8</p> <p>RMS to amend Table 7.6.2-1 in a revised DAR according BCS comment in column 2. See comment in 3(15)</p> <p>See reporting table 3(16)</p>	<p>Results from trials in accordance with Home&amp;Garden use (2x 125 g/ha, interval 10 d, PHI 3 d and maximum 2 uses per 12 months.) was included in table 7.6.2-1 to complete the results for residue trials in lettuce.</p>	<p>Not applicable.</p>		<p>Addressed</p> <p>Results from trials in accordance with the "field uses" (2x 125 g/ha, interval 10 d, PHI 3 d) have in included in Table B.7.6..2-1. In addition, table has been amended taking into account the new residue definition agreed in the TC 107.</p>

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point 3.9  RMS to amend Table 7.6.2-1 in a revised DAR according BCS comment in column 2. See comment in 3(15)  See reporting table 3(17)	Results from trials in accordance with Home&Garden use (2x 125 g/ha, interval 10 d, PHI 3 d and maximum 2 uses per 12 months.) was included in table 7.6.2-2 to complete the results for residue trials	Not applicable.		See open point 3.8
Open point 3.10  MRL proposals are pending the conclusion on the plant residue definitions.  see expert consultation in 3(8).  See reporting table 3(18)	MRL proposal was not amended at this stage. Pending the outcome of the expert consultation, MRLs may need to be revised.  Proposed import tolerances were deleted, since the ITs will not be considered at this stage. See open point 3(17).	Not applicable.		Addressed MRL proposals related to the representative uses have been amended by the RMS considering the outcome of the TC meeting on the residue definitions.  MRL proposals related to the MRL application have been reconsidered by EFSA in the LoEP,
Open point 3.11  CF proposals are pending the conclusion on the plant residue definitions. As stated by EFSA in column 2, the possible variations in the CF values at the	CFs for different PHIs were not calculated and proposed at this point pending the outcome on the discussion of the residue definition.  When a conclusion is drawn on the residue	Not applicable.		Addressed Based on the residue definitions agreed in the TC 107 meeting, the setting of CFs is no longer necessary.

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
different PHI time points should be considered.  See reporting table 3(19)	definition in the expert consultation, RMS will calculate CFs for different time points in accordance with the RD			
Open point 3.12  RMS to reconsider in a revised DAR the MRL proposal for grape, considering EFSA and BCS comments in column 2 and 3. See also expert consultation 3(8) on plant residue definitions and BCS comments 3(80) and 3(81)  See reporting table 3(20)	Proposed MRL was not reconsidered, since the data set did consist of eight independent trials instead of only four trials as it did appear due to the incorrect trial parameters.  MRL proposal is still depending on the outcome of the expert consultation regarding the residue definition. CF were not yet calculated for each time point.	Not applicable.		RMS to amend the ER of January part I and part II. MRL proposals and experimental designs for trials on grape in SEU have to be corrected.  Note: MRL proposal for grape has been reconsidered by EFSA in the LoEP.
Data requirement 3.1  Applicant to submit the embedded files in column 3, if not already included in the dossier.  See reporting table 3(20)	Embedded files were submitted. Original trial report was already available, embedded files were revised tier I summaries.	Not applicable.		Addressed  Embedded file in reporting table were submitted

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point 3.13  RMS to clarify in a revised DAR what are the studies conducted on gherkin and on cucumber. BCS comment in column 3 should be considered indeed.  See reporting table 3(21)	In tables C.3.1.2.1-8 and C.3.1.2.1-11, fruit sizes were reported to indicate whether the harvested crops could be classified as a gherkin or as a cucumber. Since residues in cucumber and gherkin are in the same order of magnitude, the data can be pooled to propose one MRL for cucumber and gherkin. This represents the practice where cucumbers can be harvested as small snack cucumbers.	Not applicable.		Addressed  4 trials were conducted on cucumbers and 4 trials on gherkins. Data have been pooled to derive an MRL for the whole group “cucumber edible peel”.
Open point 3.14  Varieties Haon, Talento and Jucar are climbing varieties. Application rates were therefore calculated taking into account the plant height (2 m), resulting in an application rate of ca 250 g/ha/treatment.  The residue levels observed in the trials conducted on climbing melons are significantly	Climbing varieties were excluded from the MRL calculations.  MRLs for watermelons were recalculated. The dataset for indoor and outdoor, excluding the climbing varieties, proved to be similar populations in a Mann-Whitney U-test.	Not applicable.		Addressed  Trials on climbing melon varieties (Haon, Talento and Jucar) have not been taken into account to derive an MRL proposal for watermelons.  These trials result in significant higher residue levels (U-test, 5%) since referring to an application rate of 250 g/ha (112.5 g/mCH x 2 m), while trials on normal varieties were conducted at a dose of 113 g/ha.

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
higher than the levels observed in non-climbing varieties (U-Test, 5%). Since watermelons are not climbing varieties, it seems not appropriate to take into account the values observed on climbing melon to derive a MRL for watermelon.  See reporting table 3(22)				MRLs of 0.15 mg/kg are proposed for flupyradifurone and DFA respectively, derived from the SEU trials .
Open point 3.15  Dates in trial Gualchos (SP) in table C.3.2.1.2-19 page 68 have to be corrected.  See reporting table 3(23)	Dates were checked against the original study report. Date of second date of treatment was corrected.	Not applicable.		RMS to correct in the ER part II, the treatment dates in Table C.3.2.1.2-19, related to the NEU trials on tomato.
Open point 3.16  RMS to reconsider the MRL proposal for apple taking into account the NEU and SEU data sets. MRL proposal should also consider the	MRL proposal in table 3.1, page 27 is based on pooled NEU and SEU apple data. The proposed MRL is lower than the proposed import tolerance, but since the ITs will not be considered at this stage, the MRL of 0.4 mg/kg will be used in the	Not applicable.		RMS to reconsider the MRL proposals in the ER part I and part II taking into account the residue definitions agreed by the TC 107 meeting and the comment in open point 3.16  MRL proposal for apple has

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>conclusion of the expert consultation on plant residue definition (see Expert consultation 3(8)).</p> <p>Note to the applicant: Since statistical calculations are more reliable when based on a larger data set, the pooling of the NEU and SEU trials is recommended (if not significantly different).</p> <p>See reporting table 3(24)</p>	<p>assessment.</p> <p>Conclusion of the expert meeting regarding the RD will be applied, if necessary.</p>			<p>been reconsidered by EFSA in the LoEP. Both NEU and SEU trials conducted according to the NEU GAP (2x 68 g/mCH) have been pooled together to derived an MRL proposal of 0.4 mg/kg (flupyradifurone) and 0.03 mg/kg (DFA)</p>
<p>Open point 3.17</p> <p>RMS to reconsider in an Evaluation Report (ER), the Import Tolerance (IT) proposals, once the documentation evidencing that authorisations have been granted in the exporting countries is provided. IT proposals should be consistent with the MRL values</p>	<p>Both RMS and BCS can understand that the import tolerances can be evaluated only at a later time point. The information regarding the ITs and the dietary burden calculations consumer RA and MRL calculations were reviewed and amended where necessary in both the ER and the DAR.</p> <p>RMS considers this open point can be closed since it</p>	<p>Not applicable.</p>		<p>Import tolerance (IT) requests will be considered in a separate EFSA reasoned opinion, once the documentation evidencing the authorisation of the active substance in the exporting countries is provided and a new application is submitted.</p> <p>ER part I and part III related to the assessment of the IT, should be reconsidered, taking into account the conclusion of</p>

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>effectively published at national level in the exporting countries, and the residue definitions finally adopted for flupyradifurone.</p> <p>By the time being, evaluation and MRL proposals are limited to the EU GAPs proposed for:</p> <p><b>Representative uses:</b></p> <ul style="list-style-type: none"> <li>- hops,</li> <li>- lettuce,</li> </ul> <p><b>MRL application:</b></p> <ul style="list-style-type: none"> <li>- apple (pear)</li> <li>- grape,</li> <li>- pepper,</li> <li>- cucumber, gherkins (zucchini)</li> <li>- water melon</li> <li>- tomato (egg plant)</li> </ul> <p>See reporting table 3(25)</p>	<p>solely concerns an import tolerance and it was decided not to include the IIs in the evaluation.</p>			<p>the peer review on the plant and animal residue definitions and considering the changes in the toxicological endpoints.</p> <p>See also comments in open points 3(28), 3(29), 3(30), 3(39)</p>
<p>Expert consultation 3.3</p> <p>Member states to discuss the residue definitions for processed</p>	<p>It should say DFA metabolite.</p> <p>The nature of DFA and DFEAF residues was not studied. Based on</p>	<p><u>Pesticides Peer Review teleconference 107 (27 November 2014):</u></p> <p>For processed commodities,</p>	<p>Processing factors for lettuce and hops were recalculated, according to the new residue definition for monitoring.</p>	<p>Addressed</p> <p>The TC 107 meeting concluded that the residue definitions proposed for raw plant commodities are</p>

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
commodities, considering the conclusion on the toxicity of the BFA metabolite.  See reporting table 3(26)	similarity between the structures RMS concluded that DFA is also stable under the processing conditions. RMS considers that toxicity of DFA was elucidated sufficiently. See expert consultation 3.1.	the residue definition for <b>risk assessment</b> is set as the sum of flupyradifurone and DFA, expressed as flupyradifurone.  The residue definition for <b>monitoring</b> is proposed as 1) flupyradifurone and 2) DFA, separately		applicable to processed commodities.
New open point 3.50:  Transfer factors for flupyradifurone and DFA, to be reconsidered according to the residue definitions proposed for primary crops and for processed commodities.		Not applicable.		PFs have been recalculated by the RMS for the representative uses only (lettuce and hops). Having regard to the two separate definitions proposed for monitoring, separate PFs are proposed for flupyradifurone and DFA respectively.  RMS to provide updated ER part I, part II and part III where PFs for flupyradifurone and DFA are reconsidered according to the residue definitions agreed during the TC 107 meeting.
Open point 3.18	Median processing factors	Not applicable.		RMS to amend the ER part I

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
RMS to reconsider in a revised DAR, the processing studies on wine, taking into account the clarification given by the applicant in column 3. Red and white wine processes should be assessed separately. Conclusion of the expert consultations 3(8) and 3(26) on residue definitions should be considered indeed.  See reporting table 3(27)	were calculated separately for red wine and white wine (bottling and taste test) in the ER.			and part III where PFs are derived for red and white wine respectively.  Considering the clarification given by the applicant; trials 10-3406-01 and -02 on variety <i>Blauer Spaetburgunder</i> (red wine) and trials 10-3406-03 and -04 on varieties <i>Riesling</i> and <i>Mueller Thurgau</i> (white wine), EFSA derived in the LoEP a PF of 0.7 and 0.3 for red and white wine respectively for flupyradifurone. PF is 1 for DFA.
Open point 3.19  RMS to amend Table 7.7.2-1 in a revised DAR according to applicant comment in column 2.  See reporting table 3(28)	Frame lines were added in table 7.7.2.-1	Not applicable.		Addressed Table 7.7.2-1 has been amended in the revised DAR of December 2014
Expert consultation 3.4	The comment on the OECD guidelines was not written	<u>Pesticides Peer Review teleconference 107 (27)</u>	Animal MRLs were recalculated.	Data gap

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>Member states to discussed whether the feeding studies conducted with the parent compound flupyradifurone are appropriate to estimate DFA residue levels in animal matrices. The approach to derived MRLs for products of animal origin should be discussed indeed (use of transfer factors, ...). See comment in 3(55)</p> <p><b>EFSA Note:</b> RMS comment on OECD studies limited to the parent active substance is surprising, as it is clearly stated in the OECD guideline 503 on metabolism in livestock that "<i>If a plant metabolite comprises a major portion of the TRR on a feed item, a livestock metabolism study involving dosing with the plant metabolite may be needed</i>". Moreover, in the guideline 505 on</p>	<p>as meant. RMS intended to say what is mentioned in DAR:</p> <p>Conducting the feeding studies with a mixture of both the parent compound and its primary food/feed-relevant metabolite, DFA, seems attractive when viewed from a 1-region "EU-only" perspective, the feeding studies for the flupyradifurone project (Joint OECD dossier) should be designed to be used in all relevant regions (NAFTA, EU, Brazil and Australia). It is in this point that weaknesses become evident: different crops, different residue levels and compositions, different "feeding tables" used for their evaluation and finally, difficulties in evaluating the results in the long term make this strategy seem less attractive.</p> <p>Performing separate feeding studies would effectively alleviate the above-</p>	<p><u>November 2014):</u></p> <p>For the time being, as an interim approach, the use of the transfer factors to estimate residues of DFA upon exposure flupyradifurone is considered to derive provisional MRLs. These provisional MRL proposals for animal matrices will have to be reviewed when DFA feeding studies and appropriate rotational crop studies are available. The requirement is in line with the OECD guidelines.</p> <p>A data gap has been identified:</p> <p>Feeding studies in hen and cow conducted with the DFA metabolite to be submitted.</p>	<p>The data gap was included in the revised DAR</p>	<p>Feeding studies in hen and cow conducted with the DFA metabolite to be submitted.</p>

