European Food Safety Authority

EFSA Scientific Report (2009) 339, 1-86

CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance spirodiclofen[1]

(Question No EFSA-Q-2009-669)

Re-Issued on 27 July 2009

EFSA changes as a result of re-discussion highlighted in yellow

SUMMARY

Spirodiclofen is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[2] The Netherlands 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 2002/593/EC[3].

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, The Netherlands, made the report of its initial evaluation of the dossier on spirodiclofen, hereafter referred to as the Draft Assessment Report (DAR), available on 21 April 2004.

The peer review was initiated on 18 May 2004 by dispatching the DAR for consultation of the Member States and the applicant. 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 on 9 February 2005. Remaining issues as well as further data made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in June – July 2005 leading to the conclusions set out in the EFSA Scientific Report (2007) 104 which was finalised on 13 June 2007.

At the request of the Commission spirodiclofen was re-discussed within a series of scientific meetings with Member States experts in April – May 2009 in the sections of physical and chemical properties, mammalian toxicology and ecotoxicology . A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member

[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance spirodiclofen. *EFSA Scientific Report* (2009) 339, 1-86

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

[3] OJ No L 192, 20.7.2002, p. 60

States in July 2009. The conclusion has been amended accordingly. This updated conclusion replaces the previous version, which was finalised on 13 June 2007 (EFSA, 2007)

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide and acaricide as proposed by the applicant which comprises of spray application to control mites and sucking insects. Full details of the GAP can be found in the table "List of representative uses evaluated" which is in the end points list in Appendix A.

The representative formulated product for the evaluation was "Envidor SC 240", a suspension concentrate containing 240 g/L spirodiclofen.

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (The German S19 method has been validated). For the other matrices only single methods are available to determine the residues of spirodiclofen and its enol metabolite[4] in soil, water and animal products and spirodiclofen in air. Sufficient 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.

Spirodiclofen is not acutely toxic via oral, dermal and inhalation routes. It is not a skin or eye irritant, but it is a skin sensitiser, therefore **R43 "May cause sensitisation by skin contact"** was proposed. The overall relevant NOAEL is 1.45 mg/kg bw/day (liver and adrenal effects) for repeated dose administration to spirodiclofen. Spirodiclofen chronic administration results in liver tumours in mice, Leydig cell tumours and uterus adenocarcinomas in rats, with clear NOAELs demonstrated. The classification **R40 "Limited evidence of a carcinogenic effect"** was proposed. Spirodiclofen has no genotoxic, reproductive and developmental toxicity potential. The subchronic NOAEL for neurotoxicity is 70 mg/kg bw/day, while the chronic neurotoxicity NOAEL is 110 mg/kg bw/day. The established Acceptable Daily Intake (ADI) is 0.015 mg/kg bw/day and the Acceptable Operator Exposure Level (AOEL) is 0.009 mg/kg bw/day (100 safety factor applied). The allocation of an Acute Reference Dose (ARfD) was not considered necessary. Estimated operator, worker and bystander exposure are below the AOEL for all uses.

The metabolism of spirodiclofen in fruit has been fully elucidated and proceeds through ester cleavage and hydrolysis steps. The parent compound was identified as the major constituent of the residue on fruit crops at various PHIs. The identified metabolites are present at very low levels but are considered as having similar toxicological properties as the parent compound. Given the predominance of spirodiclofen in the terminal residue in fruits, the residue definition can be restricted to spirodiclofen only, for both risk assessment and monitoring. Under processing, spirodiclofen is degraded only at temperatures of 100°C or higher to spirodiclofen-enol, and hence under conditions representative for fruit processing (pH 4, 90°C) no generation of spirodiclofen-enol is expected.

Upon exposure of livestock to spirodiclofen one main component of the residue in food of animal origin was identified as spirodiclofen-enol, and was defined as the residue of concern in terms of consumer exposure. Based on the results of the ruminant feeding studies MRLs for food of animal origin could be derived.

[4] BAJ 2740-enol = 3-(2,4-dichlorophenyl)-4-hydroxy-1-oxaspiro[4.5]dec-3-en-2-one

The consumer risk assessment showed that the chronic exposure to spirodiclofen residues from fruit and spirodiclofen-enol residues from food of animal origin is well below the ADI of spirodiclofen. Because an ARfD is considered not necessary, the acute risk for the consumer does not need to be assessed.

The available data demonstrate that spirodiclofen degrades in soil to the major (> 10% applied radioactivity (AR)) metabolites BAJ 2740-enol, BAJ 2740-ketohydroxy[5], BAJ 2740-dihydroxy[6] and 2,4-dichlorobenzoic acid (M16). Aerobic degradation of spirodiclofen in soil proceeds via hydrolytic and enzymatic/microbial pathways. Mineralization was significant (22.5-93.1% AR by day 120 with the dihydrofuranone-label and 69.1% AR with the cyclohexyl-label), and non extractable residues accounted for maximum 14.4 and 17.9% AR. In soil spirodiclofen, BAJ 2740-dihydroxy and 2,4-dichlorobenzoic acid exhibited low to moderate persistence, BAJ 2740-ketohydroxy exhibited very low to moderate persistence and BAJ 2740-enol can be classified as low persistent. The possibility that anaerobic conditions are encountered after application is unlikely as the proposed applications to orchard crops and grapes will occur during the spring (only for grapes) or summer months.

Adsorption coefficients of the major metabolites BAJ 2740-enol, BAJ 2740-dihydroxy and 2,4-dichlorobenzoic acid indicated that they are very highly mobile, whereas the parent spirodiclofen is strongly adsorbed to soil particles, and BAJ 2740-ketohydroxy can be classified as low mobile. There was no evidence of pH dependant adsorption. The low potential of spirodiclofen for leaching was confirmed in the aged column leaching study (<0.1% AR in leachate), but BAJ 2740-enol and 2,4-dichlorobenzoic acid were detected in the leachate at 17.4 and 19.0% AR, respectively.

FOCUS-PEARL modelling for all crops and EU-scenarios, based on average DT_{50}, Koc and 1/n values from laboratory studies, predicted 80th percentile of annual average concentrations in groundwater of < 0.001 µg/L for parent spirodiclofen, BAJ 2740-ketohydroxy, ≤ 0.001 µg/L for the metabolites BAJ 2740-enol and BAJ 2740-dihydroxy and up to 0.012 µg/L for 2,4-dichlorobenzoic acid.

In shallow natural waters, the major dissipation route of spirodiclofen will be hydrolysis, microbial degradation and partitioning to the sediment (DT_{50}system 2.3-4.2 days). Photolysis will not contribute to the dissipation of spirodiclofen in the aquatic environment. In sediment, spirodiclofen dissipates rapidly with DT_{50} values of 2.5-4.4 days. Only low levels of non-extracted residues are formed. BAJ 2740-enol is the major sediment/water metabolite (max. 84% and 30% AR in water and sediment, respectively), dissipating from the water of one system with a DT_{50} of 186 days, but stable in the water of the second system. In the sediment of both systems, the levels of BAJ 2740-enol continued to increase throughout the study. The lifetime of this metabolite in natural aquatic systems is likely to be controlled by photochemical degradation (DT_{50} in Rhine water 7.6 hours) rather than biological and chemical degradation. The pathway of anaerobic water/sediment degradation of spirodiclofen is similar, but rates of dissipation are lower (9.8 and 10 days in sediment and overall system, respectively).

The available aquatic exposure assessment is appropriate for addressing the spray drift route of entry to surface water for spirodiclofen and BAJ 2740-enol. Member States should

[5] BAJ 2740-ketohydroxy = 3-(2,4-dichlorophenyl)-3-hydroxy-1-oxaspiro[4.5]decane-2,4-dione
[6] BAJ 2740-dihydroxy = 3-(2,4-dichlorophenyl)-3,4-dihydroxy-1-oxaspiro[4.5]decan-2-one

therefore carry out a surface water exposure and consequent aquatic risk assessment from the runoff and drainage routes of exposure at the national level.

Contamination of spirodiclofen in the air compartment and transport though it is not expected to be significant.

The risk to birds and mammals was assessed as low for the representative uses evaluated. The aquatic risk assessment was based on spray drift as the only route of entry into surface water. The acute TER values for aquatic organisms were markedly above the trigger values but the long-term TER values for fish, daphnids and sediment-dwelling insects were below the Annex VI trigger of 10. Risk-mitigation measures such as no-spray buffer zones of up to 30m (early use in orchards), 15m (late use in orchards) and 10m (late use in vines) are required to mitigate the long-term risk to aquatic organisms. The acute risk to adult bees is low but larval stages are susceptible. Temporary adverse effects on bee brood development with recovery after 4 weeks were observed in field tests. Therefore it is suggested that the product should not be applied during flowering of the crop and to label the product accordingly. The standard laboratory tests suggested a high potential risk to predatory mites. Field tests with *T. pyri* showed that recovery within one year after the application is possible and the risk to non-target arthropods is considered as sufficiently addressed for the representative uses. Effects of >25% on soil nitrification were observed in tests with spirodiclofen and its major soil metabolites. The effects caused by the metabolites occurred on day 14 but were <25 % at day 28, and also the effects of spirodiclofen were <25% after day 56. Since the tested concentrations were a factor of 2 to 66 times higher than the initial PECsoil values and the effects were of a temporary nature it is assumed that the observed effects would not cause a high risk to soil functioning at the application rates suggested in the representative uses.

The risk to earthworms, other soil non-target macro-organisms, non-target plants and biological methods of sewage treatment were assessed as low for the representative uses.

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

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC The Netherlands received an application from Bayer CropScience for inclusion of the active substance spirodiclofen 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 2002/593/EC[7].

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, The Netherlands submitted the report of its initial evaluation of the dossier on spirodiclofen, hereafter referred to as the Draft Assessment Report (DAR) (The Netherlands, 2004) on 21 April 2004. The DAR was distributed for consultation to the Member States and the applicant on 18 May 2004.

The comments received on the DAR were evaluated and addressed by the rapporteur Member State. Based on this evaluation, in an Evaluation Meeting on 9 February 2005 representatives from Member States identified and agreed on data requirements to be addressed by the applicant as well as issues for further detailed discussion at expert level. A representative of both the applicant and ECPA attended this meeting.

Taking into account the information received from the applicant addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team of the Pesticide Safety Directorate (PSD) in York, United Kingdom in June and July 2005. The reports of these meetings have been made available to the Member States electronically. The outcome of the consultation led to the conclusions set out in the EFSA Scientific Report (2007) 104 (EFSA, 2007), which was finalised on 13 June 2007.

At the request of the Commission spirodiclofen was re-discussed within a series of scientific meetings with Member States experts in April – May 2009 in the sections of physical and chemical properties, mammalian toxicology and ecotoxicology. A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in July 2009. The conclusion has been amended accordingly.

During the peer review of the DAR 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 A.

The documentation developed during the peer review was compiled as a Peer Review Report (EFSA, 2009) comprising the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's DAR:

[7] OJ No L 192, 20.7.2002, p. 60

- the comments received
- the resulting reporting table (rev. 1-1 of 4 March 2005)

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. 3-2 of 30 June 2009)

Given the importance of the DAR including its Final Addendum (compiled version of June 2009 containing all individually submitted addenda, The Netherlands, 2009) 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.

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the DAR (Vol. 3 B1 - B9) which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can basically be found in the original DAR together with the peer review report which both is publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Spirodiclofen is the ISO common name for 3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl 2,2-dimethylbutyrate (IUPAC).

Spirodiclofen, belongs to the class of tetronic acid acaricides/insecticides, it is the only member of this class.

The representative formulated product for the evaluation was "Envidor SC 240", a suspension concentrate containing 240 g/L spirodiclofen.

The evaluated representative uses were as an insecticide and acaricide as proposed by the applicant which comprises spray application to control mites and sucking insects. Full details of the GAP can be found in the table “List of representative uses evaluated” which is in the end points list in Appendix A.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of spirodiclofen as manufactured should not be less than 965 g/kg which is based on full scale production.

The specification and supporting batch data for the full scale production were considered in the EPCO meeting of 30 July 2005 and were found to be acceptable, the pilot plant specification was not considered as it was superseded by the full scale production but it should be noted that the data package was not complete for the pilot plant specification. However, the EPCO meetings of experts for toxicology and ecotoxicology did not consider the full scale production specification and therefore no final conclusion was reached on this issue. During the re-discussion of this active substance, both the PRAPeR experts’ meetings on ecotoxicology and mammalian toxicology concluded that the specification is acceptable.

The technical material contains 3-(2,4-dichlorophenyl)-4-hydroxy-1-oxaspiro[4.5]dec-3-en-2-one (BAJ-2740 enol) and N,N-dimethylacetamide, which have to be regarded as relevant impurities (see justification in section 2.) The maximum content must not exceed [redacted] g/kg and [redacted] g/kg respectively.

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

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 spirodiclofen or the respective formulation.

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of spirodiclofen in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material. Methods are also available for the relevant impurities BAJ-2740-enol and N,N-dimethylacetamide in the formulation.

Therefore, sufficient data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. spirodiclofen in food of plant origin. The method is the German S 19 multi residue method with detection by GC-ECD and confirmation by GC-MS. The method of analysis for products of animal origin, soil and water is HPLC-MS/MS with validation for spirodiclofen and its metabolite BAJ 2740-enol, although spirodiclofen is not in the residue definition for surface water and products of animal origin. Air is analysed by HPLC-UV for the residue definition spirodiclofen. Methods are not required for body fluids and tissues as spirodiclofen is not classified as either toxic or very toxic.

2. Mammalian toxicology

Spirodiclofen toxicology was discussed in a meeting of experts in York in June 2005 (EPCO 28) and in the PRAPeR 69 meeting held in Parma in April 2009.

In the addendum submitted in September 2006, the RMS provided an explanation of the point raised during the EPCO 30 meeting (physical-chemical properties) regarding the new specification from the full scale production; the RMS confirmed that the new specification is acceptable. With regard to the new specification proposed EFSA noted that one of the three new impurities (N,N-dimethylacetamide) is classified in the European Union as Repro 2/R61; Xn / R 20/21. The RMS considered that the specified concentration of [redacted]% ([redacted] g/kg) is well below the Specific Concentration Limits of 5 and 25% for classification of this impurity (according to ECB decision); for the respiratory route of absorption a worst case indicative risk assessment was provided in the addendum. The dermal route was considered of even less concern. According to the RMS, the impurity was of no toxicological concern for consumers. The assessment was not peer reviewed at the time of submission.

In April 2009 the RMS presented an Addendum to the DAR with the new full scale production of spirodiclofen. The three new impurities were described. With regard to N,N-dimethylacetamide a threshold value has been set in the USA and Germany at 10 ppm (36 mg/m3). The RMS concluded that a specified limit of max. [redacted] g/kg can be supported from a toxicological perspective. It was noted that this impurity had not been tested in the technical specification. The lowest substance specific trigger value for classification (Repro2) is 5% concentration. Experts considered that the new specification from full scale production is covered by the available tox data.

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

Experimental data show that 65% of spirodiclofen is absorbed after 48 hours; it is widely distributed with the highest levels of radioactivity in liver, kidney, plasma, gastrointestinal tract and skin after 48 hours. Spirodiclofen does not show any potential for accumulation. Excretion is rapid and almost complete after 2 days from administration.

Spirodiclofen shows a marked sex difference in the metabolite profile under a quantitative rather than qualitative point of view. The main urinary metabolites are the 3- (M02[8]) and 4- (M03[9]) hydroxy-BAJ 2740-enol isomers. In plasma, liver and kidney of both male and female rats the main metabolite is BAJ 2740-enol (M01[10]).

2.2. Acute toxicity

Spirodiclofen is not acutely toxic via oral, dermal and inhalation routes in rats. It is not a skin or eye irritant, but it is a skin sensitiser, therefore **R43 "May cause sensitisation by skin contact"** was proposed to be flagged to ECHA.

2.3. Short term toxicity

Short term toxicity was investigated in rats, mice and dogs. Comparable effects were observed in all species (clinical biochemical parameters, organ weights, liver and adrenals, histopathological findings).

The experts agreed with the RMS's view that the historical control data on adrenal cortical vacuolisation in rats demonstrated that the incidence in males was within the historical control range. As a result, the NOAEL from this study was increased to 8.1 mg/kg bw/day, based on adrenal cortical vacuolisation in females at the next highest dose. In the mouse, the LOAEL was set at the lowest dose tested, 15.3 mg/kg bw/day (13 week study).

The lowest overall short term NOAEL was considered to be that of 1.45 mg/kg bw/day derived from the 1 year dog study, and was considered appropriate for the derivation of reference values.

2.4. Genotoxicity

Spirodiclofen did not induce mutations in bacteria and mammalian cells. The results of the chromosomal aberration study in mammalian cells in vitro were equivocal: the experts considered that the increased mutation frequency in the HPRT assay was not confirmed in the

[8] M02: 3-hydroxy-spirodiclofen-enol (eq=equatorial or ax=axial)
[9] M03: 4-hydroxy-spirodiclofen-enol(eq=equatorial or ax=axial)
[10] M01: BAJ 2740-enol = 3-(2,4-dichlorophenyl)-4-hydroxy-1-oxaspiro[4.5]dec-3-en-2-one

parallel culture or in a second trial and therefore it was not considered biologically relevant. It was noted that spirodiclofen did not induce micronuclei in the in vivo micronucleus assay, which covers all chromosomal aberrations, at doses at which effects on the bone marrow were demonstrated.

It was concluded that spirodiclofen has no genotoxic potential.

2.5. Long term toxicity

Long-term oral toxicity studies were performed with mice, rat and dogs.

The meeting discussed the NOAELs from the long term studies and their use in the derivation of the ADI, and concluded that the 1-year dog study was the most relevant and appropriate. The NOAEL from this study was lower than that from the rat carcinogenicity study. Furthermore, while no NOAEL was derived from the mouse carcinogenicity study (the LOAEL was 4.1 mg/kg bw/day), the application of an additional safety factor as a result of the extrapolation from a LOAEL to a NOAEL would result in a similar value to that obtained from the 1-year dog study. The NOAEL in the 2-year rat is 6 mg/kg bw/day.

