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

fipronil

finalised: 3 March 2006

(version of 12 April 2006 with minor editorial changes and corrections indicated in yellow)

SUMMARY

Fipronil is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

France being the designated rapporteur Member State submitted the DAR on fipronil in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 10 February 2004. Following a quality check on the DAR, the peer review was initiated on 15 July 2004 by dispatching the DAR for consultation of the Member States and the sole applicant BASF. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting in 9 February 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in June and July 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 7 February 2006 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide as proposed by the applicant which comprises seed dressing to control soil insects and wireworms in sunflower and maize at application rate up 30 g fipronil per hectare for sunflower (up to 500 g fipronil per 100 kg seeds) and up to 50 g per hectare for maize (up to 250 g per 100 kg seeds), respectively. It should be noted that due to the fact that the applicant has changed, some representative uses are not longer supported for the EU review by the new applicant. Fipronil can be used as insecticide and acaricide. It should be noted that during the peer review process the applicant stated that only the use as insecticide will be supported in the EU review programme.

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25

The representative formulated product for the evaluation was "Regent 500FS" ("EXP80415A"), a flowable concentrate for seed treatment (FS), registered in some Member States of the EU. The WG- and the GB formulation (EXP60720A and EXP61840A, respectively) are not longer supported for the EU review process (i.e. with respect to Annex I inclusion) by the new applicant. However, the submitted data package was evaluated in the DAR, but the peer review was not completed.

Adequate methods to monitor all compounds given in the respective residue definition are available only for food and air. Residues in food of plant origin can be determined with a multi-residue method (The German S19 method has been validated). For the other matrices only single methods are available to determine residues of fipronil.
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.

Rapidly and extensively absorbed and distributed, fipronil may bioaccumulate but is readily metabolised, and slowly excreted via faeces. Fipronil is toxic by oral, inhalation and dermal acute exposure. It is slightly skin and eye irritating, and weakly sensitising, but not sufficiently to be classified. The proposed classification is T, R23/24/25 "Toxic by inhalation, in contact with skin and if swallowed".
Adverse effects in the short term studies are observed in the central nervous system, liver and thyroid.
The proposed classification by ECB is T, R48/25 "Toxic: danger of serious damage to health by prolonged exposure if swallowed", to be voted in the 30th ATP. No genotoxic or carcinogenic potential is demonstrated. The mechanism for induction of thyroid tumours was discussed by the experts and considered rat specific and not relevant to humans.
Neither reproductive or developmental toxicity is observed. In specific neurotoxicity studies, no histopathological findings are observed in the nervous system.
The Acceptable Daily Intake (ADI) is 0.0002 mg/kg bw/day, the Acceptable Operator Exposure Level (AOEL) is 0.0035 mg/kg bw/day, and the Acute Reference Dose (ARfD) 0.009 mg/kg bw, with a safety factor of 100.
As the use of the Seed Tropex model was considered not fully appropriate by the experts, the operator exposure was evaluated with a field study, resulting in an exposure below the AOEL without PPE.
Worker exposure is 89% of the AOEL without PPE, for a 8-hour working day. Bystander exposure is not likely to be an issue for seed treatments and has to be addressed at Member State level.

The metabolism of fipronil has been investigated on five different crops representative for cereals, pulses and oilseed, roots and tubers using either soil applications or seed treatment. A common metabolic pathway could be defined for the three crop groups tested and a relevant metabolite (sulfone metabolite MB 46136) was demonstrated to be present. Even though there were concerns on an acutely toxic by oral administration photo degradation product of fipronil, MB 46513, the experts' meeting on residues concluded that the compound is basically not relevant in relation to seed treatment uses. However, a label restriction has been proposed to ensure that treated seed remains

stored in the dark to prevent photo degradation processes. In supervised residue trails no residues of fipronil and of its sulfone metabolite were observed at harvest of maize grain and sunflower seed. Trials results are suitable to propose MRLs at LOQ level.

Even though calculated animal intakes were well below the trigger of 0.1 mg/kg, there is a need to consider residues in animal products since fipronil is classified fat soluble and the ADI is very low. Based on the available livestock metabolism and feeding studies, MRLs for food of animal origin were proposed.

In a consumer risk assessment the TMDI was demonstrated to exceed the ADI for toddlers and infants, mainly due to the fact that milk consumption accounted for the most significant contribution of pesticide intake in terms of the total dietary assessment. However, in a refined chronic dietary risk assessment the IEDI/NEDI was below the ADI for all considered consumer groups (adults, toddles, infants) and thus, it is unlikely that exposure to fipronil and fipronil sulfone residues from seed treatment will pose a high chronic risk to consumers. In an acute dietary risk assessment the estimated exposure of all considered consumer groups was well below the proposed ARfD.

Under laboratory aerobic conditions fipronil is moderate to high persistent in soil. Major metabolites are the amide RPA 200766[3], the sulphone MB 46136[4] and the sulphide MB 45950[5]. Mineralization is very low.

Under dark aerobic conditions at metabolite RPA 200766 is high persistent, RPA 200761[6] moderate to high persistent, MB 45950 medium to high persistent, MB 46136 high persistent and MB 46513[7] moderate to medium persistent. Most of the measured half lives are longer than the duration of the studies and therefore uncertain.

Photolysis may contribute slightly to the environmental dissipation of fipronil in soil yielding two metabolites not previously detected in the dark aerobic degradation studies: MB 46513 (more acutely orally toxic than fipronil) and RPA 104615[8].

Available field studies confirmed that fipronil is medium to high persistent in soil when not exposed to light (soil incorporated). When exposed to light the toxic metabolite MB 46513 is detected.

Two field accumulation studies were submitted by the applicant after the DAR was finalised. A clear tendency for accumulation of fipronil metabolites is demonstrated. Plateau for metabolites had not been reached after the five or six years of repeated applications.

