EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Safety of the Food Chain
Pesticides and Biocides

COMMISSION STAFF WORKING DOCUMENT[1]

Flupyradifurone
SANTE/11649/2015/ rev 1
9 October 2015

Final Review report for the active substance **flupyradifurone**
Finalised in the Standing Committee on Plants, Animals, Food and Feed
at its meeting on 9 October 2015
in view of the approval of flupyradifurone as active substance in accordance with Regulation (EC) No 1107/2009[2]

1. Procedure followed for the evaluation process

This review report has been established as a result of the evaluation of the new active substance flupyradifurone, made in the context of the work provided for in Articles 7 to 13 of Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC, with a view to the possible approval of this substance for the use in plant protection products.

In accordance with the provisions of Article 7 of that Regulation, the authorities of the Netherlands received on 8 May 2012 an application from Bayer CropScience AG, hereafter referred to as the applicant, for the approval of the active substance flupyradifurone for use in plant protection products. The authorities of the Netherlands indicated to the Commission on 21 June 2012 the results of their examination of the completeness of the dossier satisfying the requirements of Article 8, according to the provisions of Article 9 of the Regulation. Subsequently, and in accordance with the requirements of Article 9(3), a dossier on flupyradifurone was distributed to the Member States, the European Food Safety Authority (EFSA) and the Commission.

Thereupon, the Netherlands as rapporteur Member State started the detailed examination of the dossier provided by the applicant. According to the provisions of Article 11, the rapporteur Member State shall prepare and submit to the Commission and EFSA within twelve months a report (the draft assessment report), assessing whether the active substance can be expected to meet the criteria provided for in Article 4 of the Regulation.

The Netherlands submitted that draft assessment report to the Commission and EFSA on 1 February 2014.

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1 Does not necessarily represent the views of the Commission.
2 OJ L 309, 24.11.2009, p. 1.

On 5 February 2014, EFSA circulated the draft assessment report to Member States and the applicant and, in addition, organised a public consultation on it, in line with the provisions of Article 12(1) of the Regulation.

EFSA organised a consultation to review the draft assessment report and the comments received thereon (peer review) in accordance with the provisions of Article 12(2) and 12(3). In this framework, EFSA decided to request additional information from the applicant and that there was a need to conduct an expert consultation.

According to the provisions of Article 12(2) of the Regulation, EFSA sent to the Commission its conclusion on the risk assessment [Conclusion on the peer review of the pesticide risk assessment of the active substance flupyradifurone) (approved: 30 January 2015)[3]]. This conclusion refers to background document A (draft assessment report) and background document B (EFSA peer review report).

According to the provisions of Article 13 of that Regulation, the Commission produced a draft review report and a draft Regulation on flupyradifurone. The Commission referred the draft review report to the applicant for commenting and to the Standing Committee on Plants, Animals, Food and Feed, for examination on 13 July 2015. The draft review report was finalised in the meeting of the Standing Committee on 9 October 2015.

The present review report contains the conclusions of the final examination by the Standing Committee. Given the importance of the conclusion of EFSA, and the comments and clarifications submitted after the conclusion of EFSA (background document C), these documents are also considered to be part of this review report.

2. Purposes of this review report

This review report, including the background documents and appendices hereto, has been developed and finalised in support of **Commission Implementing Regulation (EU) 2015/2084**[4] concerning the approval of flupyradifurone as active substance under Regulation (EC) No 1107/2009, and to assist the Member States in decisions on individual plant protection products containing flupyradifurone they have to take in accordance with the provisions of that Regulation, and in particular the provisions of Article 29(1) of Regulation (EC) No 1107/2009 and the uniform principles laid down in Regulation (EU) No 546/2011.

This review report provides also for the evaluation required under part I, Section A.2 (b) of the above mentioned uniform principles, as well as under several specific sections of chapter B of these principles. In these sections it is provided that Member States, in evaluating applications and granting authorisations, shall take into account the information concerning the requirements of Regulation (EU) No 544/2011, submitted for the purpose of approval of the active substances, as well as the result of the evaluation of those data.

[3] EFSA Journal 2015;13(2):4020 [101 pp.]. Conclusion on the peer review of the pesticide risk assessment of the active substance flupyradifurone. doi:10.2903/j.efsa.2015.4020 Available online: www.efsa.europa.eu/efsajournal.

[4] OJ L 302, 19.11.2015, p. 89–92.

In accordance with the provisions of Article 10 of Regulation (EU) No 188/2011, this review report will be made available to the public.

The information in this review report is, at least partly, based on information which is confidential and/or protected under the provisions of Regulation (EC) No 1107/2009. It is therefore recommended that this review report would not be accepted to support any registration outside the context of that Regulation, e.g. in third countries, for which the applicant has not demonstrated to have regulatory access to the information on which this review report is based.