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>residues in livestock it is mentioned "<i>Livestock are dosed with the representative component(s) of the residue as defined in the feed, which is derived from crop metabolism, confined rotational crop and processing studies.</i> The residue definition of a pesticide might consist of parent compound plus one or more metabolites, or a single or several metabolites or degradation products". In addition, it is also mentioned in the current EU guidance on livestock feeding studies 7031/VI/95 rev.4 "<i>The initial active substance is often the relevant part of the residue. In other instances, a metabolite or metabolite mix may also be used in the trial.</i>"</p> <p>See reporting table 3(28)</p>	<p>mentioned concerns. Dose calculation, result evaluation, and robustness in the face of parameter change are all facilitated by this concept. While it is the most straightforward, precise approach, it would require the use of many more animals.</p> <p>Seen in this light, the concept of feeding BYI 02960 parent alone and calculating transfer factors for DFA was considered as an acceptable option. While effectively yielding similarly robust data to the two-study solution, only one study for each animal type would be necessary, thus saving animal lives.</p> <p>The feeding studies were designed to allow "material balancing" in order to evaluate levels and calculate transfer factors for both the total residue (parent BYI 02960 and DFA) and DFA, despite feeding parent compound only.</p>			

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
New data gap  Feeding studies in hen and cow conducted with the DFA metabolite are missing.		Not applicable.		See expert consultation 3.4
Open point 3.20  RMS to amend Vol. 3, B.7.8.1, Livestock feeding studies according to the reporting table 3(29) – 3(34)	Frame lines were added in table 7.8.1-2	Not applicable.		Addressed  Table B.7.8.1-2 has been amended in the revised DAR of December 2014.
Open point 3.21  Table numbering in section B.7.8.1 has to be reconsidered.  See reporting table 3(35)	Table numbering was amended to chronological order	Not applicable.		Addressed  Table numbering in section B.7.8.1 has been corrected in the revised DAR of December 2014.
Open point 3.22  RMS, point to be amended in a revised DAR according to BCS comment in column 2  See reporting table	Dose level was amended to correct dose, using the recalculated dietary burden	Not applicable.		Addressed  Dose rate levels have been corrected in section B.7.8.1 according to the recalculated dietary burden in the revised DAR of December 2014.

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
3(36)				
Open point 3.23  RMS, point to be amended in a revised DAR according to BCS comment in column 2  See reporting table 3(37)	Dose level was amended to correct dose, using the recalculated dietary burden	Not applicable.		Addressed see open point 3.22
Open point 3.24  RMS, point to be amended in a revised DAR according to BCS comment in column 2  See reporting table 3(38)	Frame lines were added in table 7.8.1-16	Not applicable.		Addressed  Table 7.8.1.16 has been amended in the revised DAR of December 2014
Expert consultation 3.5  Member states to discuss if the rotational crop studies conducted with a dose rate of 2x 125 g/ha and a PHI of 30 days, are appropriate to estimate the residue levels expected in food commodities and in the feed commodities used	The dose rate of 2x 125 g as/ha is the cGAP supported in the residue dossier for lettuce (home and garden use), but also the supported use in unprotected fruiting vegetables home and garden use) of 2x 0.1125 g as/ha, PHI 3 days is the worst case to the cGAP in the DAR.	<u>Pesticides Peer Review teleconference 107 (27 November 2014):</u>  Data gap: Rotational crop trials should be submitted, conducted at realistic-worst-case plant back intervals with regard to the following crop selected, and providing in addition soil	Rotational crop MRLs were recalculated, using the HRs and rounding these up. The data gap was included in the revised DAR	Data gap  Rotational crop trials should be submitted, conducted at realistic-worst-case plant back intervals with regard to the following crop selected. In addition soil analyses should be provided in order to confirm whether the residue levels in soil are representative of the plateau levels in soil reach

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
for the animal burden calculations.  See also comment 3(5), 3(41) and 3(47)  See reporting table 3(39)	The PBI of 30 days is worst case and one can argue that the chance of crop failure and subsequent crop rotation after application is small, moreover since application of flupyradifurone is envisaged as of BBCH 12 up to BBCH 87 (fruiting vegetables) or BBCH 49 (lettuce).	analyses.  Proposed MRLs for DFA for rotational crops are provisional, pending the availability of the new data.		following several years of consecutive applications.  For the time being MRLs for rotational crops are derived from the trials performed with a total dose of 200 to 250 g/ha applied on bare soil at a plant back interval of 30 days, and considering the highest residue values observed in the different crops.
New data gap 3.1:  Rotational crop trials should be submitted, conducted at realistic-worst-case plant back intervals with regard to the following crop selected, and providing in addition soil analyses.		Not applicable.		See expert consultation 3.5
Open point 3.25  RMS to amend Vol. 3, B.7.9.1, Field rotational crops according to reporting table 3(41) -	Comments were processed and DATs and study numbers were amended.	Not applicable.		Addressed  In section B.7.9.1, study numbers and DAT have been corrected in the revised DAR of December 2014

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
3(45)				
Open point 3.26  LMRs for rotational crops are pending the conclusion of the expert meeting requested under 3(40) and related to the dose rate and PBI considered in the DAR.  See reporting table 3(46)	See response under expert consultation 5	Not applicable.		See expert consultation 3.5
Open point 3.27  EU MRL proposals are pending the conclusions of the expert meeting on plant residue definitions requested under comment 3(8)  See reporting table 3(47)	See open point 3(10)	Not applicable.		RMS to provide a revised ER part I and part II where EU MRL proposals are reconsidered taking into account the residue definitions agreed in the TC 107 meeting.
Open point 3.28  To be considered in a revised ER, once the information requested under 3(28) provided.	Concerns proposed import tolerance for dry bean and dry pea seeds. Notifier commented that it should be summarised as 'pulses' and that the IT should be 10 mg/kg (Table 7.12.1-1)	Not applicable.		See open point 3.17

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Moreover, conclusion of the expert consultation on residue definition and rotational crop studies should also be considered (see Expert consultations 3(8) and 3(40)).  See reporting table 3(49)	RMS considers this open point can be closed since it solely concerns an import tolerance and it was decided not to include the Its in the evaluation. See open point 3.17			
Open point 3.29  To be considered in a revised DAR/ER, once the information requested under 3(28) provided.  Moreover, conclusion of the expert consultations on residue definition and rotational crop studies should also be considered (see Expert consultations 3(8) and 3(40))  See reporting table 3(50)	Concerns proposed import tolerance for sweet corn grain (Table 7.12.1-1)  RMS considers this open point can be closed since it concerns an import tolerance and it was decided not to include the Its in the evaluation. See open point 3.17	Not applicable.		See open point 3(17)

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point 3.30  To be considered in a revised ER, once the information requested under 3(28) provided.  Moreover, conclusion of the expert consultations on residue definition and rotational crop studies should also be considered (see Expert consultations 3(8) and 3(40)) See reporting table 3(51)	Concerns proposed import tolerance for sweet corn grain (Table 7.12.1-1)  RMS considers this open point can be closed since it concerns an import tolerance and it was decided not to include the IIs in the evaluation. See open point 3.17	Not applicable.		See open point 3(17)
Open point 3.31  RMS to reconsider in a revised DAR the animal dietary burden based on the representative uses, the EU uses related to the MRL application and the residues expected in rotational crops. Conclusion of the expert meeting on rotational crops should be considered (See expert	Animal dietary burden calculations were revised, only by changing the input values.  Following the discussions of the expert consultation on residue definition, transfer factors and rotational crops, animal dietary burden calculations might need to be revised (completely).	Not applicable.		Addressed  Animal burden calculations have been reconsidered in the revised DAR of December 2014

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
consultation in 3(40)). See also comments in 3(6)  Possible contribution of the residues resulting from the setting of import tolerances on food/feed commodities would have to be considered in a revised ER, once the information requested under 3(28) provided.  See reporting table 3(52)				
Open point 3.32  MRL proposals for rotational crops should be reconsidered, taking into account the conclusion of the expert consultations on residue definitions and rotational crops (see Expert consultation 3(8) and 3(40))  See reporting table	MRL proposals will be amended if necessary after Exert consultation	Not applicable.		Addressed  MRL proposals for rotational crops have been amended in the revised DAR of December 2014, according to the conclusion of the TC 107 meeting.

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
3(54)				
Open point 3.33  RMS, to reconsider the MRL proposals for products of animal origin, taking into account, conclusion of the expert consultations on the residue definitions 3(13), the animal feeding studies 3(29), and the rotational crop studies 3(40). See also comments 3(53), 3(57) and 3(58)  See reporting table 3(55)	Animal MRLs were recalculated, based on changed dietary burden calculations (see open point 3.31).  Following the discussions of the expert consultation on residue definition, transfer factors and rotational crops, animal dietary burden calculations might need to be revised (completely) and consequently, proposed MRLs for products of animal origin.	Not applicable.		Addressed  MRL proposals for animal commodities have been amended in the revised DAR of December 2014, according to the conclusion of the TC 107 meeting.
Open point 3.34  RMS to reconsider in a revised DAR , the consumer risk assessment considering the conclusions of the expert meetings on residue definitions (3(8), 3(13), 3(26), the comments on plant and animal MRL proposals	Consumer risk assessment was revised, using the newly proposed toxicological endpoints and recalculated MRLs and excluding the import tolerances.  Following the discussions of the expert consultation on residue definition, transfer factors and	Not applicable.		Addressed  Consumer risk assessment has been amended in the revised DAR of December 2014, according to the conclusion of the TC 107 meeting.  However, EFSA disagree with RMS' conclusion on lettuce. EFSA is of the opinion that an

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
3(20), 3(22), 3(24), 3(25), 3(47), 3(55) and 3(56).  See also comments 3(60), 3(62) and 3(63)  See reporting table 3(58)	rotational crops, animal consumer risk assessment may need to be reconsidered.			acute risk cannot be excluded for consumer, considering the GAP proposed for indoor uses (2x 125 g/ha, 3 day PHI), since the HR value of 6.04 mg/kg results in an IESTI of 108% of the ARfD.  The absence of risk concluded by RMS (82% ARfD) is based on the use of a PF value of 0.76 taking into account the “inner leaves” only.
Open point 3.35  RMS, Typo in sentence page 278 to be corrected  See reporting table 3(60)	Typo 6-CAN was amended to 6-CNA.	Not applicable.		Addressed
Open point 3.36  RMS to amend the summary section B.7.16 considering the overall conclusion of the expert meeting consultations and the comments in 3(65), 3(66), 3(67)  See reporting table	Summary was amended to clarify the special study design. See also exert consultation 4	Not applicable.		Addressed  Section B.7.16 has been amended in the revised DAR of December 2014

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
3(63)				
Open point 3.37  RMS; point to be amended in a revised DAR according BCS comment in column 2.  See reporting table 3(67)	Metabolite name DFEAF-OH-glyc was added to metabolite M35 in annex I to the DAR (list of metabolites)	Not applicable.		Addressed  Metabolite name “DFEAF-OH-glyc” was added to metabolite M35 in annex I of the revised DAR of December 2014
Open point 3.38  RMS; point to be amended in a revised DAR according BCS comment in column 2.  See reporting table 3(68)	Metabolite name DFEAF-mercapto lactic acid was added to metabolite M41 in annex I to the DAR (list of metabolites)	Not applicable.		Addressed  Metabolite name “DFEAF-mercapto lactic acid” was added to metabolite M41 in annex I of the revised DAR of December 2014
Open point 3.39  RMS, to amend the evaluation report related to peanut.  See reporting table 3(69)	All information regarding import tolerances was deleted from the Evaluation Report since it is expected that import tolerances will not be established as MRLs in the exporting countries at the envisaged time of approval	Not applicable.		See open point 3(17)
Open point 3.40	See open point 3(10)	Not applicable.		A revised DAR dated December 2014 and considering the conclusions of

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
RMS to reconsider in a revised DAR/ER, the MRL proposals considering the conclusions of the expert meetings on residue definitions 3(8), 3(13), 3(26), the comment on Import tolerance setting 3(25) and the comments on plant and animal MRL proposals 3(20), 3(22), 3(24), 3(47), 3(55) and 3(56) and the additional BCS comments (72), 3(73), 3(79), 3(80), 3(81), 3(82), 3(83), 3(84), 3(85), 3(86) and 3(87).  See reporting table 3(70)	BCS comments  Regarding the ER (open points 3(73) to 3(98) were considered and revised in ER where agreed.  When this had effect on MRL proposal, HR and/or STMR, this was amended and consequently, these amendments were taken into account in livestock dietary burden calculations and consumer risk assessment.			the TC 107 meeting has been provided.  However, the RMS is requested to provide a revised ER part I and part II, taking into account the conclusions of the TC 107 meeting.  Amendment in the ER part III of the sections related to the import tolerance requests is pending the submission by the applicant of documentation evidencing the registration of the active substance in the exporting countries.  See also comments in open points 3(42), 3(43), 3(44), 3(45), 3(46) and 3(47)
Open point 3.41  RMS to consider BCS comment on the analytical method in a revised ER.  See also comment 3(75) and 3(76)	List of endpoints with regard to enforcement methods was amended and relevant components were copied to ER sections 1.1 and 1.2.	Not applicable.		Addressed  LOQ values have been amended in the LoEP.

