Conclusion regarding the peer review of the pesticide risk assessment of the active substance

spiromesifen

finalised: 13 June 2007

(revision of 9 July 2007 with replaced names of non-relevant impurities)

SUMMARY

Spiromesifen is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[1] United Kingdom received an application from Bayer CropScience for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/105/EC[2].

Following the agreement between the EU-Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State United Kingdom made the report of its initial evaluation of the dossier on spiromesifen, hereafter referred to as the draft assessment report (DAR), available on 20 February 2004. This draft assessment report was distributed for consultation to the Member States and the notifier on 16 April 2004.

The peer review was initiated on 16 April 2004 by dispatching the draft assessment report for consultation of the Member States and the notifier. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting in November 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in September 2006.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 26 April 2007 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide as proposed by the applicant that comprises broadcast spraying to cucumber, courgette, pepper, tomato, eggplant (aubergine), French bean, melon, strawberry and ornamentals in permanent greenhouse only. Full details of the representative uses evaluated can be found in the attached list of

[1] OJ No L 230, 19.8.1991, p.1 as last amended by OJ L 106, 24.4.2007, p.14
[2] OJ No L 43, 18.2.2003, p.45

endpoints. It should be note that this active also has acaricidal properties but only its use as an insecticide have been considered in the DAR and in this conclusion.
The representative formulated product for the evaluation was "Oberon SC 240 (BSN 2060 SC 240", a suspension concentrate (SC).

Insufficient methods are available to monitor all compounds given in the respective residue definition. Residues of spiromesifen in food of plant origin can be determined with a multi-method (The German S19 method has been validated) however, no method is currently available for spiromesifen-enol which forms part of the residue definition in plants. For the other matrices only single methods are available to determine residues of spiromesifen and spiromesifen-enol in soil and water and spiromesifen in air. However, it should be noted that the LOQ for air is not sufficient.
Some analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. There is no method available for the relevant impurity in the plant protection product.

Spiromesifen has a low acute oral, dermal and inhalational toxicity in rats. It is not a skin or eye irritant. It is a skin sensitiser (the risk phrase R43 “May cause sensitisation by skin contact” was proposed). Histological findings in adrenals due to decreased plasma cholesterol levels were seen in short-term and long-term studies in rodents, together with induction of microsomal hepatic enzymes, also present in dogs. Spiromesifen did not show any genotoxic and carcinogenic potential. The relevant repeat dose NOAEL is 3 mg/kg bw/day. Spiromesifen was tested in reproductive and developmental toxicity studies showing effects only as a consequence of maternal toxicity (reduced oestrus cycling frequency, increased number of ovarian primordial follicles, slightly delayed maturation of external sexual organs in weanlings and slightly more advanced ossification of phalangeal and skull bones). The parental and offspring NOAEL is 30 ppm (about 3.3 mg/kg bw/day), while the reproductive NOAEL is 120 ppm (equal to 14.2 mg/kg bw/day). The maternal and developmental NOAEL is 10 mg/kg bw/day. Spiromesifen did not raise any concern for neurotoxic effects. The Acceptable Daily Intake was established to be 0.03 mg/kg bw/day, based on the relevant long term toxicity NOAEL of 3 mg/kg bw/day (short term and long term toxicity in mouse) applying a safety factor of 100; an Acute Reference Dose of 2 mg/kg bw is proposed based on applying a 100-fold uncertainty factor to the NOAEL of 200 mg/kg bw/day from an acute neurotoxicity study in rats. An Acceptable Operator Exposure Level of 0.015 mg/kg bw/day was set based on the relevant NOAEL of 3 mg/kg bw/day, using an assessment factor of 100 and correction for incomplete oral absorption (50%). Levels of systemic exposure for operators applying spiromesifen are estimated to be below the AOEL for operators wearing protective gloves when mixing and loading and a protective coverall and protective gloves during application. The estimated worker exposure is 45% and 25% of the AOEL for vegetables and ornamentals, respectively. Bystanders are unlikely to be exposed to spiromesifen for applications in greenhouses.

Metabolism of spiromesifen was investigated in tomato, lettuce and cotton. The picture of metabolism was similar across the tested crops. A significant reaction in spiromesifen metabolism is

the cleavage of the ester bond forming spiromesifen-enol (M01[3]). The available data on rotational crop metabolism show a similar profile of metabolism compared to the primary crop. However, the metabolite M02[4] and its conjugates are present in higher proportions in the rotational crop compared to the primary crops and are the most abundant residues in rotated crops. Currently only rotation of soil grown fruiting vegetables with fruiting vegetables has been assessed, and therefore further data are necessary to address the potential for uptake of residues in other crops that are realistically expected to occur in crop rotations, depending on individual MS practices.

A sufficient number of valid residues trials are available to support the consumer risk assessment and MRL proposals for all notified representative uses except for the use in peppers, as these trials were not conducted at the appropriate application rate.

Investigation of metabolism and residue levels in livestock and food of animal origin respectively is currently not required as none of the crops concerned by the notified representative uses in greenhouses (primary as well as rotational crops) are usually fed to livestock.

The consumer exposure through residues from crops treated with spiromesifen according to the notified GAP is expected to be well below the toxicological reference values for spiromesifen (ADI, ARfD) for the considered consumer groups adults, children and toddlers.

Assessment on fate and behaviour in the environment was based on representative uses for glasshouse, assuming a permanent glasshouse that stays after the harvest at least until residues of parent and metabolites in soil are below the LOQ.

Spiromesifen is low to moderately persistent in soil under dark aerobic conditions at 20 ºC. It is hydrolysed to form the major soil metabolite M01 (max 85 % AR after 14 d) that oxidises to major metabolite M09[5] (max 14.1 % AR after 90 d). Both metabolites were shown to be of low to high persistence in soil.

Photolysis does not seem to contribute to the environmental degradation of spiromesifen in soil but may accelerate the degradation of its metabolite M01.

PEC soil were calculated based on worst case laboratory half lives and maximum formation of metabolites M01 and M09.

The HPLC method following draft OCDE guideline 121 was used to estimate the Koc value for spiromesifen. According to this test spiromesifen should be classified as immobile in soil. RMS proposed that, were the applicant to consider outdoor uses, a standard adsorption / desorption study at neutral conditions should be provided. According to the equilibrium batch adsorption/desorption studies, metabolites M01 and M09 were very high mobile in soil.

Hydrolysis of spiromesifen is pH dependent being faster at alkaline pH and produces the major metabolite M01 that does not hydrolyse further.

Photolytic half life of spiromesifen in water was 1.7 d in the laboratory conditions. Two major aqueous photolysis metabolites were identified. The experts' meeting agreed that in the case of

[3] M01: (BSN 2060-enol) 4-hydroxy-3-mesityl-1-oxaspiro[4.4]non-3-en-2-one

[4] M02: (4-hydroxymethyl-BSN 0546) 4-hydroxy-3-[(1E,3E)-5-hydroxy-2,4-dimethyl-1-(1-methylethenyl)penta-1,3-dien-1-yl]-1-oxaspiro[4.4]non-3-en-2-one

[5] M09: 4-(8-hydroxy-6-oxo-5-oxaspiro[3.4]oct-7-en-7-yl)-3,5-dimethylbenzoic acid

spiromesifen adsorption to sediment seems to be the dominant route of dissipation from the water phase. Therefore, no further data were required on these metabolites. M01 was found to be stable to photolysis in water. The experts' meeting agreed to propose that spiromesifen is classified as not readily biodegradable.

In the two dark aerobic water/sediment experiments with alkaline water phase, spiromesifen degraded in the whole systems with half lives of 4.1 d and 7.8 d. The only major metabolite identified in both water and sediment was M01 (max. water 89.7 % AR after 63 d; max. sed. 38 % after 90 d) that is relatively stable in the whole system. Mineralization was practically negligible and unextractable residue in the sediment amounted to 3 – 16 % AR after 120 d. PEC_{SW} were calculated using the Dutch assumption of 0.1 % loss of the active substance for the parent and metabolite M01. In the case of metabolite M01, it was assumed that no degradation occurred between applications. Worst case PEC_{SED} were calculated based on the same model assuming in this case no degradation between applications neither for the parent nor for the metabolite M01.

Potential ground water contamination by spiromesifen and soil metabolites M01 and M09 were produced by the applicant with FOCUS-PELMO and modified scenarios to represent glasshouse conditions. In this exercise, the trigger of 0.1 µg /L was not exceeded for any of the substances of concern.

Spiromesifen is not considered prone to cause contamination through atmospheric long range transport.

Spiromesifen is of low acute, short-term and chronic toxicity to birds and mammals. Direct exposure via contaminated food items is considered negligible. A risk assessment for fish-eating birds and mammals based on the PECsw calculated by the Dutch model and the reproductive NOECs indicated a low risk from secondary poisoning.

Spiromesifen is very toxic to fish and aquatic invertebrates. The risk to fish, algae and sediment dwelling insects was assessed as low based on the Dutch exposure model. However the long-term TER for daphnids was below the trigger of 10. The expert meeting concluded that the risk to aquatic invertebrates is not addressed on the basis of the Dutch exposure model and further risk refinement is required. The risk of the major metabolite in the water phase M01 and the soil metabolite M09 to aquatic organisms was assessed as low.

Adverse effects on bumblebees were observed at an exposure of 0.72 mg/bee/week. Exposure of naturally occurring bee and bumblebee species is considered to be low because of negligible exposure. If bumblebees are used as pollinators in glasshouse the observed effects should be considered further.

High mortality (>30%) of non-target arthropods was observed at application rates much lower than the recommended rate of 216 g spiromesifen/ha. Exposure of naturally occurring populations of non-target arthropods is considered to be low and hence the risk is expected to be low. If biological control is used in glasshouse then the observed effects on *Coccinella septempunctata* and *Typhlodromus pyri* need to be considered further. The risk to non-target plants and biological methods of sewage treatment was assessed as low.

No risk assessment was conducted for earthworms, other soil non-target macro- and micro-organisms because exposure was considered as negligible for uses in glasshouses which are permanent structures.

The ecotoxicological risk assessment was conducted for the use in a permanent glasshouse where exposure of wildlife is considered negligible. Member states where non-permanent structures are used should take this into consideration.

Key words: spiromesifen, peer review, risk assessment, pesticide, insecticide, acaricide.

TABLE OF CONTENTS

BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC United Kingdom received an application from Bayer CropScience for inclusion of the active substance spiromesifen in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/105/EC.

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State United Kingdom submitted the report of its initial evaluation of the dossier on spiromesifen, hereafter referred to as the draft assessment report (DAR), to EFSA on 20 February 2004. This draft assessment report was distributed for consultation to the Member States and the notifier on 16 April 2004.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 29 November 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier was attending this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised by EFSA in September 2006. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 26 April 2007 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

Following the agreement between the EU Commission and EFSA regarding the peer review of new active substances, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received
- the resulting reporting table (rev. 1-1 of 20 December 2005)
- the consultation report

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-0 of 18 April 2007)

Given the importance of the draft assessment report including its addendum (compiled version of February 2007 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Spiromesifen is the ISO common name for 3-mesityl-2-oxo-1-oxaspiro[4.4]non-3-en-4-yl 3,3-dimethylbutyrate (IUPAC).

Spiromesifen, is in the class tetronic acid insecticides/acaricides the only other member of this class is the compound spirodiclofen. Its mode of action has not yet been clearly defined but it is probably a lipid biosynthesis inhibitor.
The representative formulated product for the evaluation was "Oberon SC 240 (BSN 2060 SC 240", a suspension concentrate (SC).

The evaluated representative uses are as an insecticide as proposed by the applicant that comprises broadcast spraying to cucumber, courgette, pepper, tomato, eggplant (aubergine), French bean, melon, strawberry and ornamentals in permanent greenhouses only. Full details of the representative uses evaluated can be found in the attached list of endpoints.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of spiromesifen as manufactured should not be less than 965 g/kg which is based on full scale production no conclusion was reached on the pilot plant production and the peer review of it was not completed. At the moment no FAO specification exists.

However, as there are outstanding mammalian and ecotoxicological data required to support the specification as well as addition analytical data and the content of one impurity in the batches (see Vol. 4, addendum 2, revision 1, February 2007, C.1.2.c, (v)), the specification for the technical material as a whole should be regarded as provisional for the moment.

The technical material contains N,N-dimethylacetamide, which has to be regarded as a relevant impurity. The maximum content of this impurity in the technical material has not been concluded on as there are toxicology and ecotoxicology data gaps identified. This is in line with the previous conclusion for the similar compound spirodiclofen which also had the impurity N,N-dimethylacetamide. No other relevant impurities were identified during the peer review process.

The content of spiromesifen in the representative formulation is 240 g/L (pure).

Beside the specification, 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 spiromesifen or the respective formulation. However, the following data gaps were identified:

- spectra for the relevant impurity,
- storage stability data for the revised formulation with the lower preservative content as well as analysis of the relevant impurity before and after storage,
- validated method of analysis for the relevant impurity in the formulation,
- the analysis of one impurity (see Vol. 4, addendum 2, revision 1, February 2007, C.1.2.c, (v)) in the batch data with validated supporting method of analysis.

The main data regarding the identity of spiromesifen and its physical and chemical properties are given in appendix 1.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of spiromesifen in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material. However as mentioned above there is no method for the relevant impurity in the formulated product.

However, sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that at least limited quality control measurements of the plant protection product are possible.

Residues in food can be determined with a multi-method (the German S19 method has been validated) for spiromesifen. However, spiromesifen-enol is also included in the residue definition for food and there is no monitoring method available for this compound. This has to be considered as a critical area of concern.

For soil and water LC-MS/MS methods are available to analyse for spiromesifen and spiromesifen-enol with an LOQ of 0.01 mg/kg for each compound in soil and an LOQ of 0.05 µg/L for each compound in surface water and groundwater/drinking water. For air a validated HPLC-UV method

was supplied but the LOQ was too high at 0.01 mg/m^3 as the AOEL is 0.015 mg/kg bw/day. A new method with an LOQ of 0.0045 mg/m^3 for air is required. A method of analysis for products of animal origin is not required as MRLs will not be set. In addition to this a method for body tissues and fluids is not required as the active substance spiromesifen is not classified as toxic or very toxic.

2. Mammalian toxicology

Spiromesifen was discussed in an experts' meeting in Parma (round 1, PRAPeR meeting 4, September 2006).