Spirodiclofen administration resulted in liver tumours at 610 mg/kg bw/day in mice, Leydig cell tumours and uterus adenocarcinomas at 110 mg/kg bw/day and 153 mg/kg bw/day in rats. It was noted that tumours were observed at doses considerably higher than the NOAEL in the carcinogenicity studies; clear NOAELs for carcinogenicity were demonstrated and an appropriate margin of safety was present in the derivation of reference values from lower dose effects not related to carcinogenicity. The experts considered the classification **R40 "Limited evidence of a carcinogenic effect"** appropriate.

2.6. Reproductive toxicity

Reproductive toxicity

The experts concluded that the proposed NOAEL of 26.2 mg/kg bw/day for the reproduction toxicity studies was appropriate. It was noted that no NOAEL for parental and offspring effects was derived (NOAEL < 5.2 mg/kg bw/day). However, effects noted were consistent with those seen in general toxicity studies.

Developmental toxicity

In the teratogenicity study with rats, no toxicologically relevant effects were observed. The NOAEL for maternal and foetal toxicity in rats is 1000 mg/kg bw/day, the highest dose tested. In the rabbit, the NOAEL for maternal toxicity is 100 mg/kg bw/day, while the NOAEL for developmental toxicity is 300 mg/kg bw/day, based on liver lobulation in foetuses at maternally toxic doses.

Overall, spirodiclofen did not show any reproductive and developmental toxicity potential.

2.7. Neurotoxicity

In an acute oral neurotoxicity study, no evidence of neurotoxicity was observed, and the related NOAEL was 2000 mg/kg bw/day, the highest dose tested.

In a 13 week subchronic oral neurotoxicity study, in the highest dose group dosed of 1089 mg/kg bw/day, decreased foot splay and decreased forelimb/hindlimb grip strength were observed, possibly related to a body weight decrease in the highest dose group. The NOAEL

for neurotoxicity in this subchronic study was 70 mg/kg bw/day. In a 77 week chronic oral neurotoxicity study, no evidence of neurotoxicological effects was observed, and the NOAEL for neurotoxicity in this study was 110 mg/kg bw/day, the highest dose tested.

In the Addendum provided in September 2006 the RMS summarised a developmental neurotoxicity study (DNT), which was discussed in the PRAPeR 69 meeting, together with an additional DNT study reported in the Addendum submitted in April 2009. The meeting concluded that there were no developmental neurotoxicity effects, as in the first study an increased incidence of deceased memory performance occurred at all dose levels in females, however without dose-response relationship; in the second study no significant differences between control and treated groups were demonstrated at any dose level. The NOAEL was set as 1500 ppm (119 mg/kg bw/day).

2.8. Further studies

Immunotoxicological and mechanistic studies were provided. Spirodiclofen clearly interferes with steroid hormone synthesis. The experts in the EPCO 28 meeting agreed that it can be considered as an endocrine disruptor. It was noted that the effect on steroidogenesis is mediated by effects on general biochemical pathways, and that no androgenic or antiandrogenic effects were noted in mechanistic studies. Additionally, no reproductive toxicity was noted. While decreased spermatogenesis occurred at paternally toxic doses, this had no effect on litter parameters, demonstrating the high functional reserve capacity of this system. The application of an additional safety factor for active substances with endocrine disrupting properties (as with reproductive toxicity) was discussed. However, this was not considered necessary, as the derived reference value would be considerably higher than that derived from other adverse effects: the risk assessment driven by effects not relating to endocrine disruption provided an adequate margin of safety against potential effects resulting from endocrine disruption. It was noted that this would have no impact on classification.

As during the meeting the experts agreed on the proposed classification as R40, all rat metabolites of spirodiclofen (i.e. M1-M16) are in principle considered toxicologically relevant. The soil/water metabolites BAJ 2740-enol, BAJ 2740-ketohydroxy[11], BAJ-dihydroxy[12] and 2,4-dichlorobenzoic acid were identified to be assessed for their toxicological relevance. Neither spirodiclofen nor its metabolites were found to exceed the trigger of 0.1 µg/L in the FOCUS scenarios. BAJ 2740-enol (M01), which is also an impurity, and 2,4-dichlorobenzoic acid (M16) are rat metabolites, and are thus toxicologically relevant.

2.9. Medical data

No reports about human findings are available.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

ADI

The ADI of 0.015 mg/kg bw/day was confirmed by the experts based on the 1 year dog study with a 100 safety factor.

[11] BAJ 2740-ketohydroxy = 3-(2,4-dichlorophenyl)-3-hydroxy-1-oxaspiro[4.5]decane-2,4-dione
[12] BAJ 2740-dihydroxy = 3-(2,4-dichlorophenyl)-3,4-dihydroxy-1-oxaspiro[4.5]decan-2-one

ARfD

For spirodiclofen, no effects were observed below 2000 mg/kg bw in the acute oral toxicity study in rat, no acute neurotoxic effects were observed, there were no other indications from repeated dose toxicity studies for effects likely to occur after an acute exposure, and there were no embryotoxic or developmental effects at levels which did not induce maternal toxicity. Therefore it was concluded that allocation of an acute reference dose is not necessary.

AOEL:

The AOEL of 0.009 mg/kg bw/day was confirmed by experts based on the 1-year study in dog, considering an oral absorption correction factor of 0.65 (overall factor of 154).

2.11. Dermal absorption

In the DAR, the proposed dermal absorption value was 2% for both concentrate and diluted spirodiclofen, based on an in vivo study in male monkeys.

The experts in the EPCO 28 meeting expressed concerns relating to both the ethics of conducting dermal absorption studies on monkeys, and the quality of the data. A number of experts indicated that they would not have accepted the study initially, particularly as there were clear OECD guidelines on both in vivo and in vitro assessment of dermal absorption. The experts discussed the proposed dermal absorption value of 2%. Areas of concern with the monkey study included the fact that levels of radioactivity in the skin and body were not determined, and the level of total radioactivity recovered (92%). The low level of variation in individual animals supported the theory that the 8% of "lost" radioactivity may have been absorbed, and thus the experts concluded that this should be incorporated into the dermal absorption to give a value of 10%.

Experts considered the physical chemical properties of spirodiclofen, and considered that the molecular weight and K_{OW} supported a dermal absorption value of 10%. It was therefore concluded to set the dermal absorption at a value of 10% for the concentrate, based on physicochemical properties and supported by the studies in monkeys. It was additionally noted that no data were available on the dermal absorption potential of the formulation dilution. Therefore a value of 65% was proposed in 2005, based on the oral absorption value.

A further study in monkey and an *in vitro* study with rat and human skin, all performed with the representative formulation, were submitted and presented in the Addendum to the DAR of April 2009. The monkey study was disregarded as it was performed on one monkey; therefore only the *in vitro* study with human skin was used to make the dermal absorption proposals of the RMS, as the human skin absorption results were considered more representative. The results showed that the amount directly absorbed (amount in receptor fluid) is very low. However, the dermal depot should also be taken into account as potentially absorbed. For the concentrate a value of 0.4% (rounded value) and for the spray dilution a value of 3% (rounded value) were proposed to be used in the risk assessment. The dermal absorption values proposed by the RMS of 0.4% for the concentrate and 3% for the dilution were agreed on by the meeting.

2.12. Exposure to operators, workers and bystanders

Envidor SC 240 is a suspension concentrate containing spirodiclofen. The formulation is applied outdoor on pome fruit, stone fruit, citrus and grapes using manual and mechanical spraying techniques.

A re-calculation of the operator, worker and bystander exposure was submitted in November 2006, according to the new dermal absorption values agreed on during the EPCO experts' meeting (see table below).

In the addendum submitted in September 2006, the RMS re-assessed the EPCO meeting outcomes considering that these conclusions were drawn on wrong assumptions. In summary, the RMS claims that the concentration as tested in the in vivo study is an acceptable area dose to be used for the spray concentration. Hence the RMS now proposed a dermal absorption value of 10% for the concentrate and spray dilution.

In the risk assessment of 2009, the dermal absorption values proposed by the RMS of 0.4% for the concentrate and 3% for the dilution were agreed on by the meeting

Operator

Operator exposure levels without and with personal protective equipment (PPE) were calculated using the UK and the German model. For risk assessment purposes, the 75th percentile of the UK-model was used (and the geometric mean of the German model (DE-GM).

Model	% AOEL	
	without PPE	with PPE
Mechanical upward spraying in grapes		
UK- 75th	81	-
DE- GM	45	-
Mechanical upward spraying in pome fruits, and stone fruits		
UK- 75th	86	-
DE- GM	68	-
Mechanical upward spraying in citrus		
UK- 75th	51	-
DE- GM	68	-
Manual upward spraying in grapes		
UK- 75th	105	61*
DE- GM	16	-
Manual upward spraying in pome fruits, and stone fruits		
UK- 75th	105	61*

Model	% AOEL	
	without PPE	with PPE
DE- GM	25	-
Manual upward spraying in citrus		
UK- 75th	76	-
DE- GM	25	-

*gloves during mixing and loading

Estimated exposure was below the AOEL for all uses according to the German model, as well as with the UK POEM, with the exception of manual upward spraying in grapes, pome- and stone-fruits, for which the use of gloves during mixing and loading is needed.

Worker

The estimated exposure for workers re-entering fields after mechanical and manual upward spraying in grapes, pome fruits, stone fruits and citrus are below the AOEL (37% grapes, 56% for the other scenarios using the EUROPOEM II, 2002 model - 90th percentile).

Bystander

As an estimate, the draft values proposed for the EUROPOEM II, 2002 model were used (90th percentile). For bystanders the estimated exposure was below the AOEL (<10%) for all uses considered.

3. Residues

Spirodiclofen (BAJ 2740) was discussed in the experts' meeting (EPCO 29) in June/July 2005.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The behaviour and metabolism of ^{14}C spirodiclofen labelled in the dihydrofuranone-3-position was investigated in apples, grapes and citrus (oranges and lemons). Additionally, a translocation study in grapefruits was performed.

The available studies demonstrate that the metabolic pathway was similar in all the fruit investigated. The rate of degradation was low and the majority of the radioactivity remained on the surface of the fruits. Applications early in the growing season led to a relative higher amount of degradation products and also a higher penetration rate into the fruit flesh than applications close to harvest. However, spirodiclofen was always the predominant component of the terminal residue (34% to 89% TRR after early application and 75% to 99% TRR after late application). In the separate translocation experiment with grapefruit it was shown that

less than 0.1% of the radioactivity applied to leaves immediately surrounding the fruits were transported into the fruits.

In **apples** (ca 7N rate treatment) 89% TRR (0.35 mg/kg) and 99% (0.85 mg/kg) were identified as spirodiclofen after early and late applications, respectively. Upon characterisation and identification of the residual radioactivity the metabolites spirodiclofen-enol (M01), M03eq, M07[13] and M08[14] could be identified. Of them only metabolite M08 was found in significant quantities (0.02 mg/kg or 4% TRR) in apples having received an early application, while after a late application only trace amounts (<0.001 mg/kg) of the metabolites were detected in the fruits.

Due to the low amount of total residues in the pulp (<0.01 mg/kg) of treated oranges and lemons (at ca 4N and 3N rate, respectively) only the components present in/on the lemon and orange peel were analysed. The main component in the peel was spirodiclofen that accounted for 75% TRR (0.2 mg/kg) in lemons and 34% TRR (0.025 mg/kg) in oranges, respectively. Up to 27 metabolites could be detected, together amounting to 22% TRR (0.06 mg/kg) in lemon and 52% TRR (0.04 mg/kg) in oranges, respectively. The metabolites were identified as spirodiclofen-enol, M02eq, M03eq, M04[15], M05[16], M06[17] and M08, none of them individually exceeding 10% TRR or 0.01 mg/kg, respectively. Ca 13% TRR in the lemon peel and 31% in the orange peel remained unidentified, but none of the individual compounds exceeded 0.005 mg/kg.

In **grapes** (ca 2N rate treatment) after early application, 58% TRR (0.65 mg/kg) was identified as spirodiclofen. A total of 17 metabolites could be detected, together amounting to 41% TRR (0.46 mg/kg). Metabolites identified were M08 (12.2 % TRR) and spirodiclofen-enol, M04, M05, M02eq, M03eq (all <10%TRR). Upon characterisation of residual radioactivity further 18% TRR could be resolved into 15 compounds, amongst them four compounds containing dichloro-mandelic acid as common moiety.

After a late application 96% TRR (1.8 mg/kg) was identified as spirodiclofen. A total of 11 metabolites could be detected, together amounting to only 3.5% TRR (0.07 mg/kg). Of them six metabolites could be identified as M05, M08, M04 (0.6- 1.1% TRR; all <0.02 mg/kg) and spirodiclofen-enol, M02eq, M03eq (all <0.01 mg/kg).

It could be demonstrated that in the metabolism of spirodiclofen in plants, the initial degradation reaction is cleavage of the ester bond forming spirodiclofen-enol, followed by hydroxylation in the 3- or 4- position of the cyclohexyl ring. Cleavage of the acid ring structure leads to a ring-open mandelic acid cyclohexyl ester intermediate which is further metabolised into the free 2,4-dichloro-mandelic acid (M06), finally followed by glycosylation.

Metabolites found in plant matrices but not found in rat and livestock (goat) were M04 (7.9% TRR in grapes), M07 (1% TRR in apples) M08 (12% TRR in grapes) and M05 (9.1% TRR in oranges). Metabolites M04, M07 and M08 are sugar conjugates of the rat metabolites M09[18]

[13] M07: 2,4-dichloro-mandelic acid glucosyl cyclohexyl ester
[14] M08: 2,4-dichloro-mandelic acid glucoside
[15] M04: 2,4-dichloro-mandelic acid cyclohexyl ester glucosylpentoside
[16] M05: 2,4-dichloro-mandelic acid hydroxy-cyclohexyl ester
[17] M06: 2,4-dichloro-mandelic acid
[18] M09: 2,4-dichloro-mandelic acid cyclohexyl ester

and M06, respectively. Therefore, they were not considered of particular toxicological concern, i.e. of having higher toxicity than spirodiclofen itself, however it is noted that all rat metabolites should be considered toxicologically relevant (refer to 2.8). Toxicity data for non rat metabolites M05 are not available. The metabolite was not used as reference compound in the rat metabolism studies, so its presence or absence in rat was not verified. M05 is expected to hydrolyse into M06, which was found in rats and hence the toxicity of M05 is expected to be equal to that of spirodiclofen. It was concluded that given the predominant presence of spirodiclofen in the terminal residue on fruit after a foliar treatment none of the metabolites should be included in the residue definition. None of the metabolites is expected to be present at levels above 0.01 mg/kg upon treatment at the notified application rates. Consequently, it is proposed to define the residue in fruits and fruiting vegetables as spirodiclofen for risk assessment and monitoring purposes. The proposed residue definition has to be limited to fruit and fruiting vegetables since the metabolism of spirodiclofen was studied only in relation to the representative uses notified, i.e. citrus, pome fruit, stone fruit and grapes, and no statement about metabolism in other crops can be made.

Supervised residue trials were carried out according to the supported representative uses on mandarins, oranges, peaches in Southern Europe and apples, pears, and grapes in Northern and Southern Europe. Based on the trial results HRs (Highest Residues) and STMRs (Supervised Trials Median Residues) could be derived for each relevant data set and MRLs could be proposed for citrus fruit, pome fruit, peaches, nectarines, apricots and grapes (refer to 3.4). Valid storage stability data support the residue values found in supervised residue trials and in processing studies. No degradation of spirodiclofen occurred during storage in water containing materials. In commercial practice, a large part of the harvested citrus fruits and pome fruits will be stored in (oxygen and carbon dioxide controlled) cooled pack houses for a long time, before the product is consumed. The fate of residues during storage in cooled pack houses was not investigated. However, since the majority of the residue was located outside the fruits, hydrolysis of spirodiclofen into spirodiclofen-enol was expected to occur very slowly.

The hydrolytic degradation of spirodiclofen under representative processing conditions was investigated. The results demonstrated that spirodiclofen was significantly hydrolysed to spirodiclofen-enol under conditions representative for baking, brewing and boiling (pH 5, 100°C) and sterilisation (pH 6, 120°C). In these cases the nature of the residue in the processed commodities was different from that found in raw agricultural commodities. Under conditions representative for fruit processing such as preparation of juice, wine, sauce and preserves (pH 4, 90°C), spirodiclofen was not hydrolysed. Because spirodiclofen is intended for use on fruits only and therefore spirodiclofen-enol is not expected in processing products thereof, spirodiclofen-enol is not included in the residue definition for risk assessment. However, the residue definition for risk assessment may have to be changed into spirodiclofen plus spirodiclofen-enol in future, if uses should be extended to commodities other than fruit.

In processing studies the residues in/on apples remained nearly unchanged after washing, while a reduction of residues was observed for peaches after washing. Residue levels decreased also upon preparation of orange marmalade, apple sauce, apple juice, grape juice and wine. A considerable concentration of residues was however found in wet and dry apple pomace (mean processing factor 5.9 and 18, respectively) and preparation of raisins (mean processing factor 1.9). Processing studies provided with apples are assumed to represent the

worst case in terms of concentration of residues in dry and wet pomace and thus citrus fruits are covered by theses studies.

3.1.2. Succeeding and rotational crops

Spirodiclofen is currently intended for use in orchards and vineyards where crop rotation is usually not practised, and thus, any potential uptake of soil residues could only occur in the directly treated perennial crops. Spirodiclofen and its major soil metabolites are low to moderate persistent in soil, and no different metabolites than in treated crops are generated in soil. Therefore it is not expected, that the residue situation in the perennial crops after a direct treatment will be affected in some way by residues present in the soil. No rotational crop studies are considered necessary to support the representative uses.

3.2. Nature and magnitude of residues in livestock

The behaviour and metabolism of spirodiclofen was investigated in the lactating goat as a model for ruminants.

After oral administration of ^{14}C spirodiclofen to a lactating goat ca 45% of the applied dose was excreted through urine and faeces and 54% remained in the gastrointestinal tract, suggesting a slow absorption process. This is confirmed by a continuously increasing plasma level during 24 h after first dosage. 0.05% administered dose were recovered in milk and 0.3% in edible tissue. Total radioactive residues (TRR) in milk (0.1 mg/kg) and muscle and fat tissue (<0.2 mg/kg) were low, but slightly higher in the excretory organs liver (0.78 mg/kg) and kidney (2.92 mg/kg).