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 3(73)				
Open point 3.42  RMS, to amend in a revised ER the text related to the metabolite 6-CAN according to BCS comments in column 2.  See reporting table 3(77)	Text was amended to reflect the more accurate text proposal by BCS	Not applicable.		see open point 3(40)
Open point 3.43  RMS to reconsider in a revised DAR/ER the overview residue trial table 3-1, taking also into account the conclusion of the expert meetings requested under 3(8), 3(13), 3(26), the comment on import tolerance 3(25) and the open point 3(71). See also comments 3(91), 3(92) and 3(93)  <b>EFSA note:</b> There is no need to report OECD	Since the data regarding orange and other import tolerances were deleted from the ER, this point was not considered any further in revision of the ER.	Not applicable.		see open point 3(40)

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
calculation details (mean + 4xSD, CFx 3mean....). Unrounded and rounded OECD values are sufficient  See reporting table 3(89)				
Open point 3.44  RMS, to amend sentences related to LOQ according BCS comment in column 2.  See reporting table 3(93)	Text was amended to clarify the LOQs	Not applicable.		see open point 3(40)
Open point 3.45  RMS, to reconsider in a revised ER the processing and conversion (correction?) factors taking into account the conclusion of the expert meeting 3(8), 3(13), 3(26), on the residue definitions. See also comments 3(96), 3(97), 3(98) and 3(99)	The correction/conversion factors were reconsidered and recalculated, sometimes resulting in slightly other CFs.  PFs were also recalculated.	Not applicable.		see open point 3(40)

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 3(94)				
Open point 3.46  RMS to amend in a revised ER the sections 3.1.2.1, 3.1.2.2 and 3.1.2.3 on rotational crops, taking into account the BCS comments 3(101), 3(102), 3(103), 3(104), 3(105) and 3(106). Conclusion of the expert meeting on residue definitions 3(8), 3(13), 3(26), and rotational crops 3(40) should be considered indeed.  See reporting table 3(99)	Sections concerning rotational crops in ER were amended in accordance with comments 3(99) to 3(104) in the reporting table	Not applicable.		see open point 3(40)
Open point 3.47  RMS to align in the DAR and ER the sections related to residues in livestock  See reporting table	Livestock sections were aligned, as well as proposed MRLs and consumer risk assessment.	Not applicable.		see open point 3(40)

## section 3 – Residues

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
3(106)				
New open point 3.48: RMS to revise consumer assessment taking into consideration the revised reference values (ADI and ARfD) set by the experts.		Not applicable.	<p>Residue levels for DFA, expressed as DFA were calculated from DFA, expressed as flupyradifurone.</p> <p>Totals of flupyradifurone and DFA, expressed as flupyradifurone were recalculated.</p> <p>MRLs were calculated using the new residue definitions for monitoring, consumer risk assessment was recalculated.</p>	<p>Addressed</p> <p>Consumer risk assessment has been reconsidered in the revised DAR of December 2014.</p>

## section 4 – Environmental fate and behaviour

**4. Environmental fate and behaviour**

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point 4.1  RMS to add the k1, k2 and g values for each DFOP fit for the field degradation studies for the DFOP fits to the list of endpoints.  See reporting table 4(2)	The RMS included the k1 and k2 values and g value in the RMS remarks for the field studies	Not applicable.		Open point fulfilled  EFSA has included the k1 and k2 values and g values in the LoEPs (December 2014).
Open point 4.2  RMS to add the k1, k2 and g values for each DFOP fit for the lab degradation studies for the DFOP fits as a minimum for the (AX) and (HN) soils to the list of endpoints. (i.e. the soils where for modelling the SFO DT50 was not selected).  See also open point at comment 4(2).  It is essential that this	The RMS included the k1 and k2 values and g value in the LOEP	Not applicable.		Open point fulfilled  RMS has appropriately included the k1 and k2 values and g values in the LoEPs (December 2014).

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>information is included in the list of agreed endpoints in the rate of degradation in soil section.</p> <p>It would be appreciated if the RMS could also present the information as offered in a corrigendum or amended DAR.</p> <p>See reporting table 4(5)</p>				
<p>Expert consultation 4.1</p> <p>Member state experts to discuss the time dependent sorption dataset and the appropriateness of the tier 2b groundwater modelling approach used, including the consideration of the RMS assessment of what is provided in response to the data requirement at reporting table comment 4(12). Experts to conclude if</p>	<p>To be discussed at the expert meeting</p>	<p><u>Pesticide Peer Review expert meeting 121 (19 – 20 November 2014):</u></p> <p>A new open point was proposed (see below)</p>		<p>Expert consultation fulfilled</p> <p>In conclusion, the experts agreed that the kinetic sorption experiments were performed following the draft guidance developed by FERA and Alterra and the calculations of the model input parameters and the ground water modelling required were provided but still need to be included in an addendum or in an updated DAR. Since the experts have still doubts on the acceptability of the TDS scheme as in the draft</p>

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
the available tier 2b simulations should be relied upon. Experts to discuss the issue of parameter correlation and discuss if averaging of simulation results for each soil rather than averaging input parameters from different soils is justified or whether the results from both approaches should be considered for decision making.  See reporting table comments 4(11), 4(12), 4(13), 4(16), 4(17), 4(31), 4(32) and 4(37).				guidance developed by FERA and Alterra due to uncertainties in the validation of the scheme against accepted (and not completely clear) protection goals, experts considered that at this stage the results of these simulations should not be included in the LoEP.  Based on the ECPA paper on PUF (plant uptake factor, change in solution concentration) the applicant presented calculations using TSCF (transpiration stream concentration factors) of 0.5 for parent and metabolites. For the parent a TSCF of 0.5 for substances that uptake by root from soil is accepted here. In this case it can be accepted on basis of the following crop metabolism studies however evidence for the metabolites is not available (only generic data was provided and it is not accepted). Therefore, calculations for metabolites need to be redone using a

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
				TSCF of 0.
New open point 4.10:  RMS to remove tier 2b input parameters and results from the LoEP.  RMS to present the results of the tier 2b in and addendum or updated DAR including results of the simulations performed with PELMO and PEARL in hops and lettuce considering geomean and mean input parameters (as appropriate) and median results of the separated soils simulations.  RMS to add tier 1 and tier 2a PEC GW simulations for field lettuce to the LoEP.  RMS to check and		Not applicable.	RMS (December 2014): all points addressed in updated DAR of December 2014.	Open point fulfilled  RMS has appropriately updated the DAR and the LoEPs (December 2014).

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
confirm and update the results for PELMO tier 1 and tier 2a in the updated DAR and the LoEP.  For the metabolites the calculations presented should be performed assuming a plant uptake factor of 0.				
Data requirement 4.1  Applicant to submit reports of fitting of aged sorption experimental results, where a range of different starting parameters are investigated, with all these optimisations being transparently reported as outlined in the draft UK guidance Beulke and van Beinum (2012). Once applicant is confident that they have demonstrated that they have robust fitted parameters for each	This subject is related to the expert consultation 4.1 therefore the RMS proposes that this will be discussed further at the expert meeting  The provided reports will be evaluated and included in the updated DAR after the expert meeting. The data will be added in an addendum for the preparation of the expert meeting together with data submitted for the original dossier on TDS.	Not applicable.	Data requirement fulfilled.  The applicant has, as asked for in data requirement 4.1, submitted a report on the aged sorption experimental results. See also expert consultation 4.1.	

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>soil, applicant to rerun tier 2b simulations both averaging the input parameters from each available soil and running simulation using results for each soil as input separately and then averaging the simulation results, as outlined in the draft UK guidance Beulke and van Beinum (2012).</p> <p>Note there are no' current criteria from the TDS guidance' as there is no agreed TDS guidance.</p> <p>See reporting table 4(12)</p>				
<p>Data requirement 4.2</p> <p>Applicant to provide PEC soil for metabolites that represent and include the situation that accumulated concentrations of the precursor active</p>	<p>The results of the study provided by the applicant is included in de revised DAR.</p>	<p>Not applicable.</p>		<p>Data requirement fulfilled.</p> <p>The data have been submitted and the RMS has appropriately updated the DAR and the LoEPs (December 2014).</p>

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
substance from repeated use over the years can occur. (worst case DT values to be used in calculations).  See reporting table 4(21)				
Open point 4.3  RMS to correct the PEC soil values in the list of endpoints for parent flupyradifurone so they are consequent to what is presented in Table B.8.3-04 of Vol. 3 page 172, further details / explanation to be included regarding mixing depths and depth assumed for the applications in the final year for the two crops  See reporting table 4(22)	The list of endpoints is updated with the long term PECs for flupyradifurone and the metabolites	Not applicable.		Open point fulfilled  RMS has appropriately updated the LoEPs (December 2014).
Data Requirement 4.3  Applicant to address the	The applicant provide a statement where the PECgw and sw are related to the possible	Not applicable.		Data requirement not fulfilled. Some information was provided however the

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
effect of water treatment processes on the nature of residues present in surface and groundwater, when surface water or groundwater are abstracted for drinking water. Probably in the first instance, a consideration of the processes of ozonation and chlorination would appear appropriate. If an argumentation is made that concentrations at the point of extraction for drinking water purposes will be low, this argumentation should cover metabolites predicted to be in groundwater and surface water, as well as the active substance. Should this consideration indicate novel compounds might be expected to be formed from water treatment, the risk to	<p>concentrations at drinking water abstraction points. It is concluded that the concentrations are below the 0.1 ug/L for the active substance and metabolites.</p> <p>The RMS included the report evaluation in the revised DAR. The RMS agrees with the applicant that the PEC gw and sw concentrations are below 0.1 ug/L.</p>			assessment was not sufficient (not robust because it was very qualitative) to conclude that the effects of water treatment processes on the nature of residues of the active substance and metabolites when surface water is abstracted for drinking water and metabolites when groundwater is abstracted for drinking water to address Article 4 (approval criteria for active substances) 3(b) of Regulation (EC) No 1107/2009. Therefore a data gap was identified.

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
human or animal health through the consumption of drinking water containing them should be addressed  See reporting table 4(24)				
Open point 4.4  EFSA to indicate in its conclusion that the surface water exposure assessment for the field uses covers exposure from the assessed glasshouse uses provided that ultra low volume application techniques are not used in the glasshouses and that this application technique has not been assessed / may not be covered in the available assessment.  See reporting table 4(28)	Open point for EFSA	Not applicable.		Open point fulfilled.  EFSA has calculated PECsw values using 0.2 % emissions from glasshouses to 30cm deep static water body for a total annual dose of 250 resulting in a PEC of 0.1667 µg/L. EFSA has also calculated a long-term PECsoil for use in glasshouse. This calculation is based on the same assumptions as field use the only difference is that 2 applications are assumed according to the GAP table.
Open point 4.5	The PECsw with > 95% spray drift mitigation were	Not applicable.		Open point fulfilled

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
RMS to remove from the list of endpoints all PECsw and TER values derived from situations where spray drift has been mitigated by > 95%.  See reporting table 4(29)	indicated in the DAR and the list of endpoints.			EFSA has removed the PECsw and TER values derived from situations where spray drift has been mitigated by > 95% in the LoEPs (December 2014).
Open point 4.6  RMS to provide an evaluation of the evidence that the use of a TSCF in FOCUS modelling of 0.5 for the active substance and its metabolites was justified.  See reporting table 4(30)	The RMS included a reference to the volume B.10 where it is stated that the mode of action of the active substance is systemic.  The evaluation of the Schriever report (Schriever et al, 2013 <sup>1</sup> ) is included in a footnote.  The applicant provided new data (poster and statement) and the article Schriever et al. 2013. The RMS has the	Not applicable.		Open point fulfilled.  The active substance is considered to be systemic however the metabolites were not proven to be systemic. See also expert consultation 4.1.

<sup>1</sup> Schriever, C., Gottesbüren, B., Ebert, D., Sur, R. Schmitt, W. (January 2013). ECPA background paper. Plant uptake of compounds via roots system – A hydroponic test system to determine plant uptake as input parameter for leaching models.

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
	<p>opinion that this needs to be discussed by expert and will include the information and discussion points in the addendum for the expert meeting.</p> <p>The RMS did not yet recalculated the PECgw based on the not acceptance of the Schriever et al study. Based on the expert meeting results on the discussion on aged sorption the values for PECgw will be updated and the adjusted PUF for the metabolites will be included in these new model calculations.</p>			
Open point 4.7  RMS to update the list of endpoints GAP table row for hops to indicate that biennial (and not biannual) application is the representative use. The GAP table in the	<p>The biennial usage in hop was assessed for PECsoil, PECsw and PECgw.</p> <p>For PECsoil, plateau the annual application was assessed, a clarification is included in the updated DAR and volume 1. The</p>	Not applicable.		<p>Open point fulfilled</p> <p>RMS has clarified in the fate section that the application in hops is biennial and not biannual. However the GAP table has not been updated by the RMS and therefore EFSA has clarified in the GAP table</p>

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
DAR from the beginning has indicated the representative use on hops is only every other year. Therefore this is the representative use that has been assessed.  See reporting table 4(39)	assessment of the annual usage in hop covers the biennial usage .			that flupyradifurone is applied biennial on hops.
Open point 4.8  RMS to present an evaluation of the literature review completed by the applicant in an addendum.  See reporting table 4(42)	The evaluation is included in the literature relied on included in the updated DAR.	Not applicable.		Open point fulfilled, by the RMS as far as was possible though a data gap was identified because of the limited explanation of the applicant on the reasons why literature were not considered as needing to be added to the dossier. The data gap is : "Transparent study-by-study justification of the relevant studies found by the applicant during the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites."
Data requirement 4.4  Applicant to provide a search of the scientific	The applicant provided the search for the two metabolites. This is included and evaluated in	Not applicable.		Addressed  An additional literature search was completed for the aqueous photolysis

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, being conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) for the aqueous photolysis metabolites BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide that do not appear to have been included in the available literature review.	the reference relied on in the updated DAR			metabolites. The RMS evaluation of the information submitted (which resulted in no references being found) was presented in Vol. 3 B.8.10 of the updated DAR.