During the meeting a data gap was identified for applicant to provide a case and/or data to show that the full scale production is not significantly more toxic than the reference source, in particular with regard to reproductive toxicity, due to the toxicological properties of one of the impurities, which is classified in the European Union as Repro 2/R61; Xn / R 20/21 and, as such, should also be regarded as relevant. An addendum to Annex C was submitted by the RMS in Feb 2007 (not peer reviewed). According to ECB decision the Specific Concentration Limits for classification of this impurity are 5 and 25%. The RMS considers that the specified concentration of 0.4% (4 g/kg) is well below these limits and that no concern is expected for exposure to the impurity in the full scale production.

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Spiromesifen is rapidly but incompletely absorbed after oral administration (about 50%); it is widely distributed, with the highest levels in the gastrointestinal tract and blood. Excretion is rapid (almost complete after 72 hours) mainly via the faeces (55 - 60% of the administered dose, and approximately 40% via urine). Spiromesifen does not show any potential for accumulation. Spiromesifen is extensively metabolised in the rat. The main metabolites are M01[6] in females and M02[7] in males.

2.2. Acute toxicity

Spiromesifen has a low acute oral, dermal and inhalational toxicity in rats (LD_{50} >2000 mg/kg bw for oral and dermal toxicity and LC_{50}>4.87 mg/L for inhalation). It is not a skin or eye irritant. It is a skin sensitiser (the risk phrase **R43 "May cause sensitisation by skin contact"** was proposed).

2.3. Short term toxicity

Spiromesifen was tested in repeated dose dietary studies in rats, mice and dogs. Decreased plasma cholesterol levels were seen in short-term and long-term studies in rodents. In the mouse and also at higher doses in the rat, the decreased plasma cholesterol levels were accompanied by histological correlates indicating a depletion of the adrenal reservoirs of plasma-derived excess cholesterol.

Effects on the liver were also seen in rodents, such as induction of microsomal hepatic enzymes, linked to a thyroid activation from an increased secretion of TSH as a compensatory response to

[6] **M01**: (BSN 2060-enol) 4-hydroxy-3-mesityl-1-oxaspiro[4.4]non-3-en-2-one

[7] **M02**: (4-hydroxymethyl-BSN 0546) 4-hydroxy-3-[(1E,3E)-5-hydroxy-2,4-dimethyl-1-(1-methylethenyl)penta-1,3-dien-1-yl]-1-oxaspiro[4.4]non-3-en-2-one

increased T4-excretion (due to hepatic enzyme induction). The red and white blood cells and related organs were detected as a further target in rodents. Effects at lower doses included decreased values for haemoglobin, mean corpuscular volume, mean corpuscular haemoglobin, hematocrit and erythrocyte count.

In dogs, the predominant change was the induction of hepatic microsomal enzymes, accompanied by increased liver weights and/or respective histological liver findings. These effects were considered as adaptive. The relevant repeat dose NOAEL is 3 mg/kg bw/day (90 day mice).

No adverse systemic effects or local skin reactions were seen in a dermal study with rats exposed up to 1000 mg/kg bw/day over a 4 week period. The relevance of cholesterol decrease in this study was discussed in the experts' meeting: the effect was considered treatment related, and it was agreed to set the NOAEL at 300 mg/kg bw/day.

The NOAEL in the 4-week inhalation toxicity study in rats was of 5 and 81 mg/m^3 air (in females and males, respectively), based on affected clinical chemical liver parameters.

2.4. GENOTOXICITY

Spiromesifen was tested in a number of *in vitro* and *in vivo* tests. In particular, the micronucleus assay was discussed during the experts' meeting. No statistical significant effects were observed. The concern was related to the presentation of the study in the DAR leading to some doubts about the validity of the study. This was discussed, confirming the negative outcomes of the other studies. The experts agreed that spiromesifen has no mutagenic/genotoxic potential.

2.5. LONG TERM TOXICITY

Spiromesifen did not show oncogenic potential in rats and mice tested in long term assays.

The relevant NOAEL is 3 mg/kg bw/day (overall value from 90 day and 18 month studies in mouse).

2.6. REPRODUCTIVE TOXICITY

Reproductive toxicity was tested in two multigeneration studies in rats.

Parental toxicity consisted in marked reduced bodyweight. Reproductive toxicity (reduced oestrus cycling frequency, increased number of ovarian primordial follicles, slightly delayed maturation of external sexual organs in weanlings) was observed secondarily to general systemic toxicity. The relationship between reproductive effects in rats and depletion of plasma cholesterol was discussed by the experts. Concerns were raised with regard to the mode of action, whether the effects are related to systemic toxicity or to hormonal effects. A link between reproductive effects in rats and depletion of plasma cholesterol would show some neoplastic or pre-neoplastic effects in female reproductive tissues, which did not occur. The experts agreed that the findings are linked to the systemic toxicity, for which a clear NOAEL has been established. Both two-generation studies showed that these effects had no impact on the reproductive performance. The NOAEL for parental and offspring was 30 ppm (about 3.3 mg/kg bw/day), while the reproductive NOAEL is 120 ppm (equal to 14.2 mg/kg bw/day).

Spiromesifen was tested in developmental toxicity studies in rats and rabbits. Both developmental toxicity studies did not reveal a teratogenic potential of spiromesifen. In the developmental toxicity study in rats, a slightly more advance ossification of phalangeal and skull bones was observed at maternally toxic doses. In rabbits, abortions and resorptions occurred secondarily to severe systemic maternal toxicity. The maternal and developmental NOAEL is 10 mg/kg bw/day.

2.7. NEUROTOXICITY

No relevant findings occurred in specific neurobehavioral and neurohistopathological investigations in acute, subchronic and chronic neurotoxicity studies in rats: at high doses in rat short-term studies, the occurrence of neurobehavioral signs (including e.g. spastic gait, nervousness, aggression, spasms, increased motility, impaired reflexes) was noted. All signs were shown to be reversible. Specific neuropathological changes were not observed. The long-term rat studies revealed no indications for a neurotoxic or immunotoxic potential of spiromesifen.

2.8. FURTHER STUDIES

In short term toxicity studies, effects on the immune system were seen at high doses. The observed changes included effects on the thymus and on several morphological immunological parameters. All observed changes were assessed as secondary to the marked general systemic toxicity. Special functional immunological investigations (plaque-forming cell assay) were conducted in rats and in mice showing no significant immunotoxic hazard.

2.9. MEDICAL DATA

Since spiromesifen is a new compound, there is little information on exposure of workers or the general population. No poisoning cases are reported.

2.10. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

Acceptable daily intake (ADI)

The ADI was established to be 0.03 mg/kg bw/day, based on the relevant long term toxicity NOAEL of 3 mg/kg bw/day (short term and long term toxicity in mouse) applying a safety factor of 100.

Acute reference dose (ARfD)

An acute reference dose for spiromesifen of 2 mg/kg bw is proposed based on applying a 100-fold uncertainty factor to the NOAEL of 200 mg/kg bw/day from an acute neurotoxicity study in rats.

Acceptable operator exposure level (AOEL)

An AOEL of 0.015 mg/kg bw/day was set based on the relevant NOAEL of 3 mg/kg bw/day, using an assessment factor of 100 and correction for incomplete oral absorption (50%).

2.11. DERMAL ABSORPTION

A general concern was raised in the meeting for studies with rhesus monkeys, because of the limitations this study has, such as number of individuals, permeability variability pending on the skin sites chosen, as well as the recovery. To cover these uncertainties it was proposed to use a value of 10% instead of 3% (based on the assessment of the study). However, in the study after 120 hours between 1-3% was recovered in the excreta in the animals tested (including. cage washes). Based on these data, dermal absorption was clearly low and 3% was considered an appropriate value to use in operator/worker exposure estimates for both the concentrate and in-use dilution.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative formulation for spiromesifen is BSN 2060 240 SC, to be used on fruiting vegetables and ornamentals in greenhouses at doses of 0.144-0.216 kg as/ha.

Operator exposure

The exposure was estimated combining data from the German and/or POEM models (for mixing/loading activities) and the results of a field study performed in Germany (for application, IVA[8] exposure study).

Estimated exposure expressed as percentage of the AOEL (0.2 mg/kg bw/day):

Scenario	Model	No PPE	With PPE*
Large tank/hand lance application (maximum values are reported)	**German model/IVA**	866%	24%
	UK POEM/IVA	864%	24%
Knapsack sprayer application (maximum values are reported)	**UK POEM/IVA**	1072%	34%

* gloves during mixing/loading and gloves and coveralls during application

EFSA notes that the experts agreed to consider unrealistic for an operator to treat an area at a spray volume of 1000 to 1500 litres (according to GAPs) using a knapsack sprayer. A work rate of 400 litres (assuming a 15 litre sprayer) was considered suitable to the assessment.

Levels of systemic exposure for operators applying spiromesifen are estimated to be below the AOEL for operators wearing protective gloves when mixing and loading and a protective coverall and protective gloves during application.

[8] Industrieverband Agrar, Mich 1996

Worker exposure

Worker exposure was estimated considering DFR values ranging from 30000 cm^2/hr (unrealistic case) to 8000 cm^2/hr for fruiting vegetables and 4500 cm^2/hr for ornamentals.

Considering the more realistic values of 8000 and 4500 cm^2/hr, the estimated exposure was 45% and 25% of the AOEL for vegetables and ornamentals, respectively.

Bystander exposure

Bystanders are unlikely to be exposed to spiromesifen from applications in greenhouses.

3. Residues

Spiromesifen was discussed in the meeting of experts in Parma in September 2006 (PRAPeR 05).

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

In all studies the molecule was ^{14}C radio labelled in the 3-position of the dihydrofuranone ring.

3.1.1. PRIMARY CROPS

Metabolism of spiromesifen was investigated in tomato, lettuce and cotton, under polytunnel or glasshouse conditions. The application was broadly in line with the notified representative uses, and application rates were relevant to the proposals at moderately exaggerated rates.

With 86% of the total radioactive residue (TRR) spiromesifen was the most abundant component in mature **tomato** fruits treated twice at a 2N application rate. Metabolite spiromesifen-enol (M01) was observed in fruits at only *ca* 0.5% TRR. Another metabolite present in relatively big amounts was spiromesifen-4-hydroxymethyl glucoside (M03[9]) (5.4-7%TRR). In addition, the unconjugated spiromesifen-4-hydroxymethyl (M02) was present at up to 0.5% TRR. Other components were present at low amounts (<0.5% TRR and <0.005 mg/kg) and thus were not identified.

In **cotton**, spiromesifen and spiromesifen-enol (M01) were significant compounds in both cotton seed and gin trash. Spiromesifen and spiromesifen-enol (M01) were present in these products at 17 to 56% TRR and 3.5 to 50% TRR respectively. Other metabolites were relatively minor in cotton. For the treatment using three applications at 1.4N rate, unknown metabolites were individually present at very low levels (up to 0.001 mg/kg in cotton seed).

In **lettuce**, spiromesifen was with 58% TRR the main component of the residue. M03 and M04[10] were the major metabolites (13% and 6% TRR respectively), with other metabolites (M02, M06[11] and M01) present at low levels, each at <3% TRR. Unknown components in lettuce were individually present at low levels in the range of <0.2% to 4% of the TRR.

[9] **M03**: glucose conjugate of 4-hydroxy-3-[(1E,3E)-5-hydroxy-2,4-dimethyl-1-(1-methylethenyl)penta-1,3-dien-1-yl]-1-oxaspiro[4.4]non-3-en-2-one

[10] **M04**: dihydroxy spiromesifen enol (the exact position of the OH groups could not be determined)

[11] **M06**: 4,7-dihydroxy-3-(2,4,6-trimethyl-phenyl)-1-oxa-spiro[4.4]non-3-en-2-one

The studies also showed that residues were not translocated to a significant extent. The picture of metabolism was similar across the tested crops, although fewer metabolites were detected in the metabolism study on tomato representative for fruit crops.
The initial reaction in the plant metabolism of spiromesifen is the cleavage of the ester bond forming spiromesifen-enol (M01). Further metabolic steps are hydroxylation of the spiromesifen-enol in the 3-position of the cyclopentyl ring, hydroxylation in the methyl side-chain of the spiromesifen-enol followed by hydroxylation in the 3-position of the cyclopentyl ring, conjugation and hydroxylation of the spiromesifen-enol.

A sufficient number of residues trials are available in climbing French beans, cucumbers, peppers, tomatoes, strawberries and melons, grown in greenhouses across Europe. PRAPeR 05 noted that not all trials, in particular in peppers, were conducted at the appropriate application rate. In the addendum of February 2007 the RMS provided a revised evaluation of the trials pepper supporting a lower water volume ($\leq$ 1000 L/ha) and therewith lower application rate, than initially notified by the applicant as the representative use. However, this evaluation was neither peer reviewed or discussed in an expert's meeting. According to the applicant, new residue data supporting the notified GAP with a higher water volume (1500 L/ha) will be submitted at MS level.
In all the trials spiromesifen and spiromesifen-enol (M01) were separately analysed for, and their sum was expressed as spiromesifen. At the notified PHI of 3 days spiromesifen-enol (M01) was present at 5% to 60% of the amount of spiromesifen present. The trial results are supported by validated analytical methods and acceptable storage stability data. Although in some crops significant degradation of spiromesifen to spiromesifen-enol (M01) was found upon freezer storage over two years, metabolite M01 seemed to be sufficiently stable. Based on the consistent conclusion across the three crops tested (cucumber, melon, French beans), that residues do not degrade significantly beyond metabolite M01 in all crops over a two year storage period, it is considered that the residues trials are sufficiently supported by freezer storage stability data.
Residues trials data for tomatoes are including four trials in cherry tomatoes. Residues were slightly higher in cherry tomatoes, and therefore cherry tomato data were used in the consumer risk assessment. As no individual residue trials were submitted for aubergines, residue levels found in the larger tomatoes were used to assess potential residues in aubergines by extrapolation in accordance with current guidance.

A radio-labelled hydrolysis study is available together with processing studies on the influence of processing on levels of spiromesifen and spiromesifen-enol (M01) in tomatoes, beans and strawberries. The radiolabelled hydrolysis study covered a range of hydrolytic conditions and demonstrated that spiromesifen was hydrolytically unstable. Spiromesifen was primarily altered to spiromesifen-enol (M01) which was present at up to 89%TRR at the end of the study. Other degradation products were not significant.
Generally residues of spiromesifen decrease over processing. All processing studies showed the potential for hydrolysis of spiromesifen to spiromesifen-enol (M01), in particular as a result of the heat treatment over a process. Therefore levels of spiromesifen-enol (M01) were at times observed at

significantly higher levels after processing compared to before processing. Residue processing factors were calculated on the basis of the sum of residues of spiromesifen and spiromesifen-enol (M01) expressed as spiromesifen. The processing of tomatoes into tomato juice and tomato preserves (canned tomatoes), of strawberries into strawberry jam and strawberry preserves (canned strawberries) and cooking of beans reduced the residue levels, while a concentration of residues was observed in tomato puree.