The PEC soil calculation submitted by the applicant after the DAR was finalised do not represents a worst case with respect to the parent compound. Furthermore, the assumptions taken in the

[3] RPA 200766: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylsulfonyl-1*H*-pyrazole-3-carboxamide

[4] MB 46136: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylsulfonylpyrazole-3-carbonitrile

[5] MB 45950: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylthio-1-pyrazole-3-carbonitrile

[6] RPA 200761: 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonylpyrazole-3-carboxylic acid

[7] MB 46513: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylpyrazole-3-carbonitrile

[8] RPA 104615: 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl) pyrazole-4-sulfonic acid, potassium salt

calculation are not well justified. Calculation of the initial and 21 d TWA-PEC_S for the parent compound and soil metabolites are also needed to finalise the ecotoxicological risk assessment.
According adsorption / desorption studies fipronil is low to medium mobile, MB 45950 and MB 46136 are immobile to low mobile, MB 46513 is low mobile and RPA 200766 is medium to high mobile.
Hydrolysis will not contribute to the degradation of fipronil in the environment. However, photolysis may contribute to the degradation of fipronil and its major metabolites in water. Fipronil is not readily biodegradable in water.
In water/sediment system fipronil is adsorbed on the sediment where degrades to MB 45950. In the water phase fipronil and the major metabolite RPA 200766 reached levels above 10 % AR.
$PEC_{SW/SED}$ were provided by the applicant after the DAR was finalised. However, new calculations are needed with parameters updated following FOCUS guidance. New PEC_{GW} were provided by the applicant after the DAR had been finalized. Only the application rate of 50 g/ha for maize has been simulated. Results of these new calculations show that metabolite RPA 200766 exceeds the trigger of 0.1 µg / L for five of the seven scenarios simulated. This metabolite has been assessed to be not toxicological relevant (see 2.8) but it is considered ecotoxicological relevant (see 5.2). Due to the deviations with respect to guidelines on the input parameters selection and the need of justification for the use of field kinetic parameters a data gap for new FOCUS PEC_{GW} calculation with appropriate input parameters has been identified.
Long range transport and deposition of fipronil may be considered negligible.

A high acute, short and long term risks to granivorous birds were identified in the first tier risk assessment for the representative use as a seed treatment in maize and sunflower. The risk to birds should focus on the acute and short term risk as there is no indication that fipronil is a reproductive toxin. A new risk assessment for granivorous birds taking into account the concerns raised at the EPCO 27 experts' meeting is required. The risk to small and large granivorous birds must be quantified. The current proposed extrapolation from maize to sunflowers is not acceptable.
Also for granivorous mammals a high acute and long term risk were identified in the first tier risk assessment for the representative use as a seed treatment in maize and sunflower. A revised risk assessment for granivorous mammals taking into account the concerns raised at EPCO 27 is required. The availability of treated seeds for mammals should be assessed to indicate whether mice consumed drilled maize and sunflower seeds.
The risk to granivorous birds and mammals from the use of fipronil as a seed treatment in maize and sunflower can only be concluded once recently submitted data are evaluated.
The risk to herbivorous birds and mammals from the representative uses of fipronil as a seed dressing is considered to be low. The risk to earthworm and fish-eating birds and mammals can be considered low based on the currently available PECs and PECsw-values. The risk to earthworm and fish eating birds and mammals from the representative uses with the FS formulation can not be concluded due to still open questions regarding the calculation of PEC in surface water and soil.

The risk to aquatic organisms is based on the most sensitive species, *Mysidopsis bahia*. If the applicant would like to pursue the argument that marine species are more sensitive than freshwater species then a more robust justification must be provided. The risk to aquatic organisms from the representative uses with the FS formulation can not be concluded due to still open questions regarding the calculation of PECsw values. Based on the available provisional PECsw values a high acute and long term risk to aquatic organisms was identified for the representative use as a seed treatment in maize. The risk to aquatic organisms for the representative use in sunflower can be regarded as low. The RMS proposed to refine the long term risk by using an endpoint for *M. bahia* from a study in the presence of sediment. The EFSA considers that in order to accept this refinement option, an assessment in line with the conclusion of the PPR Panel on dimoxystrobin should be presented. The experts' meeting agreed that it might be possible to reduce the standard uncertainty factor due to the number of species tested. The EFSA would like to refer to the opinion of the PPR Panel regarding the reduction of the uncertainty due to the availability of several single species studies and proposes to take this opinion into account at MS-level. Based on the present PECsw values the risk from the metabolites MB 46136, MB 45950 and RPA 200766 for the representative uses as a seed treatment in maize and sunflower can be regarded as low except for the long term risk to aquatic invertebrates from MB 46136 in maize. Also for the refinement of this risk the EFSA would like to refer to the opinion of the PPR Panel on the lowering of aquatic trigger values.
The risk for bioaccumulation in fish from fipronil is considered to be low. The EFSA proposes that a study on bioaccumulation in fish from the metabolites MB 46136, MB 45950 and RPA 200766 should be submitted as the Log Pow of these metabolites exceeds 3.

A very high acute contact and oral toxicity of fipronil to bees were observed in the laboratory toxicity studies. The metabolite MB 46136 showed a similar toxicity to bees as fipronil and the metabolite RPA 200761 showed a lower toxicity to bees than fipronil. The EPCO experts' meeting considered the risk to adult bees for the representative uses as a seed treatment in maize and sunflower addressed based on the low exposure situation observed in monitoring studies and the observation of no adverse effects in the tunnel studies. The risk to bees can only be concluded once recently submitted data on the risk to bee brood are evaluated. Furthermore the EFSA would like to highlight that the available monitoring studies were mainly performed in France and MS should consider the relevance of these studies for the circumstances in their country.

A high toxicity to NTA was observed in the laboratory. The EPCO experts' meeting identified the need for a new risk assessment for soil dwelling arthropods taking into account final results from the ongoing aged residue studies on *A. bilineata* and *F. candida*. This assessment should cover the potential for recovery of impacted species in the field. Furthermore the meeting noted that the risk assessment should cover the plateau soil PEC for total residues (parent + metabolites). The risk to non-target arthropods from the representative uses with the FS formulation can only be concluded once recently submitted studies on *A. bilineata* and *F.* candida are evaluated and the open questions for the calculation of PECsoil have been solved.

The risk to soil macro-organisms can be considered low at a concentration of 0.785 mg a.s./kg soil and the risk to soil micro-organisms can be considered as low at a concentration of 0.667 mg a.s./kg soil for fipronil and 0.60, 0.133 and 0.267 mg/kg soil for MB 46136, MB 45950 and RPA 200766 respectively. The risk to soil non-target macro- and micro-organisms from the representative uses with the FS formulation can not be concluded due to still open questions regarding the calculation of PECsoil.

The risk to earthworms, non-target plants and biological methods for sewage treatment is considered to be low.

Key words: fipronil, peer review, risk assessment, pesticide, insecticide, acaricide

Table of Contents

BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Fipronil is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating France as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, France submitted the report of its initial evaluation of the dossier on fipronil, hereafter referred to as the draft assessment report, to the EFSA on 10 February 2004. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 15 July 2004 to the Member States and the main applicant BASF as identified by the rapporteur Member State following acquisition of the fipronil business from the original notifier Aventis.