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 4(42)				
Open point 4.9  RMS to provide in an addendum to volume 1, Level 3 their assessment against the annex II approval criteria; please also include short explanatory notes how the decisions were derived and which data were used to decide on the separate criteria.. It is suggested to follow Guidance Document SANCO/12592/2012 – rev. 0 November 2012 (Template to be used for Assessment Reports). The substance is assessed / will be approved under Regulation (EC) No 1107/2009, therefore a conclusion against these criteria is a responsibility of the RMS.	Included in updated volume 1.	Not applicable.		The open point remains open the assessment provided by the RMS is minimal and lacks transparency.

## section 4 – Environmental fate and behaviour

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting/EFSA request for RMS' action	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 4(45)				

## section 5 - Ecotoxicology

## 5. Ecotoxicology

Column A Conclusions from the Reporting Table	Column B Rapporteur Member State comments (reference to addenda where necessary)	Column C Recommendations of the Pesticides Peer Review Meeting	Column D Rapporteur Member State homework (reference to addenda where necessary)	Column E EFSA conclusion
<p>Expert consultation 5.1</p> <p>The residue decline data was not used because based on the NOEAL of 34 mg/kg bw/d, a refined risk assessment is not necessary. However if the 1-year dog study is considered to be relevant, a refined risk assessment may be needed. Depending on the outcome of the expert consultation 5(8), the experts may need to discuss if the 21-d ftwa approached proposed for lettuce and hops can be considered acceptable.</p> <p>In all trials residue were determined after the second treatment, but for four trials residues were also determined after the first application and DT50 values were estimated for each decline interval. Some of the DT50 values were</p>	<p>NL (Oct 2014): Please see the discussion on the 21-d ftwa approach in the DAR B.9.3, and the applicant's position in the reporting table 5(5).</p>	<p><u>Pesticides Peer Review Meeting 124 (3 – 5 December 2014):</u></p> <p>A new open point has been proposed, see open point 5.26 below.</p>	<p>See open point 5.26 below</p>	<p>Expert consultation fulfilled</p> <p>The residue decline data was discussed during the Pesticides Peer Review Meeting 124 (3 – 5 December 2014). The data was considered suitable to be used in the risk assessment for the representative crops and the risk assessment has been updated with the appropriate fTWA.</p> <p>It was noted that the approach in which the 21-d ftwa is calculated from measurements which started at the last application (in trials with two applications) is acceptable for the current GAP, since this has only one application per year. It was discussed that it may not cover GAPs which have multiple applications, as the 21-d exposure window may be higher at an earlier stage. Therefore, for other GAPs it needs to be carefully considered how to use these data.</p>

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
calculated with DFOP (both kfast and kslow was used). For most of the sites in lettuce only 5 sampling points were available. A geometric mean 21-day fTWA is proposed for the refined long-term exposure assessment. There are some uncertainties for lettuce whether the residue values is applicable to the full application period. Only one of the four doubly analysed trials was performed at a relatively early BBCH stage in lettuce.  See reporting table 5(5)				
New open point 5.26:  The RMS to include a refined risk assessment in an updated DAR and the LoEP taking account of the appropriate fTWA, in addition to the NOAEL of 100 ppm (see the open point on the experts- consultation 2)		Not applicable.	NL (Dec 2014): The discussion on the relevant long-term endpoint and the revised long-term risk assessment are included in the revised DAR.	Open point fulfilled  The RMS has included a refined risk assessment in the updated DAR (December 2014) and the LoEPs taking into account the appropriate ftwa in addition to the NOAEL of 100 ppm.

rapporteur NL

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Open point (EFSA) 5.1  EFSA to make it clear in the conclusion that there is possible effects of the surrounding habitat in the species composition in a crop.  See reporting table 5(7)	-	Not applicable.	-	The generic field monitoring study was not used in a significant way in the risk assessment. The study was therefore not mentioned in the conclusion. However if the study is used in future assessments it should be noted that there can be possible effects of the surrounding habitat in the species composition in a crop.
Expert consultation 5.2  Should the 1-year dog study, with an endpoint of 7.8 mg/kg bw, be considered relevant in the risk assessment of other terrestrial vertebrates, mammals?  See reporting table 5(8)	NL (Oct 2014): One-year dog studies are to our knowledge never considered for ecotoxicological risk assessment. The EFSA GD for birds and mammals of 2009 does not include this study in the list of mammalian tests relevant for the reproductive risk assessment.  It was noted that changes were made by the RMS to certain long-term endpoints in the mammalian tox section based on comments from MS and EFSA. These changes may be of	<u>Pesticides Peer Review Meeting 124 (3 – 5 December 2014):</u>  A new open point has been proposed, see open point 5.27 below.	See open point 5.27.	Expert consultation fulfilled  The one-year dog study was discussed at the Pesticides Peer Review Meeting 124 (3 – 5 December 2014). It was concluded that the one-year dog study was not considered relevant for ecotoxicology reproductive risk assessment. It was concluded that a NOAEL of 100 ppm from the 2-generation rat study should be used in the risk assessment.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
	influence for the discussion on the relevant endpoint for the ecotox assessment. The outcome of the mamtox peer review meeting, scheduled for 17/18 November, is awaited and can be taken into account in the ecotox peer review meeting.			
New open point 5.27:  RMS to provide a revised DAR or addendum and to update the LoEP with the revised long-term risk assessment based on the NOAEL of 100 ppm.		Not applicable.	NL (Dec 2014): The discussion on the relevant long-term endpoint and the revised long-term risk assessment are included in the revised DAR.	Open point fulfilled  The RMS has provided a revised DAR and updated the LoEPs with the revised long-term risk assessment based on the NOAEL of 100 ppm.
Open point 5.2  RMS to correct the timescale of the acute study with 6-CAN on Chironomus tentans to 96 h in the LoEP.  See reporting table 5(10)	NL (Oct 2014): Corrected in the revised DAR in the endpoint overview table and the LoEP.	Not applicable.	-	Open point fulfilled  The RMS has corrected the timescale of the acute study with 6-CAN on Chironomus tentans to 96 h.
Open point 5.3  RMS to put a footnote in the LoEP:s that clarifies that the NOEC has some uncertainties and that a ~30% difference on	NL (Oct 2014): Footnote added to LoEP.	Not applicable.	-	Open point fulfilled  The RMS has put a footnote in the LoEPs that clarifies that the NOEC has some uncertainties and that a ~30% difference on

rapporteur NL

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
average from the control was seen in the study.  See reporting table 5(15)				average from the control was seen in the study.
Expert consultation 5.3 Experts to discuss if a test on mayflies should be considered needed in the aquatic risk assessment.  Reporting table comment 5(18); "Even if the butenolide flupyradifurone (nicotinic acetylcholine receptor (nAChR) agonist) is not as toxic to Chironomides as the closely related neonicotinoids, such as imidacloprid, the concerns about possible effects on mayflies (Ephemeroptera) should be investigated and discussed further because mayflies show higher sensitivity to neonicotinoids compared to Chironomides. The aquatic risk could be well addressed exploring sensitivity of mayflies to	NL (Oct 2014): The applicant provided a position paper with input for this discussion. Hager, J. 2014. Flupyradifurone (BYI 02960): BCS opinion on the need for additional data on mayflies (Ephemeroptera). This document is included as Appendix 1 to the addendum, and can also be found under Q14/01 in the BCS Scientific Response Document to EFSA questions, in the applicant's dossier.	<u>Pesticides Peer Review Meeting 124 (3 – 5 December 2014):</u>  A new open point has been proposed, see open point 5.28 below.	See open point 5.28.  Please note that the conclusion from the position paper from the applicant has now been included in the revised DAR.	Expert consultation fulfilled  The Pesticides Peer Review Experts Meeting 124 (December 2014) discussed if mayflies (Ephemeroptera) should be considered in the aquatic invertebrate risk assessment since mayflies seems to have higher sensitivity to the group of pesticides that flupyradifurone belongs to than Chironomus tentans or Chironomus riparius. The meeting concluded that not enough data were available to support such a requirement. Furthermore the meeting concluded that the endpoints for Chironomus should be expressed in terms of mean measured concentration in water column when the analytical measurement concentrations are outside of the range 80 – 120 % and when concentrations in the sediment are not available.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
the a.s."  See reporting table 5(18)				
New open point 5.28:  RMS to amend the risk assessment to aquatic organisms in a revised DAR and in the LoEP by considering the endpoint for chironomus expressed as mean measured concentration in the water column.		Not applicable.	NL (Dec 2014): The NOECs for Chironomus from the a.s. and the formulation study have been recalculated to mean measured concentrations and the risk assessment has been updated.  For Step 3 and 4, the TER values were only presented for the biennial use in lettuce, but since this does not completely cover the annual use in lettuce, TER values are now also presented for the annual use.	Open point fulfilled  The RMS has included the mean measured concentrations and updated the risk assessment for Chironomus.  For the representative use in lettuce in glasshouse EFSA has calculated TER values for the most sensitive species Chironomus for flupyradifurone. For the metabolites the field use was considered to cover the use in glasshouse.
Data requirement 5.1  To support the discussions in the expert meeting the Applicant should submit any information available, which might even be a position paper or an argumentation.  See reporting table 5(18)	NL (Oct 2014): The applicant has provided a position paper. See above, Expert consultation 5.3.	Not applicable.	-	Data requirement fulfilled  The applicant has provided a position paper.
Open point 5.4	NL (Oct 2014): The term biannual is corrected to	Not applicable.	-	Open point fulfilled

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
RMS to clarify in the LoEP:s and a revised DAR that the application on hops is biennial and not biannual.  See reporting table 5(19)	biennial in the revised DAR and the LoEP.			The RMS has updated the LoEPs and a revised DAR that the application on hops is biennial and not biannual.
Open point 5.5  RMS to update the LoEP:s with acute and chronic TER calculations for <i>Chironomus</i> and the 4 relevant metabolites (DFA, 6-CNA, BYI 02960-succinamide and BYI 02960-zabicyclosuccinamide).  See reporting table 5(22)	NL (Oct 2014): Corrected in/added to the revised DAR and the LoEP.	Not applicable.	-	Open point fulfilled  The RMS has updated the LoEPs with acute and chronic TER calculations for <i>Chironomus</i> and the 4 surface water metabolites (DFA, 6-CNA, BYI 02960-succinamide and BYI 02960-zabicyclosuccinamide).
Open point 5.6  RMS to clarify in the LoEP:s which mitigation measures that are assumed in the higher tiers.  See reporting table 5(23)	NL (Oct 2014): Clarifications added to the revised DAR and the LoEP.	Not applicable.	-	Open point fulfilled  The RMS has clarified in the LoEPs which mitigation measures that are assumed in the higher tiers.
Open point 5.7  RMS to indicate in the LoEP (e.g. via a	NL (Oct 2014): Footnote added to LoEP.	Not applicable.	-	Open point fulfilled  An appropriate footnote was added to the LoEP.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>footnote) that there are some uncertainties of the results of the chronic lab. studies arising from the lack of toxic standard and the lack of information on the history of the used bees. The lack of experience of conducting these kind of tests and the lack of experience for the interpretation of these tests might also be mentioned.</p> <p>Notes: Currently no agreed reference performance is available for any potential toxic standard.</p> <p>EFSA considers the current period as an interim period, when there is some room for some flexibility with this new type of studies, when the design and the results (including the control mortality) were reasonable.</p> <p>See also open points in</p>				<p>Note: Although the uncertainties exist, the information provided by these studies is considered as very valuable and was considered for the conclusion.</p>

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
5(29) and 5(31).  See reporting table 5(28)				
Open point 5.8  RMS to indicate in the LoEP (e.g. via a footnote) that there are some uncertainties of the results of the larval test arising from the lack of experience of conducting and the interpretation these kind of tests.  Notes: EFSA agrees that some uncertainties exist around this NOEC value. In some (valid) test runs the mortality in the treated groups was consistently higher than in the controls. On the other hand at least test run No.4 indicated a lack of effects up to 10 ppm and the performance of the reference item clearly indicated the sensitivity of larvae to chemical stress in all runs.  See also open points in	NL (Oct 2014): Footnote added to LoEP.	Not applicable.	-	Open point fulfilled  An appropriate footnote was added to the LoEP.  Note: Although the uncertainties exist, the information provided by these trials is considered as very valuable and was considered for the conclusion.