Even though spirodiclofen is classified as fat-soluble according to its log pow, it was not found in the analysed goat matrices, indicating its full metabolisation in the animal body. The major metabolic product in goat tissues and milk was the hydrolysed derivative spirodiclofen-enol (81%-95% TRR). The oxygenated derivative of spirodiclofen-enol (M03) was also present in milk, liver and kidney but at lower levels.

All metabolites found in goat were also found in rat. However, absorption and metabolism in goat are not completely comparable to those in rat. The absorption process in the goat was slower than in rat. The metabolite pattern observed in rat was different depending of the administered dose and hence the dose rate was shown to have consequences for the absorption and metabolism. Because spirodiclofen-enol is the main component of the residue in the goat study, the residue definition for monitoring and risk assessment in animal products was proposed by EPCO 29 as spirodiclofen-enol, expressed as spirodiclofen. The toxicological reference values of spirodiclofen should be applied in the risk assessment (refer to 2.8).

Fruit pomace (from citrus fruit and pome fruit) is used as feed item for two of the indicator livestock species (dairy cattle, beef cattle). Because estimated residue levels in the livestock diet are higher than 0.1 mg/kg, feeding studies with lactating ruminants were performed. Based on the results of the ruminant feeding studies MRLs for food of animal origin could be derived (refer to 3.4). The estimates of potentially occurring residues in food of animal origin and the subsequent MRL proposals have been presented in an addendum that was, however, not peer reviewed.

Because fruit pomace is not fed to chickens and pigs, they will normally not be exposed to spirodiclofen residues and thus metabolism and feeding studies for poultry and pigs are not required.

3.3. Consumer risk assessment

Long term exposure:
A calculation of the provisional TMDI has been carried out using the WHO standard European diet and the National Dutch diet. In this calculation the MRLs as proposed by the rapporteur Member State (refer to 3.4) are used. Under these conditions the TMDI covered 1.9% of the ADI (0.015 mg/kg bw/d) for the European diet and 3.5% of the ADI for the Dutch diet (general population) or 9.4% of the ADI for the Dutch diet (1-6 yr old children). Considering the above TMDI calculations, the actual dietary intake of spirodiclofen residues is estimated to be well below the ADI.

Acute exposure
Because an ARfD is considered not necessary, the acute risk for the consumer does not need to be assessed.

3.4. Proposed MRLs

Plant products (spirodiclofen)	
citrus fruit	0.1 mg/kg
pome fruit	0.1 mg/kg
peach, nectarine, apricots	0.2 mg/kg
Grape	0.2 mg/kg

Animal products (spirodiclofen-enol expressed as spirodiclofen) – Proposals not peer reviewed	
Milk	0.005 mg/kg
Fat ruminant	0.01 mg/kg
Muscle ruminant	0.01 mg/kg
Kidney ruminant	0.05 mg/kg
Liver ruminant	0.05 mg/kg

4. Environmental fate and behaviour

The fate and behaviour in the environment of spirodiclofen (BAJ 2740) was discussed in the experts' meeting (EPCO 26) of June 2005 on basis of the revised DAR of April 2004[19].

[19] Last updated version: September 2006

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

The route of degradation of spirodiclofen in soil under dark aerobic conditions at 20ºC and 40% maximum water holding capacity (MWHC) or 75% field capacity (FC), was investigated with ^{14}C-3-dihydrofuranone-label or 14C-1-cyclohexyl-label compound. The five soils covered a range of pH (5.8-7.2 measured in $CaCl_2$), organic carbon (OC) content (0.17-2.62%) and clay content (1-10 %). No studies conducted at lower temperatures were available.

Aerobic degradation of spirodiclofen in soil proceeds by ester-cleavage to give the major (> 10% of the applied radioactivity) metabolite BAJ 2740-enol (max. 51.9% AR on day 2), which is metabolised to another major metabolite BAJ 2740-ketohydroxy (max. 44.4% AR on day 30) by oxidation of the dihydrofuranone ring. BAJ 2740-lactide[20] (<3.0% AR) and the major metabolite BAJ 2740-dihydroxy (max. 16.4% AR on day 120) are formed from BAJ 2740-ketohydroxy by rearrangement and reduction, respectively. Hydrolytic or oxidative ring-opening leads to the formation of the major metabolite 2,4-dichlorobenzoic acid (max. 39.6% AR on day 120) from the former 3 metabolites. The ultimate and major breakdown product is carbon dioxide (22.5-93.1% AR by day 120 with the dihydrofuranone-label and 69.1% AR with the cyclohexyl-label) together with low levels of non-extractable residues (max. 14.4 and 17.9 % AR on day 120 with the dihydrofuranone-label and the cyclohexyl-label, respectively).

Due to the proposed pattern of use applied for, it can be justified that spirodiclofen will not be exposed to anaerobic conditions, and therefore no study under these conditions has been performed.

Photolytic degradation of spirodiclofen (14C-3-dihydrofuranone) is insignificant, but photolysis may contribute to the disappearance of BAJ 2740-enol and BAJ 2740-ketohydroxy from soil in the environment. Only one minor photoproduct accounting for a maximum of 4.4% AR was observed in irradiated samples.

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

The rate of soil degradation of spirodiclofen was investigated in the same soils used in the aerobic degradation studies discussed in section 4.1.1. Degradation rates were recalculated by the RMS through the analysis of degradation curves for a hinge point and then using first order regression analysis. Spirodiclofen is low to moderate persistent in soil (DT_{50} = 1.1 – 13 days). An experiment in one of the four soils showed that there was no effect of the dose on degradation rate. First order half-lives of the major metabolites BAJ 2740-enol and BAJ 2740-ketohydroxy were calculated from results obtained in the same study with soils dosed with the parent compound. First order DT_{50} values estimated by the applicant by curve fitting with the ACSL Optimize program package ranged from 1.9 to 9.8 days for BAJ 2740-enol. After recalculation performed by RMS using Modelmanager, first order DT_{50} values for BAJ 2740-ketohydroxy ranged from 0.6 to 27 days.

[20] BAJ 2740-lactide = 3-(2,4-dichlorophenyl)-1,4-dioxaspiro[5.5]undecane-2,5-dione

The rate of degradation of [oxolan-3-14C]-BAJ 2740-dihydroxy was investigated in two soil degradation studies at 20ºC and 49% of MWHC (3 soils, pH ($CaCl_2$): 6.9-7.4; O.C.: 0.69-2.62 %; clay: 10-33%). In the original DAR first order DT_{50} and DT_{90} values were recalculated by the RMS with the same approach used for the parent. Re-analysis of the raw data in soil Laacher Hof A III showed a biphasic decline curve, resulting in a DT_{50} of 49 days. However, following a further inspection of the study, it was considered that this value is indeed too worst case and it was agreed (EPCO 26) to use the value reported by the applicant (= 29.5 days) for TWA (Time Weighted Average) PECsoil calculations (Revised addendum B8 dated September 2006, The Netherlands, 2009).

An aerobic soil degradation study conducted with [phenyl-U-14C]-2,4-dichlorobenzoic acid allowed the calculation of the rate of degradation of this metabolite (4 soils; pH ($CaCl_2$): 5.9-7.4; O.C.: 0.19-2.62 %; clay: 1-33%). The RMS recalculated 1st order DT_{50} values at 20ºC and these were in the range 3.5-11 days, indicating that 2,4-dichlorobenzoic acid is low to moderate persistent in soil.

As the single first order DT_{50} (at 20ºC and pF2) were < 60 days, no field dissipation studies were provided.

PECsoil calculations[21] for spirodiclofen and its soil major metabolites were based on worst case laboratory DT_{50} values as revised by the RMS, and assuming a crop interception of 50% agreed by the Member States experts (EPCO 26).

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

Parent spirodiclofen and the metabolite BAJ 2740-ketohydroxy are not stable in 0.01 M calcium chloride and no batch sorption studies were performed. KFoc values were therefore determined using the HPLC method, resulting in 31037 L/kg for spirodiclofen and 612 L/kg for the metabolite. Reliable KFoc values were determined in laboratory batch sorption studies with [dihydrofuranone-3-14C]-BAJ 2740-enol, [oxolan-3-14C]-BAJ 2740-dihydroxy and [phenyl-U-14C]-2,4-dichlorobenzoic acid. Results showed that BAJ 2740-enol and 2,4-dichlorobenzoic acid are very high mobile (4 soils, KFoc = 12.1-28.6 L/kg and KFoc = 4.7-8.8 L/kg, respectively), and that BAJ 2740-dihydroxy is very high to high mobile (3 soils, KFoc = 8.9-105 L/kg). No clear relationships were observed between soil pH and adsorption or between % clay content and adsorption for any of the metabolites.

A 9-day aged column leaching study, performed in one soil (pH, 6.2, OC content 0.34%, sand 65%), showed 34.5% AR in the eluted soil column and 52.8% AR in the leachate. Parent compound was only detectable in the treated soil plug and in the 0-6 cm layer (total in column 15.4% AR) and metabolite BAJ 2740-ketohydroxy was detectable down to 12 cm (total in column 4.4% AR). Metabolites BAJ 2740-dihydroxy, BAJ 2740-enol and 2,4-dichlorobenzoic acid were detected in all soil layers (total in column 1.8, 3.8 and 1.4% AR respectively).

Parent compound was not detectable in the leachate (<0.1% AR). Metabolites BAJ 2740-enol and 2,4-dichlorobenzoic acid were present in the leachate at > 10% AR (17.4% AR and 19.0% AR respectively), whereas BAJ 2740-ketohydroxy and BAJ 2740-dihydroxy were

[21] Revised addendum B8 dated September 2006.

detected at 5.2% AR and 2.0% AR respectively. Further 7-8 unidentified fractions were present in the soil column and the leachate, none of them individually accounting for > 1.2% AR and > 3.1% AR respectively.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

In sterile aqueous buffer solutions, spirodiclofen hydrolysed with first order DT_{50} of 119.6 (pH 4), 52.1 days (pH 7) and 2.5 days (pH 9) at 20ºC. The hydrolytic stability of spirodiclofen decreases as temperature and pH increase. The main hydrolysis product was BAJ 2740-enol (max. 28.9, 52.2 and 100.8% AR after 30 days at pH 4, 7 and 9, respectively).

The aqueous photolysis of spirodiclofen was studied at pH 4 to minimise any effects of hydrolysis. When irradiated with a xenon lamp (equivalent light intensity of midsummer sunlight, 40ºN latitude) the reliable half-life corresponding to natural irradiation with a 12 hour photoperiod was 123 days. Irradiated and dark solutions contained low levels of BAJ 2740-enol (≤ 3.3% AR) and up to 6 unidentified fractions (none > 7.7% AR).

The aqueous photolysis of BAJ 2740-enol was studied in laboratory with Rhine water. When irradiated with a xenon lamp (equivalent light intensity of midsummer sunlight, 40ºN) the half-life was 7.6 hours. BAJ 2740-dioxoketone was the only photodegradate formed at > 10% AR (max. 25.6% AR).

No study on ready biodegradability was submitted and therefore it was proposed to classify spirodiclofen as “non-readily biodegradable” taking into account the results of the water/sediment study.

In water/sediment systems (2 systems studied in laboratory at 20ºC; pond sediment: pH 5.8 and total O.C. 4.0%; pit sediment: pH 7.1 and total OC 0.9%) spirodiclofen degraded in the whole system with first order DT_{50} of 4.2 and 2.3 days, respectively, as re-calculated by the RMS. Mineralisation was at comparable low level in both systems (CO_2 max. 2.1-2.6% AR by day 110). A slightly higher proportion of applied radioactivity partitioned into the pond sediment (max. 78.7% AR after 1 day) compared to the sediment (max. 64.5% AR after 1 day). Spirodiclofen was rapidly lost from the water phase of both systems, with first order DT_{50} values of 0.3 days (DT_{90} <1d) for the pond and 1.1 days (DT_{90} <3d) for the pit. Maximum levels of spirodiclofen in sediment occurred on day 1 (58-68% AR), declining thereafter with DT_{50} values in sediment of 4.4 days (pond) and 2.5 days (pit). The major metabolite was BAJ 2740-enol, with maximum levels of 84% AR (day 14-59) and 30% AR (day 110) in water and sediment, respectively. The total levels of other degradates in any system were = 5.0% AR. DT_{50} values for BAJ 2740-enol were based on few data points late in the pond study, when microbial activity was low and sediment not anaerobic, and resulted in 186 and 393 days for the water and system respectively. In the pit system, no degradation of BAJ 2740-enol was apparent until study end (day 110) and therefore no degradation rates could be calculated.

In an anaerobic water/sediment study conducted at 20ºC, spirodiclofen was almost quantitatively lost from the water phase at the first sampling, with a maximum level occurring in sediment of 91.9% AR on day 0. Spirodiclofen dissipated from sediment and overall system with a first order DT_{50} of 9.8 and 10 days, respectively. The metabolite BAJ 2740-enol

was detected in the water phase (max. 71-80% AR between day 34 and 365) as well as in the sediment phase (max. 15.6% AR on day 246, thereafter declining to 9.6% AR at study end, 365 days). Other degradates individually never exceeded 4.8% AR in the system.

The available surface water exposure assessment considered the spray drift route of entry to surface water according to the Guidance Document on Aquatic Ecotoxicology (European Commission, 1997). The potential exposure of surface water via the drainage and runoff routes of entry has not been assessed in the EU level exposure assessment. Member States should therefore carry out a surface water exposure and consequent aquatic risk assessment for spirodiclofen and its major metabolites from the runoff and drainage routes of exposure at the national level, should spirodiclofen be included in annex 1. PECsw estimations for parent spirodiclofen were performed by the RMS for single application of 96 (vine) or 144 g a.s./ha (orchards crops), using drift values for early and late stage for vine and orchard crops, with the exception of citrus (application in leafy stage only). An equal distribution in a static water body of 30 cm depth was assumed. Time weighted average concentrations were calculated based on dissipation DT_{50} of 1.1 days from water (maximum 1st order DT_{50} from water phase). Because limited or no degradation of BAJ 2740-enol was observed in the water/sediment systems, TWA PECsw values for this metabolite were considered to be equal to the initial PECsw values.

Predicted concentrations in sediment were not calculated as the end points of the toxicity tests with sediment-dwelling organisms were expressed in concentrations in the overlaying water.

4.2.2. Potential for ground water contamination of the active substance, their metabolites, degradation or reaction products

Predicted concentrations in groundwater for spirodiclofen and its soil major metabolites (BAJ 2740-enol, BAJ 2740-dihydroxy, BAJ 2740-ketohydroxy and 2,4-dichlorobenzoic acid), were recalculated by RMS with FOCUS-PEARL using the revised degradation rates and adsorption values. Simulations were carried out for the good agricultural practice (GAP) of 1 application of spirodiclofen of 0.144 kg a.s./ha for apple and citrus (0.0504 and 0.0432 kg a.s./ha accounting for 65 and 70% crop interception, respectively). The date of application was taken to be the latest date of application in supervised residues trials in northern or southern Europe, and as a result simulations were based on late application. Therefore, Member States should pay particular attention to ensure that earlier applications to vine are adequately assessed at national level. The arithmetic mean of laboratory soil first order DT_{50} values were used as input and Koc values were converted into Kom values, excluding those values determined in soil with low organic carbon content (0.19%) and with an associated Freundlich exponent $1/n < 0.7$. In all scenarios, estimated 80th percentile of annual average concentrations in groundwater were <0.001 µg/L for parent spirodiclofen and the metabolite BAJ 2740-ketohydroxy, and ≤0.001 µg/L for the metabolites BAJ 2740-enol and BAJ 2740-dihydroxy. Estimated 80th percentile of annual average concentrations in groundwater of the metabolite 2,4-dichlorobenzoic acid were ≤0.001-0.012 µg/L in all the relevant FOCUS scenarios.

4.3. Fate and behaviour in air

Measured volatilisation of spirodiclofen from soil and leaf surfaces under field conditions was negligible. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals (1.5 x 106 radicals cm^{-3} and a 12 hour photoperiod) resulted in an estimated atmospheric half-life of 2.67 hours. This estimated degradation rate and the Henry's Law constant of 2 x 10-3 Pa/mol.m^3 and the 24 hour volatilisation results, suggested that the concentrations of spirodiclofen in air are likely to be negligible.

5. Ecotoxicology

Spirodiclofen was discussed at the experts' meeting for ecotoxicology (EPCO 27) in June 2005 and at PRAPeR 68 in May 2009, based on the Draft Assessement Report of April 2004, the Addendum of May 2005 - revised September 2006, and the Addendum of April 2009.

Spirodiclofen is a new acaricide / insecticide proposed for use on apple and pear (northern and southern EU), southern EU peach, apricot, nectarine, orange and mandarin (all single application at 0.144 kg a.s./ha), and on northern and southern EU grapevines (single application 0.096 kg a.s./ha). The proposed formulated product, Envidor SC 240, is a SC formulation containing 240 g/L spirodiclofen.

EPCO 30 (phys chem) asked for ecotoxicological confirmation of the new specification from the full scale production. The RMS confirmed that the new specification is acceptable for toxicology, which would also cover the ecotoxicological relevance with regard to wild living mammals. The studies related to the ecotoxicological non-relevance of the three new impurities (impurities 7, 8 and 9) with regard to aquatic organisms and soil-dwelling organsims were submitted by the applicant in 2007, and assessed by the RMS in an addendum (The Netherlands, 2009).

No significant change in the hazard potential of the new material was evidenced from the submitted aquatic toxicity data (impurities 8 and 9) and the impurities were not anticipated to contribute to the toxicity of spirodiclofen, considering the specified limit of 4 - 5 g/kg. The potential contribution of impurity 7 to the overall toxicity of the new material was also assessed as low, based on QSAR assumptions or a toxicity of 10 times higher than the parent substance. New acute toxicity studies on earthworms and micro-organisms exposed to the new material containing the three impurities 7, 8 and 9 at the maximum specified limit did not indicate any changes in the toxicity. Based on the submitted studies it was concluded that none of the new impurities were of ecotoxicological significance. The assessment was endorsed at PRAPeR 68 (May 2009).