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

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised 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.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 7 February 2006 leading to the conclusions as laid down in this report.

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

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, 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 provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

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

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

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

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-1 of 1 March 2006)

Given the importance of the draft assessment report including its addendum (compiled version of January 2006 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B (part 1 and part 2) 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 draft assessment report (Volume 3, B.5, rev 2 of July 2005) which take into account mostly editorial changes and open points of the reporting table. 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 draft assessment report together with the peer review report which both is publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Fipronil is the ISO common name for 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile (IUPAC).

Fipronil belongs to the class of pyrazole insecticides and pyrazole acaricides such as acetoprole and tebufenpyrad. Fipronil has activity against various soil insects during their larval growth stage by contact and ingestion. It interferes with the passage of chloride ion through the GABA chloride channel.

The representative formulated product for the evaluation was "Regent 500FS" ("EXP80415A"), a flowable concentrate for seed treatment (FS), registered in some Member States of the EU. It should be noted that the WG- and the GB formulations (EXP60720A and EXP61840A, respectively) for "in

furrow" applications at drilling are not supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion). However, the submitted data package was evaluated in the DAR, but the peer review was not completed.

Fipronil can be used as insecticide and acaricide. It should be noted that during the peer review process it was stated that only the use as insecticide will be supported in the EU review programme. The evaluated representative uses as insecticide which comprises seed dressing to control soil insects and wireworms in sunflower and maize at application rate up 30 g fipronil per hectare (sunflower; up to 500 g fipronil per 100 kg seeds) and up to 50 g per hectare (maize; up to 250 g per 100 kg seeds), respectively.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of fipronil as manufactured should not be less than 950 g/kg, which is higher than the minimum purity given in the FAO specification 581/TC/S/F (1998) of 925 g/kg. The higher value relates to the submitted results of current batch analysis and not to any toxicological concern to increase the minimum purity.
The technical material contains no relevant impurities.

The content of fipronil in the representative formulation is 500 g/L (pure).

The assessment of the data package revealed no particular area of concern for "Regent 500FS (EXP80415A) as well as for the formulations "EXP61840A" (GB) and EXP60720A (WG) not supported by BASF for the EU review process (i.e. with respect to Annex I inclusion).

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of fipronil in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough 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. fipronil and the sulfone metabolite MB 46136[9] in food of plant origin and animal origin (seed treatment, only); fipronil in air.
In the case of soil only a method for the determination of fipronil, MB 46136, MB 45950[10], is available. ~~No~~ A method for the determination of the metabolite RPA 200766[11] in soil was submitted but it has not been evaluated or peer reviewed. Analytical methods for the determination of fipronil in water (ground and surface) are available. For the metabolite RPA 200766 no sufficiently validated methods are available. The submitted method for water (surface and ground) is not sufficiently validated to fulfil the requirements (no confirmatory method is available and the LOQ of 1 µg/L is too high for drinking water). It is understood that a method is under development but it has not been submitted yet.
Residues in food can be determined with a multi-residue method (the German S19 method has been validated). For the other matrices only single methods are available to determine the respective residues.
The methodology used is GC with EC or MS detection. It was shown that a multi-residue method (the German S19 was validated) is applicable for the determination of residues in food.

The discussion in the expert meeting on identity, physical and chemical properties and analytical methods (EPCO 30, July 2005) was limited to certain physical, chemical and technical properties, analytical methods and the manufacturing process. It should be noted that a data requirement for a new shelf-life study was erroneous associated with the "Regent 500FS" formulation, but this data gap belongs to the formulation "EXP 80416A". However, this formulation was not included in the dossier and therefore not evaluated.

2. Mammalian toxicology

Fipronil was discussed at the EPCO expert meeting for mammalian toxicology (EPCO 28) in June-July 2005.
Due to the fact that the applicant has changed during the peer review process, some representative uses have been deleted. The GB and the WG formulations (EXP61840A and EXP60720A, respectively, for “furrow” applications) are not supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion). However, the submitted data package was evaluated by the RMS but excluded from the discussions at the expert meeting.

[9] MB 46136: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylsulfonylpyrazole-3-carbonitrile
[10] MB 45950: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylthio-1-pyrazole-3-carbonitrile
[11] RPA 200766: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylsulfonyl-1*H*-pyrazole-3-carboxamide

2.1. ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Fipronil is rapidly and extensively absorbed (>80% within 72 hours).

The potential for accumulation was discussed by the experts. Some data suggest that fipronil or its metabolites may accumulate: a long half life (up to 245 hours), a large distribution in tissues (with a predominance in fatty tissues) and levels in fat always higher than in blood. (fat:blood 20:1 at high dose, fat:blood 70-90:1 at low dose, log P 3.5-4).

The major residue in tissues is MB 46136 (sulphone derivative). Fipronil is mainly excreted via faeces (up to 71% in 7 days, with up to 10 metabolites), but also via urine (6-26%) and via bile (7-18%, high degree of biliary excretion).

2.2. ACUTE TOXICITY

Fipronil is toxic following oral (rat LD_{50} 97 mg/kg bw) , inhalation (rat LC_{50} 0.39 mg/L) and dermal (rabbit LD_{50} 354 mg/kg bw) acute exposure. It is slightly irritating to skin and eyes, and is a weak sensitizer in the Magnusson and Kligman test, but not sufficiently to be classified.

The proposed classification and risk phrases are: **T, R23/24/25 "Toxic by inhalation, in contact with skin and if swallowed"**.

2.3. SHORT TERM TOXICITY

The short term effects of fipronil were studied in 28-day and 90-day studies in rats and dogs, as well as in 1-year dog study by oral administration. Repeated dermal exposure was performed in a 21-day rabbit study.

Target organs were the central nervous system (all species), the liver (rat and dog) and the thyroid (rat). The findings observed were clinical signs of neurological disturbance, increased liver weight and hepatocyte enlargement, as well as thyroid follicular hypertrophy/hyperplasia. The relevant short term NOAEL agreed by the experts, based on the 1-year dog and 90-day rat and dog studies, is 0.35 mg/kg bw/day.

The dermal NOEL for the 21-day dermal rabbit study is 5 mg/kg bw/day.

The proposed classification by ECB is **T, R48/25 "Toxic: danger of serious damage to health by prolonged exposure if swallowed"** (to be voted in the 30th ATP).

2.4. GENOTOXICITY

Five *in vitro* and three *in vivo* studies were performed to investigate the genotoxic potential of fipronil. The *in vitro* chromosome aberration test with Chinese hamster lung cells is positive at toxic dose levels, with and without metabolic activation. As the two micronucleus tests and the additional UDS test *in vivo* are negative, the experts considered that fipronil has no genotoxic potential.