rapporteur NL

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
5(28) and 5(34).  See reporting table 5(29)				
Open point 5.9  RMS to make clear the control mortality and the analytical findings for the test item stability for all chronic adult tests in an addendum.  See reporting table 5(31)	NL (Oct 2014): The control mortality data and the analytical findings for the test item stability for all chronic adult tests were included in the study summaries in the addendum (and also in the revised DAR).	Not applicable.	-	Open point fulfilled  The DAR was updated with the required information (an addendum was prepared).
Open point 5.10  RMS to remove the NOEC values from the LoEP.  Notes: EFSA just noted that there are some uncertainties around some NOEC values if a read-across for all the available data (including also the acute oral test) is done. This is might be partly due to the correction procedure (the alternative would be do not apply the correction and consider the NOEC where actually 0 % effect	NL (Oct 2014): The NOEC values from the chronic toxicity studies with adult honeybees were removed from the LoEP.	Not applicable.	-	Open point fulfilled  The LoEP was amended as requested.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>was seen). It does not mean that the information on the likely no effect levels is ignored. EFSA agrees that the available data suggest rather a lack of potential for accumulative effect at least for the a.s., which should be taken into consideration.</p> <p>It is likely that the new template for LoEP will ask only the LC50 (LD50) as this will be used in the follow up risk assessments in the future.</p> <p>See also comments in 5(26), 5(27), 5(28) and in 5(44).</p> <p>See reporting table 5(31)</p>				
<p>Open point 5.11</p> <p>RMS to confirm (if possible) that the question regarding the identity of the test item used in the acute test (first study under</p>	<p>NL (Oct 2014): RMS confirms that this issue is resolved. The acute bee toxicity test was performed with a batch that is considered equivalent to the technical specification of the active substance. See the</p>	<p>Not applicable.</p>	<p>-</p>	<p>Open point fulfilled</p> <p>A clarification was added to the DAR (an addendum was prepared).</p>

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
B.9.4.1.1) is resolved and indeed technical flupyradifurone was used with comparable profile with other studies and the specification.  Note: EFSA do not disagree that the acute and chronic studies indicated similar results, but numerically the chronic endpoint is higher than the acute one. Since the difference is rather small, this does not trigger a particular concern provided that the test items used in these tests are comparable  See reporting table 5(33)	revised DAR and the revised Volume 4.			
Open point 5.12  RMS to include the endpoint for honeybee larvae expressed in mass of the total intake of a.i./larvae throughout the exposure period in LoEP (e.g. ug/larvae	NL (Oct 2014): Nominal value of 1.32 ug a.s./larvae (accumulated exposure on day +4, +5 and +6 after grafting of the larvae) added to LoEP.	Not applicable.	-	Open point fulfilled  The endpoint in question was further clarified (an addendum to the DAR was prepared). The LoEP was amended accordangly.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
over 3 days). If only nominal values are available than please indicate clearly that these values are nominal and it cannot be excluded that the real test item intake was lower. If more than one value are available than the range from the valid test runs could be indicated.  See reporting table 5(34)				
Expert consultation 5.4  Experts from Member States to discuss the design and the results of the available higher tier studies for bees. Experts from Member States to discuss the risk assessment and conclude the risk to bees for the representative uses.  Beside the available higher tier effect studies, the experts should/may pay attention to the - available	NL (Oct 2014): EFSA requested an addendum for formal reasons. For ease of reference, the whole bee section from the DAR was copied to the addendum, with the requested additions highlighted in yellow. Note that some of the requested additions to the study summaries are also included in yellow in the revised DAR, but not all – thus, please use section B.9.4 of the addendum as input for the discussion.	<u>Pesticides Peer Review Meeting 124 (3 – 5 December 2014):</u>  Two new open points have been proposed, see open points 5.29 and 5.30 below.	See open point 5.30.	Expert consultation fulfilled  The higher tier studies and some other considerations were discussed. Overall, a low risk to honey bees was agreed for the representative uses.  However two open points (5.29 and 5.30, see below) were also agreed.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<ul style="list-style-type: none"> <li>- laboratory endpoints</li> <li>- available residue data</li> <li>- off-field risk assessment</li> <li>- sub-lethal effects observed in laboratory studies</li> <li>- repellent effects seen in some higher tier studies</li> <li>- risk via honeydew</li> <li>- risk to wild pollinators</li> </ul> <p>See also comments in 5(26), from 5(37) to 5(45), from 5(47) to 5(50) and from 5(52) to 5(55). In some of these points some open points were set for further information to ease the discussion.</p> <p>See reporting table 5(36)</p>				
New open point 5.29:  EFSA to reflect in the conclusion that the		Not applicable.	-	Open point fulfilled  The issue was included in the conclusion.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
available assessment does not cover the risk to pollinators other than honey bees.				
New open point 5.30:  RMS to update the LoEP to ensure that the text is in line with the conclusions of the meeting.		Not applicable.	NL (Dec 2014): The LoEP is updated. The conclusions of the expert meeting on the individual semi-field and field effect studies and the overall conclusion of the expert meeting are included in the revised DAR.	Open point fulfilled  The LoEP was updated.
Open point 5.13  RMS to provide more detailed data (i.e. for each repetition for each day) at least for adult and larvae/pupa mortality in an addendum from the study by Schnorbach, 2012b. Table and/or graphical presentations are preferred.  Note: this information will be used for the expert discussion (see in 5(36)).  See also point for expert consultation in 5(36), above.	NL (Oct 2014): The requested data were included in the study summary in the addendum.	Not applicable.	NL (Dec 2014): For the pesticide peer review meeting, an addendum was prepared as a discussion paper. This addendum has now been incorporated in the revised DAR of December 2014.	Open point fulfilled  The information as requested was included in an addendum.

rapporteur NL

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 5(39)				
<p>Open point 5.14</p> <p>RMS to provide more detailed data for adult and larvae/pupa mortality or abundance separately in an addendum from the study by Rentschler, 2012a. Table and/or graphical presentations are preferred.</p> <p>Note: The more formal format (i.e. addendum) is needed for transparency reason and because this information will be used for the expert discussion (see in 5(36)).</p> <p>See also point for expert consultation in 5(36), above.</p> <p>See reporting table 5(40)</p>	<p>NL (Oct 2014): The requested data were included in the study summary in the addendum.</p>	Not applicable.	<p>NL (Dec 2014): For the pesticide peer review meeting, an addendum was prepared as a discussion paper. This addendum has now been incorporated in the revised DAR of December 2014.</p>	<p>Open point fulfilled</p> <p>The information as requested was included in an addendum.</p>
<p>Open point 5.15</p> <p>RMS to provide more detailed data for adult mortality and adult and brood abundance in an</p>	<p>NL (Oct 2014): The requested data were included in the study summary in the addendum.</p>	Not applicable.	<p>NL (Dec 2014): For the pesticide peer review meeting, an addendum was prepared as a discussion paper. This addendum has now been incorporated in the revised DAR</p>	<p>Open point fulfilled</p> <p>The information as requested was included in an addendum.</p>

rapporteur NL

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>addendum from the study by Pröbsting, 2012b. Table and/or graphical presentations are preferred.</p> <p>Note: this information will be used for the expert discussion (see in 5(36)).</p> <p>See also point for expert consultation above</p> <p>See reporting table 5(42)</p>			of December 2014.	
<p>Open point 5.16</p> <p>RMS to provide more detailed data for adult and larvae/pupa mortality separately in an addendum from the study by Rentschler, 2012b. Table and/or graphical presentations are preferred. As an alternative solution, clearly confirm that the contribution of pupae mortality was negligible throughout the study and this does not disturb the interpretation of the adult mortality from the DAR</p>	<p>NL (Oct 2014): Additional information is added to the addendum. Based on the separate results for dead bees in the dead bee traps and the linen sheets, there is no indication that pupae mortality is higher in the treatment than in the control.</p>	<p>Not applicable.</p>	<p>NL (Dec 2014): For the pesticide peer review meeting, an addendum was prepared as a discussion paper. This addendum has now been incorporated in the revised DAR of December 2014.</p>	<p>Open point fulfilled</p> <p>The information as requested was included in an addendum (the information was not included in the document called as addendum, but in a document called as updated DAR).</p>

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
(i.e. the overall picture suggested by Figure 9.4.2-29 would be the same for adult mortality).  Note: The more formal format (i.e. addendum) is needed for transparency reason and because this information will be used for the expert discussion (see in 5(36)).  See also point for expert consultation in 5(36), above.  See reporting table 5(43)				
Data requirement 5.2  Applicant to submit more comprehensive study summary of the two studies Aldershof S. & Bakker F. (2012). Furthermore the present table B.9.5.2-02 should be presented in a readable version. More detailed information will be necessary to understand the visualised results and	NL (Oct 2014): The applicant submitted more extended summaries, including an improved quality of the graphs and tables. To avoid loss of graphical quality by copy-and-paste-work, these summaries are not included in the addendum but added in a separate document as an appendix to the addendum.	Not applicable.	NL (Dec 2014): For the pesticide peer review meeting, an addendum was prepared as a discussion paper. This addendum has now been incorporated in the revised DAR of December 2014.	Data requirement fulfilled  More extended study summaries had been submitted. These were transformed in an appendix (Appendix 2) to the addendum by the RMS. The information was considered in the related expert discussion (Expert consultation 5.5). The way how the studies were summarised (including readability) were good enough to be used in the meeting.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>especially the data standing behind it (e.g. validity criterion).</p> <p>See also expert consultation 5(60).</p> <p>See reporting table 5(58)</p>				
<p>Expert consultation 5.5             Experts to discuss the two non-target arthropod field studies (off-crop) from the authors Aldershof S. and Bakker F. (2012). Can they be considered acceptable to be used in the risk assessment?             See reporting table comment 5(60).            "DE: The two non-target arthropod field studies (off-crop) from the authors Aldershof S. and Bakker, F. (2012) are quite comprehensive and a summary of it is obviously labour-intensive. Nevertheless, in the study summary more readable (e.g.</p>	<p>NL (Oct 2014): As background for the discussion, please see the study summaries from RMSin the DAR, the extended study summaries from the applicant in the Appendix to Addendum 1, and the reporting table.</p>	<p><u>Pesticides Peer Review Meeting 124 (3 – 5 December 2014):</u>             For any action points, see related discussion under expert consultation 5.6 below.</p>	<p>NL (Dec 2014): See expert consultation 5.6. Please note that for the pesticide peer review meeting, an addendum was prepared as a discussion paper, which has now been incorporated in the revised DAR of December 2014.</p>	<p>Expert consultation fulfilled             The off-crop non-target arthropod field studies had been discussed.            See also Expert consultation 5.6.</p>

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Table on page 367) as well as more detailed information will be necessary to understand the visualised results and especially the data standing behind it (e.g. validity criterion). It will also be helpful to provide more information within the summary to avoid misinterpretation of the results. Furthermore, there are some shortcomings of the studies that question the applicability for the refinement in off-crop risk assessment as well as the reliability of the selected endpoints: In an off-crop field study suitable for the refinement of the off-field risk assessment it has to be shown that toxic effects are not overlaid by re-colonisation, but the studies were conducted to show NOER/NOEAER by recovery, thus the focus was different influencing				

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>the design and outcome of the study. In the two conducted (off-crop) field studies the plots were established in a checkerboard design with open (uncovered) plots, which makes it difficult to conclude on the reliability of the study results on toxic effects. Furthermore, arthropods were sampled one, two, four and eight weeks after treatment. Thus, overlaying of toxic effects by re-colonisation cannot be excluded, and a clear separation of NTA-communities between treated and non-treated plots in the off-field is missed.</p> <p>The off-crop field studies were performed only on grassland and are, therefore, insufficient as surrogate for the variability of possible off-field habitats around arable land. The study is not representative for 100% of existing worst</p>				

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
case landscape. Standing alone, these field studies are insufficient for the refinement of the NTA off-crop risk assessment (please see DE comment 3, below "reduction of the correction factor"). The study design is not suitable to show time and concentration related trends of toxic effects. Therefore, reliability of population related endpoints, such as NOER an NOEAER is questionable and conclusions on recovery and dose effect relationships are not reliable Information on the mode of action as well as physical-chemical properties of the test substance flupyradifurone and the reference substance lambda-cyhalothrin should be used to underline and interpret the results in				

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
observations of treated plots. „  See reporting table 5(59) a				
Expert consultation 5.6  Experts to discuss the off-field arthropod risk assessment. Can the refined risk assessment for off-field arthropods be accepted?  See reporting table comment 5(61). “Reduction of the correction factor for the off-field PEC calculations from 5 to 1 is not acceptable, considering the shortcomings of the available off-crop field studies (please see DE comment (1) above). The uncertainty concerning the sensitivity of off-field arthropod species cannot be clarified. A correction factor of 5 will clearly result in a risk for off-crop NTAs. A study design for the refinement	NL (Oct 2014): As background for the discussion, please see the revised DAR and the reporting table.	<u>Pesticides Peer Review Meeting 124 (3 – 5 December 2014):</u>  N new open point has been proposed, see open point 5.31 below.	See open point 5.31.	Expert consultation fulfilled  The risk assessment for non-target arthropod had been discussed. The discussion has resulted in an open point (see open point 5.31, below).