The impurity BAJ 2740-enol in the new technical specification is also a metabolite in the environment. The risk to the environment was assessed as low. Therefore BAJ 2740-enol was not considered to be an ecotoxicologically relevant impurity.

5.1. Risk to terrestrial vertebrates

The risk assessment for birds and mammals was conducted according to SANCO 4145/2000 (European Commission, 2002). The RUD values were based on an older draft version of the

guidance document from February 2001. Therefore an updated risk assessment with RUD values from the final version of the guidance document (September 2002) was presented in the addendum of May 2005 and discussed in the experts` meeting. The representative uses are in orchards and grapevine (Northern and Southern EU). Therefore the standard risk assessment scenarios for insectivorous birds and herbivorous mammals were chosen. The acute, short-term and long-term TER values for insectivorous birds exceeded the Annex VI trigger values indicating a low risk for all representative uses evaluated.

The risk to birds from bio-accumulation via uptake of contaminated earthworms or fish was assessed as low since the long-term TERs were markedly above the Annex VI trigger of 5 for all representative uses.

The first tier risk assessment for herbivorous mammals resulted in acute TER values above the trigger of 10. The long-term TERs of 1.2 (orchard) and 1.8 (grapevine) indicated a potential high risk to mammals. The NOEC used in the risk assessment was based on slight (about 5%) but statistically significant effects on body weight of F0 male adults and F1 pup weight. Since no effects on embryo/foetal development were observed in a developmental study with rats up to the highest tested dose of 1000 mg/kg bw/d the effect on initial pup weight recorded in the 2-generation study at 26.2 mg/kg bw/d was considered to be an effect due to the prolonged exposure of the parental generation. Since only one application per year is recommended in the representative uses it was considered that in a realistic exposure scenario the animals would not be exposed to constant high levels of spirodiclofen for 16 weeks due to residue decline. Besides the effect on pup weight a slight increase in vacuolisation of adrenals of F1 adult rats was observed at a dose of 26.2 mg/kg bw/d. The meeting agreed that the lowest observed effect level of 26.2 mg/kg bw/d could be used in the risk assessment because of the low magnitude of effect and the likelihood that exposure would be much shorter in reality.

The end points based on the end point of 26.2 mg/kg bw/d are 5.3 and 8.1 for the use in orchards and grapevine, respectively.

The risk to mammals from bioaccumulation via uptake of contaminated earthworms or fish was assessed as low since the long-term TERs were above the Annex VI trigger of 5 for all representative uses.

The metabolite BAJ 2740-enol is a major metabolite in soil and water. BAJ 2740-enol is found in the rat metabolism and hence the risk to mammals is considered to be covered by the risk assessment for spirodiclofen. BAJ 2740-enol was also found in metabolism studies with goat, fish and plants suggesting that ester cleavage of spirodiclofen is the first step in the metabolism in different groups of organisms. Therefore it was assumed that BAJ 2740-enol is also formed in birds and that the toxicity of the metabolite would be covered by the study with the parent spirodiclofen. The log Pow for the metabolite is 3. Therefore the risk from bioaccumulation to earthworm- and fish-eating birds and mammals was assessed. The TER values for the long-term risk to earthworm- and fish-eating birds were more than one order of magnitude above the trigger of 5 (based on the assumption that the metabolite would have the same toxicity as spirodiclofen) suggesting a low risk to birds. The long-term TERs for fish- and earthworm-eating mammals were in the range of 29.8 to 1310 (based on the long-term endpoint of 26.2 mg spirodiclofen/kg bw/d).

2,4-Dichlorobenzoic acid, BAJ 2740-ketohydroxy and BAJ 2740-dihydroxy are major soil metabolites. The metabolites were not found in the metabolism studies with rats, goat, fish or plants except 2,4-Dichlorobenzoic acid which was found in rats. Long-term exposure via uptake of contaminated earthworms was considered as a route of exposure. Since the log-Pow of 2,4-Dichlorobenzoic acid is <3 the risk from uptake of contaminated earthworms was not considered further. For BAJ 2740-ketohydroxy and BAJ 2740-dichlorobenzoic acid the TER values for birds were more than one order of magnitude above the trigger of 5 and for mammals the TER values were calculated to be in the range of 25 to 66 (based on the assumption that the metabolites would be as toxic to birds and mammals as spirodiclofen).

The toxicity of metabolites is usually less than that of the parent and in tests with other organisms no indication was found that the metabolites would be more toxic than spirodiclofen. Therefore the margin of safety was considered as large enough to conclude that the risk to birds and mammals from metabolites in soil and water is low.

Potential endocrine effects of spirodiclofen and the explanation for the observed effects included in the addendum were discussed in the EPCO meeting. The meeting concluded that the effects on spermatogenesis observed in rats at the highest tested dose are due to interference at the general biochemical pathways (Krebs cycle and pyruvate/citrate shuttle). Systemic toxic effects were observed at lower dose levels and the reproductive performance was not affected at the highest tested dose. Therefore the meeting agreed that no further studies on the endocrine disrupting properties of spirodiclofen are required.

The acute TER values for the risk from uptake of contaminated drinking water were calculated to be more than 5 orders of magnitude above the Annex VI trigger of 10. The calculation presented in the addendum was based on PECsw values instead of the 5 fold dilution of the sprayed solution as suggested in the guidance document on birds and mammals (European Commission, 2000). If the 5 fold dilution of the sprayed solution is used than the TER values would still be above the trigger suggesting a low risk to birds and mammals from uptake of contaminated drinking water.

Overall it is concluded that the risk to birds and mammals is low for all representative uses.

5.2. Risk to aquatic organisms

A new risk assessment was presented in the addendum of May 2005. No effects were observed in acute tests with technical spirodiclofen in fish, daphnids and algae at concentrations close or above the limit of solubility in water. End points from tests with the formulation (with higher concentrations of dissolved spirodiclofen) were used in the risk assessment. For the calculation of PECsw values only spray drift was considered as a route of entry. The acute risk to aquatic organisms was assessed as low for the representative uses evaluated. However the long-term TERs for fish and daphnids were below the Annex VI trigger of 10.

The applicant suggested to refine the risk assessment by using PECtwa values. However the tests with fish and daphnids did not allow a conclusion on the time period to onset of effects and therefore the meeting considered it not appropriate to use PECtwa values in the risk assessment. A new study with fish (early life stage test) was conducted under static conditions and the presence of sediment. The meeting agreed that pulsed exposure is more realistic compared to flow through conditions and that the behaviour of the test substance observed in

the test system matched the behaviour in the water-sediment study. The meeting suggested that the end point (NOEC = 20 µg/L) should be used in the long-term risk assessment and compared to the initial PECsw value. Based on the new end point the no-spray buffer zone could be reduced to 20m (early use in orchards) and 10m (late use in orchards) to achieve TERs >10 for fish. A new flow-through study with Daphnia magna was also submitted. The meeting agreed to use the end point from this new study in the risk assessment since the end point was lower than in the study provided earlier (NOEC of 11 µg/L instead of 24.8 µg/L). However the use of a 21-d PECtwa was rejected since it was not possible from the study observations to draw a conclusion on the time to onset of effects. Based on the NOEC of 11 µg/L buffer zones of 30m (early use in orchards), 15m (late use in orchards) and 10m (late use in vine) would be required to achieve a TER of >10 for all representative uses evaluated. Since spirodiclofen is an insecticide and it partitions rapidly to the sediment phase a risk assessment for sediment dwelling insects was conducted. The TER values for *Chironomus riparius* were below the trigger of 10 requiring no-spray buffer zones of 15m and 10m for the early and late use in orchards while for the use in vine the TERs are >10 at the standard distance from the field of 3m.

The major metabolite in water BAJ 2740-enol is persistent in the water phase and degrades slowly in the sediment phase (DT_{50} = 186 d). The acute toxicity of BAJ 2740-enol to aquatic organisms is lower but the chronic toxicity is similar to spirodiclofen. The PEC values of BAJ 2740-enol of 9, 4.8, 0.55 and 1.6 µg/L for the uses in orchards early and late and grapevine early and late were based on the maximum formation rate of 84.3 % of the parent spirodiclofen. The acute TER values for fish, daphnids and algae were well above the Annex VI triggers and also the chronic TERs for fish, daphnids and *Chironomus* were above the trigger of 10 indicating a low risk.

Concerns were raised on potential endocrine disrupting effects of BAJ 240-enol in the evaluation meeting in March 2005, based on observations on sex ratio in the fish full life cycle study of Dionne E., 2001 (The Netherlands, 2004, B.9.2.2.3.1). Further details on the study and an evaluation of potential endocrine effects were given in the addendum from May 2005. The experts´ meeting agreed that the study gives no rise to concern of endocrine effects since no compound related anomalies were found in the gross pathological evaluation of the gonads and reproduction was not affected. The lower percentage of male fish in the F0 generation was due to higher mortality because of aggressive behaviour of male fish.

Overall it is concluded that the acute risk to aquatic organisms is low but a high long-term risk was indicated requiring no-spray buffer zones of 30m (early use in orchards), 15m (late use in orchards) and 10m (late use in vine) to mitigate the long-term risk.

5.3. Risk to bees

The acute oral and contact toxicity of technical and formulated spirodiclofen to honeybees is low. The HQ values for the orchard and grapevine use are in the range of <0.48 to <0.73 indicating a low acute risk to bees from both representative uses.

Larval stages of insects are particularly susceptible to spirodiclofen. Temporary adverse effects on bee-brood with recovery after 4 weeks were observed in two semi-field studies where worker bees were foraging exclusively on plants treated at rates of 0.144 kg a.s./ha and 0.146 kg spirodiclofen/ha. The experts' meeting concluded that no further studies are required

and suggested as a risk mitigation measure the following labelling: No use during flowering of the crop and avoiding that flowering weeds are present (e.g. mowing the weeds).

After the peer review concern was raised by beekeepers' associations that exposure from potential plant residues should be addressed and taken into account in a risk assessment, or used to establish a waiting time between the application and the plant flowering. EFSA noted that the route of honeybee exposure to plant protection products, which is considered in calculating HQ, is a direct contact through sprays. HQ values were calculated for both contact and oral absorption of the product and were below 1. Exposure to residues on flowers, and in particular leaves, will comparatively have much less importance. Risk assessment through direct sprays can be considered fully to cover risk via exposure to residues.

5.4. Risk to other arthropod species

Effects of BAJ 2740 240 SC were tested in standard laboratory tests with *Aphidius rhopalosiphi*, *Trichogramma caccoeciae*, *Chrysoperla carnea*, *Pardosa sp*., *Poecilus cupreus* and *Typhlodromus pyri*. Spirodiclofen is an insecticide/acaricide with an insect growth regulator related mode of action. Hence it is expected that larval stages of insects and mites are particularly sensitive to spirodiclofen. Not surprisingly only slight effects were observed at dose rates ranging from 0.029 to 0.144 kg spirodiclofen/ha in the tests with adult insects while in the test with *T. pyri* treatment with 0.0533 kg spirodiclofen/ha caused 100% mortality suggesting a high in-field risk to predatory mites from both representative uses. Two extended lab tests were conducted with *T. pyri*. The LR_{50} was determined as 0.024 g spirodiclofen/ha. No LR_{50} from a standard laboratory study was available and hence the LR_{50} from the extended laboratory study was used instead to calculate TER values for different distances from the treated area (90th percentile drift data and a vegetation distribution factor of 10 were used in the calculations). The TER value was compared to a trigger value of 5. The TER of 5 would be exceeded at distances of 20m (orchard early use), 15m (orchard late use), 3m (grapevine early use) and 5m (grapevine late use) from the treated area. Three field studies were conducted. The number of mites and mite eggs was reduced at 7 and 28 d after treatment at a rate of 0.096 kg spirodiclofen/ha (the effect was statistically not significant). The number of *T. pyri* was reduced by up to 54% after treatment at a rate of 0.144 kg/ha. After one year the difference to the control was 27% (but not statistically significant). It was suggested that recovery within one year was shown in the field experiment. The risk assessment provided by the RMS was discussed and accepted by the experts' meeting. The meeting concluded that the relevant routes of exposure were covered by the risk assessment and that the specificity to target organisms (mites) is high. Overall the risk to non-target arthropods is considered to be low for the representative uses.

5.5. Risk to earthworms

The acute LC_{50} values for spirodiclofen and its major soil metabolites BAJ 2740-enol, BAJ 2740-ketohydroxy, BAJ 2740-dihydroxy were > 500 mg /kg soil and for the major metabolite 2,4-dichloro-benzoic acid the LC_{50} was 281 mg /kg soil (end points were corrected by a factor of 2 to account for the log Pow>3 and the organic matter content in the test systems). The TER values were markedly above the trigger of 10 indicating a low risk to earthworms from the representative uses. No chronic

risk assessment is required since the DT_{90} for spirodiclofen and its metabolites is less than 100 d and it is applied only once per year.

5.6. Risk to other soil non-target macro-organisms

No testing with other soil non-target macro-organisms is triggered because the DT90 of spirodiclofen and its soil metabolites is <100 days. Nevertheless the toxicity of the major metabolites in soil was tested with *Folsomia candida*. The NOEC values were determined as 100 mg BAJ 2740-enol/kg soil, 1000 mg BAJ 2740-dihydroxy/kg soil and 18 mg 2,4-dichlorobenzoic acid/kg soil. The TERs based on initial PECsoil values are markedly above the trigger of 10 indicating a low risk. In the test with BAJ 2740-ketohydroxy no effects in terms of number of offspring were observed but the body size of juveniles was reduced at all concentration levels tested. The TER values for BAJ 2740-ketohydroxy are <183 (orchard) and <271 (grapevine) based on the lowest tested concentration. Since only the size of offspring was affected but not the number of offspring and because the TER values are well above the trigger of 10 it is concluded that the risk to collembola from BAJ 2740-ketohydroxy is likely to be low.

5.7. Risk to soil non-target micro-organisms

The effects of spirodiclofen and its major soil metabolites on soil nitrification and respiration were investigated. The formation of nitrate-N was increased by >25 % at days 28 and 42 but returned to levels <25% after day 56. Effects on nitrification of > 25% were also observed in the tests with the metabolites BAJ 2740-enol, BAJ 2740-ketohydroxy, BAJ 2740-dihydroxy and 2,4-dichlorobenzoic acid on day 14. But all effects were <25% at day 28. Since the tested concentrations were a factor of 10 to 66 times higher than the initial PECsoil values and the effects were of temporary nature it is assumed that the observed effects would not cause a high risk to soil functioning at the application rates suggested in the representative uses.

5.8. Risk to other non-target-organisms (flora and fauna)

No herbicidal effects were detected in two screening studies at application rates of up to 2 kg spirodiclofen/ha. The tested application rates were about 14 and 21 times higher than the rates of the representative uses. Therefore the risk to non-target plants is considered to be low.

5.9. Risk to biological methods of sewage treatment

Only slight effects on respiration of activated sewage sludge were observed at the tested concentrations of up to 10000 mg spirodiclofen/L. The EC50 is therefore > 10000 mg spirodiclofen/L. If the product is applied as suggested in the list of representative uses it is expected that the concentrations of spirodiclofen reaching sewage treatment plants are far below the EC50 value and hence the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

6.1. Soil

Definitions for risk assessment: spirodiclofen, BAJ 2740-enol, BAJ 2740-ketohydroxy, BAJ 2740-dihydroxy, 2,4-dichlorobenzoic acid

Definitions for monitoring: spirodiclofen

6.2. Water

6.2.1. Ground water

Definitions for exposure assessment: spirodiclofen, BAJ 2740-enol, BAJ 2740-ketohydroxy, BAJ 2740-dihydroxy, 2,4-dichlorobenzoic acid

Definitions for monitoring: spirodiclofen

6.2.2. Surface water

Definitions for risk assessment: spirodiclofen, BAJ 2740-enol

Definitions for monitoring: BAJ 2740-enol (spirodiclofen is not a suitable marker for monitoring as DT_{90}water <3d)

6.3. Air

Definitions for risk assessment: spirodiclofen

Definitions for monitoring: spirodiclofen

6.4. Food of plant origin

Definitions for risk assessment: spirodiclofen

Definitions for monitoring: spirodiclofen

6.5. Food of animal origin

Definitions for risk assessment: spirodiclofen-enol expressed as spirodiclofen

Definitions for monitoring: spirodiclofen-enol expressed as spirodiclofen

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

6.6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Spirodiclofen	Low to moderately persistent (first order $DT_{50\,lab}$ 1.1-13 d, 20°C 40% MWHC or 75% FC)	Low risk to earthworms and collembola, temporary effects of > 25% at concentrations of 0.2 and 0.98 mg/kg soil which is more than 2 times and 10 times the initial PECsoil
BAJ 2740-enol	Low persistent (first order $DT_{50\,lab}$ 1.9-9.8 d, 20°C 40% MWHC or 75% FC)	Low risk to earthworms, collembola and soil micro-organisms
BAJ 2740-ketohydroxy	Very low to moderately persistent (first order $DT_{50\,lab}$ 0.6-27 d, 20°C 40% MWHC or 75% FC)	Low risk to earthworms, collembola and soil micro-organisms
BAJ 2740-dihydroxy	Low to moderately persistent (first order $DT_{50\,lab}$ 3.8-29.5 d, 20°C 49% MWHC)	Low risk to earthworms, collembola and soil micro-organisms
2,4-dichlorobenzoic acid	Low to moderately persistent (first order $DT_{50\,lab}$ 3.5-11 d, 20°C 49% MWHC)	Low risk to earthworms, collembola and soil micro-organisms

6.6.2. 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 -activity
Spirodiclofen	Immobile (K_{oc}= 31037 L/kg, estimated with HPLC method)	FOCUS: no	Yes	Yes	Yes
BAJ 2740-enol	Very high mobility (K_{Foc}= 12.1-28.6 L/kg)	FOCUS: no	No data available No data required	Assessment not necessary	The acute toxicity to aquatic organisms is lower but the chronic toxicity is similar to spirodiclofen. The risk to aquatic organisms in surface water is low.
BAJ 2740-ketohydroxy	Low mobility (K_{oc}= 612 L/kg, estimated with HPLC method)	FOCUS: no	No data available No data required	No data available, not required	No data available No data required
BAJ 2740-dihydroxy	Very high to high mobility (K_{Foc}= 8.9-105 L/kg)	FOCUS: no	No data available No data required	No data available, not required	No data available No data required
2,4-dichloro-benzoic acid	Very high mobility (K_{Foc}= 4.7-8.8 L/kg)	FOCUS: no	No data available No data required	Assessment not necessary	No data available No data required

6.6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Spirodiclofen	See point 5.2.
BAJ 2740-enol	The acute toxicity to aquatic organisms is lower but the chronic toxicity is similar to spirodiclofen. The risk to aquatic organisms is low.