2.5. LONG TERM TOXICITY

The long term effects of fipronil were studied in a 2-year rat study and an 18-month mouse study.

In the rat study, effects are observed in the liver, thyroid and kidneys at the high dose. Dose-related incidence of convulsive episodes is also observed, except at the low dose. Slight effects on circulating

T4 and cholesterol are noted at the low dose, but considered as not toxicologically relevant. The relevant NOAEL is 0.019 mg/kg bw/day.

The mechanism for induction of thyroid tumours at the high dose was discussed by the experts. Taking into consideration the results of mechanistic studies, they agreed that thyroid tumours are induced by the increased clearance of T4 in the bile, rather than a direct effect, and that they are rat specific and not relevant to humans.

In the mouse study, the proposed NOAEL is 0.05 mg/kg bw/day. It is based on decreased body weight gain, increased liver weight and increased incidence of periacinar microvesicular vacuolation of hepatocytes (mainly in males). No evidence of carcinogenicity was observed.

2.6. REPRODUCTIVE TOXICITY

The effects of fipronil on reproductive parameters were studied in a two-generation reproduction study in rats, and in two teratogenicity studies (in rats and rabbits).

In the rat reproductive study, the maternal NOAEL is 0.25 mg/kg bw/day, based on liver and thyroid changes. Adverse effects on the offspring or on the reproductive parameters are only observed at maternal toxic doses (convulsions, body weight changes, delays in pre-weaning development). Based on this, the offspring and the reproductive NOAEL is 2.5 mg/kg bw/day.

In the rat and rabbit teratogenicity studies, there is no effect upon litter parameters or on embryofoetal development. The rabbit is the most sensitive species with a maternal NOAEL of 0.2 mg/kg bw/day and a developmental NOAEL > 1.0 mg/kg bw/day, whereas the rat maternal NOAEL is 4 mg/kg bw/day and the rat developmental NOAEL > 20 mg/kg bw/day.

2.7. NEUROTOXICITY

In two rat acute studies, the overall NOEL for neurobehavioural and general toxicity is 2.5 mg/kg bw, based on reduced body weight gain (females) and decreased hind leg splay (males). No neuropathological changes are observed.

In the dog 14-day study, functional observations and loss of body weight are observed at 20 mg/kg bw/day (single dose tested), but no histopathological changes in the nervous system.

In the rat 90-day study, there is no evidence of any neurological effect and the NOEL for neurotoxicity is 8.9 mg/kg bw/day. The NOAEL for general toxicity is 0.3 mg/kg bw/day, based on reduced bodyweight gain and food consumption.

In the rat developmental neurotoxicity study, the NOAEL for developmental neurotoxicity and parental toxicity is 0.91 mg/kg bw/day, based on neurobehavioural effects but without evidence of neuropathological changes in offspring and on reduced body weights and food consumption in dams at 15 mg/kg bw/day. The overall systemic NOAEL is 0.05 mg/kg bw/day, based on reduced body weights in the offspring during lactation.

2.8. FURTHER STUDIES

Rat metabolites

The metabolite **MB 45897**[12] was neither toxic after acute exposure by oral or percutaneous administration (LD_{50} > 2000 mg/kg bw) , nor skin or eye irritant.

The metabolite **MB 45950** had an acute oral LD_{50} of 69 mg/kg bw/day. The acute dermal LD_{50} was between 500 and 4000 mg/kg bw, and it was not irritant to rabbit skin and eye. The NOAEL in a 28-day dog study was 1 mg/kg bw/day, based on a marginal increase in alkaline phosphatase activity, and the 90-day rat study showed a similar NOAEL of 0.7 mg/kg bw/day, based on increased liver weight and thyroid hypertrophy. The mutagenicity tests performed *in vitro* with bacterial strains and human lymphocytes were negative.

The oral LD_{50} of the metabolite **MB 46136** was 184 mg/kg bw and the dermal LD_{50} > 2000 mg/kg bw, and it was not demonstrated to be skin or eye irritant in the rabbit. The bacterial reverse mutation test and the mammalian cytogenetic test *in vitro* with human lymphocytes gave both negative results.

The metabolite **RPA 200766** has an LD_{50} > 2000 mg/kg bw. The NOAEL in a 28-day rat study is 3.8 mg/kg bw/day. It was not mutagenic in an Ames test, but clastogenic in human lymphocytes in the presence of S9 mix, only at cytotoxic dose levels. A rat micronucleus *in vivo* showed negative results but there was no evidence of toxicity to bone marrow cells and no systemic toxicity.

Based on their binding potential with the GABA receptor and on toxicity data, the metabolites MB 45950 and MB 46136 are comparable to fipronil in toxicity and the same reference values are considered justified. On the contrary, MB 45897 and RPA 200766 do not show binding at the GABA receptor and are considerably less toxic than fipronil.

Soil/water metabolites

The metabolite **MB 46513**[13] showed a similar toxicokinetic behaviour as fipronil. It was very toxic orally (LD_{50} 16 mg/kg bw) but not toxic by dermal administration (LD_{50} > 2000 mg/kg bw). In the 28-day and 90-day studies performed in rats, the NOAEL was 0.2 mg/kg bw/day based on decreased body weight and clinical signs. Repeated dose studies (28-day and 90-day) in dogs resulted in a NOAEL of 0.3 mg/kg bw/day. The NOAEL from a 90-day mouse study was 0.3 mg/kg bw/day based on deaths and liver findings. There was no genotoxic effect *in vitro* and *in vivo*. A 2-year rat carcinogenicity study showed no evidence of neoplastic changes, with a NOAEL of 0.03 mg/kg bw/day based on clinical signs (convulsions in females, higher agressivity in males). In a teratogenicity study in rats, no developmental effect was demonstrated; the maternal NOAEL was 0.2 mg/kg bw/day, and the developmental NOAEL was 1.0 mg/kg bw/day. An acute neurotoxicity study in rats showed behavioural changes but no neuropathological changes, with a NOAEL of 2.0 mg/kg bw. A dermal absorption study *in vivo* resulted in a maximum value of 6.61% including skin.

The metabolite **RPA 105048**[14] had a moderate acute oral toxicity (LD_{50} 467 mg/kg bw).