In toxicological studies, it is expected that spiromesifen is rapidly converted to spiromesifen-enol (M01), and therefore it is not possible to draw conclusions on the relative toxicology of spiromesifen-enol (M01) to parent spiromesifen. This conversion was also seen in processing data, particularly for processes involving heat, and in freezer storage stability studies. In the residues trials, spiromesifen-enol was present at 5% to 60% of the amount of parent present. Therefore the residue definition in crops for risk assessment should be spiromesifen and spiromesifen-enol expressed as spiromesifen equivalents. Given the instability of spiromesifen residues under freezer storage conditions, PRAPeR 05 recommended the same residue definition be applied for monitoring purposes.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Based on soil degradation rates (refer to 4.1.2 below) it was considered that rotational crop data were required to address the potential for uptake of residues by soil grown crops grown in rotation in the glasshouse. Soil based greenhouse systems are considered relevant due to their importance in southern European greenhouse agriculture.

The fate of spiromesifen in rotational crops was investigated with radio-labelled material. After application (at 0.9 N rate) the soil was aged for a period of 30, 120-187 and 365 days before replanting of wheat, spinach and turnip. Total radioactive residues varied according to following crop and replanting timing, but were significant in all tested crops. The data show a similar profile of metabolism compared to the primary crop. However some of the metabolites that appear in the metabolic pathway beyond spiromesifen-enol (M01) were present in higher proportions in the rotational crop compared to the primary crop (levels of individual metabolites varied according to crop and ranged up to 0.44 mg/kg). A major part of residue in rotated crops was represented by metabolite M02 and conjugates. Metabolites with hydroxylation of the cylcopentane ring or hydroxylation of other sites in the molecule accounted for less significant proportions of the residue. In few samples (mainly of spinach and turnip), proportions of metabolite M06 were similar or slightly higher than M02 and conjugates. In addition there were unknowns present in varying amounts; individual unknowns were present up to 0.04 mg/kg in consumable crop parts (spinach) and 0.09 mg/kg in crops relevant for livestock feeding (wheat straw). Investigations of the unextractable radioactivity in wheat straw and grain suggested that significant proportions of the radioactivity were associated with polymeric plant wall constituents, including lignin, or incorporated into starch respectively.

Given the predominance of metabolite M02 and its conjugates (including glucose conjugate M03) in the total radioactive residue in the tested crops it is currently proposed to define the sum of metabolites M02 (BSN 2060-4-hydroxymethyl), M03 (BSN 2060-4-hydroxymethyl-glucoside) and M02-conjugates (BSN 2060-4- hydroxymethyl conjugates) as the relevant residue in rotational crops. These compounds are accounting for a significant part of the total radioactive residue in all sample materials except wheat grains. However, the above proposal cannot be considered a finalised and agreed residue definition as the situation in rotational crops is still unclear for some rotational practices. Further consideration might be needed when these practices will have been addressed.

All the timings tested (30 to 365 days) are relevant to the requested glasshouse uses where soil may be re-used in the glasshouse and following crops may be grown in quick succession. For the representative uses there could be a timing of as low as 2 to 4 weeks before the next glasshouse crop is sown.

Rotational crop residue trial were conducted with tomatoes in two greenhouse systems, one with the Enarenado soil system and the other with uncovered natural soil, to reflect the most intensively used practices in Southern Europe. A primary crop of tomatoes was treated according to the notified cGAP, and after 30 and 45 days, respectively, following crops of tomatoes were planted and grown to maturity. Samples of tomato fruits were analysed for M02 and its conjugates measured as the common moiety M02 with validated analytical methods. No residues above the LOQ of 0.01 mg/kg were found in tomato fruit from the following crop indicating that residues in these crops are unlikely to be of significance. However, no crops other than tomatoes were studied, but rotation sequences applied in Member States may vary from the assessed one of fruiting vegetables rotated with fruiting vegetables.

Based on data from the confined rotational metabolism study it is considered possible, that residues in following crops particularly leafy crops could be of concern. Therefore PRAPeR 05 agreed to the RMS' view that for risk assessment purposes further residues trials are necessary to address the potential for uptake of residues in other crops that are realistically expected to occur in crop rotations, depending on individual MS practices (i.e. to cover other relevant crop groups, and depending on the potential for residues to arise these data may also need to cover fruiting crop(s) additional to tomatoes relevant to the expected rotations). Depending on the significance of the residue levels in these quantitative trials with alternative rotational crops, it may also be necessary to give consideration to the nature of the unknowns observed in the confined rotational crop metabolism study.

As soil based systems are expected to involve crop rotations, the restriction to grow greenhouse crops other than fruiting vegetables on inert media/substrates or by nutrient film technique only should remain to protect consumers from potential residues arising in following crops grown in soil systems. This allows for use on glasshouse crops using a non-soil based system.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Data were submitted on metabolism of spiromesifen in goat and hens.

Upon evaluation of the data the RMS noted that the basic premise of metabolism studies, that a reasonable level of radioactivity should be accountable, was not fulfilled by the submitted studies in goat and hens.
However, no such studies are currently required as none of the crops concerned by the notified representative uses in greenhouses (primary and rotational crops) are fed to livestock animals.

Therefore a residue definition is not proposed at present for animal products and further consideration is required if authorisation of uses relevant for animal feeding is sought in future.

No animal feeding studies are currently available or required.

3.3. CONSUMER RISK ASSESSMENT

Following the discussions in PRAPeR 05 there was the need to recalculate consumer exposure. An updated consumer risk assessment was submitted in the addendum of February 2007, that was however not peer reviewed.
The TMDIs calculated by the RMS using the consumption data of the WHO GEMS/Food Standard European diet show that intakes are well below the ADI of 0.03 mg/kg bw/day. Using UK consumption data, chronic exposure estimates for long term dietary intakes are also well below the ADI of 0.03 mg/kg bw/day. The total NEDIs vary according to different consumer groups, although the values range from 2% (a number of consumer groups) to 4% (toddlers) of the ADI.
Using UK consumption data, acute exposure estimates for short term dietary intakes (NESTI) are well below the ARfD of 2 mg/kg bw/day (all ≤ 3 % of the ARfD).

EFSA noted that with the new PRAPeR model higher intakes were estimated for other diets of European Member States or regions, however all estimates showed intakes well below the toxicological reference values.
With the MRLs proposed (see 3.4 below) the highest TMDI was obtained for the WHO GEMS/Food Cluster diet B (relevant for Italy, Spain, Portugal, Greece, Cyprus) amounting to 12.5 % of the ADI of 0.03 mg/kg bw/day. An acute risk assessment confirmed that all short term dietary intakes are below 3% of the ARfD of 2 mg/kg bw/day. It is noted that peppers were not included in the assessment, as the notified critical GAP is not supported by data.

3.4. PROPOSED MRLS

As the meeting of experts PRAPeR recommended spiromesifen-enol (M01) be included in the residue definition for monitoring, the initially proposed MRLs covering only spiromesifen had to be changed. The RMS proposed the following updated MRLs in the addendum of February 2007 (not peer reviewed).

Cucumber	0.2 mg/kg
Courgette	0.2 mg/kg

Tomato	1.0 mg/kg	(Based on tomato and cherry tomato data)
Aubergine	0.5 mg/kg	(Based on extrapolation from larger tomato data)
French bean	1.0 mg/kg	
Strawberry	1.0 mg/kg	
Melon	0.1 mg/kg	

For the sake of transparency the following is noted: A proposed MRL of 0.2 mg/kg for pepper in the addendum of February 2007 is based on an alternative, less critical GAP (*ca* 0.6 N application rate or lower) to the notified GAP and has not been peer reviewed.

4. Environmental fate and behaviour

Spiromesifen fate and behaviour in the environment was discussed in the expert's meeting PRAPeR 02 of September 2006 on basis of the spiromesifen DAR of February 2004. Assessment was based on representative uses proposed only for glasshouse in North and South EU with a maximum of 4 applications at a rate of 216 g a.s/ha. The risk assessment also assumed that the glasshouse is permanent and stays after the harvest at least until residues of parent and metabolites in soil are below the LOQ.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of spiromesifen in soil under dark aerobic conditions at 20 ºC was investigated in three separated studies with [dihydrofuranone-3-^{14}C] spiromesifen in four soils (pH_{CaCl2} 6.1 – 6.8; OC 1.2 – 2.17 %; clay 5-35 %), [cyclopetyl-1-^{14}C] spiromesifen in one soil (pH_{CaCl2} 8.2; OC 0.28 %; clay 8.4 %) and [phenyl-UL-^{14}C] spiromesifen in one soil (pH_{CaCl2} 7.2; OC 0.24 %; clay 5.1 %). Under these conditions spiromesifen ester is hydrolysed to form the major soil metabolite **M01** (spiromesifen enol, max 85 % AR after 14 d) that oxidises to form the also major metabolite **M09**[12] (max 14.1 % AR after 90 d). Considerable mineralization was observed in all the soils investigated (CO_2 14.3 – 71 % AR after 90 d). Unextractable residues were formed at levels between 13.9 % AR after 120 d to 24.1 % AR after 62 d.

Degradation under anaerobic conditions was not investigated in any of the studies available in the dossier.

Photolysis was investigated in one study on one soil (pH 7.2; OC 0.64 %; clay 14.8 %) at 20 ºC with artificial light (filtered < 290 nm) from a Xenon lamp during 10 d of continuous irradiation (considered equivalent to 34 d in late June, Phoenix, Arizona, USA). Photolysis does not seem to contribute to the environmental degradation of spiromesifen but may accelerate the degradation of its enol metabolite M01. No metabolites specific to photolytic degradation were identified in this study.

[12] **M09**: 4-(8-hydroxy-6-oxo-5-oxaspiro[3.4]oct-7-en-7-yl)-3,5-dimethylbenzoic acid

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Rate of degradation of spiromesifen was determined with the data obtained in the route studies. Spiromesifen is low to moderately persistent in soil ($DT_{50\ lab}$ = 2.6 d – 17.9 d). A multi-compartmental kinetic model was employed to derive the kinetic parameter for the formation and degradation of metabolites M01 and M09 from the data on the degradation studies performed with the parent. Spiromesifen was assumed to degrade according to first order processes. Enol M01 and acid M09 were shown to be of low to high persistence in soil (M01: $DT_{50\ lab}$ = 8.8 d – 101.6 d; M09: $DT_{50\ lab}$ = 1.7 d – 223.6 d). Whereas the applicant considered that the values obtained in two of the soils tested were not relevant for metabolite M01 and M09 due to low biomass, the RMS did not consider it justified to exclude them from the risk assessment. The experts' meeting agreed and confirmed the RMS approach.

No field studies were submitted. The experts' meeting agreed that laboratory data represents a reasonable worst case for metabolites and that no further studies were needed to complete the EU risk assessment.

PEC in soil proposed by the applicant based on the use of FOCUS –PELMO (v.2.2.2) were not considered acceptable by the RMS. New PEC soil were calculated by the RMS using the standard procedure based on worst case laboratory half lives and maximum formation of metabolites M01 and M09 of 85 % and 14.1 % respectively. To estimate the potential accumulation of metabolite M09 two crops per year in the glasshouse with an application regime of 4 x 216 g/ha per crop was assumed. Using this method, a plateau of 0.169 mg/kg at the end of the 6th year was predicted.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

A batch adsorption/desorption study in soil was attempted unsuccessfully. The test solution prepared for this study was alkaline (pH ≈ 9) and at this pH spiromesifen is more instable than at neutral or acidic pH. Therefore, the HPLC method following draft OECD guideline 121 was used to estimate the Koc value for spiromesifen. According to the results of this test, spiromesifen should be classified as immobile in soil (Koc = 30900 mL / g).

In another study the soil TLC method was employed with TLC plates prepared with four soils (pH 5 – 6.7; OC 0.95 – 1.68; clay 6.8 – 32.8 %). The plates were run with reference standards of known Koc. This experiment confirmed the low mobility of spiromesifen (Koc = 42296 - 106195 mL / g). Low mobility of spiromesifen was further confirmed by the calculated values obtained from various empirical formulas and QSAR programs. For the purpose of the representative uses EU risk assessment based on protected crops the RMS considered the use of the HPLC method estimation (Koc = 30900 mL / g) acceptable. However, following the recommendations of the SCP opinion on alternative methods for the estimation of Koc,[13] the values obtained for spiromesifen should be

[13] Opinion of the Scientific Committee on plants on methods for the determination of the organic carbon adsorption coefficients (Koc) for a plant protection product active substance in the context of council directive 91/414./EEC. Brussels, 18 July 2002. SCP/KOC/002-Final. (http://ec.europa.eu/food/fs/sc/scp/out128_ppp_en.pdf)

considered to have a high degree of uncertainty. Since it seems reasonable that more accurate values for Koc could be obtained by employing a neutral vehicle in the dosing of the standard adsorption / desorption studies, RMS proposed that, were the applicant to consider outdoor uses, a standard adsorption / desorption study at neutral conditions should be provided. This is regarded as a MS data gap if outdoor uses were applied for in the future.

Equilibrium batch adsorption/desorption studies were conducted with soil metabolites M01 and M09 in four soils (M01: pH 6.1 – 7.8; OC 0.53 – 2.62 %; clay 5.0 - 39.6 %, M09: pH 6.9 – 7.6; OC 1.2 – 2.17 %; clay 5.0 – 34.8 %). According these studies both metabolites were very high mobile in soil (M01: Koc = 1.2 – 8.3 mL / g; M09: Koc = 3 mL / g for the only soil were some adsorption was measurable, for the three other soils no adsorption was observed).

A column leaching study (in four soils) and an aged column leaching study (one soil) are available. M01 was found in the leachate at maximum levels of 15.5 % AR (non aged column) and 52 % AR (aged column). M09 was only found in the non aged column study at maximum levels of 0.5 % AR. Two unidentified metabolites were found in the aged column study at levels of 0.4 and 0.6 % AR.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Aqueous hydrolysis of spiromesifen was investigated in sterile buffer solutions (pH 4, 7 and 9) at 25 ºC and 50 ºC. Also degradation half lives at 20 ºC were calculated using Arrhenius plots. Hydrolysis of spiromesifen is pH dependent being faster at alkaline pH (25 ºC: $DT_{50\ pH\ 4}$ = 53.3 d; $DT_{50\ pH\ 7}$ = 24.8 d; $DT_{50\ pH\ 9}$ = 4.3 d). The hydrolysis of spiromesifen produces the major metabolite M01 that does not hydrolyse further.