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
<p>with a correction factor of 1 for the off-crop community requires a clear separation of toxic effects, recovery and re-colonisation as well as a 100% covering of a existing worst case landscape.</p> <p>The refined risk assessment for off-field arthropods should be discussed.“</p> <p>See reporting table 5(60)</p>				
<p>New open point 5.31:</p> <p>RMS to update the risk assessment (risk mitigation) considering the agreed NOER of 1.7 g/ha in the DAR and in the LoEP. As agreed no additional safety factor is needed.</p>		<p>Not applicable.</p>	<p>NL (Dec 2014): The DAR and the LoEP have been revised. For hops, 30 m buffer zone is needed to reach an acceptable off-field risk. For lettuce, 5 m buffer zone is needed.</p>	<p>Open point fulfilled</p> <p>The RA was updated as requested in an addendum. The finally agreed value is included in the LoEP.</p>
<p>Expert consultation 5.7</p> <p>Experts to discuss the chronic risk assessment for earthworms.</p> <p>Experts to discuss the</p>	<p>NL (Oct 2014): As background for the discussion, please see the revised DAR and the reporting table.</p>	<p><u>Pesticides Peer Review Meeting 124 (3 – 5 December 2014):</u></p> <p>A new open point has been proposed, see open point 5.32 below.</p>	<p>See open point 5.32.</p>	<p>Expert consultation fulfilled</p> <p>The chronic risk assessments for earthworms had been discussed. The discussion has resulted in an open point (see open point 5.32, below).</p>

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
sublethal studies on earthworms, Leicher T. (2010c) and Leicher (2010d). Are the differences in reproductive parameters seen at the established NOECs compared to the control considered as biologically relevant? It is noted that these differences expressed in % using the average data were ~ 6.7% in the formulation study and for the metabolites > 13%.  Experts also to discuss if the earthworm field study by Menke, U. (2012, report number NMU/RG-F-8/12) is considered acceptable to be used in the refined chronic risk assessment. Is the timing of the substance application considered to be acceptable? Do the experts consider the endpoint correctly derived from the study? Should the effects seen on the number and the				

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
biomass of juveniles of <i>Lumbricus terrestris</i> considered to be relevant?  See reporting table 5(64)				
New open point 5.32:  The RMS to remove the field study from the LoEP. A statement regarding the conclusion from the experts' meeting on this study should also be reported in a revised DAR.		Not applicable.	NL (Dec 2014): DAR and LoEP updated.	Open point fulfilled  The DAR was updated as requested in an addendum. The LoEP was also updated.
Open point (EFSA) 5.17  EFSA to make clear in the conclusion that the risk to soil dwelling organisms from glasshouse uses was not assessed.  See reporting table 5(69)	-	Not applicable.	-	Open point redundant  EFSA has calculated accumulative PECsoil for 2 applications in a year (e.g. for a scenario for uses in non-permanent greenhouse). A risk assessment using this PEC would result in TER values above the trigger.
Data requirement 5.3  Applicant to submit further information on the technical specification of	NL (Oct 2014): The applicant submitted the requested information. It was included by RMS in the revised Volume 4, section	Not applicable.	-	Data requirement fulfilled  The required assessment had been submitted, included and concluded in the revised

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
the batches of the test material used in the ecotoxicity studies.  See reporting table 5(77)	C.1.4.			Volume 4 by RMS. Comments from MSs suggested that this data requirement is addressed. This is supported by EFSA.
Data requirement 5.4  The Applicant may wish to submit further information on the potential endocrine disruption properties, or for the lack of them, to the RMS.  See reporting table 5(78)	NL (Oct 2014): The applicant provided the following statement: " <i>BCS reiterates the opinion of the RMS, there is no criteria to assess whether a substance has potential for endocrine activity no additional information can be provided at this point in time.</i> "	Not applicable.	-	No additional information, only a short statement was provided.
Open point 5.18  RMS to present an evaluation of the literature review completed by the applicant in an addendum.  See reporting table 5(79)	NL (Oct 2014): This is done in the revised DAR in section B.9.12 (and a reference to the revised DAR is included in the addendum).	Not applicable.	-	Open point fulfilled  Data gap identified  The RMS has evaluated the literature reviews provided by the applicant in an addendum.  It was concluded that the search has been conducted in line with the EFSA guidance. None (except one for mammalian toxicology) of the hits was considered as relevant for regulatory use. However, as no study-by-study justifications

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
				were given, the RMS could not properly verify whether the identified, potentially relevant papers were correctly evaluated or not.  Therefore a data gap was identified for a transparent reporting of the findings from the literature search.
Data requirement 5.5  Applicant to provide a search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, being conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under	NL (Oct 2014): The applicant submitted an additional literature search. See open point 5.18.	Not applicable.	-	Data gap: An additional literature search had been submitted. Due to the lack of transparency a data gap has been identified.  See also Data gap in 5.18, above.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) for the aqueous photolysis metabolites BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide that do not appear to have been included in the available literature review.  See reporting table 5(79)				
Open point 5.19  RMS to amend the LoEP:s with the correct name of the formulation.  See reporting table 5(80)	NL (Oct 2014): Where needed, the tested formulation was corrected in the LoEP. When asked, the applicant clarified that <i>the denominations BYI 02960 SL 200 G, BYI 02960 SL 200 g/L and Flupyradifurone SL 200 G do all refer to the same formulation with the Specification number 102000021884</i> . This information is added to the LoEP and the revised DAR.	Not applicable.	-	Open point fulfilled  The LoEP was updated.
Open point 5.20  RMS to amend the LoEP:s to clarify for long-	NL (Oct 2014): Clarification added to LoEP.	Not applicable.	-	Open point fulfilled  The LoEP was updated.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
term bird endpoints whether they are based on nominal or measured concentrations.  See reporting table 5(81)				
Open point 5.21  RMS to amend LoEP:s to clarify the type of endpoint for all bird and mammal endpoints.  See reporting table 5(82)	NL (Oct 2014): Done.	Not applicable.	-	Open point fulfilled  The LoEP was updated.
Open point 5.22  RMS to amend the LoEP:s, make sure that the DDD and TER value for the pigeon scenario corresponds with those from the DAR.  See reporting table 5(83)	NL (Oct 2014): Done.	Not applicable.	-	Open point fulfilled  The LoEP was updated.
Open point 5.23  RMS to amend the LoEP:s, include all Chironomus data under 'sediment dwelling organisms' and indicate if the tests used water spiking.	NL (Oct 2014): Done.	Not applicable.	-	Open point fulfilled  The LoEP was updated.

## section 5 - Ecotoxicology

<u>Column A</u> Conclusions from the Reporting Table	<u>Column B</u> Rapporteur Member State comments (reference to addenda where necessary)	<u>Column C</u> Recommendations of the Pesticides Peer Review Meeting	<u>Column D</u> Rapporteur Member State homework (reference to addenda where necessary)	<u>Column E</u> EFSA conclusion
See reporting table 5(84)				
Open point 5.24  RMS to amend the LoEP:s, insert the correct name for the test item.  See reporting table 5(85)	NL (Oct 2014): Done.	Not applicable.	-	Open point fulfilled  The LoEP was updated.
Open point 5.25  RMS to clarify if the GAP-table for the representative use hops should have the remark biannual or biennial and to update the LoEP:s with the correct remark.		Not applicable.	NL (Dec 2014): The representative use in hops should have the remark biennial. This was updated in Vol.1. The ecotox risk assessment is based on a yearly application in hops. It seems that the biennial application was only taken into account for the groundwater exposure calculation.	Open point fulfilled  The LoEP was updated.

## TABLE OF CONTENTS

	<b>Document</b>
00	Cover page
01	Comments on the assessment report
02	Reporting table
03	Pesticides peer review meeting reports
04	Evaluation table
<b>05</b>	<b>Comments on the additional information assessment</b>
06	Comments on the draft EFSA conclusion

**Report of Pesticides Peer Review written procedure on additional information**

FLUPARADIFURONE

Rapporteur Member State: NL

Comments on the assessment report are listed in the relevant reporting table. Comments submitted during the written procedure on the assessment of the additional information are listed in Appendix 1.

Documents submitted for written procedure:

Date	Supplier	File Name
14.11.2014	NL	flupyradifurone evaluation table NAS section 1 November 2014.doc
14.11.2014	NL	flupyradifurone evaluation table NAS section 2_2014-11-21.doc
14.11.2014	NL	flupyradifurone evaluation table NAS section 3_2014-11-21.doc
14.11.2014	NL	flupyradifurone evaluation table NAS section 4_2014-11-21.doc
14.11.2014	NL	flupyradifurone evaluation table NAS section 5 November 2014.doc
14.11.2014	NL	Flupyradifurone revised DAR and addenda .zip
14.11.2014	NL	flupyradifurone updated list of end points_November 2014.doc
26.11.2014	EFSA	flupyradifurone_reporting_table_2014-06-24.doc

Appendix 1: Discussion table written procedure: Flupyradifurone

## Appendix 1: Discussion Table Written Procedure, Flupyradifurone

### 1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

Subject	Discussion Written Procedure	Conclusions Written Procedure
Data requirement 1.1  Applicant to submit the report M-402996-02-1, if not already submitted in the dossier.  See reporting table 1(14)	The summary of report M-402996-02-1 was included in the revised Volume 3 B2.	Addressed: The summary of report M-402996-02-1 was included in the revised Vol. 3 B2
Data requirement 1.2  Applicant to submit the table for plant and animal matrices, if not already included in the dossier.  See reporting table 1(64)	The table for plant and animal matrices was submitted by the applicant and included in revised Volume 3.  DE: Data requirement fulfilled.	Addressed: The table for plant and animal matrices was submitted and included in the revised Vol. 3.

## 2. Mammalian toxicology

Subject	Discussion Written Procedure	Conclusions Written Procedure
<p>Data requirement 2.1</p> <p>6-CNA cannot be regarded as a major metabolite in the rat studies (the level of 6.3% of the administered dose was obtained only in males treated with 200 mg/kg bw and was indiscriminately found in urine and faeces). Pending on the fate and behaviour section conclusion on 6-CNA calculated levels in groundwater, further toxicological data may be needed for this metabolite.</p> <p>See reporting table 2(1)</p>	<p>DE: Agreed. This assessment that was copied from the revised Volume 3 is in line with the discussion on PRAS 122 expert meeting.</p>	<p>Addressed: 6-CNA is considered a major metabolite in male rat but not in females</p> <p>Data requirement obsolete: Although insufficient data is available to assess the toxicological relevance of the metabolite in groundwater according to the respective guidance document, the assessment is not triggered according to fate and behaviour models in the environment (see section 4).</p>
<p>Data requirement 2.2</p> <p>Applicant to provide the historical control data regarding epididymis weights for the 28-day study in mice.</p> <p>See reporting table 2(10)</p>	<p>DE: Historical control data, even though not very extensive, is now included in the revised Volume 3. Thus, this requirement has been fulfilled. This historical data suggest that the lower epididymis weights in the 28-day study with flupyradifurone in mice were not abnormal but due to rather large variability. For toxicological assessment, it seems to be more important that there were no related histopathological findings and no clear dose response what one might expect if it was a real treatment-related and possible adverse effect of the test substance.</p>	<p>Addressed: The information was taken into consideration under expert consultation 2.5. The changes in epididymis weight were not considered toxicologically relevant.</p>
Data requirement 2.3	<p>DE: This additional data is given now in the revised Volume 3. Thus, the requirement has been fulfilled.</p>	<p>Addressed: The information was taken into</p>

Subject	Discussion Written Procedure	Conclusions Written Procedure
Applicant to provide the tabled results of body weight/body weight gain and haematological findings of the 2-year rat study and relevant historical control data.  See reporting table 2(18)		consideration under expert consultation 2.7 in setting the NOAEL of the 2-year rat study at 15.8 mg/kg bw per day based on reduced body weight / body weight gain, liver, lung and thyroid toxicity.
Data requirement 2.4  Applicant to provide clarification on the possible endocrine-mediated MoA of flupyradifurone. The information embedded in column 3 of the reporting table should be included.  See reporting table 2(24)	DE: According to the preliminary information from PRAS 122 (final report not available so far), no definitive conclusion on the MoA can be drawn.	Addressed: The information was taken into consideration under expert consultation 2.8 where the experts concluded that, considering the effects observed on the reproduction, an endocrine-mediated MoA could not be ruled out. A data gap was identified for level 2 tests currently indicated in the OECD Conceptual Framework, noting that further tests might be necessary pending on the outcome.
Data requirement 2.5  Applicant to provide historical control data for the in vivo micronucleus assay performed with BYI 02960-difluoroethyl-amino-furanone (study 4). See also 2(43)  See reporting table 2(38)	DE: The historical control data was provided and does not support an adverse effect of the flupyradifurone. For evaluation, the final report from the PRAS 122 meeting should be awaited. Data requirement fulfilled.	Addressed: The information has been taken into consideration under expert consultation 2.9 where the experts considered that there was sufficient evidence to conclude that DFEAF is unlikely to have genotoxic potential.