[12] MB 45897: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-1H-pyrazole-3-carbonitrile
[13] MB46513: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylpyrazole-3-carbonitrile
[14] RPA 105048: 1-(2,6-dichloro-4-trifluoromethylphenyl)-3-amino-5-amino-4-trifluoromethylsulfonylpyrazole

Plant metabolites

The metabolite **RPA 104615**[15] had a low acute oral toxicity (LD_{50} > 2000 mg/kg bw) and was not mutagenic *in vitro*. The NOAEL in a 28-day rat study was 45.7 mg/kg bw/day.

The metabolites **RPA 105320**[16] and **RPA 200761**[17] were not acutely toxic (LD_{50} > 2000 mg/kg bw). RPA 200761 was also negative in an Ames test.

Based on their binding potential with the GABA receptor and toxicity data, the metabolites RPA 105320, RPA 104615 and RPA 200761 do not show binding at the GABA receptor and are considerably less toxic than fipronil.

2.9. MEDICAL DATA

No human cases of fipronil intoxication in the course of production, transportation, formulation and packaging have been reported. Regular medical examinations do not show any related health effects including sensitisation.

Literature search on adverse reactions in humans and pets, from the use of fipronil as veterinary drug, did not raise concerns related to its use as a seed treatment.

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

A standard safety factor of 100 was used for all the reference values.

ADI

Based on the NOAEL from the rat carcinogenicity study, the ADI is 0.0002 mg/kg bw/day.

AOEL

The AOEL of 0.0035 mg/kg bw/day based on the overall NOAEL from the 90-day rat, 90-day and 1-year dog studies, was considered appropriate by the experts.

ARfD

The experts agreed that the ARfD should be derived from the developmental neurotoxicity study in the rat, with a developmental NOAEL of 0.9 mg/kg bw/day. This results in an ARfD of 0.009 mg/kg bw.

2.11. DERMAL ABSORPTION

The experts noted that in vitro dermal absorption studies with rat and human skin were conducted using an SC formulation, while in vivo studies used a WDG. The general opinion was that a WDG

[15] RPA 104615: 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl) pyrazole-4-sulfonic acid, potassium salt

[16] RPA 105320: 5-amino-3-carbamyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonylpyrazole

[17] RPA 200761: 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonylpyrazole-3-carboxylic acid

formulation would penetrate less than a SC formulation. It was additionally noted that the use of the dermal absorption value for the concentrate (1%) rather than the dilution (11%) in operator exposure calculations was acceptable due to the fact that the operator is exposed to the concentrate, as water is added to the tank. Furthermore, seed treatments are not extensively diluted prior to use.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Regent 500 FS (EXP 80415A) is a flowable concentrate for seed treatment containing 500 g fipronil/L.

In the original dossier also exposure estimates for the WG and GB formulations were submitted. Comments were made by other MSs and several open points were identified, but not discussed in an experts meeting as these formulations were not further supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion). The results should be considered at Member State level.

Operator exposure

Seed Tropex

In the DAR, results according to the Seed Tropex model are presented. The applicability of this model to the application method of the PPP for maize was discussed by the experts. They considered the model as not fully appropriate, as it is based on data from mobile units whereas maize is treated in factories. Therefore, the field exposure data provided, which are specific for the treatment method, were considered more appropriate.

Field study

The results of a field study are provided in an addendum. This was considered by the experts as a conservative risk assessment, as it included all activities (mixing/loading, calibration, bagging and cleaning). However, the activities were performed by professional seed treaters and not assessed for other uses (e.g. farm use). The RMS explained that in Europe activities with maize are confined to professionals.

The results are presented in the following table.

Measured* exposure presented as % of AOEL (0.0035 mg/kg bw/day), according to a field study during maize seed treatment with Regent 500. The default for body weight of operator is 70 kg.

Systemic exposure	Original study data (work time = 5.6h)	8h standard workday
With protective gloves during bagging	58%	63%
Without protective gloves during bagging	59%	64%

*90th percentiles for mixers/loaders and calibrators and arithmetic means for baggers and cleaners

Worker exposure

In the DAR, the Seed Tropex model was used, with a conservative assumption of a 10-hour working day. This resulted in an exposure of 112% or the AOEL when no protective equipment is worn. The use of protective equipment has not been considered further.

In an addendum, the same calculation for an 8-hour working day gave an estimated exposure of 89% of the AOEL without protective equipment. This was agreed by the experts.

Bystander exposure

The experts agreed that bystander exposure is not likely to be an issue for seed treatments. However for maize and sunflower exposure may occur depending on the sowing technology used.

This issue has to be addressed at Member State level.

3. Residues

Fipronil was discussed in the experts' meeting for residues in June/July 2005 (EPCO 29). It is pointed out that evaluation of the residue behaviour of fipronil in terms of consumer safety covers only the representative use of fipronil as a seed treatment.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of fipronil has been investigated on five different crops using either soil applications or seed treatment. These crops are representative for cereals (wheat, maize), pulses and oilseed (sunflower, cotton), roots and tubers (sugar beet). Due to the structure of the molecule, metabolism studies were performed with ^{14}C-fipronil labelled on the phenyl ring only.

Metabolism in plants following soil application or seed treatment is characterised by low uptake (less than 5% of the applied radioactivity) and low translocation of radioactive residues in sunflowers, cotton plants, maize, wheat and sugar beets. The studies indicate that a common metabolic pathway could be defined for the three crop groups tested. Fipronil is metabolised through two major pathways, on one hand by oxidation of the sulfoxide to yield the sulfone MB 46136 and on the other hand by hydrolysis of the nitrile moiety to yield the amide RPA 200766, which hydrolyses to the carboxylic acid RPA 200761.

Fipronil, metabolite MB 46136 (sulfone) and metabolite RPA 200766 (amide) were found to be the major compounds detected in the different plant parts, individually accounting for about 14-40%, 12-64% and 13-60% of the total radioactivity (TRR) respectively. Additional metabolites were characterised but generally observed at low levels (<10% TRR) with the exception of metabolite RPA 105320 in sugar beet leaves (18% TRR) and metabolite RPA 200761 in maize forage and wheat grain (11% and 37% TRR respectively). From metabolism studies with fipronil in plants treated with a foliar application the formation of the very toxic photolysis product of fipronil, MB 46513 (desulfinyl), is known. In the initially submitted plant metabolism studies with soil application or seed treatment, MB 46513 was never observed. In contrast, this photolysis compound was detected in a

sunflower study recently submitted (2004). However, metabolite MB 46513 was only detected in leaves and stalks and accounted for a very low level (0.6% TRR in the immature plant and 0.3% at harvest for the 1N treatment, 1.2% at harvest for the 5N treatment). MB 46513 was never detected in sunflower seeds where metabolites RPA 200761, RPA 200766 and RPA 104615 were seen to be major (1.7% to 17.5% TRR).