Aqueous photolysis of [dihydrofuranone-3-^{14}C] spiromesifen was investigated in a buffer solution (pH 4) at 25 ºC under artificial light (Xenon lamp filtered for λ < 290 nm) simulating midsummer conditions at 40 ºN. Photolytic half life was 1.7 d (*versus* 23.1 d in the dark control) equivalent to environmental half life of 5.8 d in midsummer. Two major aqueous photolysis metabolites were identified in this study: **M16**[14] (max. 35.8 % AR after 5 d) and **M17**[15] (max. 36.6 % AR after 5d). PRAPeR meeting agreed on the validity of this study and discussed the need to further address the aqueous photolysis metabolites. The meeting agreed that in the case of spiromesifen adsorption to sediment seem to be the dominant route of dissipation from the water phase leaving little opportunity for photolysis to play a major role on the degradation of spiromesifen. Therefore, no further data on these metabolites were required.

The aqueous photolysis of metabolite [cyclopentyl-1-^{14}C]-M01 was investigated in one study in a buffer solution (pH 7) at 25 ºC under artificial light (Xenon lamp filtered for λ < 290 nm) simulating 31 d in Phoenix, Arizona, USA. M01 was found to be stable to photolysis in water.

Ready biodegradability was not tested and the experts' meeting agreed to propose that spiromesifen is classified as not readily biodegradable.

[14] **M16**: 3,5-dimethyl-5'-oxodispiro[bicyclo[4.2.0]octa-1,3,5-triene-7,4'-furan-2',1''-cyclopentan]-3'-yl 3,3-dimethylbutanoate

[15] **M17**: 8'-hydroxy-4',6'-dimethyl-8',8a'-dihydrospiro[cyclopentane-1,1'-indeno[1,2-c]furan]-3'(3a'H)-one

Degradation of [dihydrofuranone-3-^{14}C]spiromesifen in water/sediment systems was investigated in one study with two systems (pH_{water} = 8.3 – 8.4; pH_{sed} = 5.5 – 7.0; OC 0.5 – 5.2 %; clay 4 %) under dark aerobic conditions at 20 ºC. Spiromesifen is rapidly adsorbed in the sediment and dissipation from the water phase occurs with a DT_{90} < 3d. Spyromesifen degraded in the whole systems with half lives of 4.1 d and 7.8 d. The only major metabolite identified in both water and sediment was M01 (max. water 89.7 % AR after 63 d; max. sed. 38 % after 90 d). It was not possible to derive any reliable dissipation and degradation half lives for this metabolite due to the fact that very little degradation occurs in these systems. Mineralization is practically negligible in both systems (CO_2 = 0.5 % AR– 1.2 % AR after 120 d) and unextractable residue in the sediment amounted to 3 – 16 % AR after 120 d at the end of the study. The water phase in both systems is alkaline. Due to the strong pH dependence and the faster degradation of spiromesifen under alkaline conditions the need for further data in a neutral or acidic system was discussed in the experts' meeting. The meeting agreed that with the available data it cannot be fully excluded that hydrolysis represents a important process for the whole systems in the supplied study. However, the main dissipation process form the water phase was considered to be sorption to the sediment. Therefore, it was agreed that even under neutral or more acidic conditions the 2 d half life trigger for chronic ecotoxicity assessment will not be exceeded.

All representative uses were proposed for protected crops. Therefore, the RMS chose to use the Dutch assumption of 0.1 % loss of active substance from the glasshouse to calculate indicative PEC_{SW}. PEC_{SW} were calculated for the parent and for the metabolite M01 assuming only four applications of 216 g a.s/ha per year with 10 d interval. This means that if more than one crop per season is planted in the glasshouse, the risk assessment presented would only cover the situation where spiromesifen is applied only to one of them. In the DAR the RMS also considered for the metabolite M01 the case of six applications per year assuming the product is used in two successive crops within the same year calendar (Southern Europe). In that case the product could be only applied twice for the second crop. In the case of metabolite M01, it was assumed that no degradation occurred between applications on the basis of the behaviour observed in the water sediment system. Max PEC_{SW} calculated for spiromesifen was 0.072 µg /L and for M01 0.187 µg /L.

Worst case PEC_{SED} were calculated based on the same model assuming in this case no degradation between applications neither for the parent nor for the metabolite M01.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Potential ground water contamination by spiromesifen and soil metabolites M01 and M09 were produced by the applicant with FOCUS-PELMO and modified scenarios to represent glasshouse conditions. In this exercise, the trigger of 0.1 µg /L was not exceeded for any of the substances of concern.

4.3. FATE AND BEHAVIOUR IN AIR

On basis of the vapour pressure and the volatility of spiromesifen, it is no expected that this compound will significantly volatilise. Furthermore, the calculated photochemical half life was

calculated to be 1.69 h (corresponding to chemicals life time of 2.5 h). Therefore, spiromesifen is not considered prone to cause contamination through long range transport in the atmosphere.

5. Ecotoxicology

Spiromesifen was discussed at the PRAPeR experts' meeting for ecotoxicology (PRAPeR 03) in September 2006. The risk assessment was conducted for the use in a permanent glasshouse where exposure of wildlife is considered negligible. Member states where non-permanent structures are used should take this into consideration in their national registration.

The new technical specification presented in an addendum was discussed in the expert meeting. No assessment with regard to ecotoxicity of the impurities in the new specification was made available. Therefore a data gap was identified to provide information showing that the new source is not significantly more ecotoxic than the original material used in the ecotox tests. A revised addendum to Annex C was submitted by the RMS in Feb 2007 (not peer reviewed)

5.1. RISK TO TERRESTRIAL VERTEBRATES

Spiromesifen is of low acute, short-term and chronic toxicity to birds and mammals (birds: LD_{50} >2000 mg/kg bw and >5000 ppm, reproductive NOED = 23.2 mg spiromesifen/kg bw/d, mammals: LD_{50} >2500 mg/kg bw, NOED = 3.3 mg/kg bw/d). Exposure of birds and mammals via contaminated food items is considered negligible since the representative uses of spiromesifen are glasshouse applications. It is expected that spiromesifen does not reach the surrounding environment in significant amounts. However a risk assessment was conducted by the RMS for fish-eating birds and mammals based on the PECsw of the Dutch model and the long-term endpoint from the reproductive studies. The resulting TERs of 2830 and 402 indicate a low risk from secondary poisoning.

5.2. RISK TO AQUATIC ORGANISMS

Spiromesifen is very toxic to aquatic organisms. The lowest endpoint was observed for fish (acute LC_{50} = 0.016 mg spiromesifen/L). The chronic toxicity to fish was tested in an early life stage test. The observed overall NOEC was 0.00473 mg spiromesifen/L. The 21-d NOEC for daphnids was 0.00025 mg spiromesifen/L. The risk assessment was based on the Dutch model for glasshouse uses (0.1% entry into surface water). The acute TERs were well above the trigger of 100 indicating a low acute risk to aquatic organisms. The long-term TER for fish was calculated as 65.7. The TER for daphnids was 3.5. A new daphnia reproduction study was conducted with two applications of spiromesifen (interval of 7 days) and sediment present. Effects on reproduction were observed at all tested concentrations ranging from 0.27 to 11.6 µg spiromesifen/L. Recovery was observed in the two lowest concentrations 0.25 and 0.56 µg spiromesifen/L about 4 weeks after the last application. The RMS suggested an EAC of 0.56 µg spiromesifen/L. The meeting of experts disagreed that recovery was shown for the representative use of 4 applications (only 2 applications were made in the study). It was noted that the study did not cover potential indirect effects on other aquatic organisms. Therefore

the meeting concluded that it is not possible to derive an EAC from this single study and proposed to use the TER of 3.5 based on the original long-term study. The RMSs´ argument that the flow-through test design would have led to an overestimation of the risk since the DT_{50} in water is only 0.2 days was not accepted by the meeting. It was noted that the endpoint from the flow-through study 21-d (NOEC = 0.00025 mg spiromesifen/L) is similar to that observed in the semi-static test with sediment present (NOEC < 0.00027 mg spiromesifen/L). The meeting concluded that the long-term risk to daphnids is not addressed on the basis of the Dutch exposure model and requires further risk refinement.

M01 is the only major metabolite in the water phase of the water/sediment system. M01 is of low acute toxicity to fish and daphnids (LC/EC_{50} > 100) and to algae (EbC_{50} 17.9 mg spiromesifen/L). In addition the major soil metabolite M09 was tested showing also a low toxicity to aquatic organisms. The TERs were 3 orders of magnitudes above the Annex VI triggers indicating a low risk to aquatic organisms.

No studies were submitted for the major photolysis metabolites M16 and M17 (maximum of 35.8 and 36.6 % of applied radioactivity). M16 and M17 are not expected to become major metabolites in natural surface waters for the representative uses due to fast adsorption to sediment of spiromesifen, preventing photolysis to occur (see point 4.2.). Ecotox studies with the two metabolites are not required.

The study with *Chironomus riparius* was reassessed in an addendum. The experts agreed to the new NOEC of 0.032 mg spiromesifen/L. The corresponding TER of 83 indicates a low risk to sediment dwelling organisms. The study had some shortcomings e.g. an unexpected high concentration of spiromesifen in the water phase which was not further explained by the applicant. The concentration of M01 in the sediment was not measured. However according to the guidance document on Aquatic Ecotoxicology no study with sediment dwelling organisms is triggered for the metabolite M01 since the chronic NOEC for daphnids is above the trigger of 0.1 mg/L. Overall it is concluded that the risk to sediment dwelling organisms is low for the representative uses in glasshouse.

5.3. RISK TO BEES

The acute oral and contact LD_{50} values for bees were 792 and >200 µg spiromesifen/bee, respectively. A study with bumblebees was conducted to investigate effects on brood development. A statistically significant reduction in the number of drones was observed at an exposure of 0.72 mg/bee/week (average value based on the observation that the bees in each hive consumed 50 mL of treated sugar solution).

No risk assessment was conducted by the RMS based on the argument that naturally occurring bees are not exposed. It was suggested by the RMS that a risk assessment is conducted for bumblebees when they are used as pollinators at MS level. It was agreed to the argument of the RMS in the expert meeting and it was concluded that no risk assessment for honeybees is required for the representative uses in glasshouse.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory tests were conducted with *Aphidius rhopalosiphi, Typhlodromus pyri, Chrysoperla carnea, Coccinella septempunctata, Poecilus cupreus* and *Aleochara bilineata*. No effects of >30% were observed for *A. rhopalosiphi*, *C. carnea*, *P. cupreus* and *A. bilineata* at application rates similar to the representative uses. Mortality of >30% was observed in the tests with *C. septempunctata* and *T. pyri* at application rates much lower than the recommended rate of 216 g spiromesifen/ha. Since the representative uses are in glasshouse the risk to naturally occurring populations of non-target arthropods is considered to be low. However if biological control is used in glasshouse then the observed effects on *C. septempunctata* and *T. pyri* need to be considered further.

5.5. RISK TO EARTHWORMS

The toxicity of technical and formulated spiromesifen was tested with earthworms. The acute LC_{50} was >1000 mg spiromesifen/kg soil. The chronic NOEC was at the highest tested concentrations of 4.32 mg spiromesifen/kg soil and 1 mg spiromesifen/kg soil (values not corrected by a factor of 2). The acute LC_{50} for the metabolite M01 was >1000 mg/kg soil. Effects on body weight were observed at the two highest tested doses of 316 and 1000 mg M01/kg soil. No risk assessment was conducted since exposure of naturally occurring populations of earthworms is considered negligible. A risk assessment is required at MS level for uses on natural soil and glasshouses which are non-permanent structures.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

The soil metabolites M01 and M09 have DT_{50}s of 101.6 and 223.6 days (exceeding the trigger of DT_{90} = 100 days). Studies with collembola resulted in LC_{50} values of >1000 mg M01/kg soil and 273 mg M09/kg soil. No risk assessment was conducted since exposure of naturally occurring populations of soil non-target macro-organisms is considered negligible. A risk assessment is required at MS level for uses on natural soil and glasshouses which are non-permanent structures.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects of >25% on soil respiration and nitrification were observed at rates of 2.96 mg spiromesifen/kg. No effects on soil nitrification were observed in tests with the soil metabolites M01 and M09 at 1.07 mg M01/kg soil and 3.25 mg M09/kg soil. No risk assessment was conducted since exposure of naturally occurring populations of earthworms is considered negligible. A risk assessment is required at MS level for uses on natural soil and glasshouses which are non-permanent structures.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

Phytoxicity was investigated in a pre-emergence test with 5 monocotyledon and 6 dicotyledon plant species. Effects of up to 35% visual damage were observed in 3 monocotyledon plant species at application rates of 144 and 216 g spiromesifen/ha. Exposure of non-target plants in the vicinity of

glasshouses is considered to be low and hence the risk is assumed to be low for the representative uses.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No effects on respiration of activated sewage sludge were observed up to the highest tested concentration of 1000 mg spiromesifen/L. It is assumed that spiromesifen does not enter sewage treatment plants in concentrations of >1000 mg/L if applied according to the representative uses. The risk to biological methods of sewage treatment plants is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: spiromesifen, M01 and M09.

Definitions for monitoring: spiromesifen and M01 (spiromesifen-enol).

Water

Ground water

Definitions for exposure assessment: spiromesifen, M01 (spiromesifen-enol) and M09.

Definitions for monitoring: spiromesifen (only glasshouse use considered).