3. Overall conclusion in the context of Regulation (EC) No 1107/2009

The overall conclusion from the evaluation is that it may be expected that plant protection products containing flupyradifurone will fulfil the safety requirements laid down in Article 4(1) – (3) of Regulation (EC) No 1107/2009. This conclusion is however subject to compliance with the particular requirements in sections 4, 5, 6 and 7 of this report, as well as to the implementation of the provisions of Article 29(1) of Regulation (EC) No 1107/2009 and the uniform principles laid down in Regulation (EU) No 546/2011, for each flupyradifurone containing plant protection product for which Member States will grant or review the authorisation.

Furthermore, these conclusions were reached within the framework of the uses which were proposed and supported by the data submitter and mentioned in the summary of representative uses evaluated (attached as Appendix II to this review report).

Extension of the use pattern beyond those described above will require an evaluation at Member State level in order to establish whether the proposed extensions of use can satisfy the requirements of Article 29(1) of Regulation (EC) No 1107/2009 and of the uniform principles laid down in Regulation (EU) No 546/2011.

The following reference values have been finalised as part of this evaluation:
ADI: 0.064 mg/kg bw per day,
ARfD: 0.15 mg/kg bw,
AOEL: 0.064 mg/kg bw per day.

With particular regard to residues, the review has established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The maximum international estimated daily intake (IEDI) was estimated to be 17% of the Acceptable Daily Intake (ADI), based on EFSA PRIMo Model rev.2. Regarding acute exposure, the International Estimated Short-Term Intake (IESTI) is not higher than 57% of the Acute Reference Dose (ARfD).

The review has identified acceptable exposure scenarios for operators, workers and bystanders, which require however to be confirmed for each plant protection product in accordance with the relevant sections of the above mentioned uniform principles.

The review has also concluded that under the proposed and supported conditions of use there are no unacceptable effects on the environment, as provided for in Article 4(3)(e) of Regulation (EC) No 1107/2009, provided that certain conditions are taken into account as detailed in section 6 of this report.

The following points were considered as open by the EFSA (2015) for flupyradifurone:

- *Assessment of the relevance of individual impurities present in the technical specification in comparison with the toxicological profile of the parent compound.*

  As the specification is based on pilot plant production and needs to be confirmed following commercial scale production, the equivalence of the final specification with the batches used in the toxicological assessment should be confirmed at this stage including the relevance of impurities. This is requested as confirmatory information.

- *Flupyradifurone is not classified or proposed to be classified as carcinogenic category 2 or toxic for reproduction category 2, in accordance with the provisions of Regulation (EC) No 1272/2008, and therefore the conditions of the interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine disrupting properties are not met. However, an endocrine-mediated mode of action could not be ruled out regarding the reproductive effects observed in the multigeneration toxicity study (reduced number of implantation sites and oestrus cycle, reduced litter size - reduced number of pups born and higher number of stillborn) and the potential for endocrine disrupting effects could not be finalised.*

  As regards the current regulatory framework, flupyradifurone shall not be considered an endocrine disruptor since it does not fulfil the interim criteria to identify endocrine disruptors, as set in Annex II paragraph 3.6.5. As regards the adverse effects highlighted by EFSA, they were considered when deciding on the NOAEL that has been retained for setting the AOEL and the ADI. As a consequence, it can be considered that these adverse effects are adequately covered by the current risk assessment.

4. Identity and Physical/chemical properties

The main identity of flupyradifurone is given in Appendix I.

At the time of evaluation no FAO specification was allocated.

The active substance shall have a minimum purity of 960 g/kg.

The review has established that for the active substance as specified by Bayer CropScience AG in the application, there are no manufacturing impurities which are considered to be of toxicological, ecotoxicological and/or environmental concern.

5. Endpoints and related information

In order to facilitate Member States, in granting or reviewing authorisations, to apply adequately the provisions of Article 29(1) of Regulation (EC) No 1107/2009 and the uniform principles laid down in Regulation (EU) No 546/2011, the most important endpoints were identified during the evaluation process. These endpoints are listed in the conclusion of EFSA, and in section 3 of this report.

6. Particular conditions to be taken into account on short term basis by Member States in relation to the granting of authorisations of plant protection products containing flupyradifurone.

On the basis of the proposed and supported uses (as listed in Appendix II), the following issue has been identified as requiring particular and short term attention from all Member States, in the framework of any authorisations to be granted, varied or withdrawn, as appropriate:

Member States shall pay particular attention to:

- the protection of workers and operators;
- the risk to non-target arthropods, aquatic invertebrates and small herbivorous mammals;
- the protection of groundwater, when the substance is applied in regions with vulnerable soil and/or climatic conditions;
- residues in animal matrices and rotational crops.