It can be concluded that in terms of the representative use under evaluation (seed treatment) only fipronil, metabolite MB 46136 (sulfone) and metabolite RPA 200766 (amide) appeared to be major metabolites in plants. However, since metabolite RPA 200766 was not found to be of toxicological relevance (refer to 2.8), it was proposed to limit the residue definition in plants to the parent compound fipronil and its sulfone metabolite MB 46136. The experts' meeting for residues also discussed whether or not the desulfinyl metabolite MB 46513 should be included in the residue definition, as done in previous JMPR evaluations. It was concluded that this definition was mainly based on studies with foliar application. Following consultation with EPCO 28 (toxicology), for seed treatment uses the residue definition for risk assessment and monitoring was proposed as the sum of fipronil and sulfone metabolite (MB 46136) expressed as fipronil. However, based on the concern that the desulfinyl metabolite MB 46513 forms as a result of photodegradation and as the metabolism studies with seed treatment or soil incorporation would have prevented photodegradation, it was proposed that treated seed must be kept in the dark prior to use. Therefore, a label restriction is considered necessary to ensure that treated seed remains in sealed bags to keep treated seed stored in the dark. If the use is to be extended for soil treatment with soil incorporation it will be necessary to consider whether a label statement to ensure that the soil is incorporated straight after application of the pesticide is needed.

Extensive residue data have been generated for maize and sunflower following seed treatment. Field trials were conducted over several growing seasons from the 1990's to 2004 in both southern and northern Europe. Although residue in plants was defined as sum of fipronil and MB 46136, also the metabolites MB 45590, MB 46513 and RPA 200766 have been monitored in most of the residue trials in order to ascertain that these compounds would not be found at levels greater than the limit of quantification (LOQ). The analytical limits of quantification gradually improved over the duration of these studies. It decreased from 0.010-0.020 mg/kg in the residue trials performed prior to 1994 to 0.0005 mg/kg mg/kg (for each individual compound) in the most recent ones performed in 2004.
No residues of fipronil and of its metabolites were observed at harvest of maize grain. In three out of seven treated maize silage samples fipronil residues were found between 0.0006 and 0.0021 mg/kg, in the other four samples no measurable residues (<0.005 mg/kg) were observed. The highest residue level for the metabolite MB 46136 was 0.0023 mg/kg in one sample.
In sunflower seed no residue of fipronil and of its metabolites were observed at harvest (<0.002 mg/kg for each analyte).
The experts' meeting noted that all LOQs were low and supported by suitably validated analytical methods (LC-MS/MS). The methods of analysis determined fipronil and the sulfone metabolite MB

46136 simultaneously and information provided by the residues trials was sufficient to propose MRLs for maize grain, sweet corn and sunflower.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

A confined rotational crop study has been performed using ^{14}C fipronil labelled on the phenyl ring at a 1.6N dose rate. Following an ageing period of 30, 153 and 365 days, respectively, the treated soil was planted with cereal crops (wheat, sorghum) root vegetable (carrot, radish) and leafy vegetable (lettuce). Residue analyses were performed on crops at maturity as well as at half maturity for sorghum and wheat. Of the total extractable residues, fipronil, MB 46136 and RPA 200766 were the major constituents. Therefore, the plant residue definition derived from the primary plant metabolism studies corresponds with the residues observed in rotational crops.

Apart from the residue observed in the wheat straw (0.172 mg/kg at 153 days), the total radioactive residues found in the crops, at various rotational intervals, were low (from 0.003 mg/kg to 0.036 mg/kg). Toxicological relevant residues above 0.010 mg/kg were only observed in one item intended for human food (carrot roots) and in only one crop part used for animal feed (wheat straw). Unfortunately information on these crops was incomplete since data were provided for a single sowing date only. Moreover, it is a common agricultural practice to have a sequence of two maize crops over two successive years in the same plot. Such a practice has to be taken into account and additional data on cumulative applications over two years have been requested in order to conclude that no significant residues are expected in rotational crops (especially in root crops such as carrot and in cereal crops such as wheat). The RMS outlined the new data in an addendum for the potential for residues arising in rotational crops and in particular regarding the possibility of the desulfinyl metabolite to be present. In the new rotational crop field study (non-radiolabelled) long term accumulation was assessed as fipronil was applied each year from 2000 to 2003 in N and S Europe at a rate of 4X (followed by incorporation into the soil). Whilst residues of fipronil and the sulfone were occasionally found in following crops (highest level was the sulfone found in wheat straw up to 0.011mg/kg), residues of the sulphide and the desulfinyl metabolite were always less than the LOQ (0.001-0.002 mg/kg). This study confirmed that increased residues as a result of accumulation are not expected. The experts' meeting concluded that there was no concern with rotational crops due to the low levels detected in the studies, and that following seed treatment residues of fipronil desulfinyl metabolite would not be expected to be found.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The metabolism of fipronil has been investigated in lactating goats and laying hens using ^{14}C-fipronil labelled on the phenyl ring. Fipronil was administrated for 7 and 28 consecutive days to goats and hens, respectively at the nominal dose levels of 0.05 - 2.0 and 10.0 mg/kg feed dry matter/day.

In the study with lactating goats approximately 77%-83% of the total administered dose was recovered. The majority of the radioactivity was observed in the faeces (ca 65%) demonstrating an extensive excretion of the administered material. The radioactivity found in urine, milk and tissues

indicated a minimum absorption of 15-19%. Small amount of radioactivity (<5% TRR) was observed in milk with a maximum level of 0.001 mg/kg for the goat with the lowest dose level. At a dose level of 10 mg/kg feed, radiolabelled fipronil derived material partitioned into milk with residue level increasing over study duration and a maximum value of 0.166 mg/kg. Consistent with the lipophilic nature of the compound and its metabolites, fipronil derived residues were preferentially observed in fat matrices (omental/renal). Fipronil and metabolite MB 46136 (sulfone) were found to be the major components in milk, muscle, omental fat and renal fat, accounting for 60–75% and ca 20% of the TRR respectively. MB 46136 was also major in kidney and liver (50-75 % TRR).

In a study with laying hen a large proportion of the administered dose was eliminated and recovered in the faeces (ca. 28% to 42%). As evidenced by the lipophilic nature of the compound, a low radioactivity was found in the lean tissues (muscle, liver) whereas a larger proportion of it was observed in the fat matrices (skin, fat, egg yolk). The metabolite MB 46136 was also reported to be the major constituent of the fipronil derived residues in any of the investigated tissues, accounting for more than 95% of the total radioactivity.