Surface water

Definitions for risk assessment: spiromesifen, M01(spiromesifen-enol), M16 and M17

Definitions for monitoring: spiromesifen

Air

Definitions for risk assessment: spiromesifen

Definitions for monitoring: spiromesifen

Food of plant origin

Definitions for risk assessment: spiromesifen and spiromesifen-enol expressed as spiromesifen

Definitions for monitoring: spiromesifen and spiromesifen-enol expressed as spiromesifen

Food of animal origin

Definitions for risk assessment: not required for representative uses evaluated

Definitions for monitoring: not required for representative uses evaluated

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Spiromesifen	Low to moderately persistent in soil ($DT_{50\ lab}$ = 2.6 d – 17.9 d)	Spiromesifen is of low acute toxicity to earthworms (LC_{50} > 1000 mg/kg soil)
M01	Low to high persistent ($DT_{50\ lab}$ = 8.8 d – 101.6 d)	Similar toxicity to earthworms as spiromesifen (LC_{50} >1000 mg/kg soil)
M09	Low to high persistent ($DT_{50\ lab}$ = 1.7 d – 223.6 d)	Similar toxicity to earthworms as spiromesifen (LC_{50} >1000 mg/kg soil)

Ground water

Compound (name and/or code)	**Mobility in soil**	**> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)**	**Pesticidal activity**	**Toxicological relevance**	**Ecotoxicological relevance**
Spiromesifen	Estimated to be immobile in soil (Koc = 30900 mL / g)	FOCUS PELMO. Scenarios modified to represent glasshouse conditions. No scenario exceeded 0.1 µg / L	Yes	Yes	Yes

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
M01	very high mobile (Koc = 1.2 – 8.3 mL / g)	No scenario exceeded 0.1 µg / L	No data available, no data required	No data available, no data required	No. About 3 orders of magnitude less toxic to aquatic organisms compared to spiromesifen.
M09	very high mobile (Koc = 3 mL / g)	No scenario exceeded 0.1 µg / L	No data available, no data required	No data available, no data required	No. About 3 orders of magnitude less toxic to aquatic organisms compared to spiromesifen.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Spiromesifen (water and sediment)	See point 5.2.
M01 (water and sediment)	About 3 orders of magnitude less toxic to aquatic organisms compared to spiromesifen. The risk to aquatic organisms from the use in glasshouse is assumed to be low.
M09 (water and sediment)	About 3 orders of magnitude less toxic to aquatic organisms compared to spiromesifen. The risk to aquatic organisms from the use in glasshouse is assumed to be low.

M16	Major aqueous photolysis metabolite, not expected to become major metabolite in natural SW for the representative uses proposed due to fast adsorption to sediment of Spiromesifen, preventing photolysis to occur. Further assessment by ecotoxicology considered not necessary.
M17	Major aqueous photolysis metabolite, not expected to become major metabolite in natural SW for the representative uses proposed due to fast adsorption to sediment of Spiromesifen, preventing photolysis to occur. Further assessment by ecotoxicology considered not necessary.

Air

Compound (name and/or code)	**Toxicology**
Spiromesifen	Low toxicity via inhalation after acute and repeat dose exposure

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Spectra data for the relevant impurity N,N-dimethylacetamide (relevant for all uses identified, data gap identified by EFSA, March 2007, date of submission unknown, refer to chapter 1)
- 2 year storage stability data for the formulation is required as the original formulation tested had a much higher preservative content (relevant for all uses identified, data gap identified by PRAPeR 01 meeting of experts September 2006, date of submission unknown, refer to chapter 1). Also in this study the content of the relevant impurity N,N-dimethylacetamide should be measured before and after storage (relevant for all uses identified, data gap identified by EFSA, March 2007, date of submission unknown, refer to chapter 1)
- Validated method of analysis for the relevant impurity N,N-dimethylacetamide in the Plant Protection Product (relevant for all uses identified, data gap identified by EFSA, March 2007, date of submission unknown, refer to chapter 1)
- The content of one impurity (see Vol. 4, addendum 2, revision 1, February 2007, C.1.2.c, (v)) must be analysed in the 5 batch study in order to derive a specification for this compound. In addition to this a supporting validated method of analysis is required (relevant for all uses identified, data gap identified by EFSA, March 2007, date of submission unknown, refer to chapter 1)
- Validation data for the yield of the derivatisation step for the determination of one impurity (see Vol. 4, addendum 2, revision 1, February 2007, C.1.2.c, (ii)) are required to enable a full consideration of the method of analysis used. (relevant for all uses identified, data gap identified by Rapporteur in Addendum 2 ,Vol 4 June 2006, date of submission unknown, refer to chapter 1)
- A validated method of analysis for the monitoring of residues of spiromesifen-enol in plants is required (relevant for all uses identified, data gap identified by EFSA, March 2007, date of submission Autumn 2007, refer to chapter 1)
- A validated method of analysis for air is required with an LOQ of <0.0045 mg/m^3. (relevant for all uses identified, data gap identified by PRAPeR 01 meeting of experts September 2006, date of submission unknown, refer to chapter 1)
- Data gap was identified for applicant to provide a case and/or data to show that the full scale production is not significantly more toxic than the reference source, in particular with regard to reproductive toxicity, due to the toxicological properties of one of the impurities, which is classified R 20/22 and Cat 2 R61 (relevant for all representative uses; an addendum to Annex C submitted by the RMS in Feb 2007 – not peer reviewed; refer chapter 2 Mammalian toxicology)
- Residues trials data to support the representative GAP in peppers (relevant for the use in peppers, data gap identified by RMS in the DAR, date of submission unknown, refer to chapter 3.1.1 above). The currently available trials for pepper only support an alternative GAP based on lower water volumes.

- For soil based greenhouse systems rotational crop data in other crops than fruiting vegetables that are realistically expected to occur in crop rotations (relevant for all representative uses, data gap identified by RMS in the DAR, date of submission unknown, refer to chapter 3.1.2 above).
- Batch equilibrium adsorption/ desorption study in soil (relevant for field uses in case they are applied for at MS level; not relevant for the representative EU uses proposed refer to point 4.1.3).
- The long-term risk to daphnids needs to be addressed further (relevant for all representative uses evaluated based on the Dutch exposure model for glasshouse use; data gap identified in the experts` meeting (PRAPeR 03 in September 2006); the applicant indicated that a freshwater mesocosm study will be submitted by March 2007; refer to point 5.2.)
- Information (or data) showing that the new source is not significantly more ecotoxic than the original material used in the ecotox tests (relevant for all representative uses; data gap identified in the experts` meeting (PRAPeR 03 in September 2006); new information was provided in a non peer reviewed addendum; the applicant proposed the submission of new studies by May 2007; refer to point 5)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide as proposed by the applicant that comprises broadcast spraying to cucumber, courgette, pepper, tomato, eggplant (aubergine), French bean, melon, strawberry and ornamentals in permanent greenhouse only. Full details of the representative uses evaluated can be found in the attached list of endpoints. It should be note that this active also has acaricidal properties but only its use as an insecticide have been considered in the DAR and in this conclusion.

The representative formulated product for the evaluation was "Oberon SC 240 (BSN 2060 SC 240", a suspension concentrate (SC).

Insufficient methods are available to monitor all compounds given in the respective residue definition. Residues of spiromesifen in food of plant origin can be determined with a multi-method (The German S19 method has been validated) however, no method is currently available for spiromesifen-enol which forms part of the residue definition in plants. For the other matrices only single methods are available to determine residues of spiromesifen and spiromesifen-enol in soil and water and spiromesifen in air. However, it should be noted that the LOQ for air is not sufficient.

Some analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. There is no method available for the relevant impurity in the plant protection product.

Spiromesifen has a low acute oral, dermal and inhalational toxicity in rats. It is not a skin or eye irritant. It is a skin sensitiser (the risk phrase **R43 "May cause sensitisation by skin contact"** was

proposed). Spiromesifen did not show any genotoxic and carcinogenic potential. The relevant repeat dose NOAEL is 3 mg/kg bw/day. Spiromesifen was shown not to be a reproductive and developmental toxicant. The ADI is 0.03 mg/kg bw/day, the ARfD 2 mg/kg bw and the AOEL is 0.015 mg/kg bw/day. Operator, worker and bystander exposure are estimated to be below the AOEL.

Metabolism of spiromesifen was investigated in tomato, lettuce and cotton. The picture of metabolism was similar across the tested crops. A significant reaction in spiromesifen metabolism is the cleavage of the ester bond forming spiromesifen-enol (M01). The available data on rotational crop metabolism show a similar profile of metabolism compared to the primary crop. However, the metabolite M02 and its conjugates are present in higher proportions in the rotational crop compared to the primary crops and are the most abundant residues in rotated crops. Currently only rotation of soil grown fruiting vegetables with fruiting vegetables has been assessed, and therefore further data are necessary to address the potential for uptake of residues in other crops that are realistically expected to occur in crop rotations, depending on individual MS practices.
A sufficient number of valid residues trials are available to support the consumer risk assessment and MRL proposals for all notified representative uses except for the use in peppers, as these trials were not conducted at the appropriate application rate.
Investigation of metabolism and residue levels in livestock and food of animal origin respectively is currently not required as none of the crops concerned by the notified representative uses in greenhouses (primary as well as rotational crops) are usually fed to livestock.
The consumer exposure through residues from crops treated with spiromesifen according to the notified GAP is expected to be well below the toxicological reference values for spiromesifen (ADI, ARfD) for the considered consumer groups adults, children and toddlers.

Assessment on fate and behaviour in the environment was based on representative uses proposed only for glasshouse in North and South EU with a maximum of 4 applications at a rate of 216 g a.s/ha. The risk assessment also assumed that the glasshouse is permanent and stays after the harvest at least until residues of parent and metabolites in soil are below the LOQ.
Under dark aerobic conditions in soil at 20 ºC, spiromesifen is low to moderately persistent ($DT_{50\ lab}$ = 2.6 d – 17.9 d).Its ester is hydrolysed to form the major soil metabolite **M01** (max 85 % AR after 14 d) that oxidises to form the also major metabolite **M09** (max 14.1 % AR after 90 d). Enol M01 and acid M09 were shown to be of low to high persistence in soil (M01: $DT_{50\ lab}$ = 8.8 d – 101.6 d; M09: $DT_{50\ lab}$ = 1.7 d – 223.6 d). Considerable mineralization was observed in all the soils investigated (CO_2 14.3 – 71 % AR after 90 d). Unextractable formed at levels of 13.9 % to 24.1 % AR. Photolysis does not seem to contribute to the environmental degradation of spiromesifen in soil but may accelerate the degradation of its enol metabolite M01.
PEC soil were calculated by the RMS using the standard procedure based on worst case laboratory half lives and maximum formation of metabolites M01 and M09 of 85 % and 14.1 % respectively. To estimate the potential accumulation of metabolite M09 two crops per year in the glasshouse with an application regime of 4 x 216 g/ha per crop was assumed. Using this method, a plateau of 0.169 mg/kg at the end of the 6th year was predicted.

The HPLC method following draft OECD guideline 121 was used to estimate the Koc value for spiromesifen. According to the results of this test spiromesifen should be classified as immobile in soil (Koc = 30900 mL / g). For the purpose of the representative uses EU risk assessment based on protected crops the RMS considered the use of the HPLC method estimation acceptable. However, following the recommendations of the SCP opinion on alternative methods for the estimation of Koc, the values obtained for spiromesifen should be considered to have a high degree of uncertainty. RMS proposed that, were the applicant to consider outdoor uses, a standard adsorption / desorption study at neutral conditions should be provided. This is regarded as a MS data gap if outdoor uses were applied for in the future.

According to the equilibrium batch adsorption/desorption studies, metabolites M01 and M09 were very high mobile in soil (M01: Koc = 1.2 – 8.3 mL / g; M09: Koc = 3 mL / g for the only soil were some adsorption was measurable, for the three other soils no adsorption was observed).

Hydrolysis of spiromesifen is pH dependent being faster at alkaline pH (25 ºC: $DT_{50\ pH\ 4}$ = 53.3 d; $DT_{50\ pH\ 7}$ = 24.8 d; $DT_{50\ pH\ 9}$ = 4.3 d). The hydrolysis of spiromesifen produces the major metabolite M01 that does not hydrolyse further.

Photolytic half life of spiromesifen in water was 1.7 d equivalent to environmental half life of 5.8 d in midsummer. Two major aqueous photolysis metabolites were identified: **M16** (max. 35.8 % AR after 5 d) and **M17** (max. 36.6 % AR after 5d). The experts'meeting agreed that in the case of spiromesifen adsorption to sediment seem to be the dominant route of dissipation from the water phase leaving little opportunity for photolysis to play a major role on the degradation of spiromesifen. Therefore, no further data were required on these metabolites. M01 was found to be stable to photolysis in water. The experts' meeting agreed to propose that spiromesifen is classified as not readily biodegradable.

In the two dark aerobic water/sediment experiments with alkaline water phase, spyromesifen degraded in the whole systems with half lives of 4.1 d and 7.8 d. The only major metabolite identified in both water and sediment was M01 (max. water 89.7 % AR after 63 d; max. sed. 38 % after 90 d) that is relatively stable in the whole system. Mineralization was practically negligible in both systems (CO_2 = 0.5 % AR– 1.2 % AR after 120 d) and unextractable residue in the sediment amounted to 3 – 16 % AR after 120 d at the end of the study. The experts' meeting agreed that even under neutral or more acidic conditions the 2 d half life trigger for chronic ecotoxicity assessment will not be exceeded.

PEC_{SW} were calculated using the Dutch assumption of 0.1 % loss of active substance for the parent and for the metabolite M01 assuming only four applications of 216 g a.s/ha per year with 10 d interval. In the case of metabolite M01, it was assumed that no degradation occurred between applications on basis of the behaviour observed in the water sediment system. Worst case PEC_{SED} were calculated based on the same model assuming in this case no degradation between applications neither for the parent nor for the metabolite M01.

Potential ground water contamination by spiromesifen and soil metabolites M01 and M09 were produced by the applicant with FOCUS-PELMO and modified scenarios to represent glasshouse conditions. In this exercise, the trigger of 0.1 µg /L was not exceeded for any of the substances of concern.

On basis of the vapour pressure, the volatility and the calculated photochemical half life, spiromesifen is not considered prone to cause contamination through atmospheric long range transport.

The risk to wildlife except aquatic invertebrates was considered as low based on the assumption that exposure will be neglible. A potential high long-term risk to aquatic invertebrates was indicated on the basis of the Dutch exposure model. Further risk refinement is needed to address the long-term risk to aquatic invertebrates. Adverse effects are expected for bumblebees and non-target arthropods if they are exposed to the recommended application rate of 216 g spiromesifen/ha. This should be considered further if bumblebees are used as pollinators and arthropods are used as biological control agents in the glasshouse. No risk assessment was conducted for earthworms, other soil non-target macro- and micro-organisms because exposure was considered as negligible for uses in glasshouses which are permanent structures.
The ecotoxicological risk assessment was conducted for the use in a permanent glasshouse where exposure of wildlife is considered negligible. Member states where non-permanent structures are used should take this into consideration.