6.6.4. Air

Compound (name and/or code)	Toxicology
Spirodiclofen	Not acutely toxic via inhalation

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

- none

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide and acaricide as proposed by the applicant which comprises of spray application to control mites and sucking insects. Full details of the GAP can be found in the table "Summary of representative uses evaluated" which is in the end points list.

The representative formulated product for the evaluation was "Envidor SC 240", a suspension concentrate containing 240 g/L spirodiclofen.

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (The German S19 method has been validated). For the other matrices only single methods are available to determine the residues of spirodiclofen and its enol metabolite in soil, water and animal products and spirodiclofen in air. Sufficient 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.

Spirodiclofen is not acutely toxic via oral, dermal and inhalation routes. It is not a skin or eye irritant, but it is a skin sensitiser, therefore **R43 "May cause sensitisation by skin contact"** was proposed. The overall relevant NOAEL is 1.45 mg/kg bw/day (liver and adrenal effects) for repeated dose administration to spirodiclofen. Spirodiclofen chronic administration results in liver tumours in mice, Leydig cell tumours and uterus adenocarcinomas in rats, with clear NOAELs demonstrated. The classification **R40 "Limited evidence of a carcinogenic effect"** was proposed. Spirodiclofen has no genotoxic, reproductive and developmental toxicity potential. The subchronic NOAEL for neurotoxicity is 70 mg/kg bw/day, while the chronic neurotoxicity NOAEL is 110 mg/kg bw/day. The established Acceptable Daily Intake (ADI) is 0.015 mg/kg bw/day and the Acceptable Operator Exposure Level (AOEL) is 0.009 mg/kg bw/day (100 safety factor applied). The allocation of an Acute Reference Dose (ARfD) was not considered necessary. The estimated operator, worker and bystander exposure are below the AOEL for all uses as well as for the workers and bystanders.

The metabolism of spirodiclofen in fruit has been fully elucidated and proceeds through ester cleavage and hydrolysis steps. The parent compound was identified as the major constituent of the residue on fruit crops at various PHIs. The identified metabolites are present at very low levels but are considered as having similar toxicological properties as the parent compound. Given the predominance of spirodiclofen in the terminal residue in fruits, the residue definition can be restricted to spirodiclofen only, for both risk assessment and monitoring. Under processing, spirodiclofen is degraded only at temperatures of 100°C or higher to spirodiclofen-enol, and hence under conditions representative for fruit processing (pH 4, 90°C) no generation of spirodiclofen-enol is expected.

Upon exposure of livestock to spirodiclofen one main component of the residue in food of animal origin was identified as spirodiclofen-enol, and was defined as the residue of concern in terms of consumer exposure. Based on the results of the ruminant feeding studies MRLs for food of animal origin could be derived.

The consumer risk assessment showed that the chronic exposure to spirodiclofen residues from fruit and spirodiclofen-enol residues from food of animal origin is well below the ADI of spirodiclofen. Because an ARfD is considered not necessary, the acute risk for the consumer does not need to be assessed.

The information available on the fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at the EU level. The drainage and runoff routes of exposure to surface water for parent spirodiclofen and its major metabolites have not been covered in the available EU level assessment. These exposure assessments and the associated risk assessment to aquatic organisms should be completed in national assessments made by member states should spirodiclofen be included in annex 1. For the notified intended field uses, the potential for groundwater exposure by spirodiclofen or its soil metabolites BAJ 2740-enol, BAJ 2740-ketohydroxy, BAJ 2740-dihydroxy and 2,4-dichlorobenzoic acid above the parametric drinking water limit of 0.1 µg/L is considered negligible.

The risk to birds and mammals was assessed as low. The aquatic risk assessment was based on spray drift as the only route of entry into surface water. The acute TER values for aquatic organisms are markedly above the trigger values but the long-term TER values for fish, daphnids and sediment dwelling insects were below the Annex VI trigger of 10. Risk-mitigation measures such as no-spray buffer zones of up to 30m (early use in orchards), 15m (late use in orchards) and 10m (late use in vine) are required to mitigate the long-term risk to aquatic organisms. The acute risk to adult bees is low but larval stages are susceptible. Temporary adverse effects on bee brood development with recovery after 4 weeks were observed in field tests. Therefore it is suggested that the product should not be applied during flowering of the crop and to label the product accordingly. The standard laboratory tests suggested a high potential risk to predatory mites. Field tests with *T. pyri* showed that recovery within one year after the application is possible. The expert´s meeting agreed that the risk to non-target arthropods is sufficiently addressed for the representative uses. Effects of >25% on soil nitrification were observed in tests with spirodiclofen and its major soil metabolites. The effects caused by the metabolites occurred on day 14 but were <25 % at day 28 and also the effects of spirodiclofen were <25% after day 56. Since the tested concentrations were a factor of 10 to 66 times higher than the initial PECsoil values and the effects were of temporary nature it is assumed that the observed effects would not cause a high risk to soil functioning at the application rates suggested in the representative uses.

The risk to earthworms, other soil non-target macro organisms, non-target plants and biological methods of sewage treatment were assessed as low for the representative uses.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Risk-mitigation measures such as no-spray buffer zones of up to 30m (early use in orchards), 15m (late use in orchards) and 10m (late use in vine) are required to mitigate the long-term risk to aquatic organisms (see point 5.2).
- The following labelling is suggested to mitigate the risk to bees: No use during flowering of the crop and avoiding that flowering weeds are present (e.g. mowing the weeds) (see point 5.3).

ISSUES THAT COULD NOT BE FINALISED

- None

CRITICAL AREAS OF CONCERN

- None

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APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

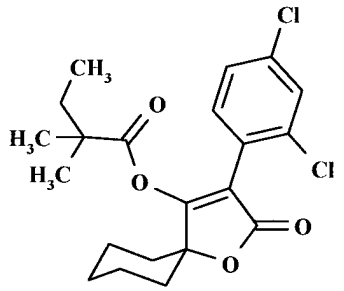
In April 2009 the list of endpoints is also changed into the new format. These changes are not highlighted.

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Spirodiclofen
Function (e.g. fungicide)	Acaricide/insecticide

Rapporteur Member State	The Netherlands
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl 2,2-dimethylbutyrate
Chemical name (CA) ‡	3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl 2,2-dimethylbutanoate
CIPAC No ‡	737
CAS No ‡	148477-71-8
EEC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification ‡ (including year of publication)	No FAO specification established
Minimum purity of the active substance as manufactured ‡ (g/kg)	965 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	3-(2,4-dichlorophenyl)-4-hydroxy-1-oxaspiro[4.5]dec-3-en-2-one (BAJ-2740 enol) (max. [redacted] g/kg) and N,N-dimethylacetamide (max. [redacted] g/kg)
Molecular formula ‡	$C_{21}H_{24}Cl_2O_4$
Molecular mass ‡	411.3
Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	94.8 °C (99%)
Boiling point (state purity) ‡	Not determined due to thermal decomposition
Temperature of decomposition	A weight loss was observed at 160 °C (99%)
Appearance (state purity) ‡	White powder (99%)
Relative density (state purity) ‡	Density: 1.29 g/cm^3 (99%)
Surface tension	Not required, water solubility < 1 mg/L
Vapour pressure (in Pa, state temperature) ‡	at 20 °C < 3 x 10^{-7} Pa (99%)
Henry's law constant (Pa m^3 mol $^{-1}$) ‡	at 20 °C < 2 x 10^{-3} Pa m^{3}mole^{-1}
Solubility in water ‡ (g/L or mg/L, state temperature)	pH 4: 50 µg/L at 20 °C (99%) pH 7: 190 µg/L at 20 °C (99%)
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	at 20 °C, 99 % pure: ethyl acetate: > 250 g/L xylene: > 250 g/L 2-propanol: > 47 g/L acetonitril: > 250 g/L acetone: > 250 g/L n-heptane: 20 g/L 1-octanol: 44 g/L dichloromethane: 250 g/L
Partition co-efficient (log POW) ‡ (state pH and temperature)	log Pow 5.83 at 20 °C and pH 4 (99%) log Pow 5.1 at 20 °C and pH 7 (99%)
Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	pH_4__: DT_{50}= 119.6 days at 20 °C pH_7__: DT_{50}= 52.1 days 20 °C pH_9__: DT_{50}= 2.5 days 20 °
Dissociation constant ‡	The active substance contains no ionisable functional groups, no dissociation in water can occur
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	Neutral: λ 201 nm with ε = 37869 L/mol.cm; No absorption at 300-400 nm
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	DT $_{50}$= 28.8 hours at pH4 and 25 °C
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	1.44 x 10^{-2} moles/einstein
Flammability ‡	Not highly flammable (97.8 %)
Explosive properties ‡	Not explosive (97.8 %)

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 a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Apple (MABSD) **Pear** (PYUCO)	EU North	Envidor SC 240	F	mites and sucking insects	SC	240 g/L	overall spray	BBCH 51 – 57 or 69 - 85	1	n.a.	0.0096	1500	0.144	14	
Grape (VITVI)	EU North	Envidor SC 240	F	mites	SC	240 g/L	overall spray	BBCH 03 – 57 or 69 - 85	1	n.a.	0.0096	1000	0.096	14	
Apple (MABSD) **Pear** (PYUCO)	EU South	Envidor SC 240	F	mites and sucking insects	SC	240 g/L	overall spray	BBCH 51 – 57 or 69 - 85	1	n.a.	0.0096	1500	0.144	14	
Peach (PRNPS) **Apricot** (PRNAR) **Nectarine** (PRNPN)	EU South	Envidor SC 240	F	mites	SC	240 g/L	overall spray	BBCH 69 – 85	1	n.a.	0.0096	1500	0.144	14	

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 a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Orange (CIDSI) **Mandarin** (CIDRE)	EU South	Envidor SC 240	F	mites	SC	240 g/L	overall spray	BBCH 69 – 85	1	n.a.	0.0048	3000	0.144	14	
Grape (VITVI)	EU South	Envidor SC 240	F	mites	SC	240 g/L	overall spray	BBCH 03 – 57 or 69 - 85	1	n.a.	0.0096	1000	0.096	14	

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

Chapter 2: Methods of Analysis

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

Technical as (principle of method)	Reversed phase HPLC -UV
Impurities in technical as (principle of method)	Reversed Phase HPLC -UV and GLC-MS
Plant protection product (principle of method)	Spirodiclofen: GC -MS Spirodiclofen, N,N-dimethylacetamide and BAJ 2740-enol: HPLC-UV (method AM011108MF1): LOQ 0.05% for N,N-dimethylacetamide and 0.08% for BAJ 2740-enol

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	GC-ECD method 00086/M030, confirmation by GC-MS. Analyte spirodiclofen LOQ 0.02 mg/kg for fruits with high acid content (oranges and apples, except orange peel LOQ=0.1 mg/kg), commodities with high water content (apples), cereals and other dry crops (wheat), and commodities with high fat content (rape seed).
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Residue analytical method 00919 for the determination of residues BAJ 2740-enol by HPLC-MS/MS BAJ 2740-enol[22] LOQ 0.005 mg/kg for milk, 0.01 mg/kg for fat and muscle, and 0.05 mg/kg for kidney and liver
Soil (principle of method and LOQ)	Extraction with acetonitrile, analysis by HPLC-MS/MS Spirodiclofen LOQ 0.01 mg/kg
Water (principle of method and LOQ)	Acidification, clean-up on polymer cartridge, analysis by HPLC-MS/MS Spirodiclofen and BAJ 2740-enol LOQ (surface water) 0.05 µg/L spirodiclofen and 0.05 µg/L BAJ 2740-enol.
Air (principle of method and LOQ)	Air is sampled with TENAX, TENAX is extracted with acidified acetonitrile, analysis by HPLC/UV Spirodiclofen LOQ 0.0015 mg/m^3

[22] BAJ 2740 = Spirodiclofen; BAJ 2740-enol = BAJ 2510 = spirodiclofen-enol (M01)

Body fluids and tissues (principle of method and LOQ)	No method available. However, a method was not required since spirodiclofen is not classified for acute toxicity.

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	Not classified

Chapter 3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapidly absorbed: 65% based on excretion in urine (48h) after single oral dose of 2 mg/kg bw.
Distribution ‡	Liver, kidneys, plasma, GI-tract, skin. In females, organ and tissue levels were about 5-15 times lower than in males. Compared to single dosed males, tissue levels in males treated for 15 days were 4 times lower.
Potential for accumulation ‡	No potential for accumulation
Rate and extent of excretion ‡	Rapid: 88% of the administered dose (99% of the recovered radioactivity) within 48 h after single oral dose of 2 mg/kg bw (64-66% in urine and 33-35% in feces)
Metabolism in animals ‡	Sex difference; higher capacity in the metabolisation of BAJ-enol (first metabolite) in male rats. In urine, plasma, liver and kidney samples the levels of the 3- and 4- hydroxy-BAJ-enol isomers were higher in males than in females
Toxicologically significant compounds ‡ (animals and plants)	Spirodiclofen (BAJ 2740) and rat metabolites (BAJ 2740-enol and 2,4-dichlorobenzoic acid) (toxicologically relevant)
Toxicologically significant compounds ‡ (environment)	Spirodiclofen (BAJ 2740)

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 2500 mg/kg bw	
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 5 mg/L	
Skin irritation ‡	Not irritating	
Eye irritation ‡	Not irritating	
Skin sensitization ‡	Sensitising to skin (Maximisation test)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver, adrenals, clinical biochemical parameters	
Relevant oral NOAEL ‡	1-y dog: 1.45 mg/kg bw/day 14-week rat: 8.1 mg/kg bw/day	
Relevant dermal NOAEL ‡	28-d rat: not determined (LOAEL 1000 mg/kg bw/day)	

Relevant inhalation NOAEL ‡	No data – not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

……..	No genotoxic potential	

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

Target/critical effect ‡	Liver, adrenals, amyloidosis	
Relevant NOAEL ‡	18-m mouse: NOAEL not determined – LOAEL 4.1 mg/kg bw/d 2-y rat: 5.9 mg/kg bw/day	
Carcinogenicity ‡	Liver tumors at 610 mg/kg bw/day (mouse). Leydig cell tumors testes, and uterus adenocarcinomas at 110 mg/kg bw/day and 153 mg/kg bw/d (rat)	**R40**

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: Reduced body weight and clinical chemistry changes. F1: decreased spermatogenesis at parentally toxic doses but no effects on litter parameters. Offspring: decreased body weight at birth and during lactation.	
Relevant parantal NOAEL ‡	< 5.2 mg/kg bw/day (rat)	
Relevant reproductive NOAEL ‡	26.2 mg/kg bw/day	
Relevant offspring NOAEL	5.2 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Liver lobulation in fetuses (rabbit) at maternally toxic doses	
Relevant maternal NOAEL ‡	Rat: 1000 mg/kg bw/day Rabbit: 100 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 1000 mg/kg bw/day Rabbit: 300 mg/kg bw/day	

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

Acute neurotoxicity NOAEL	2000 mg/kg bw/day (rat), no evidence of	

	neurotoxicity	
Semi-chronic neurotoxicity NOAEL	70 mg/kg bw/day (13-w rat), decreased foot splay and forelimb/hindlimb grip strength; decreased (loco)motor activity	
Chronic neurotoxicity NOAEL	110 mg/kg bw/day, no evidence of neurotoxicity (77 week rat) (satellite group from the chronic study)	
Developmental neurotoxicity NOAEL	119 mg/kg bw/day	

Other toxicological studies ‡ (Annex IIA, point 5.8)

……..	Immunotoxicology and mechanistic studies were provided. Based on these studies, BAJ 2510-enol interferes with steroid hormone synthesis at the level of general biochemical pathways. Evidence of endocrine disruption.

Medical data ‡ (Annex IIA, point 5.9)

……	New active substance – no data

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.015 mg/kg bw/day	1-year dog	100
AOEL ‡	0.009 mg/kg bw/day	1-year dog	100, corrected by oral absorption of 65 %
ARfD ‡ (acute reference dose)	Not allocated	-	-

Dermal absorption (Annex IIIA, point 7.3)

Formulation Envidor SC 240	0.4% for the concentrate and 3% for the spray dilution, based on an *in vitro* study, supported by *in vivo* studies.