These two metabolism studies with goats and hens demonstrate that fipronil and metabolite MB 46136 are the major components of the various investigated matrices, both accounting for more than 70% of the TRR. Therefore the residue definition proposed for animal products is: Sum of fipronil and sulfone metabolite (MB 46136) expressed as fipronil.

Fipronil livestock feeding studies were carried out for dairy cows and laying hens. Daily oral doses of fipronil were administered for several consecutive days to the cows (35 days) and hens (42 days).
Fipronil was found to be a compound reaching a plateau slowly in the milk (4 weeks) and egg (3 weeks). The sulfone metabolite MB 46136 was the major component in any of the animal tissues whereas fipronil was observed in negligible amounts in the various investigated animal matrices (milk included). Due to the lipophilic character of the molecule, fipronil derived residues were preferentially located in fat matrices (cow fat, skin fat with adhering fat for poultry). The residues observed in milk, egg and animal tissues were found to be strictly linearly related to the residue dose levels in animal feed. Maximum and mean transfer factors were calculated for every tissues as well as, linear regressions.
Even though calculated animal intakes were well below the trigger of 0.1 mg/kg, as the ADI is low (0.0002 mg/kg bw/day) there is a need to consider residues in animal products. Based on the residues in the livestock feeding studies, MRLs were proposed.

3.3. CONSUMER RISK ASSESSMENT

Calculations of potential intakes of fipronil residues in food have been carried out using the WHO/FAO model (sum of all intakes) based on the GEMS/food European regional diet (60 kg bw adult), the UK/PSD model for four subgroups (adult, school children, toddler and infant) and the French model for three subgroups (adult, toddler and infant). Aside from the WHO calculation both

the French and the UK models summed only the 97.5th percentile intakes for the two highest commodity intakes and the mean intakes for the other commodities.
The TMDI was calculated using the proposed MRLs for plant and animal products. When MRLs were not proposed for animal products a default value of 0.005 mg/kg was used. The TMDI estimates indicate that for adult consumers the intake was well below the ADI (max 24% ADI), for toddlers and infants, however, the TMDI exceeds the ADI (max 136% ADI, infant, French model), since milk consumption accounted for the most significant contribution of pesticide intake in terms of the total dietary assessment.
Since the TMDI is representing an overestimate of exposure in a refined risk assessment the IEDI/NEDI was calculated using the STMR values for plant and animal products. IEDI values are always below 20% ADI, even for infant and toddler. Based on these results, it is concluded that the use of fipronil on maize and sunflower as seed treatment with a maximum application rate of 30 g a.s./ha and 50 g a.s./ha respectively, is not likely to pose a high chronic risk for any population subgroup.

The acute exposure was performed using the consumption data from UK acute exposure model for adult and toddler. The NESTI value represents less than 5% of the ARfD. Based upon these data, it is concluded that from the use of fipronil on maize and sunflower as seed treatment a high acute risk for the consumer is not likely.

3.4. PROPOSED MRLS

MRLs are proposed on the basis of the above proposed residue definition for plant and animal products.
Thereby, the following MRLs are proposed for maize and sunflower on the basis of the lowest LOQ of 0.004 mg/kg (sum) achieved in the residue trials.

Maize grain	0.005 mg/kg
Sweet corn	0.005 mg/kg
Sunflower grain	0.005 mg/kg

MRLs for animal products were based on the maximum transfer factors and linear regression curves elaborated in the feeding studies. For the purposes of MRL setting it is necessary to classify the residues as fat soluble.

Milk (whole)	0.002 mg/kg
Milk fat	0.010 mg/kg
Eggs	0.010 mg/kg
Animal fat	0.010 mg/kg

However, the experts' meeting concluded that MRLs should be proposed for all animal products, and subsequently RMS proposed an MRL of 0.005* mg/kg for muscle, liver and kidney. (not peer reviewed)

4. Environmental fate and behaviour

Fate and behaviour in the environment of fipronil was discussed in the experts' meeting EPCO 26 of June 2005 on basis of the DAR (April 2004) and the Addendum 1 (May 2005).

Use pattern as soil application, band application & incorporation at sowing / planting for maize at 100 g/ha has not been addressed at all and should be labelled in grey in the table of representative uses. Maximum application rate partially addressed in the fate and behaviour in the environment is 50 g / ha applied in furrow at drilling of maize with subsequent incorporation or as seed treatment. For sunflower seed treatment at application rates of 30 g/ha has been also partially addressed. However, data gaps have been identified also for these use patterns and therefore have been labelled in grey.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of phenyl ^{14}C labelled fipronil in soil under laboratory dark aerobic conditions at 25 ºC was investigated in one study with two soils (pH (KCl) = 5.9 – 7.1; OC = 1.0 – 1.9 %; Clay = 3 – 9 %; 75 % moisture of 0.33 bar). Formation of main metabolites was also investigated in the rate of degradation study performed on four soils (pH (KCl) = 4.5- 8.2; OC = 1.1 – 4.1 %; Clay = 10.8 – 34.4 %; moisture: 45 % MWHC) at 20 ºC under dark aerobic conditions.

Main degradation processes were hydrolysis to the amide **RPA 200766** (max. 38.4 % AR after 219 d), oxidation to the sulphone **MB 46136** (max. 34.3 % AR after 162 d) and reduction to the sulphide **MB 45950** (max 17 % AR after 91 d). Mineralization was very low (< 2.6 % AR after 336 d) and bound residues were formed at amounts between 3.1 and 7.7 % AR after 219 d and up to 15.1 % AR after 336 d. At the end of the corresponding studies (219 d or 336 d) most of the radioactivity remained as fipronil and its main metabolites.

Degradation of phenyl ^{14}C labelled fipronil was also investigated under dark anaerobic conditions in one sandy loam soil (pH (KCl) = 7.1; OC = 1.0 %) at 25 ºC. No new metabolites were identified under these conditions.

Photedegradation in soil at 25 ºC was investigated in one study with fipronil ^{14}C-labelled at the pyrazole ring. Irradiation with a xenon lamp with 8 h dark / 16 h light irradiation cycle was intended to mimic a typical day in Florida. Two main metabolites, not previously detected in the aerobic degradation studies, were identified as MB 46513 (max. 6.9 % AR after 30 d) and RPA 104615 (max. 7.2 % AR after 21d).