Particular conditions proposed to be taken into account to manage the risk(s) identified

- The use of PPE has to be considered to reach exposure levels below the AOEL (see 2.12).
- A restriction to grow greenhouse crops other than fruiting vegetables on inert media/substrates or by nutrient film technique only should be put in place to protect consumers from potential residues arising in following crops grown in soil systems.
- The environmental risk assessment was conducted for the use in a permanent greenhouse where exposure of wildlife except aquatic organisms is considered negligible. A risk assessment for soil dwelling organisms is required at MS level for uses on natural soil and greenhouses which are non-permanent structures.

Critical areas of concern

- A finalised specification is not available and there are outstanding issues over the relevant impurity.
- Monitoring method of analysis for residues of spiromesifen-enol in plants is not available.
- The residue situation in following crops is not fully addressed.
- The available risk assessment to aquatic invertebrates that is based on a Dutch exposure model for greenhouse identified a high first tier risk (Annex VI triggers not met). Further data are required to refine the risk assessment.

APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

(Abbreviations used in this list are explained in appendix 2)

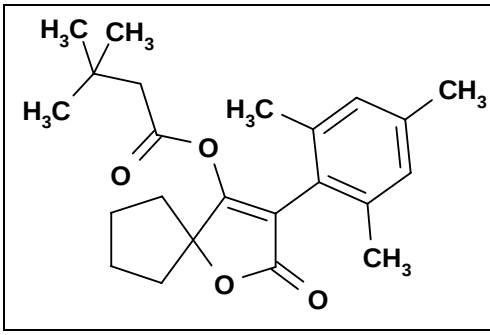
Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Spiromesifen
Function (e.g. fungicide)	Insecticide, acaricide
Rapporteur Member State	United Kingdom
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3-mesityl-2-oxo-1-oxaspiro[4.4]non-3-en-4-yl 3,3-dimethylbutanoate
Chemical name (CA) ‡	Butanoic acid, 3,3-dimethyl-, 2-oxo-3-(2,4,6-trimethylphenyl)-1-oxaspiro[4.4]non-3-en-4-yl ester (9CI)
CIPAC No ‡	747
CAS No ‡	283594-90-1
EEC No (EINECS or ELINCS) ‡	-
FAO Specification ‡ (including year of publication)	-
Minimum purity of the active substance as manufactured ‡ (g/kg)	965 g/kg full scale production
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	N,N-dimethylacetamide The maximum level for this impurity has not been concluded on.
Molecular formula ‡	$C_{23}H_{30}O_4$
Molecular mass ‡	370.49 g/mol

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	96.7-98.7°C
Boiling point (state purity) ‡	Not determined due to decomposition
Temperature of decomposition	Colour change during test (at unspecified temperature) ; the limiting temperature of this test was 375°C; exothermic decomposition starts above 300 °C.
Appearance (state purity) ‡	Colourless crystals
Relative density (state purity) ‡	1.13 at 20°C
Surface tension	Not determined due to low solubility
Vapour pressure (in Pa, state temperature) ‡	At 20°C at 20°C 7 x 10^{-6} Pa
Henry's law constant (Pa m^3 mol^{-1}) ‡	2 x 10^{-2} Pa m^3 mol^{-1} at 20°C
Solubility in water ‡ (g/L or mg/L, state temperature)	pH 4: 0.10 to 0.13 mg/L at 20°C pH 7: 0.10 to 0.13 mg/L at 20°C pH 9: 0.10 to 0.13 mg/L at 20°C
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	At 20°C aliphatic hydrocarbon: n-heptane 23 g/L aromatic hydrocarbon: xylene >250 g/L halogenated hydrocarbon: 1,2-dichloromethane >250 g/L alcohol: 2-propanol 115 g/L 1-octanol 60 g/L ketone: acetone >250 g/L ester: ethyl acetate >250 g/L acetonitrile >250 g/L polyethylene glycol 22 g/L dimethylsulfoxide 55 g/L

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Partition co-efficient (log POW) ‡ (state pH and temperature)	log Pow measured as 4.552
Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	At 50°C pH 4 2.2 days pH 7 1.7 days pH 9 2.6 hours At 25°C pH 4 53.3 days pH 7 24.8 days pH 9 4.3 days
Dissociation constant ‡	Dissociation is not expected to occur.
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	neutral medium ε($Lmol^{-1}cm^{-1}$)@214nm=2.34 $x10^4$ the UV spectra show no significant absorbance above 290 nm
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	DT_{50}: 1.7 experimental days= 5.8 solar days. ($k=0.4\ day^{-1}$) derived using first order kinetics DT90: 5.8 experimental days = 19.9 solar days.
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	Φ = 0.00101
Flammability ‡	Not highly flammable
Explosive properties ‡	Not explosive

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

List of representative uses evaluated*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests Controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number max (k)	interval between applications	kg as/hL (n)	water L/ha max	kg as/ha max		
Cucumber / Courgette	EU North / South	Oberon SC 240_(BSN 2060 SC 240)	G	mites and white flies	SC	240 g/L	overall spray	1st-4th app : start at begin of infestation	4	10 - 12	0.0144	1500	0.216	3	
Pepper	EU North / South	Oberon SC 240_(BSN 2060 SC 240)	G	mites and white flies	SC	240 g/L	overall spray	1st-4th app : start at begin of infestation	4	10 - 12	0.0144	1500	0.216	3	[1]
Tomato / Eggplant	EU North / South	Oberon SC 240_(BSN 2060 SC 240)	G	mites and white flies	SC	240 g/L	overall spray	1st-4th app : start at begin of infestation	4	10 - 12.	0.0144	1500	0.216	3	
French Beans	EU South	Oberon SC 240_(BSN 2060 SC 240)	G	mites and white flies	SC	240 g/L	overall spray	1st-4th app : start at begin of infestation	4	10 - 12	0.0144	1000	0.144	3	
Melon	EU South	Oberon SC 240_(BSN 2060 SC 240)	G	mites and white flies	SC	240 g/L	overall spray	1st-4th app : start at begin of infestation	4	10 - 12	0.0144	1000	0.144	3	

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests Controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number max (k)	interval between applications	kg as/hL (n)	water L/ha max	kg as/ha max		
Strawberry	EU North / South	Oberon SC 240 (BSN 2060 SC 240)	G	mites and white flies	SC	240 g/L	overall spray	1st-4th app : start at begin of infestation	4	10 - 12	0.0144	1000	0.144	3	
Ornamentals	EU North / South	Oberon SC 240 (BSN 2060 SC 240)	G	mites and white flies	SC	240 g/L	overall spray	1st-4th app : start at begin of infestation	4	10 - 12	0.0144	1000	0.144	n.a.	

[1] No residue data available that support the cGAP for peppers; no consumer risk assessment and MRL proposal that comply with the notified GAP

Remarks:
* Uses for which risk assessment could not been concluded due to lack of essential data are marked grey
(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(g) All abbreviations used must be explained
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(i) g/kg or g/L
(j) Growth stage at 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) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.2: Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (principle of method)	GC FID
Impurities in technical as (principle of method)	HPLC UV
Plant protection product (principle of method)	HPLC UV (DAD)

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Spiromesifen: GC MSD LOQ 0.01 mg/kg Open method for the enol metabolite is required.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required as no MRLs will be proposed
Soil (principle of method and LOQ)	Spiromesifen: HPLC MS/MS LOQ 0.01 mg/kg Spiromesifen-enol: HPLC MS/MS LOQ 0.01 mg/kg
Water (principle of method and LOQ)	Spiromesifen: HPLC MS/MS LOQ 0.05 µg/L Spiromesifen-enol: HPLC MS/MS LOQ 0.05 µg/L (the residue definition for monitoring and enforcement purposes is proposed as parent spiromesifen only.)
Air (principle of method and LOQ)	Open new method for air is required
Body fluids and tissues (principle of method and LOQ)	Not required as the active substance is not classified as toxic or very toxic.

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	No classification required

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.3: Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism in mammals (Annex IIA, point 5.1)

Rate and extent of absorption ‡	Rapid, but incomplete total rate of absorption amounted to at least 48%
Distribution ‡	Widely
Potential for accumulation ‡	Negligible
Rate and extent of excretion ‡	Rapid, only negligible radioactivity was found in the tissues and organs 72 hours after the administration
Metabolism in animals ‡	Complete
Toxicologically significant compounds ‡ (animals, plants and environment)	None

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	>2000 mg/kg
Rat LD_{50} dermal ‡	>2000 mg/kg
Rat LC_{50} inhalation ‡	>4.87 mg/L (highest achievable concentration)
Skin irritation ‡	None
Eye irritation ‡	None
Skin sensitization ‡ (test method used and result)	Positive in a Magnusson & Kligman assay **R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Adrenals and metabolic disturbance (reduced cholesterol)
Lowest relevant oral NOAEL / NOEL ‡	3 mg/kg bw/day (mouse)
Lowest relevant dermal NOAEL / NOEL ‡	1000 mg/kg bw/day (rat, not most sensitive species)
Lowest relevant inhalation NOAEL / NOEL ‡	5.0 mg spiromesifen/m^3/day for four weeks (rat)

Genotoxicity ‡ (Annex IIA, point 5.4)

……..	Negative *in vitro* (Ames test, a mammalian cell gene mutation assay with V79 cells, and a cytogenetic test in V79 cells) and *in vivo* (mouse bone marrow micronucleus test)

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Adrenal glands
Lowest relevant NOAEL / NOEL ‡	3 mg/kg bw/day
Carcinogenicity ‡	Not carcinogenic

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect	Reduced oestrous cycling frequency, increased number of ovarian primordial follicles (both considered related to strong general systemic toxicity)
Lowest relevant reproductive NOAEL / NOEL	14.2 mg/kg bw/day
Parental Toxicity/critical target	Decreased bodyweights in F1 males and F1 females
Lowest relevant parental NOAEL / NOEL	3.3 mg/kg bw/day
Neonatal Toxicity/critical target	Bodyweights during lactation at 120 ppm
Lowest relevant neonatal NOAEL / NOEL	30 ppm (3.3 mg/kg bw/day)
Developmental target / critical effect	Slightly more advanced ossification of phalangeal and single skull bones (toxicological relevance equivocal)
Lowest relevant developmental NOAEL / NOEL	10 mg/kg bw/day
Maternal toxicity/critical target	Decreased feed intake and amount of faeces, transient bodyweight loss, decreased bodyweight gain, decreased corrected bodyweight gains
Lowest relevant Maternal NOAEL / NOEL	5 mg/kg bw/day

Neurotoxicity / Delayed neurotoxicity ‡ (Annex IIA, point 5.7)

……..	No clear evidence of neurotoxicity.

Other toxicological studies ‡ (Annex IIA, point 5.8)

……..	None

Medical data ‡ (Annex IIA, point 5.9)

.....	No negative effects on the health of workers have been reported as a result of experimental biological testing or field testing of spiromesifen formulations.

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.03 mg/kg bw/day	90 day and 18 month mouse studies	100
AOEL ‡	0.015 mg/kg bw/day	90 day mouse study	100 (correction of incomplete oral absorption a factor of 0.5)
ARfD ‡ (acute reference dose)	2 mg/kg bw	Acute neurotoxicity study	100

Dermal absorption (Annex IIIA, point 7.3)

Oberon SC 240	3% for dermal absorption is assumed for both the concentrate and the in-use dilution

Acceptable exposure scenarios (including method of calculation)

Operator	Levels of systemic exposure to spiromesifen for operators applying 'Oberon SC 240' are estimated to be below the AOEL (24% hand lance application and 34% knapsack application) for operators wearing protective gloves when mixing and loading and a protective coverall and protective gloves during application.
Workers	Levels of systemic exposure for spiromesifen for re-entry workers are 45% and 25% of the AOEL for vegetables and ornamentals, respectively.
Bystanders	Bystanders are unlikely to be exposed to spiromesifen from applications in greenhouses.

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	Irritant R43 May cause sensitisation by skin contact S24 Avoid contact with skin S37 Wear suitable gloves

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.4: Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Fruit (tomato); oilseed (cotton); leafy (lettuce)
Rotational crops	Leafy (spinach); cereals (wheat); root (turnip)
Plant residue definition for monitoring	Parent spiromesifen and spiromesifen-enol (M01) expressed as spiromesifen equivalents *(factor of 1.3583 is applied to convert the enol to parent equivalents).*
Plant residue definition for risk assessment	Parent spiromesifen and spiromesifen-enol (M01) expressed as spiromesifen equivalents *(factor of 1.3583 is applied to convert the enol to parent equivalents).*
Conversion factor (monitoring to risk assessment)	None

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Ruminant (Goat); poultry (hen)
Animal residue definition for monitoring	No proposal *(deficiencies in the studies are noted)*
Animal residue definition for risk assessment	No proposal *(deficiencies in the studies are noted)*
Conversion factor (monitoring to risk assessment)	not applicable
Metabolism in rat and ruminant similar (yes/no)	yes
Fat soluble residue: (yes/no)	yes

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

……..	Based on the rotational crop metabolism it is considered that further rotational crop residues trials data are required to support the requested uses in soil grown crops that may be used in rotations in the greenhouse (not applicable for rotation of fruiting vegetables with fruiting vegetables)

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 introduction)

……..	Data for up to 2 years have been evaluated. Based on a residue definition of spiromesifen plus spiromesifen-enol (M01) expressed as spiromesifen, 'total residues' (parent+ M01) are sufficiently stable over freezer storage for up to two years. There is evidence of conversion of parent to metabolite M01, and residues of parent alone are not stable over significant periods of freezer storage (varies according to crop but residues of parent were for example only stable for up to 6 months in French bean).