Conditions of use shall include risk mitigation measures, where appropriate.

7. List of studies to be generated

Further studies were identified which were at this stage considered necessary in relation to the approval of flupyradifurone under the current approval conditions.

The applicant shall submit confirmatory information as regards:

1. The technical specification of the active substance as manufactured (based on commercial scale production) including the relevance of some individual impurities;
2. The compliance of the toxicity batches with the confirmed technical specification;

The applicant shall submit that information mentioned in points 1 and 2 to the Commission, the Member States and the Authority by 18/5/2016.

3. The effect of water treatment processes on the nature of residues present in surface and groundwater, when surface water or groundwater is abstracted for drinking water.

The applicant shall submit the relevant information mentioned in point 3 to the Commission, the Member States and the Authority two years after adoption of a guidance document on evaluation of the effect of water treatment processes on the nature of residues present in surface and groundwater.

Some endpoints however may require the generation or submission of additional studies to be submitted to the Member States in order to ensure authorisations for use under certain conditions.
A complete list of studies to be generated, still ongoing or available but not peer reviewed can be found in the relevant part of the EFSA Conclusion (page 20).

8. Information on studies with claimed data protection

For information of any interested parties, the rapporteur Member State will keep available a document which gives information about the studies for which the sole data submitter has claimed data protection and which during the evaluation process were considered as essential with a view to approval under Regulation (EC) No 1107/2009. This information is only given to facilitate the

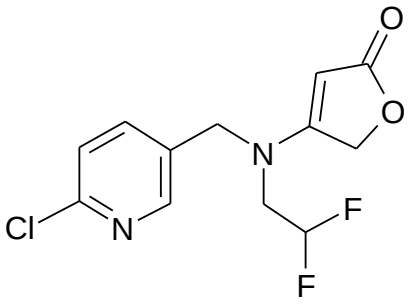
operation of the provisions of Article 62 of Regulation (EC) No 1107/2009 in the Member States. It is based on the best information available but it does not prejudice any rights or obligations of Member States or operators with regard to its uses in the implementation of the provisions of Article 62 of Regulation (EC) No 1107/2009 and neither does it commit the Commission.

9. Updating of this review report

The information in this report may require to be updated from time to time in order to take account of technical and scientific developments as well as of the results of the examination of any information referred to the Commission in the framework of Articles 13, 21, 38, 44, 56 of Regulation (EC) No 1107/2009. Any such adaptation will be finalised in the Standing Committee on Plants, Animals, Food and Feed, in connection with any amendment of the approval conditions for flupyradifurone.

APPENDIX I
Main identity

FLUPYRADIFURONE

Common Name (ISO)	Flupyradifurone
Chemical name (IUPAC)	4-[(6-chloro-3-pyridylmethyl)(2,2-difluoroethyl)amino]furan-2(5H)-one
Chemical name (CA)	4-[[(6-chloro-3-pyridinyl)methyl](2,2-difluoroethyl)amino]-2(5H)-furanone
CIPAC No	not allocated
CAS No	951659-40-8
EEC No (EINECS or ELINCS)	not allocated
FAO Specification	not applicable
Minimum purity of the active substance as manufactured (g/kg)	Min. 960 g/kg
Molecular formula	C12 H11Cl F2 N2 O2
Molar mass	288.68 g/mol
Structural formula	

APPENDIX II

Summary of representative uses evaluated

FLUPYRADIFURONE

Crop and/or situation (a)	Country	Product Name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (m)	Remarks:
					Type (d-f)	Conc. of as (i)	method kind (f-h)	BBCH stage & season (j)	number min-max (k)	interval between appls (min days)	g a.s./ hL min-max (l)	Water L/ha min-max	g a.s./ ha min-max (l)		
Representative uses															
Hops	N-EU (residue zone)	Sivanto SL 200	F	Aphids Phorodon humuli	SL	200	spray	31-75 May-July.	1	n.a.	4.5-7.5	2000-3300	150	21	Biennial application proposed
Lettuce	N/S-EU (residue zone)	Sivanto SL 200	F	Aphids, Nasonovia ribisnigri	SL	200	spray	12-49 May-Oct	1	n.a.	12.5-25	500-1000	125	10	Max 1 application per 24 months
Lettuce	N/S-EU (residue zone)	Sivanto SL 200	F	Aphids, Nasonovia ribisnigr	SL	200	spray	41-49 May-Oct	1	n.a.	12.5-25	500-1000	125	3	Max 1 application per 12 months

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide formulation types and international coding system
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(j) Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of applications possible under practical conditions of use
(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI - minimum pre-harvest interval