Acceptable exposure scenarios (including method of calculation)

Operator	Mechanical spraying in grapes UK-POEM: 81% of AOEL without PPE German model (GM): 45% of AOEL without PPE Mechanical spraying in pome and stone fruits UK-POEM: 86% of AOEL without PPE German model (GM): 68% of AOEL without PPE Mechanical spraying in citrus UK-POEM: 51% of AOEL without PPE German model (GM): 68% of AOEL without PPE Manual spraying in grapes UK-POEM: 105% of AOEL without PPE 61% with PPE German model (GM): 16% of AOEL without PPE Manual spraying in pome and stone fruits UK-POEM: 105% of AOEL without PPE 61% with PPE German model (GM): 25% of AOEL without PPE Manual spraying in citrus UK-POEM: 76% of AOEL without PPE German model (GM): 25% of AOEL without PPE
Workers	Re-entry activities in grapes EUROPOEM II: 37% of AOEL without PPE Re-entry activities in pome/stone fruits and citrus EUROPOEM II: 56% of AOEL without PPE
Bystanders	EUROPOEM II: 6-8% of AOEL (for grapes, pome and stone fruits and citrus)

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	**Xn** "Harmful" **R43** "May cause sensitisation by skin contact" **R40** "Limited evidence of a carcinogenic effect"

Chapter 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 (lemon, orange, grapefruit, apple, grapes); other categories not required
Rotational crops	No data available, data not required
Plant residue definition for monitoring	Spirodiclofen (no metabolites)
Plant residue definition for risk assessment	Spirodiclofen (no metabolites)
Conversion factor (monitoring to risk assessment)	1

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

Animals covered	Lactating ruminants (goat);
Animal residue definition for monitoring	Spirodiclofen-enol (M01) expressed as spirodiclofen
Animal residue definition for risk assessment	Spirodiclofen-enol (M01) expressed as spirodiclofen
Conversion factor (monitoring to risk assessment)	1
Metabolism in rat and ruminant similar (yes/no)	yes
Fat soluble residue: (yes/no)	Partly fat-soluble log Kow (spirodiclofen) = 5.83 (i.e. fat soluble) log Kow (sprirodiclofen-enol) = 0 (pH 7) (i.e. not fat soluble)

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

……...	No data available, data not required

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

water containing plant materials (oranges, grapes)	18 months at –19±1 °C
oil containing plant materials	No data available, data not required
protein containing plant materials	No data available, data not required
starch containing plant materials	No data available, data not required
tissues (muscle, liver, kidney, fat)	5 months at –20°C
milk	5 months at –20°C
eggs	No data available, data not required

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

intakes by livestock: 0.38 mg/kg dry feed:	ruminant: 3.8 – 2.9 mg/kg dry feed	poultry: no	pig: no
Muscle	0.01		
Liver	0.05		
Kidney	0.05		
Fat	0.01		
Milk	0.004		
Eggs	-		

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) (mg/kg)	Recommendation/comments	MRL (mg/kg)	STMR (b) (mg/kg)
Mandarin	S	0.021, 0.034, 0.042, 0.047, 0.050, 0.053, 0.059, 0.076	critical GAP: spray application; 1x 0.0048±25% (=0.0036-0.0060) kg a.s./hL; PHI = 14±25% (= 10-18) d;	0.1	0.049
Orange	S	<0.02, 0.030, 2x0.034, 0.047, 0.049, 0.053, 0.055	Idem	0.1	0.041
Citrus fruit (whole group)	**S**	**<0.02, 0.021, 0.030, 3x0.034, 0.042, 2x0.047, 0.049, 0.050, 2x0.053, 0.055, 0.059, 0.076**	**Idem**	**0.1**	**0.047**
Apple	N	0.025, 0.035, 0.039, 0.043, 2x0.049, 0.059,0.077	critical GAP: spray application; 1x 0.0096±25% (=0.0072-0.0120) kg a.s./hL PHI = 14±25% (= 10-18) d;	0.1	0.046
	S	<0.02, 0.024,0.046, 0.055	Idem	0.1	0.035
Pear	N	None	Idem	None	None
	S	0.027, 0.035, 0.039, 0.043	Idem	0.1	0.037
Pome fruit (whole group)	N	0.025, 0.035, 0.039, 0.043, 2x0.049, 0.059, 0.077	Idem	0.1	**0.046**
	S	<0.02, 0.024, 0.027, 0.035, 0.039, 0.043, 0.046, 0.055	Idem	0.1	**0.037**
Pome fruit (whole group)	**N and S**	**<0.02, 0.024, 0.025, 0.027, 0.035, 0.035, 0.039, 0.039, 0.043, 0.043, 0.046, 2x0.049, 0.055, 0.059, 0.077**	**Idem**	**0.1**	**0.042**
Peach	S	2x<0.02, 0.020, 0.027, 0.037, 0.047, 0.065, 0.096	Idem	0.1	0.032

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a) (mg/kg)	Recommendation/comments	MRL (mg/kg)	STMR (b) (mg/kg)
Peaches, nectarines, apricots (whole group)	**S**	**2x<0.02, 0.020, 0.027, 0.037, 0.047, 0.065, 0.096**	**Idem**	**0.2**	**0.032**
Grapes, (table, wine)	N	0.044, 0.045, 0.058, 0.064, 0.069 0.072, 0.063, 0.10	RAC = bunches of grapes; critical GAP: normal spray application; 1x0.096±25% (=0.072-0.120) kg a.s./ha; PHI=14±25% (= 10-18) d; residue trials with low volume spraying not included (no GAP)	0.2	0.067
	S	0.025, 0.030, 0.034, 0.037, 0.052, 0.066, 0.071, 0.11	Idem	0.2	0.045

(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
bold: group MRLs

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

ADI	0.015 mg/kg bw/day	
TMDI (European Diet) (% ADI)	WHO/EU diet: Dutch diet (adults) : Dutch diet (children 1-6y) :	1.9% 3.5% 9.4%
NEDI (% ADI)	Not necessary	
Factors included in NEDI	-	
ARfD	Not necessary	
Acute exposure (% ARfD)	Not necessary, no acute risk for consumers	

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

crop/processed crop:	Number of studies	Processing factor	% Transference*
orange/marmalade	1 (3 repeats)	<0.56	<39%
apple/washed	2 (3 repeats each)	0.65, 1.3	130%
apple/sauce	1 (3 repeats)	<0.71	<63%
apple/pasteurised juice	2 (3 repeats each)	0.02, <0.71	<25%
apple/wet pomace	2 (3 repeats each)	3.9, 5.9	140%
apple/dry pomace	1 (3 repeats)	18	100%
Apple/concentrated juice	1 (3 repeats)	0.02	
Apple/dried fruit	1 (3 repeats)	0.02	
peach/washed	1 (3 repeats)	<0.75	<74%
peach/preserve	1 (3 repeats)	not valid	not valid
grapes/raisins	2 (2 repeats each)	1.5; 2.3; mean 1.9	37%; 52%; mean 89%
grapes/pasteurised juice	1 (3 repeats)	<0.54	<28%

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

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

Crops	Citrus:	0.1 mg/kg
	Pome fruit:	0.1 mg/kg
	Peaches, nectarines, apricots:	0.2 mg/kg
	Grapes:	0.2 mg/kg

*) LOQ

Chapter 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 ‡	22.5 – 93.1% AR after 120 d (14C-3-dihydrofuranone-label, 4 soils) 69.1% AR after 119 d (14C-1-cyclohexyl-label, 1 soil)
Non-extractable residues after 100 days ‡	6.8 – 14.4% AR after 120 d (14C-3-dihydrofuranone-label, 4 soils) 17.9% AR after 119 d (14C-1-cyclohexyl-label, 1 soil)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	**BAJ 2740-enol** 14.5 – 51.9% AR after 2 – 9 d (4 soils) **BAJ 2740-ketohydroxy** 8.4 – 44.4% AR after 3 – 30 d (4 soils) **BAJ 2740-dihydroxy** 1.0 – 16.4% AR after 2 – 120 d (4 soils) **2,4-dichlorobenzoic acid** 2.0 – 39.6% AR after 3 – 120 d (4 soils)

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

Anaerobic degradation ‡	Not available and not required for the intended patterns of use applied for
Soil photolysis ‡	Moist soil: no important effect of irradiation on rate and route of degradation of spirodiclofen (14C-3-dihydrofuranone); degradation of metabolites BAJ 2740-enol and BAJ 2740-ketohydroxy enhanced by irradiation; no photo-products >10% AR
Field dissipation	Not available and not required

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

Method of calculation	Spirodiclofen and 2,4-dichlorobenzoic acid hinge point analysis, then first-order kinetics BAJ 2740-dihydroxy Curve fitting assuming first order kinetics BAJ 2740-enol & BAJ 2740-ketohydroxy from studies with soils treated with parent Spirodiclofen; method: curve fitting with ACSL Optimise program package or Modelmanager, assuming first-order kinetics

Laboratory studies ‡ (range or median, with n value, with r^2 value)	DT_{50lab} (20°C, aerobic): **Spirodiclofen** (4 soils) 7.8 d (r^2 0.99) 1.1 d (r^2 0.97) 7.4 d (r^2 1.00) 13 d (r^2 0.96) average DT_{50} value: 7.3 d **BAJ 2740-enol** (4 soils) 1.9 d 2.8 d 9.8 d 3.0 d average DT_{50} value: 4.4 d **BAJ 2740-ketohydroxy** (4 soils) 3.4 d 0.6 d 27 d 14 d average DT_{50} value: 11.2 d **BAJ 2740-dihydroxy** (3 soils) 3.8 d (r^2 1.00) 3.9 d (r^2 0.97) 29.5 d (r^2 0.96) average DT_{50} value: 12.4 d **2,4-dichlorobenzoic acid** (4 soils) 9.3 d (r^2 0.93) 10 d (r^2 0.89) 3.5 d (r^2 0.99) 11 d (r^2 0.96) average DT_{50} value: 8.5 d
	DT_{90}lab (20°C, aerobic): DT_{90}, lab (20◦C, aerobic): extrapolated from average DT_{50} values as $3.3 \cdot DT_{50}$, assuming first order exponential decay **Spirodiclofen** 24 d **BAJ 2740-enol** 15 d **BAJ 2740-ketohydroxy**

37 d **BAJ 2740-dihydroxy** 41 d **2,4-dichlorobenzoic acid** 28 d
DT_{50lab} (10°C, aerobic): calculated from DT_{50}, lab (20◦C, aerobic) using a Q10 factor of 2.2 **Spirodiclofen** (4 soils) 17 d 2.4 d 16 d 29 d average DT_{50} value: 16 d **BAJ 2740-enol** (4 soils) 4.2 d 6.2 d 22 d 6.7 d average DT_{50} value: 9.7 d **BAJ 2740-ketohydroxy** (4 soils) 7.6 d 1.3 d 59 d 30.8 d average DT_{50} value: 24.7 d **BAJ 2740-dihydroxy** (3 soils) 8.5 d 8.7 d 65 d average DT_{50} value: 27.4 d **2,4-dichlorobenzoic acid** (4 soils) 21 d 22 d 7.8 d 24 d average DT_{50} value: 19 d
DT_{50lab} (20°C, anaerobic): not available and not required

	Degradation in the saturated zone ‡: not available and not required
Field studies ‡ (state location, range or median with n value)	Not available and not required
Soil accumulation and plateau concentration ‡	Not relevant

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

Anaerobic degradation	Not available and not required
Soil photolysis	DT_{50}: **Spirodiclofen** Moist soil: no effect of irradiation on rate of degradation **BAJ 2740-enol & BAJ 2740-ketohydroxy** Moist soil: rate of degradation enhanced by irradiation (not further quantifiable)

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	K_F, K_{Foc} and 1/n values are listed in corresponding order of soils **Spirodiclofen** HPLC method: 31037 L/kg **BAJ 2740-enol** (4 soils) K_F values: 0.0641, 0.372, 0.114 and 0.293 L/kg 1/n: 1.01, 0.906, 0.945 and 0.898 (average 0.941) K_{Foc} values 12.1, 28.6, 19.3 and 11.2 L/kg (average 17.8 L/kg) no pH dependence **BAJ 2740-ketohydroxy** HPLC method: 612 L/kg **BAJ 2740-dihydroxy** (3 soils) K_F values: 0.1, 1.1 and 0.9 L/kg 1/n: 0.854, 0.863, and 0.900 (average 0.872) K_{Foc} values 8.9, 40.2 and 105 L/kg (average 51.3 L/kg) no pH dependence, no clear correlation with any soil property

	2,4-dichlorobenzoic acid (4 soils) K_F values: 0.046, 0.122, 0.045 and 0.062 L/kg 1/n: 0.815, 0.914, 0.716 and 0.619 (average 0.766) K_{Foc} values 8.8, 4.7, 8.4 and 7.0 L/kg (average 7.2 L/kg) no pH dependence (pH range tested 5.8-7.4)

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

Column leaching ‡	Not available and not required
Aged residues leaching ‡	biologically aged for 9 d, sandy loam soil (0.34% oc), leached (about 500 mm) for 5 d at 10 cm 0.01M $CaCl_2$/d In 9-day aged soil: Total RA in soil 85.9% AR; Spirodiclofen (24.1% AR), BAJ 2740-enol (17.7% AR), BAJ 2740-ketohydroxy (20.6% AR), BAJ 2740-dihydroxy (2.8% AR), 2,4-dichlorobenzoic acid (11.1% AR), non-extractable (4.4% AR), CO2 6.5% AR). In eluted soil column: Total RA 34.5% AR; Spirodiclofen 15.4% AR (only down to 6 cm), BAJ 2740-dihydroxy, BAJ 2740-enol and 2,4-dichlorobenzoic acid in all layers (1.8, 3.8 and 1.4% AR respectively); BAJ 2740-ketohydroxy 4.4% AR (only down to 12 cm). In leachate: Total RA 52.8% AR; Spirodiclofen n.d. (<0.1% AR), BAJ 2740-ketohydroxy 5.2% AR, BAJ 2740-dihydroxy 2.0% AR, BAJ 2740-enol 17.4% AR and 2,4-dichlorobenzoic acid 19.0% AR.
Lysimeter/ field leaching studies ‡	Not available and not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	Spirodiclofen: 50% crop interception 5 cm soil incorporation soil density 1.5 g/cm^3 DT_{50} used: 13 d (worst case laboratory) **Metabolites:** highest percentage of formation, correction for molar mass ratio (MMR) **BAJ 2740-enol** DT_{50} 9.8 d; max. % = 51.9; MMR = 313.2/411.3 BAJ 2740-ketohydroxy DT_{50} 27 d; max. % = 44.4; MMR = 329.2/411.3 BAJ 2740-dihydroxy DT_{50} 29.5 d; max. % = 16.4; MMR = 331.2/411.3 2,4-dichlorobenzoic acid DT_{50} 11 d; max. % = 39.6; MMR = 191.0/411.3
Application rate	Single treatment to orchard crops at 0.144 kg as/ha

PEC_S (mg/kg)

Application rate:	single treatment to orchard crops at 0.144 kg as/ha									
day after	Spirodiclofen		BAJ 2740-enol		BAJ 2740-ketohydroxy		BAJ 2740-dihydroxy		2,4-dichloro-benzoic acid	
appln.	actual	TWA	actual	TWA	actual	TWA	actual	TWA	actual	TWA
0	0.096	-	0.038	-	0.034	-	0.013	-	0.018	-
1	0.091	0.093	0.035	0.037	0.032	0.033	0.012	0.013	0.017	0.017
2	0.086	0.091	0.033	0.035	0.031	0.032	0.012	0.012	0.016	0.017
4	0.078	0.086	0.029	0.033	0.028	0.031	0.012	0.012	0.014	0.016
7	0.066	0.080	0.023	0.030	0.024	0.029	0.011	0.012	0.011	0.014
21	0.031	0.058	0.009	0.020	0.012	0.021	0.008	0.010	0.005	0.010
28	0.022	0.050	0.005	0.017	0.009	0.018	0.007	0.009	0.003	0.008
50	0.007	0.034	0.001	0.010	0.003	0.013	0.004	0.007	0.001	0.005
100	0.0005	0.018	0.00003	0.005	0.000	0.007	0.001	0.005	0.00003	0.003
Application rate:	single treatment to grapevine at 0.096 kg as/ha									
day after	Spirodiclofen		BAJ 2740-enol		BAJ 2740-ketohydroxy		BAJ 2740-dihydroxy		2,4-dichloro-benzoic acid	
appln.	actual	TWA	actual	TWA	actual	TWA	actual	TWA	actual	TWA
0	0.064	-	0.025	-	0.023	-	0.009	-	0.012	-
1	0.061	0.062	0.024	0.024	0.022	0.022	0.008	0.008	0.011	0.011
2	0.058	0.061	0.022	0.024	0.022	0.022	0.008	0.008	0.010	0.011
4	0.052	0.058	0.019	0.022	0.021	0.022	0.008	0.008	0.009	0.010
7	0.044	0.053	0.015	0.020	0.019	0.021	0.007	0.008	0.008	0.010
21	0.021	0.039	0.006	0.013	0.013	0.018	0.005	0.007	0.003	0.007
28	0.014	0.033	0.003	0.011	0.011	0.016	0.004	0.006	0.002	0.006
50	0.004	0.022	0.001	0.007	0.006	0.013	0.003	0.005	0.001	0.004
100	0.0003	0.012	0.00002	0.004	0.002	0.008	0.001	0.003	0.00002	0.002

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)	**Spirodiclofen** pH 4, 25°C: 29.7% hydrolysed after 30 d, DT_{50} 63.6 d (DT_{50} at 20°C: 119.6 d) pH 7, 25°C: 49.0% hydrolysed after 30 d, DT_{50} 30.8 d (DT_{50} at 20°C: 52.1 d) pH 9, 25°C: 98.9% hydrolysed after 30 d, DT_{50} 1.9 d (DT_{50} at 20°C: 2.5 d) Major hydrolysis product: BAJ 2740-enol (max. 28.9, 52.2 and 100.8% AR after 30 d at pH 4, 7 and 9 respectively) **BAJ 2740-enol** pH 4, 25°C: stable pH 7, 25°C: stable pH 9, 25°C: stable
Photolytic degradation of active substance and relevant metabolites ‡	**Spirodiclofen** buffer pH 4 with 20% acetonitrile, 25°C, Xenon light >290 nm equivalent to midsummer sunlight at 40°N: DT_{50} corresponding to natural irradiation under midday midsummer conditions at 40°N: 123 d. water/acetonitrile (1/1), 25°C, polychromatic light from mercury lamp (>295 nm): quantum yield 0.0144. **BAJ 2740-enol** Rhine water, 25°C, Xenon light >290 nm equivalent to midsummer sunlight at 40°N: DT_{50} 7.6 h.
Readily biodegradable (yes/no)	Not available and not required
Degradation in water/sediment	**Aerobic** study (2 systems), 20°C, first order kinetics: Spirodiclofen $DT_{50,\ water}$: 0.3 d ($r^{2:}$ -) and 1.1 d (r^2 0.95) $DT_{50,\ sediment}$: 4.4 d (r^2 0.99) and 2.5 d (r^2 1.00) $DT_{50,\ system}$: 4.2 d (r^2 1.00) and 2.3 d (r^2 0.99) BAJ 2740-enol $DT_{50,\ water}$: 186 d (extrapolated, r^2 0.96); no dissipation in 2nd system $DT_{50,\ sediment}$: - $DT_{50,\ system}$: 393 d (extrapolated, r^2 0.86); no degradation in 2_{nd} system

Anaerobic study (1 system), 20°C:

Spirodiclofen

$DT_{50, water}$: << 1 d (1.3% AR in water on day 0)

$DT_{50, sediment}$: 9.8 d (r^2 0.99)

$DT_{50, system}$: 10.0 d (r^2 0.99)