Subject	Discussion Written Procedure	Conclusions Written Procedure
<p>Data requirement 2.6</p> <p>Applicant to provide historical control data for the in vivo micronucleus assay performed with BYI 02960-difluoroethyl-amino-furanone (study 4).</p> <p>See reporting table 2(54)</p>	<p>DE: see above.</p>	<p>Data gap: A typographical error has occurred in the transcription of the data requirement (this data requirement is repeated from the above 2.5). The original data requirement in reporting table comment 2(54) was for the applicant to assess the relevance of the individual impurities present in the technical specification in comparison with the toxicological profile of the parent compound. As this issue has not been addressed, a data gap has been identified.</p>

### 3. Residues

Subject	Discussion Written Procedure	Conclusions Written Procedure
Data requirement 3.1  Applicant to submit the embedded files in column 3, if not already included in the dossier.  See reporting table 3(20)	Embedded files were submitted. Original trial report was already available, embedded files were revised tier I summaries.  DE: No comments.	Addressed  Embedded files in reporting table were submitted

#### 4. Environmental fate and behaviour

Subject	Discussion Written Procedure	Conclusions Written Procedure
Data requirement 4.1  Applicant to submit reports of fitting of aged sorption experimental results, where a range of different starting parameters are investigated, with all these optimisations being transparently reported as outlined in the draft UK guidance Beulke and van Beinum (2012). Once applicant is confident that they have demonstrated that they have robust fitted parameters for each soil, applicant to rerun tier 2b simulations both averaging the input parameters from each available soil and running simulation using results for each soil as input separately and then averaging the simulation results, as outlined in the draft UK guidance Beulke and van Beinum (2012).  Note there are no' current criteria from the TDS guidance' as there is no	DE: Robust fitted parameters for 4 soils are useful for PECgw calculation.	Data requirement fulfilled.  The applicant has, as asked for in data requirement 4.1, submitted a report on the aged sorption experimental results. See also expert consultation 4.1.

Subject	Discussion Written Procedure	Conclusions Written Procedure
agreed TDS guidance.  See reporting table 4(12)		
Data requirement 4.2  Applicant to provide PEC soil for metabolites that represent and include the situation that accumulated concentrations of the precursor active substance from repeated use over the years can occur. (worst case DT values to be used in calculations).	DE: Agreed.	Data requirement fulfilled.  The data have been submitted and the RMS has appropriately updated the DAR and the LoEP:s (December 2014).
See reporting table 4(21)  Data requirement 4.3  Applicant to address the effect of water treatment processes on the nature of residues present in surface and groundwater, when surface water or groundwater are abstracted for drinking water. Probably in the first instance, a consideration of the processes of ozonation and chlorination would appear appropriate. If an argumentation is made that	DE: Agreed.	Data gap:  Some information was provided however the assessment was not sufficient to conclude that the effects of water treatment processes on the nature of residues of the active substance and metabolites when surface water is abstracted for drinking water and metabolites when groundwater is abstracted for drinking water to address Article 4 (approval criteria for active substances) 3(b) of Regulation (EC) No 1107/2009. Therefore a data gap was identified.

Subject	Discussion Written Procedure	Conclusions Written Procedure
concentrations at the point of extraction for drinking water purposes will be low, this argumentation should cover metabolites predicted to be in groundwater and surface water, as well as the active substance. Should this consideration indicate novel compounds might be expected to be formed from water treatment, the risk to human or animal health through the consumption of drinking water containing them should be addressed  See reporting table 4(24)		
Data requirement 4.4  Applicant to provide a search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, being conducted and reported in accordance with the Guidance of EFSA on the	DE: Agreed.	Data gap: A data gap was identified. Submission of the studies found by the applicant during the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites also to clarify if all relevant metabolites were included in the search. It is not clear if all relevant metabolites were included in the scientific peer-reviewed open literature search.

Subject	Discussion Written Procedure	Conclusions Written Procedure
<p>submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) for the aqueous photolysis metabolites BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide that do not appear to have been included in the available literature review.</p> <p>See reporting table 4(42)</p>		

## 5. Ecotoxicology

Subject	Discussion Written Procedure	Conclusions Written Procedure
Data requirement 5.1  To support the discussions in the expert meeting the Applicant should submit any information available, which might even be a position paper or an argumentation.  See reporting table 5(18)	DE: BCS states that flupyradifurone is the first synthetic insecticide based on novel butenolide chemistry addressing nicotinic ACh receptors and that based on the chemical structure the compounds cannot be considered similar. It can be agreed that the chemical structure is not similar. However, since the compound is designed to act comparable to a neonicotinoid, it cannot be excluded that the effect on sensitive species is similar. Therefore, since this is the first synthetic insecticide based on the butenolide chemistry, a study on mayflies should be conducted to prove the assumption that the effect of flupyradifurone will be different compared to imidacloprid.  According to the expert meeting on imidacloprid in June 2014 (PPR Meeting 116) the study by Roessink et al. was considered reliable. In the case of imidacloprid it was considered not suitable to derive a RAC, due to the specific application pattern of imidacloprid. In fact, the study is considered suitable for deriving a RAC on national level under specific conditions (in case of imidacloprid, when exposure is only in autumn).  For this reason in our opinion the argumentation by the notifier is not sufficient to exclude a potential higher risk to ephemeroptera due to the exposure to flupyradifurone.	Data requirement fulfilled  The applicant has provided a position paper
Data requirement 5.2  Applicant to submit more comprehensive study summary of the two studies Aldershof S. & Bakker F. (2012). Furthermore the present table B.9.5.2-02 should be presented in a readable version. More detailed information will be necessary to understand the visualised results and	DE: The presentation of table B.9.5.2-02 and table B.9.5.2-03 (in the appendix document Table NL-03 and Table SWF-03) has not changed. The “new” version is exactly the same as in the updated DAR. The data needs to be presented in a readable way.  Except for presenting a statistical evaluation of the PRC in tabular form, adding a figure that demonstrates the proportion of Abbott values > 50% in the reference treatment, changing the presentation of the effect classes according to De Jong et al. (2010) and adding a plot chart the study summary for Aldershof, S: & Bakker, F: (2012a and b) provided in the Appendix is apparently the same as in the updated DAR Vol. 3 B.9.	Data requirement fulfilled  More extended study summaries had been submitted. These were transformed in an appendix (Appendix 2) to the addendum by the RMS. The information was considered in the related expert discussion (Expert consultation 5.5). The way how the studies were summarised (including readability) were good enough to be used in the meeting.

Subject	Discussion Written Procedure	Conclusions Written Procedure
<p>especially the data standing behind it (e.g. validity criterion).</p> <p>See also expert consultation 5(60).</p> <p>See reporting table 5(58)</p>		
<p>Data requirement 5.3</p> <p>Applicant to submit further information on the technical specification of the batches of the test material used in the ecotoxicity studies.</p> <p>See reporting table 5(77)</p>	<p>DE: In our opinion the data requirement is addressed.</p>	<p>Data requirement fulfilled</p> <p>The required assessment had been submitted, included and concluded in the revised Volume 4 by RMS.</p> <p>Comments from MSs suggested that this data requirement is addressed. This is supported by EFSA.</p>
<p>Data requirement 5.4</p> <p>The Applicant may wish to submit further information on the potential endocrine disruption properties, or for the lack of them, to the RMS.</p> <p>See reporting table 5(78)</p>	<p>DE: At least a section/chapter should be added addressing this issue.</p>	<p>No additional information, only a short statement was provided by the applicant. Therefore MSs could not further assess this issue.</p>
<p>Data requirement 5.5</p> <p>Applicant to provide a search of the scientific peer-reviewed open literature</p>	<p>DE: A study by study justification should be added by the applicant in order to make transparent why studies were considered not relevant.</p>	<p>Data gap:</p> <p>An additional literature search had been submitted. Due to the lack of transparency a data gap has been identified (see open point 5.18)</p>

Subject	Discussion Written Procedure	Conclusions Written Procedure
<p>relevant to the scope of the application, dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of dossier, being conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) for the aqueous photolysis metabolites BYI 02960-succinamide and BYI 02960-azabicyclosuccinamide that do not appear to have been included in the available literature review.</p> <p>See reporting table 5(79)</p>		

## TABLE OF CONTENTS

	<b>Document</b>
00	Cover page
01	Comments on the assessment report
02	Reporting table
03	Pesticides peer review meeting reports
04	Evaluation table
05	Comments on the additional information assessment
<b>06</b>	<b>Comments on the draft EFSA conclusion</b>

<b>Background</b>			
<b>No.</b>	<b>Reference (e.g. conclusion text, list of endpoints, evaluation table etc)</b>	<b>Member State comment</b>	<b>EFSA response to comment</b>
1	Summary	NL: There is a general sentence that a data gap was identified in relation to the search of the open literature. This point is also addressed in the “mammalian tox” section of the summary.	Agreed; the sentence has been deleted in the mammalian toxicology paragraph.
2	7. Data gaps, 7.1 data gaps identified for the representative uses evaluated, 1 <sup>st</sup> point (also reference to sections 2, 4 and 5)	<p>NL: It was already clarified that all relevant metabolites were included in the search.</p> <p>A literature search and review was provided by the applicant. The search has been conducted in line with the EFSA guidance. Of all identified papers (342) the relevant ones (136) have been selected by the applicant in a transparent way using a text mining filter. The applicant provided a general justification for evaluating the relevant papers. As no study-by-study justifications were given the RMS can not properly verify whether the 136 relevant papers were correctly evaluated in terms of reliability/validity/acceptability for regulatory use. The one study that was considered relevant by the applicant is evaluated in the DAR. RMS notes that flupyradifurone is a new active substance worldwide. Therefore, public literature is not expected to be an important new information source for the active substance itself.</p> <p>NL proposes the following wording for the data gap on literature search: “Transparent study-by-study justification of the relevant studies found by the applicant during the search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 2, section 4 and section 5)”</p> <p>(Explanation: the notifier selected in the literature search 342 papers of which they thought 136 could be relevant but only 1</p>	EFSA agrees that it was clarified in the amended DAR that the two aqueous photolysis metabolites had been the subject of a second literature search, section 7 of the conclusion and the evaluation table entry against Data requirement 4.4 have been amended accordingly. We also agree that our guidance does not immediately require all papers to be provided. We agree that in the first instance the data gap should be for a study by study justification. The wording has been updated as suggested.

**Member States' comments on the draft EFSA Conclusion on Flupyradifurone (RMS: NL)**  
**Pesticides Peer Review Written Procedure: January 2015**

(30-01-2015) 2/10

<b>Background</b>			
<b>No.</b>	<b>Reference</b> (e.g. conclusion text, list of endpoints, evaluation table etc)	<b>Member State comment</b>	<b>EFSA response to comment</b>
		study was indeed relevant. This study was submitted and evaluated in the DAR. However, the RMS could not verify whether the other 135 studies were indeed not relevant as only a general justification was given for all 135 studies. Therefore we think that the data gap should be as stated above.)	
3	7. Data gaps, 7.1 data gaps identified for the representative uses evaluated, 7 <sup>th</sup> point	NL: Please correct the sentence: <i>Further information is required to address the long-term risk to small herbivorous mammals from dietary routes in lettuce (relevant for the representative field uses on field-lettuce; submission date proposed by the applicant: unknown; see sections 5).</i>	Thank you for your comment, the document has been amended
4	7. Data gaps, 7.1 data gaps identified for the representative uses evaluated, 8 <sup>th</sup> point	NL: Please correct the sentence: <i>Further information is required to address the chronic risk to aquatic invertebrates (relevant for the representative field uses on field-lettuce; submission date proposed by the applicant: unknown; see section 5).</i>	Thank you for your comment, the document has been amended
5	8.1 Particular conditions proposed for the representative uses evaluated, 3 <sup>rd</sup> bullet point	NL: Please add: <i>Mitigation measures comparable to the effects of a 30-metres non-spray buffer zone for hops or 5-metres non-spray buffer zone for field uses in lettuce were needed to address the risk for non-target arthropods (see Section 5).</i>	Thank you for your comment, the document has been amended

<b>Identity, physical/chemical/technical properties and methods of analysis</b>			
<b>No.</b>	<b>Reference</b> (e.g. conclusion text, list of endpoints, evaluation table etc)	<b>Member State comment</b>	<b>EFSA response to comment</b>
1	EFSA conclusion, <b>CONCLUSIONS OF THE EVALUATION IDENTITY, PHYSICAL/CHEMICAL/TECHNICAL</b>	NL: The following is stated here:  The proposed specification is based on batch data from pilot scale production. <i>It should be noted that the 5-batch analysis from full</i>	Disagree:  In Vol. 4 RMS states: "Specification limits are now based on a pilot plant scale and to set the

<b>Identity, physical/chemical/technical properties and methods of analysis</b>			
<b>No.</b>	<b>Reference (e.g. conclusion text, list of endpoints, evaluation table etc)</b>	<b>Member State comment</b>	<b>EFSA response to comment</b>
	PROPERTIES AND METHODS OF ANALYSIS	<p><i>scale production will need to be reconsidered.</i> The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of flupyradifurone or the representative formulation.</p> <p>NL would like the italic text to be removed, since when industrial full scale data will be available, technical equivalence evaluation will be performed. And as this will have no consequences on the inclusion of Flupyradifurone at the moment, since appropriate batch data are available and as pilot batch data can be considered as such, this should be removed.</p> <p>Furthermore, no data gaps were identified in the area of identity, physical/chemical/technical properties and methods of analysis. To avoid confusion here is an extra argument to delete the indicated text as indicated above in italic.</p>	<p>specification there are some uncertainties. End of 2014 batch data on the industrial scale is supposed to be available. If for procedural reasons these data could not be included the issues to be clarified regarding the pilot batch remain open, see justification of the specified limits.”</p> <p>In the RT 1(5) on supporting comment of one MS the RMS agreed to conclude on the final specification when data from full scale production are available. (see p. 3/330)</p>
2	List of end points, Analytical methods for residues, residue definitions	<p>NL: Please clarify the difference between Flupyradifurone, DFA, sum of both expressed as flupyradifurone equivalents</p> <p>As stated originally in the List of end points and Two separate residue definitions:</p> <ol style="list-style-type: none"> <li>1) Flupyradifurone</li> <li>2) DFA, expressed as DFA</li> </ol> <p>as is stated now as residue definition since EFSA dec 2014 amendment of the list of end points.</p>	<p>For enforcement, the residue definition was intensively discussed in the teleconference meeting 107, where the three following different proposals were considered:</p> <ol style="list-style-type: none"> <li>1) Residue definition limited to flupyradifurone only: This definition was concluded to be inappropriate, since unable to consider the significant DFA residue levels in rotational crops, where parent flupyradifurone is almost not present. Moreover for primary crops, the setting of reliable conversion factors (CF) for risk assessment is not possible for some plant commodities, since the ratio (flupyradifurone + DFA)/flupyradifurone is constantly changing with the PHI (e.g. CF 2 and 10</li> </ol>