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: no	Poultry: no	Pig: no
Muscle			
Liver			
Kidney			
Fat			
Milk			
Eggs			

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Cucumber	Glasshouse (N and S)	0.03, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.14		0.2	0.06
Tomato	Glasshouse (N and S)	0.09, 0.12, 0.16, 0.19, 0.19, 0.20, 0.22 Cherry tomato: 0.15, 0.10, 0.24, 0.17, 0.42, 0.11, 0.09, 0.50		1.0	0.17
French bean	Glasshouse (S only)	0.04, 0.06, 0.07, 0.08, 0.09, 0.14, 0.26, 0.64		1.0	0.085
Strawberry	Glasshouse (N and S)	0.08, 0.10, 0.12, 0.14, 0.19, 0.19, 0.29, 0.53		1.0	0.165
Melon	Glasshouse (S only)	0.03, 0.04, 0.04, 0.04, 0.05. 0.06, 0.07, 0.07		0.1	0.045
Pepper	*Glasshouse (N)*	*insufficient data available to support representative use,* *only non peer reviewed data available that support an alternative, less critical GAP (ca 0.6 fold application rate or lower)*		none for representative use	

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Consumer risk assessment [16] (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.03
TMDI (European Diet) (% ADI)	Regional: 0.001108 mg/kg bw /day (4%) Cluster diet B: 0.00418 mg/kg bw /day (12.5%)
NEDI (% ADI)	Across various consumer groups, based on UK consumers, total NEDIs range from 0.00050 mg/kg bw/day (2%) [11-14 year old] to 0.0013 mg/kg bw/day (4%) [toddler]
Factors included in NEDI	STMR (and with regard to processing only a 2.1 x concentration processing factor for tomatoes (puree))
ARfD	2
Acute exposure (% ARfD)	NESTI based on UK diet: Worst case tomato[17]: 0.0507 mg/kg bw/day (infant, tomato) i.e. 2.5% ARfD

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/processed crop	Number of studies	Transfer factor[18]	% Transference *[19]
Canned strawberry preserves	2	0.4	Parent 68%
Strawberry jam	2	0.6	Parent 62%
Washed and boiled beans	2	0.4	Parent 12%
Peeled tomatoes	2	0.1	-
Raw tomato juice	2	0.3	Parent 10%
Tomato juice	2	0.3	Parent 5%
Tomato puree	2	2.1	Parent 7%
Wet tomato pomace	2	7.5	Parent 39%
Canned tomato preserves	2	0.3	-

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

[16] not peer reviewed as recalculated after the meeting of experts PRAPeR 05
[17] pepper data, that would support the notified cGAP not considered, as insufficient
[18] calculated on the basis of the 'total residue' (spiromesifen and spiromesifen-enol expressed as spiromesifen equivalents)
[19] only calculated for spiromesifen residues as the RMS considered that spiromesifen-enol had been produced in part by conversion of spiromesifen during processing

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Proposed MRLs

Note: Proposals were amended after the Meeting of experts and are not peer reviewed.

Cucumber	0.2 mg/kg
Courgette	0.2 mg/kg
Tomato	1.0 mg/kg
Aubergine	0.5 mg/kg
(based on larger tomato data)	
French bean	1.0 mg/kg
Strawberry	1.0 mg/kg
Melon	0.1 mg/kg

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.5: Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	Dihydrofuranone label: 50.5 – 71.0% AR (90 days) Cyclopentyl label: 14.3% AR (90 days) Phenyl label: 21.9% AR (90 days)
Non-extractable residues after 100 days ‡	Dihydrofuranone label: 16.2 – 22.9% AR (90 days) Cyclopentyl label: 13.9% AR (90 days) Phenyl label: 18.6% AR (90 days)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	M01: 28.4 – 85.0% AR (7-14 days) M09: 2.8 – 14.1% AR (14-90 days)

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡	Not presented
Soil photolysis ‡	Study end: 72.9% AR spiromesifen (73.9% AR dark control); 11.6% AR M01 (24.1% AR dark control); 7.5% AR unextracted (1.9% AR dark control); CO^2 not measured.

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Method of calculation	Parent, 1st order kinetics; metabolites 1st order 4 compartment model (ModelMaker)
Laboratory studies ‡ (range or median, with n value, with r^2 value)	DT_{50lab} spiromesifen (20°C, aerobic): (all r^2 >0.99) 3.5, 2.9, 11.7, 17.9, 3.8, 2.6 days DT_{50lab} M01 (20°C, aerobic): 8.8, 13.3, 12.6, 13.6, 101.6, 53.7 days DT_{50lab} M09 (20°C, aerobic): 8.2, 14.1, 73.2, 1.7, 223.6, 100.5 days
	DT_{90lab} spiromesifen (20°C, aerobic): (all r^2 >0.99) 11.6, 9.6, 38.8, 59.4, 12.7, 8.6 days DT_{90lab} M01 (20°C, aerobic): 29.4, 43.4, 42.1, 45.4, 337.6, 178.4 days DT_{90lab} M09 (20°C, aerobic): 27.4, 47.1, 244.5, 5.7, 742.8, 333.7 days
	DT_{50lab} (10°C, aerobic): 5.7-39.2 days by calculation assuming Q10 of 2.2
	DT_{50lab} (20°C, anaerobic): not available

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

	Degradation in the saturated zone ‡: not available, not required
Field studies ‡ (state location, range or median with n value)	DT_{50f}: Not submitted (field studies not triggered by DT_{50} of parent compound)
	DT_{90f}: Not submitted
Soil accumulation and plateau concentration ‡	Not submitted

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡	Spiromesifen: estimated K_{oc} 30900 mL/g by the HPLC method
K_d ‡	M01 (K_{oc};1/n)
pH dependence ‡ (yes / no) (if yes type of dependence)	8.3; 0.9313 3.4; 0.7491 3.7; 0.8843 1.2; 0.7223 M09 – tested on four soils, but Koc could only be determined on one soil (K_{oc} = 3 mL/g) No pH dependence expected or determined for parent or metabolites

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	Leachate: spiromesifen <LOD; M01 4.7 – 15.5% AR; M09 0.4 – 0.5% AR
Aged residues leaching ‡	Leachate: spiromesifen 0.0% AR; M01 52.1% AR
Lysimeter/ field leaching studies ‡	Not submitted

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	Crop interception of 50% Soil bulk density of 1.5 g/cm^3 Equal distribution in the top 5cm soil layer Spiromesifen, 1st order DT_{50} of 17.9 days M01, 1st order DT_{50} of 101.6 days, 85.0% AR formation, molecular weight correction factor of 0.725 M09, 1st order DT_{50} of 223.6 days, 14.1% AR formation, molecular weight correction factor of 0.819

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

	In order to calculate PECsoil values for the metabolites, it must be assumed that there is there is no degradation between applications. This is due to uncertainties with respect to the formation profile of metabolites under multiple application regimes that are difficult to account for when using simple calculation approaches.
Application rate	Four applications of 216 g a.s./ha per crop 10 day interval between applications

Spiromesifen

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial			0.353	0.353
Short term 24h			0.340	0.346
2d			0.327	0.340
4d			0.303	0.327
Long term 7d			0.269	0.309
28d			0.119	0.216
50d			0.051	0.156
100d			0.007	0.089

M01

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial			0.355	0.355
Short term 24h			0.353	0.354
2d			0.350	0.353
4d			0.345	0.350
Long term 7d			0.338	0.347
28d			0.293	0.323
50d			0.252	0.301
100d			0.179	0.257

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

M09

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial				0.066	0.066
Short term	24h			0.066	0.066
	2d			0.066	0.066
	4d			0.066	0.066
Long term	7d			0.065	0.066
	28d			0.061	0.064
	50d			0.057	0.062
	100d			0.049	0.057

Accumulation potential of M09 addressed as follows:
two crops per year in a glasshouse,
each crop treated with 216 g a.s./ha x4,
10 day spray interval in each crop,
intervals between the finish and start of spray programmes of 76 days and 229 days (as proposed in the applicants groundwater modelling),
50% interception,
1st order DT_{50} of 223.6 days, 14.1% AR formation, molecular weight correction factor of 0.819

Due to uncertainties in respect to the profile of formation and decline of M01 under multiple application regimes, it is assumed that there is no degradation of the parent between each set of four applications. Thus for the purposes of calculation, it is assumed that there are two applications of 864 g a.s./ha with intervals of 106 and 259 days between the applications every year.

Using this method, the peak concentration of M09 would be predicted to plateau at 0.169 mg/kg at the end of the 6th year of applications.

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	20°C DT_{50} pH 4: 107.3 days Major metabolite M01, max. formation @ 25°C, pH 4, 30 DAT, 27.5% AR pH 7: 44.7 days Major metabolite M01, max. formation @ 25°C, pH 7, 30 DAT, 54.3% AR pH 9: 4.8 days Major metabolite M01, max. formation @ 25°C, pH 9, 30 DAT, 95.7% AR

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Photolytic degradation of active substance and relevant metabolites ‡	Spiromesifen DT_{50} 1.7 days (equivalent 5.8 days Arizona, USA mid summer) Major metabolites at 5 DAT: M01, 12.3 %AR; M16, 35.8% AR; M17, 36.6% AR M01 stable with respect to photolysis
Readily biodegradable (yes/no)	No study submitted therefore considered not readily biodegradable.
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡	Water phase, spiromesifen DT_{50} 0.1 – 0.2 day DT_{90} 2 days (Timme et al, √1st order, r2 0.96 – 0.98)
- DT_{50} whole system ‡ - DT_{90} whole system ‡	Whole system, spiromesifen DT_{50} 4.1 – 7.8 days DT_{90} 13.6 – 26.0 days (1st order, r2 0.9821 – 0.9866)
Mineralization	Mineralisation: 1.4 – 2.1% AR
Non-extractable residues	Max. 3.0 – 16.7 % AR
Distribution in water / sediment systems (active substance) ‡	Spiromesifen 20.7 – 44.1% AR water phase day 0; 20.7 – 75.0% AR sediment day 0; max sediment 83.6% AR, 2 DAT
Distribution in water / sediment systems (metabolites) ‡	M01, max. water 84.1% AR; max. sediment 38.0% AR

PEC (surface water) (Annex IIIA, point 9.2.3)

Spiromesifen

Method of calculation	Water depth 30cm Sediment depth 5cm with bulk density 1.3 g/cm^3 Spiromesifen, sq. rt. 1st order DT_{50} of 0.2 days from water phase.
Application rate	Four applications of 216 g a.s./ha per crop 10 day interval between applications
Main routes of entry	0.1% emission into surface water (Dutch scenario, example purposes in absence of agreed European method for calculation of $PEC_{(sw)}$ from glasshouse use)

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

PEC$_{(sw)}$ (µg / l)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.072			
Short term 4h	0.015			
2d	0.008			
4d	0.003			
Long term 7d	0.001			
14d	0.000			
21d	0.000			
28d	0.000			
42d	0.000			

Due to rapid dissipation in surface water, there are no differences between single or multiple applications.

Pseudo-PECsw for spiromesifen for use in the sediment dwelling organisms risk assessment was calculated assuming 0.1% emission of the maximum total dose of 864 g a.s./ha per crop. This results in a concentration of 0.288 µg/L. This would increase to 0.384 µg/L for 6 applications per year if the product is use in a second crop within the same calendar year with only two applications (assumes four applications of 216 g a.s./ha + 2x 144 g a.s./ha)
The maximum formation of metabolite M01 was 89.7% AR; a molecular weight correction factor of 0.725 from the parent is appropriate. Given that peak concentrations were formed with only four sample times remaining in the study, reliable dissipation rates for the water phase cannot be calculated. However, data from Fresno system would suggest that dissipation of M01 may be relatively slow. Thus a maximum PECsw has been calculated on the assumptions given above. Given the relative apparent persistence of this metabolite, no degradation between applications is assumed. The peak concentration following four applications would be 0.187 µg/L. This would increase to 0.250 µg/L for six applications per year.

PEC (sediment)

Method of calculation	Water depth 30cm Sediment depth 5cm with bulk density 1.3 g/cm^3 Spiromesifen, 1st order DT_{50} 10 days following final application (note no degradation assumed between applications) 0.1% emission into surface water (Dutch scenario, example purposes in absence of agreed European method for calculation of PECsw from glasshouse use)
Application rate	Four applications of 216 g a.s./ha per crop 10 day interval between applications
Main routes of entry	Undefined emission route

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

PEC$_{(sed)}$ (µg / l)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial			1.111	1.111
Short term 2d			0.967	1.038
Long term 28d			0.160	0.490

No increased sediment concentrations would be expected following six applications per year.

Metabolite M01 occurred in sediment at a maximum of 38.0% AR at study termination. Thus a maximum PECsed has been calculated using standard water body assumptions above, no degradation between applications and a molecular weight correction factor of 0.725. The maximum PECsed would be 0.366 µg/kg. This would increase to 0.488 µg/kg for 6 applications as notified.

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)

FOCUS PELMO modelling modified to consider use under glasshouse conditions.

Scenario parameters modified from FOCUS defaults:

Crop related parameters

Sim. ID	*Region*	*Crop*	*Emergence Date*	*Date of Max. LAI*	*Harvest Date*
#1 - #4	Northern Europe	Tomatoes	20.4.	20.5.	10.7.
#5 - #8	Northern Europe	Tomatoes	15.7.	15.8.	30.9.
#9 - #12	Southern Europe	Pepper	10.10.	20.11.	15.1.
		Melon	1.3.	10.4.	10.6.

Temperature related statistics

Region	*Mean Daily Minimum Temperatures (°C)*	*Mean Daily Average Temperatures (°C)*	*Mean Daily Maximum Temperatures (°C)*
Northern Europe	13	18	25
Southern Europe	13	19	27

NE temperatures based on Hamburg scenario but modified according to:

- daily min temperatures = daily mean temperature x 0.7
- daily max temperatures = daily mean temperature x 1.4

SE temperatures based on measured data in Spanish greenhouse situations

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Daily irrigation (l/m2/day)

	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sep.	Oct.	Nov.	Dec.	Annual Sum (mm)
Northern Europe	0 a)	0 a)	1	2	3	4	4	4	3	2	1	0 a)	~720
Southern Europe	1	1	2	3	3	4	0 a)	0 a)	3	2	1	1	~630

a) no cultivation

Application rate

N. Europe – 4 x 0.216 kg a.s./ha/year
S. Europe - 4 x 0.216 + 4 x 0.144 kg a.s./ha/year
Application regime

Sim. ID	Region	Intended BSN2060 Application Rate (g a.s./ha)	Potential Amount of BSN2060 Reaching the Soil Surface a) (g a.s./ha)	Dates of Application
#1 - #4	Northern Europe	4 x 216	65, 43, 108, 108	15.5., 25.5., 4.6., 14.6.
#5 - #8	Northern Europe	4 x 216	65, 43, 108, 108	10.8., 20.8., 30.8., 9.9.
#9 - #12	Southern Europe	4 x 216 + 4 x 144 b)	4 x 108 + 4 x 72 b)	10.12., 20.12., 30.12.,9.1. + 26.3., 5.4., 15.4., 25.4.

a) Amount of BSN2060 applied onto the bare ground within the simulations
b) Combined application sequence for two consecutively cultivated crops in Southern Europe

PEC$_{(gw)}$

Maximum concentration	Not calculated by FOCUS model shells, not required.
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance) concentration (80th percentile)	Spiromesifen - <0.001 µg/L M01 - <0.001 µg/L M09 - <0.001 µg/L

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	Not available, not required.
Quantum yield of direct phototransformation	Φ = 0.00101 (from photolysis in water)
Photochemical oxidative degradation in air ‡	Latitude: ..... Season: ..... DT_{50} ..... 1.69 hours
Volatilization ‡	from plant surfaces: Not available, not required. from soil: Not available, not required.