BAJ 2740-enol

$DT_{50, water}$: no dissipation (71-80% AR on d 34-365)

$DT_{50, sediment}$: 175 d (extrapolated, r^2 0.96)

$DT_{50, system}$: no degradation (82-94% AR on d 34-365)

DT^{90} extrapolated from DT_{50} values as $3.3 \cdot DT_{50}$, assuming first order exponential decay (unless stated otherwise)

Aerobic study (2 systems), 20°C:

Spirodiclofen

$DT_{90, water}$: <1 and <3 days (graphical estimation)

$DT_{90, sediment}$: 14 and 8.2 d

$DT_{90, system}$: 14 and 7.5 d

BAJ 2740-enol

$DT_{90, water}$: 618 d; no dissipation in 2nd system

$DT_{90, sediment}$: -

$DT_{90, system}$: 1306 d; no degradation in 2nd system

Anaerobic study (1 system), 20°C:

Spirodiclofen

$DT_{90, water}$: << 1 d (1.3% AR in water on day 0)

$DT_{90, sediment}$: 32.4 d

$DT_{90, system}$: 33.2 d

BAJ 2740-enol

$DT_{90, water}$: no dissipation

$DT_{90, sediment}$: 582 d

$DT_{90, system}$: no degradation

Mineralization	**Aerobic** study with 14C-3-dihydrofuranone Spirodiclofen (2 systems), 20°C: max. 2.6 and 2.1% after 110 d (end) **Anaerobic** study with 14C-3-dihydrofuranone Spirodiclofen (1 system), 20°C: max. 1.0% after 183 d
Non-extractable residues	**Aerobic** study with 14C-3-dihydrofuranone Spirodiclofen (2 systems), 20°C: max. 6.8 and 1.5% after 110 d (end) **Anaerobic** study with 14C-3-dihydrofuranone Spirodiclofen (1 system), 20°C: max. 4.3% after 246 d
Distribution in water / sediment systems (active substance) ‡	**Aerobic** study (2 systems), 20°C: Rapid dissipation of Spirodiclofen from water (1.3-6.9% AR in water on d 3), mainly due to sorption to sediment. The high initial residues of Spirodiclofen in sediment (max. 58-68% AR after 1 d) declined to 1.6% AR on day 14-30 (=0.1% AR after 110 d = study end). **Anaerobic** (1 system), 20°C: Near complete loss from water due to sorption on day 0 (1st sampling), with Spirodiclofen at 1.3 and 91.9% AR in water and sediment, respectively. Spirodiclofen in sediment declined to 8.0% AR on day 34, 1.0% AR on day 120 and 0.0% AR after 365 d = study end.
Distribution in water / sediment systems (metabolites) ‡	Metabolites >10% AR: **Aerobic** study (2 systems), 20°C: Water: BAJ 2740-enol, max. 73.8-84.3% AR (d 37-59), 54.9-83.4% AR (d 110 = end) Sediment: BAJ 2740-enol, max. 14.0-29.6% AR (d 110 = end) **Anaerobic** (1 system), 20°C: Water: BAJ 2740-enol, max. 80.0% AR (d 56), 74.6% AR after 365 d = end Sediment: BAJ 2740-enol, max. 15.6% AR (d 246), 9.6% AR (d 365 = end)

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

Parent

Method of calculation	Static water layer 30 cm deep Spirodiclofen worst case DT_{50} (water) = 1.1 d BAJ 2740-enol highest percentage of formation in water (84.3%); correction for molar mass ratio = 313.2/411.3; TWA PECsw values equal to initial PECsw values.
Application rate	
Main routes of entry	Spray-drift emission (values taken from Guidance Document on Aquatic Ecotoxicology (8075/VI/97 rev 8))

PEC_{sw} (µg/L)

day after	**pome and stone fruit, 0.144 kg as/ha**, **early** application; PECsw of **Spirodiclofen** at distance (drift %):															
	3 m (29.20%)		5 m (19.89%)		10 m (11.81%)		15 m (5.55%)		20 m (2.77%)		30 m (1.04%)		40 m (0.52%)		50 m (0.30%)	
app.	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC
0	14	-	9.5	-	5.7	-	2.7	-	1.3	-	0.50	-	0.25	-	0.14	-
4	1.1	5.1	0.77	3.5	0.46	2.1	0.21	1.0	0.11	0.49	0.040	0.18	0.020	0.091	0.012	0.053
10	0.026	2.2	0.018	1.5	0.010	0.90	0.005	0.42	0.002	0.21	0.001	0.079	0.000	0.040	0.000	0.023
21	0.000	1.1	0.000	0.7	0.000	0.43	0.000	0.20	0.000	0.10	0.000	0.038	0.000	0.019	0.000	0.011
28	0.000	0.8	0.000	0.54	0.000	0.32	0.000	0.15	0.000	0.075	0.000	0.028	0.000	0.014	0.000	0.008
65	0.000	0.34	0.000	0.23	0.000	0.14	0.000	0.065	0.000	0.032	0.000	0.012	0.000	0.006	0.000	0.004
97	0.000	0.23	0.000	0.16	0.000	0.09	0.000	0.044	0.000	0.022	0.000	0.008	0.000	0.004	0.000	0.002
115	0.000	0.19	0.000	0.13	0.000	0.078	0.000	0.037	0.000	0.018	0.000	0.007	0.000	0.003	0.000	0.002

day after	**citrus, pome and stone fruit**, **late** application; PECsw of **Spirodiclofen** at distance (drift %):															
	3 m (15.73%)		5 m (8.41%)		10 m (3.60%)		15 m (1.81%)		20 m (1.09%)		30 m (0.54%)		40 m (0.32%)		50 m (0.22%)	
app.	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC
0	7.6	-	4.0	-	1.7	-	0.87	-	0.52	-	0.26	-	0.15	-	0.11	-
4	0.61	2.8	0.32	1.5	0.14	0.63	0.070	0.32	0.042	0.19	0.021	0.095	0.012	0.056	0.008	0.039
10	0.014	1.2	0.007	0.64	0.003	0.27	0.002	0.14	0.001	0.083	0.000	0.041	0.000	0.024	0.000	0.017
21	0.000	0.57	0.000	0.31	0.000	0.13	0.000	0.07	0.000	0.040	0.000	0.020	0.000	0.012	0.000	0.008
28	0.000	0.43	0.000	0.23	0.000	0.10	0.000	0.049	0.000	0.030	0.000	0.015	0.000	0.009	0.000	0.006
65	0.000	0.18	0.000	0.10	0.000	0.04	0.000	0.021	0.000	0.013	0.000	0.006	0.000	0.004	0.000	0.003
97	0.000	0.12	0.000	0.07	0.000	0.028	0.000	0.014	0.000	0.009	0.000	0.004	0.000	0.003	0.000	0.002
115	0.000	0.10	0.000	0.056	0.000	0.024	0.000	0.012	0.000	0.007	0.000	0.004	0.000	0.002	0.000	0.001

day after	**grapevine**, **early** application; PECsw of **Spirodiclofen** at distance (drift %):															
	3 m (2.70%)		5 m (1.18%)		10 m (0.39%)		15 m (0.20%)		20 m (0.13%)		30 m (0.07%)		40 m (0.04%)		50 m (0.03%)	
app.	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC
0	0.86	-	0.38	-	0.12	-	0.064	-	0.042	-	0.022	-	0.013	-	0.010	-
4	0.069	0.32	0.030	0.14	0.010	0.046	0.005	0.023	0.003	0.015	0.002	0.008	0.001	0.005	0.001	0.004
10	0.002	0.14	0.001	0.060	0.000	0.020	0.000	0.010	0.000	0.007	0.000	0.004	0.000	0.002	0.000	0.002
21	0.000	0.065	0.000	0.029	0.000	0.009	0.000	0.005	0.000	0.003	0.000	0.002	0.000	0.001	0.000	0.001
28	0.000	0.049	0.000	0.021	0.000	0.007	0.000	0.004	0.000	0.002	0.000	0.001	0.000	0.001	0.000	0.001
65	0.000	0.021	0.000	0.009	0.000	0.003	0.000	0.002	0.000	0.001	0.000	0.001	0.000	0.000	0.000	0.000
97	0.000	0.014	0.000	0.006	0.000	0.002	0.000	0.001	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000
115	0.000	0.012	0.000	0.005	0.000	0.002	0.000	0.001	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000

day after	**grapevine**, **late** application; PECsw of **Spirodiclofen** at distance (drift %):															
	3 m (8.02%)		5 m (3.62%)		10 m (1.23%)		15 m (0.65%)		20 m (0.42%)		30 m (0.22%)		40 m (0.14%)		50 m (0.10%)	
app.	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC
0	2.6	-	1.2	-	0.39	-	0.21	-	0.13	-	0.070	-	0.045	-	0.032	-
4	0.21	0.94	0.093	0.42	0.032	0.14	0.017	0.076	0.011	0.049	0.006	0.026	0.004	0.016	0.003	0.012
10	0.005	0.41	0.002	0.18	0.001	0.062	0.000	0.033	0.000	0.021	0.000	0.011	0.000	0.007	0.000	0.005
21	0.000	0.19	0.000	0.088	0.000	0.030	0.000	0.016	0.000	0.010	0.000	0.005	0.000	0.003	0.000	0.002
28	0.000	0.15	0.000	0.066	0.000	0.022	0.000	0.012	0.000	0.008	0.000	0.004	0.000	0.003	0.000	0.002
65	0.000	0.063	0.000	0.028	0.000	0.010	0.000	0.005	0.000	0.003	0.000	0.002	0.000	0.001	0.000	0.001
97	0.000	0.042	0.000	0.019	0.000	0.006	0.000	0.003	0.000	0.002	0.000	0.001	0.000	0.001	0.000	0.001
115	0.000	0.035	0.000	0.016	0.000	0.005	0.000	0.003	0.000	0.002	0.000	0.001	0.000	0.001	0.000	0.000

		dose (kg	**PEC (initial) = TWA PEC** of **BAJ 2740-enol** at:							
crop	appl.	a.s./ha)	3 m	5 m	10 m	15 m	20 m	30 m	40 m	50 m
pome & stone fruit	early	0.144	9.0	6.1	3.6	1.7	0.85	0.32	0.16	0.092
citrus, pome & stone fruit	late	0.144	4.8	2.6	1.1	0.56	0.34	0.17	0.10	0.068
grapevine	early	0.096	0.55	0.24	0.080	0.041	0.027	0.014	0.008	0.006
grapevine	late	0.096	1.6	0.74	0.25	0.13	0.086	0.045	0.029	0.021

PEC (sediment)

PEC_{SED} (mg/kg dw): not calculated as the endpoints of the toxicity tests with sediment-dwelling organisms were expressed in concentrations in the overlying water

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Modelling using FOCUS-PEARL, with appropriate FOCUS gw scenarios, according to FOCUS Guidance. Scenarios: apple (Chateaudun, Hamburg, Jokoinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva); citrus (Piacenza, Porto, Sevilla, Thiva) and vine (Chateaudun, Hamburg, Kremsmünster, Piacenza, Porto, Sevilla, Thiva). Average Kom, 1/n and DT_{50} values (corrected to pF 2) were used. Kom values with 1/n <0.7 and derived from soils with low OC content were excluded. The dose of the parent was corrected for interception by the crop (65, 70 and 40% for apple, citrus and grape, respectively, with a resulting corrected dose of 0.0504, 0.0432 and 0.0576 kg as/ha) and the substance was applied directly to the ground at the corrected dose. The dose of metabolites (modelled as parent compounds) was corrected for max. percentage of formation and molar mass ratio (MMR) Spirodiclofen: DT_{50} (20°C, pF 2) 6.3 d Kom 18002.9 L/kg (1/n = 0.9; default value) **BAJ 2740-enol** DT_{50} (20°C, pF 2) 3.6 d Kom 10.3 L/kg (1/n = 0.9406) max. 51.9%, MMR = 313.2/411.3 BAJ 2740-ketohydroxy DT_{50} (20°C, pF 2) 11 d Kom 355 L/kg (1/n = 0.9; default value) max. 44.4%, MMR = 329.2/411.3 **BAJ 2740-dihydroxy** DT_{50} (20°C, pF 2) 15 d Kom 29.7 L/kg (1/n = 0.8725) max. 16.4%, MMR = 331.2/411.3 **2,4-dichlorobenzoic acid** DT_{50} (20°C, pF 2) 7.2 d Kom 4.2 L/kg (1/n = 0.8150) max. 39.6%, MMR = 191.0/411.3
Application rate	Single application. Uncorrected dose: 0.144 g as/ha (apple, citrus)

	0.096 g as/ha (vine) The dose for apple, citrus and grape, respectively, corrected for interception by the crop: Spirodiclofen: 0.0504, 0.0432 and 0.0576 g as/ha BAJ 2740-enol 0.0199, 0.0171 and 0.0228 g as/ha BAJ 2740-ketohydroxy 0.0179, 0.0154 and 0.0205 g as/ha **BAJ 2740-dihydroxy** 0.0067, 0.0057 and 0.0076 g as/ha 2,4-dichlorobenzoic acid 0.0093, 0.0079 and 0.0106 g as/ha Time of application: September 17 (apple, Europe-N), August 24 (apple, Europe-S), August 18 (citrus, Europe-S), August 27 (vine, Europe-N) and September 02 (vine, Europe-S).
$PEC_{(gw)}$	
Maximum concentration	-
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Average annual concentration (80th percentile) according to FOCUS guidance: active substance: <0.001 µg/L **BAJ 2740-enol**: ≤0.001 µg/L BAJ 2740-ketohydroxy: <0.001 µg/L BAJ 2740-dihydroxy: ≤0.001 µg/L 2,4-dichlorobenzoic acid: 0.001-0.012 µg/L (see detailed results in table below)

PEC(gw) - FOCUS modelling results

FOCUS	scenario	80th percentile concentration in groundwater [µg/L] of:				
crop	location	Spirodiclofen	BAJ 2740-enol	BAJ 2740-ketohydroxy	BAJ 2740-dihydroxy	2,4-dichloro-benzoic acid
apple	Chateaudun	<0.001	<0.001	<0.001	<0.001	0.001
	Hamburg	<0.001	0.001	<0.001	<0.001	0.012
	Jokioinen	<0.001	0.001	<0.001	<0.001	0.003
	Kremsmünster	<0.001	<0.001	<0.001	<0.001	0.003
	Okehampton	<0.001	0.001	<0.001	<0.001	0.007
	Piacenza	<0.001	0.001	<0.001	0.001	0.009
	Porto	<0.001	<0.001	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001	<0.001	<0.001
citrus	Piacenza	<0.001	0.001	<0.001	0.001	0.008
	Porto	<0.001	<0.001	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001	<0.001	<0.001
vine	Chateaudun	<0.001	<0.001	<0.001	<0.001	0.001
	Hamburg	<0.001	<0.001	<0.001	<0.001	0.004
	Kremsmunster	<0.001	<0.001	<0.001	<0.001	0.001
	Piacenza	<0.001	<0.001	<0.001	0.001	0.008
	Porto	<0.001	<0.001	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001	<0.001	<0.001

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

Direct photolysis in air ‡	Not available and not required
Quantum yield of direct phototransformation	Not available and not required
Photochemical oxidative degradation in air ‡	DT_{50} 2.67 h (Atkinson method, based on 1.5 x 10^6 OH radicals/cm^3, 12 h. day)
Volatilization ‡	from plant surfaces: **Spirodiclofen** 1.4% after 24 h
	from soil: **Spirodiclofen** 2.7% after 24 h

PEC (air)

Method of calculation	Results for photochemical oxidative degradation (DT_{50} 2.67 hours), the Henry's Law constant of 2 x 10^{-3} Pa/mol.m^3 and the 24 hour volatilisation results (maximum 2.7% within 24 hours), suggest that the concentrations of spirodiclofen in air are likely to be negligible.