<b>Identity, physical/chemical/technical properties and methods of analysis</b>			
<b>No.</b>	<b>Reference (e.g. conclusion text, list of endpoints, evaluation table etc)</b>	<b>Member State comment</b>	<b>EFSA response to comment</b>
			<p>respectively, at 3 and 14 day PHI on cucurbits).</p> <p>2) Residue definition proposed as sum of flupyradifurone and DFA: This residue definition was indeed concluded to be inappropriate to monitor flupyradifurone residues, since the MRLs derived from the uses of flupyradifurone on primary crops would be covered by the default MRL values proposed for rotational crops and resulting from the significant presence of DFA in rotational crops.</p> <p>3) Two separate residue definitions for monitoring, flupyradifurone and DFA, respectively: It was finally agreed that two separate residue definitions would be required, as "flupyradifurone"; to consider the residues resulting from the uses of the active substance on primary crops, and as "DFA"; to consider DFA residues in rotational crops.</p>

<b>Mammalian toxicity</b>			
<b>No.</b>	<b>Reference (e.g. conclusion text, list of endpoints, evaluation table etc)</b>	<b>Member State comment</b>	<b>EFSA response to comment</b>
		NL: No comments.	Noted.
1	7. Data Gaps	DE: The data gap regarding the outstanding assessment of the toxicological relevance of the individual impurities is supported. In case of an approval of flupyradifurone the information should be required as Confirmatory Information.	Noted. Decisions regarding confirmatory information requests are outside EFSA's remit.

<b>Residues</b>			
<b>No.</b>	<b>Reference (e.g. conclusion text, list of endpoints, evaluation table etc)</b>	<b>Member State comment</b>	<b>EFSA response to comment</b>
1	Conclusion text, 3.1, pag 10, 2 <sup>nd</sup> paragraph	NL: typo, metabolism in plant proceeds via	Addressed
2	Conclusion text, 3.1, pag 11, 3 <sup>rd</sup> paragraph	NL: typo, dosed with the DFA metabolite should be requested to derived	Addressed
3	LoEP; consumer risk assessment	NL: rows with TMDI endpoints to be removed, since text is crossed out?	Addressed
4	LoeP, processing factor	NL: table with processing factors is crossed out. To be removed? If yes, then why?	Processing factor table, where separate PFs for flupyradifurone and DFA are proposed and considering the representative crops and the crops listed in the MRL applications has been added in the LoEP (unfortunately, this amended table has been omitted in the draft LoEP circulated for commenting).
5	Overall	NL: it appears that the transfer factors for calculating animal MRLs were not taken into consideration (also not in the revised DAR of December).	MRL calculations for animal matrices using transfer factor and taking into account the HR values observed in animal matrices at the relevant feeding level, have been considered by EFSA and are effectively not available in the revised DAR. Revised ER (part I and part II) considering the intended EU uses listed in the MRL application and the setting of MRLs according to the residue definitions agreed in the conclusion of the peer review is missing indeed. MRL proposals have been reconsidered by EFSA and reported in the LoEP (residue trials summary table).
6	Appendix A	NL: Appendix A containing the MRL evaluation was not available for commenting	Appendix A of the EFSA conclusion is the list of end points as explained in the relevant header fort that

**Member States' comments on the draft EFSA Conclusion on Flupyradifurone (RMS: NL)**  
**Pesticides Peer Review Written Procedure: January 2015**

(30-01-2015) 6/10

<b>Residues</b>			
<b>No.</b>	<b>Reference</b> (e.g. conclusion text, list of endpoints, evaluation table etc)	<b>Member State comment</b>	<b>EFSA response to comment</b>
			section. For the written procedure the list of end points is frequently provided as a separate document, like in this case of flupyradifurone.
7	7. Data Gaps	DE: The data gap regarding missing field rotational crop studies considering realistic plant back intervals for the crops considered providing information on the flupyradifurone and DFA residue levels in soil is supported. In case of an approval of flupyradifurone the studies should be required as Confirmatory Information.	Sentences have been added in section 8 of the conclusion to make clear that residues in animal matrices and in rotational crops have not been sufficiently addressed and therefore, additional studies are required (see data gap in sections 7).
8	7. Data Gaps	DE: The data gap regarding missing animal feeding studies conducted with the metabolite DFA is supported. In case of an approval of flupyradifurone the studies should be required as Confirmatory Information.	See comments 7
9	9. Concerns	DE: The concern regarding the indoor use of flupyradifurone on lettuce for consumers is supported. Conditions of authorisation must include risk mitigation measures, where appropriate.	Concern related to the indoor use of flupyradifurone on lettuce is confirmed in the conclusion.

<b>Environmental fate and behaviour</b>			
<b>No.</b>	<b>Reference (e.g. conclusion text, list of endpoints, evaluation table etc)</b>	<b>Member State comment</b>	<b>EFSA response to comment</b>
1	Conclusion text, section 4, pag 13, 1 <sup>nd</sup> paragraph	NL: the percentage used in the LoEP is 0.2 % instead of 2.0 % mentioned in the text. According to FOCUS AIR this should be 0.2 %	Agreed. This has been corrected and a reference to the FOCUS (2008) report has been included in the text as the source of the 0.2% value.
2	Conclusion text, section 4, pag 13, 3 <sup>rd</sup> paragraph	NL: typo 6-CAN should be 6-CNA	Agreed. Thank for identifying this.
3	Conclusion text, section 7.1, pag 20, paragraph	NL: Information on the effect of water treatment processes is requested and referred to section 4. Since in the DAR this point is addressed and accepted by the RMS, this is to the RMS opinion not a data gap and should be removed from the section 7.1. In section 4 there is also no data gap mentioned for this point.	Whilst EFSA acknowledges some argumentation was provided by the applicant to address this issue, we have a difference in opinion to the RMS on how acceptable the argumentation was. EFSA considers that the information submitted is rather qualitative in nature and not robust enough, being more an expectation of low residues at the point of water abstraction than having been demonstrated. We have therefore maintained the data gap in the conclusion. We have added text to section 4 and in this text have acknowledged that there is a difference of opinion between EFSA and the RMS regarding this issue.
4	LoEP longterm PECsoil of BYI02960	NL: The calculated long term PECsoil should be 0.310 mg/kg instead of 0.2766. The PECs, max over 5 cm is 0.250 mg/kg and the PECs long term plateau background is 0.06 mg/kg resulting in a total of 0.31 mg/kg	Disagreed, we have rechecked and the value EFSA calculated was correct. The long term plateau concentration over 20cm is 0.0618 and when the last 2 applications in the final year are added over 5cm this becomes 0.2766 (when assuming 25% crop interception and a 10 day application interval). The application interval assumed for the calculation was not indicated in the list of endpoints. EFSA has now added this information (which was defined by the applicant in their GAP table and is in line with the PECgw calculations). Note EFSA calculated these

<b>Environmental fate and behaviour</b>			
<b>No.</b>	<b>Reference (e.g. conclusion text, list of endpoints, evaluation table etc)</b>	<b>Member State comment</b>	<b>EFSA response to comment</b>
			concentrations using the tool ESCAPE: 1.0 (12 Jan 2011).
5	LoEP PECsw	NL: please include the volume used for static water body per m <sup>2</sup> in the initial box this makes it easier to calculate the PECsw. According to the FOCUS TOXWA ditch the volume is 300 L for 1 m <sup>2</sup> . If this is used the PECsw is 0.1667 mg/L with an aerial loading of 50 ug/m <sup>2</sup> (based on the 0.2% emission).	Agreed, the list of endpoints has been corrected as indicated.
6	LOeP PECgw	NL: two input boxes for flupyradifurone and the metabolites are presented. Remove the last ones.	Agreed the excess redundant repeated boxes have been removed.
7	LOeP PECgw application rate box	NL: Application rate remove the “annual and” for hops Number of application remove the “annual and” for hops Time of application remove the “annual and” for hops Plant interception remove the “annual and” for hops NL: typo glasshouse instead of glass (at the interval of the lettuce) NL: remove footnote *** glass house applications worst....	Agreed, the list of endpoints has been corrected as indicated.
8	9. Concerns	DE: Member states must pay particular attention to the potential for ground water contamination where flupyradifurone is applied. Conditions of authorisation must include risk mitigation measures, where appropriate.	Your comment is noted. However what action members states might need to take and the need for risk mitigation measures are management issues and not the role of EFSA. We only provide exposure / risk assessments incorporating mitigation when this has already been proposed by the applicant and or RMS, which is not the case here in relation to the groundwater exposure assessment. Therefore no change has been made to section 9 of the conclusion as a result of this comment.

<b>Ecotoxicology</b>			
No.	Reference (e.g. conclusion text, list of endpoints, evaluation table etc)	Member State comment	EFSA response to comment
1	5. Ecotoxicology, 3 <sup>rd</sup> paragraph (b&m), 2 <sup>nd</sup> sentence	NL: LT risk for mammals is only identified for the field uses in lettuce. Please correct the sentence: <i>for long-term risk assessment to mammals and all the representative field uses a high risk was identified at first tier.</i>	This sentence is explaining the situation only for the 1rst tier (as indicated in the sentence). After refinement (called as 2 <sup>nd</sup> tier in the LoEP), the hop scenario was indeed resolved. This is appropriately acknowledged in the following part of the paragraph. Also the data gap in section 7 includes only lettuce. No changes in the text are deemed necessary.
2	5. Ecotoxicology, 4 <sup>th</sup> paragraph (aquatic organisms), 4 <sup>th</sup> sentence	NL: Please correct a typo, and consider to revise the sentence on the type of substance that flupyradifurone is: .. <i>since mayflies seems to have a high sensitivity to the a group of pesticides that flupyradifurone belongs to is related to.</i>	The text was amended accordingly.
3	5. Ecotoxicology, 4 <sup>th</sup> paragraph (aquatic organisms), 6 <sup>th</sup> sentence	NL: Tyop: 6-CAN should be 6-CNA	Thanks, the name of the metabolite was corrected.
4	LoEP, bee studies, semi-field/field	NL: I noticed only now that I stated in the LoEP that the feeding phase of the long-term feeding study took seven weeks. This should be six (42 days). It would be good if you could correct this.	Thanks, EFSA made this correction in the LoEP.
5	Final addendum (pdf file)	NL: Three ecotox documents from November 2014 (Addendum 1 to B.9 and two appendices to addendum 1) are included in the 'Final Addendum' (pdf file). It is not really clear to me what the intention of this 'final addendum' is, but it seems to be the collected dossier that people can consult after inclusion. It should be noted that the addendum from November is only a working document, made for the ppr meeting, and it should not be included in the final dossier. The updated DAR of December 2014 contains all information that is included in the documents of November 2014 (so, also the information from the appendices), plus additional considerations from the ppr meeting. Therefore, it	Thank you for your clarification. The 'final addendum' will be amended.

<b>Ecotoxicology</b>			
<b>No.</b>	<b>Reference</b> (e.g. conclusion text, list of endpoints, evaluation table etc)	<b>Member State comment</b>	<b>EFSA response to comment</b>
		is recommended that the addendum 1 and its two appendices are removed from the 'Final addendum'.	
6	List of endpoints, classification and proposed labelling	DE: The respective M-Factors for the acute and chronic classification are missing. (Acute should be 10 for EC50 ( <i>C. riparius</i> ) = 0.0617 mg a.s./L and chronic should be 10 for NOEC ( <i>C. riparius</i> ) = 0.00681 mg a.s./L). Please add accordingly.	Strictly considering the relevant regulation, the classification should be based on crustaceans (and not necessarily on chironomus). The C&L in the List of endpoints is only a proposal from the RMS/peer review (no comments were made during the peer review) and should not be considered as a formal proposal. The formal C&L will be considered by European Chemicals Agency in due time. MSs may establish or amend C&L of authorised products for their own purposes.
7	EFSA Conclusion 8.1	DE: Mitigation measures such as a 30 m non spray buffer zone are not assigned in Germany. A product with this substance would not be approved in Germany under these conditions if it is not possible to mitigate exposure accordingly by other measures.	Noted.

<b>Other</b>			
<b>No.</b>	<b>Reference</b> (e.g. conclusion text, list of endpoints, evaluation table etc)	<b>Member State comment</b>	<b>EFSA response to comment</b>
		No comments	Addressed.