PEC (air)

Method of calculation	Not done, no guidance available

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

PEC$_{(a)}$

Maximum concentration	Not available, not required.

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil: spiromesifen, M01 and M09 Surface water: spiromesifen, M01, M16*) and M17*) Sediment: spiromesifen and M01 Groundwater: spiromesifen, M01 and M09 Air: spiromesifen *) the photolysis metabolites M16 and M17 are major metabolites in the photolysis study. However, they do not need to be assessed in ecotoxicology as sorption to sediment will be the main route of dissipation and these metabolites are not expected to be formed in significant amounts under natural conditions.

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R53 May cause long-term adverse effect in the aquatic environment

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.6: Effects on non-target Species

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Acute toxicity to mammals ‡(*Rattus rattus*)	LD_{50} > 2500 mg a.s./kg bw (from study with 'BSN 2060 240 SC')
Acute toxicity to birds ‡(*Rattus rattus*)	NOEC 30 ppm a.s. NOED 3.3 mg a.s./kg bw/d
Dietary toxicity to birds ‡(*Colinus virginianus*)	LD_{50} > 2000 mg a.s./kg bw
Reproductive toxicity to birds ‡ (*Colinus virginianus* and *Anas platyrhynchos*)	LC_{50} >5000 ppm a.s. (*Colinus virginianus* and *Anas platyrhynchos*) LD_{50} > 1165 mg a.s./kg bw (*Colinus virginianus*)
Reproductive toxicity to birds (*Anas platyrhynchos*	NOEC 229 ppm a.s. NOED 23.2 mg a.s./kg bw/d

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.216	Various crops under protection	fish eating mammal	long term	268	5
0.216	Various crops under protection	fish eating bird	long term	2830	5

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Laboratory tests ‡				
Fish (*Oncorhynchus mykiss*)	spiromesifen	96h	LC_{50}	0.016 a.s.
Fish (*Lepomis macrochirus*)	spiromesifen	96h	LC_{50}	> 0.034 a.s.
Free swimming invertebrate (*Daphnia magna*)	spiromesifen	48h	EC_{50}	> 0.092 a.s.
Alga (*Pseudokirchneriella subcapitata*)	spiromesifen	96 h	ErC_{50} EbC_{50}	> 0.094 a.s. > 0.094 a.s.

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Fish (*Oncorhynchus mykiss*)	M01	96h	LC_{50}	> 100 M01
Fish (*Oncorhynchus mykiss*)	M09	96h	LC_{50}	> 87.4 M09
Free swimming invertebrate (*Daphnia magna*)	M01	48h	EC_{50}	> 100 M01
Free swimming invertebrate (*Daphnia magna*)	M09	48h	EC_{50}	> 100 M09
Alga (*Pseudokirchneriella subcapitata*)	M01	72h	ErC_{50} EbC_{50}	50.2 M01 17.9 M01
Alga (*Pseudokirchneriella subcapitata*)	M09	72h	ErC_{50} EbC_{50}	64 M09 71 M09
Fish (*Oncorhynchus mykiss*)	'BSN 2060 240 SC'	96h	LC_{50}	0.105 a.s.
Fish (*Lepomis macrochirus*)	'BSN 2060 240 SC'	96h	LC_{50}	0.057 a.s.
Free swimming invertebrate (*Daphnia magna*)	'BSN 2060 240 SC'	48h	EC_{50}	15.9 a.s.
Alga (*Pseudokirchneriella subcapitata*)	'BSN 2060 240 SC'	72h	ErC_{50} EbC_{50}	>1.48 a.s. >1.48 a.s.
Fish (*Oncorhynchus mykiss*)	spiromesifen	97d	NOEC	0.00473 a.s.
Free swimming invertebrate (*Daphnia magna*)	spiromesifen	21 d	NOEC	0.00025 a.s.
Sediment dwelling invertebrate (*Chironomus riparius*)	spiromesifen	28 d	NOEC	0.032 a.s.
Fish (*Oncorhynchus mykiss*)	M01	88 d	NOEC	> 9.2 M01
Free swimming invertebrate (*Daphnia magna*)	M01	21 d	NOEC	0.186 M01

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Microcosm or mesocosm tests Not submitted

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

Application rate (kg as/ha)	Crop	Organism	Time-scale	TER	Annex VI Trigger
Spiromesifen					
0.216	Various crops under protection	Fish (*Oncorhynchus mykiss*)	96 h	222	100
0.216	Various crops under protection	Free swimming invertebrate (*Daphnia magna*)	48 h	> 1278	100
0.216	Various crops under protection	Alga (*Pseudokirchneriella subcapitata*)	96 h	> 1306	10
0.216	Various crops under protection	Fish (*Oncorhynchus mykiss*)	97 d	65.7	10
0.216	Various crops under protection	Free swimming invertebrate (*Daphnia magna*)	21 d	**3.5**	10
0.216	Various crops under protection	Sediment dwelling invertebrate (*Chironomus riparius*)	28 d	83	10
M01					
0.216	Various crops under protection	Fish (*Oncorhynchus mykiss*)	96 h	> 400000	100
0.216	Various crops under protection	Free swimming invertebrate (*Daphnia magna*)	96 h	> 400000	100
0.216	Various crops under protection	Algae (*Pseudokirch-neriella subcapitata*)	72 h	71600	10
0.216	Various crops under protection	Fish (*Oncorhynchus mykiss*)	88 d	> 36800	10
0.216	Various crops under protection	Free swimming invertebrate (*Daphnia magna*)	21 d	744	10

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Bioconcentration

Bioconcentration factor (BCF) ‡	545
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	0.7 d 6.9 d
Level of residues (%) in organisms after the 14 day depuration phase	1% of that at day 28 of exposure to 0.1 µg/L 1.8% of that of day 28 of exposure to 1.0 µg/L

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Acute oral toxicity ‡	LD_{50} 792.4 µg a.s./bee (a.s. test) LD_{50} > 60.2 µg a.s./bee (product test)
Acute contact toxicity ‡	LD_{50} > 200 µg a.s./bee (a.s.test) LD_{50} > 200 µg a.s./bee (product test)

Field or semi-field tests
30 day study with *Bombus terrestris*. Fed sugar syrup containing 144 mg a.s./L and pollen sprayed 4 x with solution containing 0.06% BSN 2060 SC 240 ((240 g spiromesifen/L). 0.72 mg a.s./bee/week consumed as sugar syrup. Intake as pollen not defined. No effects on adult survival or behaviour. Statistically significant reduction in number of drones produced.

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Not relevant as use only under protection

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests ‡						
Aphidius rhopalosiphi (Laboratory)	Adult	BSN 2060 SC240	9 mL/ha 18 mL/ha 45 mL/ha 110 mL/ha 270 mL/ha	M F M F M F M LR_{50}	7.5% 59.22% 10% 45.43% 57.5% NA 97.5% NA 100% NA 40.63 mL/ha (95% CL 31.18-48.87)	30% effects
Aphidius rhopalosiphi (Extended laboratory)	Adult	BSN 2060 SC240	600 g a.s./ha 864 g a.s./ha	M F M F	2.7% 79% -2.7% 91.33%	30% 30%
Typhlodromus pyri	Adult	BSN 2060 SC240	12 g a.s./ha 24 g a.s./ha 50.4 g a.s./ha 105.6 g a.s./ha 216 g a.s./ha	M F M F M F M F M F	17% 18% 7% 5% 54% 28% 64% NA 76% NA LR_{50} 68.4 g a.s/ha (95%CL 38.9-108)	30%

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Chrysoperla carnea	Larvae	BSN 2060 SC240	0.9 L prod/ha 1.8 L prod/ha 3.6 L prod/ha	M F H M F H M F H	-0.02% 105% 102% -0.02% 108% 100% 6.9% 105% 100%	30%
Coccinella septempunctata	Larvae	BSN 2060 SC240	45 mL prod/ha 95 mL prod/ha 200 mL prod/ha 425 mL prod/ha 900 mL prod/ha	M F M F M M M	12.9% 98% 33.1% 54% 50.8% 81.1% 92.4% LR_{50} 169 mL prod/ha	30%
Poecilus cupreus	Adult		0.9 L prod/ha 1.8 L prod/ha 2.7 L prod/ha	M 0% C 93% M 0% C 117% M 0% C 114%	30%	
Aleochara bilineata	Larvae		224.2 g a.s./ha 4x at 7 day intervals	Emergence	92%	
Field or semi-field tests NA						

M = % mortality (corrected for control mortality)
F = fecundity as % of control fecundity
H = hatching rate as % of control hatching rate
C = food consumption

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Effects on earthworms (Annex IIA, point 8.4, Annex IIIA, point 10.6)

Acute toxicity ‡	LC_{50} > 1000 mg a.s./kg soil (a.s. and product tests) LC_{50} > 1000 mg M01/kg soil LC_{50} > 1000 mg M09/kg soil
Reproductive toxicity ‡	Based on study with active substance LC_{50} > 4.32 mg a.s./kg NOEC 4.32 mg a.s./kg
	Based on study with formulated product, 'BSN 2060 SC 240' LC_{50} >1 mg a.s./kg NOEC 1 mg a.s./kg soil

Endpoints adjusted (x 0.5) for organic matter content of test soil.

Acute toxicity	LC_{50} > 500 mg a.s./kg soil (a.s. and product tests)
Reproductive toxicity	Based on study with active substance LC_{50} > 2.16 mg a.s./kg NOEC 2.16 mg a.s./kg
	Based on study with formulated product, 'BSN 2060 SC 240' LC_{50} > 0.50 mg a.s./kg NOEC 0.50 mg a.s./kg soil

Toxicity/exposure ratios for earthworms (Annex IIIA, point 10.6)

Not relevant as use only under protection.

Effects on soil micro-organisms (Annex IIA, point 8.5, Annex IIIA, point 10.7)

Nitrogen mineralization ‡	No effect at 2.96 mg a.s./kg soil (=2.16 kg a.s./ha) No effect at 11.9 µl 'BSN 2060 SC240'/kg soil (-9 L/ha) No effect at 1.07 mg M01/kg soil (= 0.8 kg/ha) No effect at 3.25 mg M09/kg soil (= 2.435 kg/ha)
Carbon mineralization ‡	No effect at 2.96 mg/kg soil (=2.16 kg a.s./ha) No effect at 11.9 µl 'BSN 2060 SC240'/kg soil (-9 L/ha)

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	Dangerous for the environment R50 Very toxic to aquatic organisms R53 May cause long term adverse effects in the aquatic environment S60 This material and its container must be disposed of as hazardous waste S61 Avoid release to the environment. Refer to special instructions/Safety Data

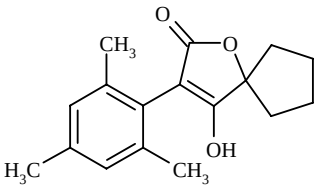
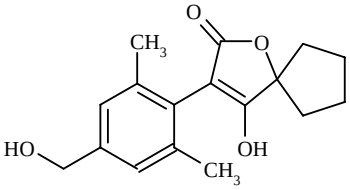
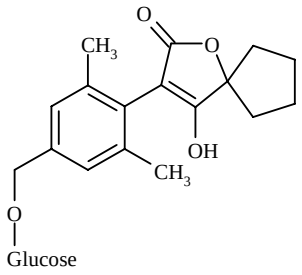
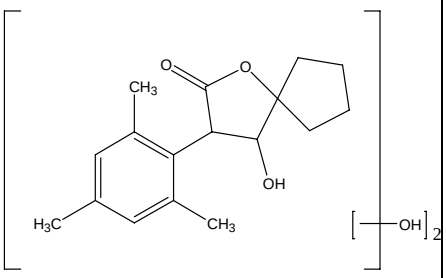
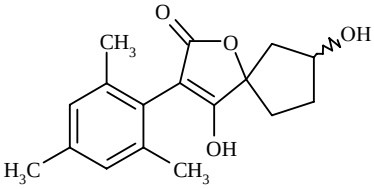
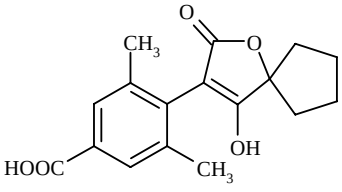
‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

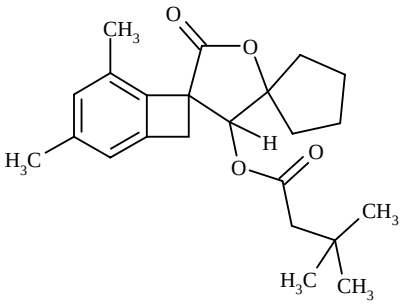
APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median

LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
M01 / Spiromesifen enol, BSN 2060-enol, BSN 0546	4-hydroxy-3-mesityl-1-oxaspiro[4.4]non-3-en-2-one	
M02 / 4-hydroxymethyl-BSN 0546	4-hydroxy-3-[(1E,3E)-5-hydroxy-2,4-dimethyl-1-(1-methylethenyl)penta-1,3-dien-1-yl]-1-oxaspiro[4.4]non-3-en-2-one	
M03 / 4-hydroxymethyl-glucoside-BSN 0546	glucose conjugate of 4-hydroxy-3-[(1E,3E)-5-hydroxy-2,4-dimethyl-1-(1-methylethenyl)penta-1,3-dien-1-yl]-1-oxaspiro[4.4]non-3-en-2-one	
M04 / dihydroxy-BSN 0546	*the exact position of the OH groups could not be determined* *only tentative structure is available*	
M06 / cis- or trans-3-hydroxy-BSN 0546	4,7-dihydroxy-3-(2,4,6-trimethyl-phenyl)-1-oxa-spiro[4.4]non-3-en-2-one	
M09	4-(8-hydroxy-6-oxo-5-oxaspiro[3.4]oct-7-en-7-yl)-3,5-dimethylbenzoic acid	

Code/Trivial name	Chemical name	Structural formula
M16	3,5-dimethyl-5'-oxodispiro[bicyclo[4.2.0]octa-1,3,5-triene-7,4'-furan-2',1''-cyclopentan]-3'-yl 3,3-dimethylbutanoate	
M17	8'-hydroxy-4',6'-dimethyl-8',8a'-dihydrospiro[cyclopentane-1,1'-indeno[1,2-c]furan]-3'(3a'H)-one