$PEC_{(a)}$

Maximum concentration	Not calculated

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	For risk assessment **soil** spirodiclofen BAJ 2740-enol BAJ 2740-ketohydroxy BAJ 2740-dihydroxy 2,4-dichlorobenzoic acid groundwater spirodiclofen BAJ 2740-enol BAJ 2740-ketohydroxy BAJ 2740-dihydroxy 2,4-dichlorobenzoic acid surfacewater and sediment Spirodiclofen BAJ 2740-enol **air** Spirodiclofen For monitoring soil, groundwater, air Spirodiclofen surface water and sediment BAJ 2740-enol

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	R53 May cause long-term effects to the aquatic environment

Chapter 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 ‡	LD_{50} >2500 mg/kg bw
Reproductive toxicity to mammals	Overall NOEC: 70 mg/kg feed (6.0 mg/kg bw/d) Ecotoxicologically relevant NOEC: 350 mg/kg feed (26.2 mg/kg bw/d)
Acute toxicity to birds ‡	Spirodiclofen LD_{50} >2000 mg/kg bw (bobwhite quail) BAJ 2740-enol LD_{50} >2000 mg/kg bw (bobwhite quail) BAJ 2740-4-hydroxy-enol LD_{50} >2000 mg/kg bw (bobwhite quail)
Dietary toxicity to birds ‡	LC_{50} >5000 mg/kg feed (>1061 mg/kg bw/d) (bobwhite quail) LC_{50} >5000 mg/kg feed (>2274 mg/kg bw/d) (mallard duck)
Reproductive toxicity to birds ‡	NOEC 720 mg/kg feed (51 mg/kg bw/d) (bobwhite quail) NOEC 734 mg/kg feed (111 mg as/kg bw/d) (mallard duck)

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

Toxicity/exposure ratios for **birds** (Annex IIIA, points 10.1)
Bird of 10 g bw, DFI 10.4 g/d, DWI 2.7 mL/d (insects, drinking water)
Bird of 100 g bw, DFI 113 g/d (earthworms)
Bird of 1000 g bw, DFI 206 g/d (fish)
Assessment in agreement with Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC (Working Document Sanco/4145/2000, September 2002).

appln.	Time scale	Toxicity endpoint (mg a.s./kg bw/day)	route	ETE (mg/kg bw/d)	TER	Annex VI trigger
orchard	acute	LD_{50}: >2000	insects	7.8	>256	10
	acute	LD_{50}: >2000	water	0.0038	>529120	10
vine	acute	LD_{50}: >2000	insects	5.2	>385	10
	acute	LD_{50}: >2000	water	0.00069	>2889706	10
orchard	short-term	LC_{50}: >1061	insects	4.3	>247	10
vine	short-term	LC_{50}: >1061	insects	2.9	>366	10

appln.	Time scale	Toxicity endpoint (mg a.s./kg bw/day)	route	ETE (mg/kg bw/d)	TER	Annex VI trigger
orchard	long-term	NOEC: 51	insects	4.3	12	5
vine	long-term	NOEC: 51	insects	2.9	18	5
orchard	long-term	NOEC: 51	earthworms	0.71	72	5
	long-term	NOEC: 51	fish	0.16	319	5
vine	long-term	NOEC: 51	earthworms	0.47	108	5
	long-term	NOEC: 51	fish	0.03	1700	5
vine	long-term	NOEC: 51	insects	2.9	18	5
orchard	long-term	NOEC: 51	earthworms	0.71	72	5
	long-term	NOEC: 51	fish	0.16	319	5
vine	long-term	NOEC: 51	earthworms	0.47	108	5
	long-term	NOEC: 51	fish	0.03	1700	5

Toxicity/exposure ratios for **mammals** (Annex IIIA, points 10.3)
Mammal of 25 g bw, DFI 34.8 g/d, DWI 2.7 mL/d (short grass, drinking water)
Mammal of 10 g bw, DFI 14 g/d (earthworms)
Mammal of 3000 g bw, DFI 390 g/d (fish)
Assessment in agreement with Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC (Working Document Sanco/4145/2000, September 2002).

appln.	Time scale	Toxicity endpoint (mg a.s./kg bw/day)	route	ETE (mg/kg bw/d)	TER	Annex VI trigger
orchard	acute	LD_{50}: >2500	short grass	17.0	>147	10
	acute	LD_{50}: >2500	water	0.0020	1245876	10
vine	acute	LD_{50}: >2500	short grass	11.3	>221	10
	acute	LD_{50}: >2500	water	0.00037	6804159	10
orchard	long-term	NOEC: 26.2	short grass	4.9	5.3	5
vine	long-term	NOEC: 26.2	short grass	3.22	8.1	5
orchard	long-term	NOEC: 26.2	earthworms	0.88	29.8	5
	long-term	NOEC: 26.2	fish	0.10	262	5
vine	long-term	NOEC: 26.2	earthworms	0.59	44.4	5
	long-term	NOEC: 26.2	fish	0.02	1310	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 ‡				
Algae				
Pseudokirchneriella subcapitata	Spirodiclofen	96 h	EbC_{50} and ErC_{50}	>0.060
Pseudokirchneriella subcapitata	BAJ 2740-enol	96 h	EbC_{50} / ErC_{50}	82.8 / >100
Selenastrum capricornutum	BAJ 2740 240 SC	96 h	EbC_{50} and ErC_{50}	>4.62
Invertebrates				
Daphnia magna	Spirodiclofen	48 h	EC_{50}	>0.0508
Daphnia magna	BAJ 2740-enol	48 h	EC_{50}	>100
Daphnia magna	BAJ 2740 240 SC	48 h	EC_{50}	>100
Fish				
Oncorhynchus mykiss	Spirodiclofen	96 h	LC_{50}	>0.0351
Oncorhynchus mykiss	BAJ 2740-enol	96 h	LC_{50}	>73
Lepomis macrochirus	BAJ 2740 240 SC	96 h	LC_{50}	>58.3
Oncorhynchus mykiss	Spirodiclofen	97 d	NOEC (ELS)	0.00195
Oncorhynchus mykiss	Spirodiclofen	42 d	NOEC (ELS, indoor, microcosm)	0.020
Oncorhynchus mykiss	BAJ 2740-enol	97 d	NOEC (ELS)	>0.115
Cyprinodon variegatus	BAJ 2740-enol	115 d	NOEC (full fish life cycle)	0.0213
Invertebrates				
Daphnia magna	Spirodiclofen	21 d	NOEC	0.0248
Daphnia magna	Spirodiclofen	21 d	NOEC	0.0111
Daphnia magna	BAJ 2740-enol	21 d	NOEC	32
Sediment-dwelling invertebrates				
Chironomus riparius	Spirodiclofen	28 d	NOEC (initial concentration in overlying water)	0.032
Chironomus riparius	BAJ 2740-enol	28 d	NOEC (initial concentration in overlying water)	3.2

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Microcosm or mesocosm tests				
Not provided				

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

crop	Application rate (kg as/ha)	Organism	Time-scale	Distance (m)	TER[a]	Annex VI Trigger
orchard	0.144 (1X)	*Pseudok. subcapitata*	acute	3	>330	10
		Daphnia magna	acute	3	>7135	100
		Oncorhynchus mykiss	acute	3	>4160	100
orchard (early)	0.144 (1X)	*Oncorhynchus mykiss*	long-term	3	0.14	10
				5	0.20	10
				10	0.34	10
				15	0.73	10
				20	1.5	10
				30	3.9	10
				40	7.8	10
				50	14	10
orchard (late)	0.144 (1X)	*Oncorhynchus mykiss*	long-term	3	0.26	10
				5	0.48	10
				10	1.1	10
				15	2.2	10
				20	3.7	10
				30	7.5	10
				40	13	10
vine (early)	0.096 (1X)	*Oncorhynchus mykiss*	long-term	3	2.3	10
				5	5.2	10
				10	16	10

crop	Application rate (kg as/ha)	Organism	Time-scale	Distance (m)	TER[a]	Annex VI Trigger
vine (late)	0.096 (1X)	*Oncorhynchus mykiss*	long-term	3	0.76	10
				5	1.7	10
				10	5.0	10
				15	9.4	10
				20	15	10
orchard (early)	0.144 (1X)	*Daphnia magna*	long-term	3	0.8	10
				5	1.2	10
				10	1.9	10
				15	4.1	10
				20	8.5	10
				30	22.2	10
orchard (late)	0.144 (1X)	*Daphnia magna*	long-term	3	1.5	10
				5	2.8	10
				10	6.5	10
				15	12.8	10
vine (early)	0.096 (1X)	*Daphnia magna*	long-term	3	12.9	10
vine (late)	0.096 (1X)	*Daphnia magna*	long-term	3	4.3	10
				5	9.3	10
				10	28.5	10
orchard (early)	0.144 (1X)	*Chironomus riparius*	long-term	3	2.3	10
				5	3.4	10
				10	5.6	10
				15	12	10
orchard (late)	0.144 (1X)	*Chironomus riparius*	long-term	3	4.2	10
				5	7.9	10
				10	19	10
vine (early)	0.096 (1X)	Chironomus riparius	long-term	3	37	10
vine (late)	0.096 (1X)	Chironomus riparius	long-term	3	12	10

[a] based on test with formulation

Long-term toxicity/exposure ratios for fish, based on the indoor microcosm ELS study (NOEC = 0.020 mg/L)

crop	Application rate (kg as/ha)	Organism	Time-scale	Distance (m)	TERlt	Annex VI Trigger
orchard (early)	0.144 (1X)	*Oncorhynchus mykiss*	long-term	3	1.4	10
				5	2.1	10
				10	3.5	10
				15	7.4	10
				20	15.4	10
orchard (late)	0.144 (1X)	*Oncorhynchus mykiss*	long-term	3	2.6	10
				5	5.0	10
				10	11.8	10
vine (early)	0.096 (1X)	*Oncorhynchus mykiss*	long-term	3	23.3	10
vine (late)	0.096 (1X)	*Oncorhynchus mykiss*	long-term	3	7.7	10
				5	16.7	10

Bioconcentration

Bioconcentration factor (BCF) ‡	**Spirodiclofen** 491 L/kg wwt (based on total radioactivity)
Annex VI Trigger:for the bioconcentration factor	100 for not readily biodegradable compounds
Clearance time (CT_{50}) (CT_{90})	CT_{50}: **Spirodiclofen** 0.79 d (exposure to 1.6 µg/L) 0.66 d (exposure to 11.4 µg/L)
	CT_{90}: 2 d
Level of residues (%) in organisms after the 14 day depuration phase	3% after 13 d depuration

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

Acute oral toxicity ‡	LD_{50} >196 µg/bee (spirodiclofen) LD_{50} >100 µg as/bee (240 SC formulation)
Acute contact toxicity ‡	LD_{50} >200 µg/bee (spirodiclofen) LD_{50} >100 µg as/bee (240 SC formulation)

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

Formulation	Application rate (kg as/ha)	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
orchards	0.144	oral	<0.73	50
		contact	<0.72	50
vine	0.096	oral	<0.49	50
		contact	<0.48	50

Field or semi-field tests				
Species	Test type	Dose [kg as/ha]	Parameter	Effect
Apis mellifera	semi field (tunnel)	0.144	mortality foraging behaviour brood development	no effect no effect effect
Apis mellifera	semi field (tunnel)	0.146	mortality foraging behaviour brood development	no effect no effect effect
		0.045	mortality foraging behaviour brood development	no effect no effect no effect(A)

(A) Toxic standard (fenoxycarb, 150-200 g a.s./ha) did not produce an effect on bee brood development

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

Species	Test type and exposure duration	Test Sub-stance	Dose (g as/ha)	Endpoint	Effect (%)	Annex VI Trigger (%)
Laboratory tests						
Predatory mites						
Typhlodromus pyri	laboratory, glass plate, 14 d	240 SC	53.3	survival	100	30
Typhlodromus pyri	extended laboratory(A), 14 d	240 SC	1.6 2.8 4.8 8.7 16.2	survival / reproduction / overall (E) LR_{50}	14 / 34 / 43 75 / 36 / 84 85 / n.a.(B) / - 100 / n.a. / - 100 / n.a. / - 2.4 g as/ha	25
Typhlodromus pyri	extended laboratory(C), 14 d	240 SC	0.54 0.93 1.67 2.94 5.25	no. of eggs / nymphs / adults	4 / -14 / 4 -5 / 7 / 2 4 / -5 / 7 2 / 2 / -1 3 / -7 / 2	25
Foliage dwelling predators						
Chrysoperla carnea	laboratory, glass plate, 9 weeks	240 SC	144	survival reproduction overall (E)	7 -17 -10	30
Parasitoids						
Aphidius rhopalosiphi	laboratory, glass plate, 48 h	240 SC	29 58	parasitism	13 22	30
Trichogramma cacoeciae	laboratory, glass plate, 9-12 d	240 SC	58 144	parasitism	-32 7	30

(A) Exposure to dry residues on laboratory treated isolated apple leaves.

(B) n.a. = not applicable (insufficient survivors from initial phase to assess reproduction).

(C) Exposure of all mite stages to residues on apple tree

Species	Test type and exposure duration	Test Substance	Dose (g as/ha)	Endpoint	Effect (%)	Annex VI Trigger (%)
Ground dwelling predators						
Poecilus cupreus[(D)]	lab, direct spray of beetles and food on sand, 14 days	240 SC	144	survival food consumption	-3[(D)] 11[(D)]	30
Pardosa sp.	lab, direct spray of beetles and food on sand, 14 days	240 SC	72 144	survival food consumption	-3 -3 0 -9	30
Field or semi-field tests						
Typhlodromus pyri	field, sprayed vineyard, 4 weeks	240 SC	96	abundance	<25	25
Typhlodromus pyri	field, sprayed apple orchard, ±4 weeks	240 SC	144	abundance	<25 after 6 d 55 after 27 d	25
Typhlodromus pyri	field, sprayed apple orchard, ±1 year	240 SC	144	abundance	23 after 7 d 35 after 27 d 47 after 66 d 54 after 89 d 27 after 353 d	25

(D) Test result considered insufficiently reliable due to low response (E=24%) for reference item.

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

Acute toxicity ‡	**Spirodiclofen** LC_{50} >1000 mg/kg(A) **BAJ 2740-enol** LC_{50} >1000 mg/kg(A) **BAJ 2740-ketohydroxy** LC_{50} >1000 mg/kg(A) **BAJ 2740-dihydroxy** LC_{50} >1000 mg/kg(A) **2,4-dichlorobenzoic acid** LC_{50} 562 mg/kg(A) **240 SC formulation** LC_{50} >226 mg as/kg(A)
Reproductive toxicity ‡	Not available

(A) Not corrected for organic content of OECD 207 substrate

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
0.144	orchards	acute	>5208	10
0.096	vine	acute	>7813	10

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

Nitrogen mineralization ‡	**Spirodiclofen** At 0.20 and 0.98 mg/kg resp., maximum effect 55 and 47% after 28 d, effects <25% after 42 d. **BAJ 2740-enol** At 0.73 mg/kg, maximum effect 40% after 14 d, effects <25% after 28 d. **BAJ 2740-ketohydroxy** At 0.77 mg/kg, maximum effect 44% after 14 d, effects <25% after 28 d. **BAJ 2740-dihydroxy** At 0.84 mg/kg, maximum effect 30% after 14 d, effects <25% after 28 d. **2,4-dichlorobenzoic acid** At 0.45 mg/kg, maximum effect 36% after 14 d, effects <25% after 28 d
Carbon mineralization ‡	Spirodiclofen At 0.20 and 0.98 mg/kg: effects <25%.

Effects on other non-target organisms (Annex IIA, point 8.6, Annex IIIA, point 10.8)

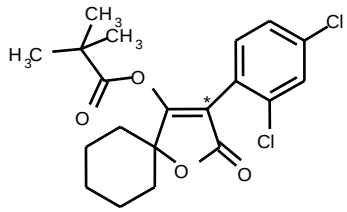
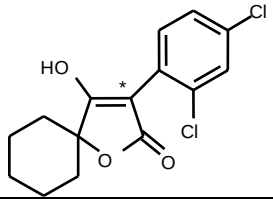
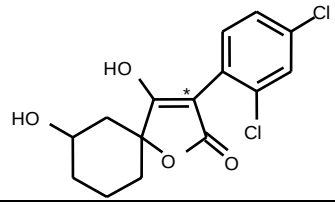
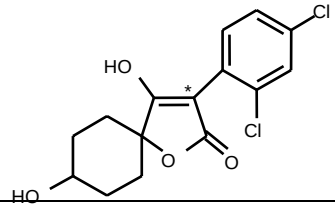
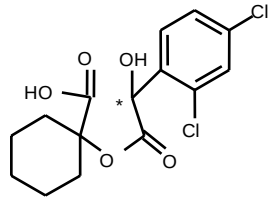
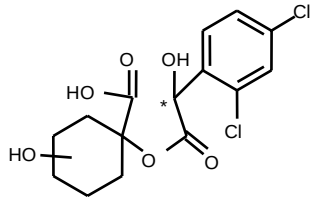
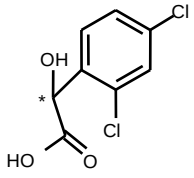
Collembola	**BAJ 2740-enol** NOEC reproduction 100 mg/kg(A) **BAJ 2740-ketohydroxy** NOEC reproduction 100 mg/kg(A) **BAJ 2740-dihydroxy** NOEC reproduction 1000 mg/kg(A) **2,4-dichlorobenzoic acid** NOEC reproduction 18 mg/kg(A)

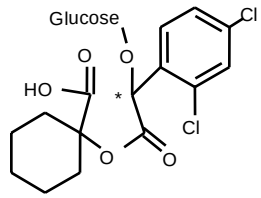
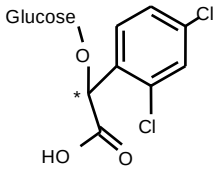
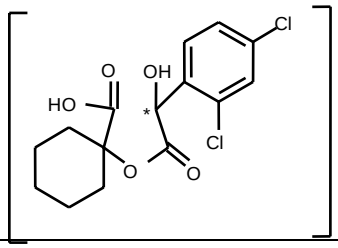
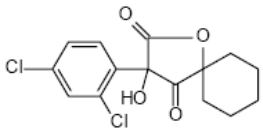
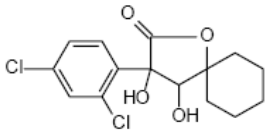
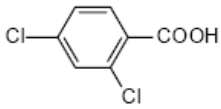
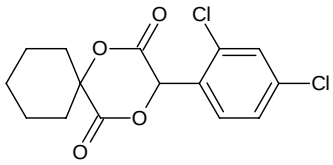
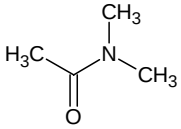
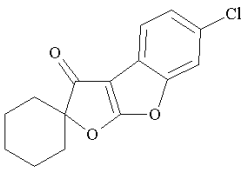
(A) Not corrected for organic content of OECD 207 substrate

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	R52/53: Harmful to aquatic organisms, may cause long-term effects to the aquatic environment S60: This material and its container must be disposed of as hazardous waste S61: Avoid release to the environment

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
Parent, BAJ 2740	spirodiclofen	
M01, BAJ 2510 BAJ 2740-enol	spirodiclofen-enol 3-(2,4-dichlorophenyl)-4-hydroxy-1-oxaspiro[4.5]dec-3-en-2-one	
M02	3-hydroxy-spirodiclofen-enol (eq=equatorial or ax=axial);	
M03	4-hydroxy-spirodiclofen-enol (eq=equatorial or ax=axial)	
M04	2,4-dichloro-mandelic acid cyclohexyl ester glucosylpentoside	
M05	2,4-dichloro-mandelic acid hydroxy-cyclohexyl ester	
M06	2,4-dichloro-mandelic acid	

M07	2,4-dichloro-mandelic acid glucosyl cyclohexyl ester	
M08	2,4-dichloro-mandelic acid glucoside	
M09	2,4-dichloro-mandelic acid cyclohexyl ester	
2740-ketohydroxy BAJ 2740-ketohydroxy	3-(2,4-dichlorophenyl)-3-hydroxy-1-oxaspiro[4.5]decane-2,4-dione	
BAJ-dihydroxy BAJ 2740-dihydroxy	3-(2,4-dichlorophenyl)-3,4-dihydroxy-1-oxaspiro[4.5]decan-2-one	
M16	2,4-dichlorobenzoic acid	
BAJ 2740-lactide	3-(2,4-dichlorophenyl)-1,4-dioxaspiro[5.5]undecane-2,5-dione	
-	N,N-dimethylacetamide	
BAJ 2740-dioxoketone		

ABBREVIATIONS

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