Two field dissipation studies in six sites of South of Europe (Italy (Bologna, 2 sites), France (Chazay, Mereville) and Spain (Seville, 2 sites) are available. Depending on the site, sepiolite formulation with 2 % fipronil (EXP60166B), 0.1 % granular (EXP 60507A) and 20 % liquid formulation (EXP 60145A) were applied (broadcast or spray) on bare ground soil at 50 or 200 g / ha. Fipronil and

metabolites RPA 200766, MB 46136, MB 45950 and MB 46513 (photolysis metabolite only detected in Sevilla and Bologna when product was applied on bare soil and not incorporated) are found as soil residue components in these studies.

Additionally, a summary of a field study performed in four USA sites (California, Nebraska, North Carolina and Washington) was used by the applicant to derive degradation rates in the original dossier. Complete reports of these studies were provided by the applicant after the DAR was finalised and have been summarized by the RMS in Addendum 1. Fipronil and metabolites RPA 200766, MB 46136, MB 45950 are found as soil residue components in these experiments. Fipronil was incorporated to the soil and the photolysis metabolite MB 46513 was not found in these experiments.

The interim and final report of a new field study in northern EU (Kortenaken, Belgium) was provided by the applicant after the DAR had been finalised, and summarized in Addendum 1 by the RMS. In this study, a wettable granule formulation (EXP60720A) was homogeneously sprayed and then incorporated prior to planting maize seeds; metabolites RPA 200766, MB 46136, MB 45950 achieved maximum residues of up to 28 %, 50 % and 13 % respectively.

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

Under laboratory aerobic conditions at 20 or 25 ºC fipronil is moderate to high persistent in soil (DT_{50} = 31 – 304 d; new kinetic analysis in the Addendum 1: DT_{50} = 32 – 346 d). At 10 ºC longer half lives were observed (DT_{50} = 515 - 747 d). As the major metabolites appear late in the experiment and hardly decrease, it was not possible to assess their persistence in the studies performed with the parent compound.

Assessment of the degradation rates of metabolites was required by the RMS in the original DAR. New studies submitted in response to it have been summarized in the Addendum 1 by the RMS. Applicant submitted a new multicompartmental kinetic analysis on the original parent degradation studies. Expert's meeting confirmed the conclusions of the RMS with respect to this analysis. It was concluded that it may be used to derive the formation fractions for the different metabolites; however, it is not possible to derive reliable degradation constants from it. Therefore, a new study to investigate the degradation of metabolites RPA 200766, RPA 200761, MB 45950, MB 46136 and MB 46513 (photolysis metabolite) under dark aerobic conditions at 27 ºC and 40 % MWHC in three soils (pH = 7.3 – 7.4; OC = 1.3 – 2.3 % and clay 11.6 – 18.3 %) was provided by the applicant. In this study RPA 200766 shows to be high persistent (DT_{50} = 107 – 149 d), RPA 200761 moderate to high persistent (DT_{50} = 43.5 – 139 d), MB 45950 medium to high persistent (DT_{50} = 89 – 224 d), MB 46136 high persistent (DT_{50} = 185 – 280.5 d) and MB 46513 moderate to medium persistent (DT_{50} = 46.5 – 98 d). These values were normalized to reference temperature and soil moisture. Experts' meeting noted that most of these half lives are longer than the duration of the studies and therefore uncertain.

Under anaerobic conditions in soil fipronil is also highly persistent (DT_{50} = 161 d).

Photolysis may contribute slightly to the environmental dissipation of fipronil in soil. Main photolysis metabolite is MB 46513 (max. 6.9 % after 30 d).

Available field studies confirmed that fipronil is medium to high persistent in soil (DT_{50} = 96 – 135 d). In the field studies performed under conditions where photodegradation could occur (Bologna and Seville) a faster degradation was observed (DT_{50} = 5.6 – 22.2 d).

A new kinetic analysis of the eight studies (4 EU and 4 USA) where fipronil was incorporated in furrows was provided after the DAR had been finalised and has been summarised in Addendum 1 by the RMS. A scaling procedure to reduce the scattering of data due to sampling heterogeneity and a multicompartmental model was used in this analysis to derive the first order degradation half lives of fipronil (DT_{50} = 33 – 120 d) and metabolites MB 46136 (DT_{50} = 147 – 430 d), MB 45950 (DT_{50} = 82 – 112 d, only data from two USA sites) and RPA 200766 (DT_{50} = 167 – 266 d).This methodology to reduce scattering in raw data was discussed in the experts' meeting. This approach was novel and the experts considered that the notifier should produce a kinetic analysis based on the original unscaled data to investigate the effect of the scaling procedure. This was identified as a new data gap. Expert's meeting also agreed that the RMS will produce an updated addendum to clarify different aspects of this kinetic analysis (see EPCO 26 Discussion table and updated Evaluation table for details). A comparison of DT_{50} values estimated for 4 soils, with and without scaling, is reported in the updated addendum (January 2006). It shows slight differences for the parent and more significant differences for some of the metabolites for which the scaling procedure results in shorter half lives for metabolites MB 46136 and MB 45950 and longer half life for metabolite RPA 200766. However, this does not have any effect on the EU risk assessment presented by the RMS that was finally based on the parameters derived from the most recent field study in northern EU (Kortenaken, Belgium).

Also the kinetic analysis of the new field study in northern EU (Kortenaken, Belgium) where fipronil was sprayed and incorporated was presented in the Addendum 1. No scaling procedure was employed in this case. A multicompartmental model was used to estimate the first order half lives of fipronil (DT_{50} = 49 d) and metabolites MB 46136 (DT_{50} = 231 d), MB 45950 (DT_{50} = 264 d) and RPA 200766 (DT_{50} = 259 d). Experts' meeting agreed that RMS should provide the range of the soil moisture contents and temperature in an updated addendum. This information has been summarized by the RMS in the updated addendum (January 2006).

Since DT_{90} of fipronil was above one year in some studies, field accumulation studies were required by the RMS in the original DAR. Two field accumulation studies were presented by the applicant and summarised in Addendum 1. One of the studies was carried out for six years in two sites of Southern Europe (Bologna, Italy and Saulce sur Rhône, France). Soil in both sites was slightly alkaline (pH = 7.5) with low organic carbon content (OC = 0.9 %). Fipronil was sprayed and then incorporated at 200 g a.s. / ha, prior to planting maize seeds. The major metabolite found was MB 46136 with significant amounts of RPA 200766. Metabolite MB 45950 was found at low levels, between LOQ (2 µg/kg) and twice LOQ. Photolysis metabolite MB 46513 remained below LOQ except for a data point close to LOQ (which is consistent with the soil incorporation practice employed in the trial). Fipronil residues decreased below LOQ after one year. The second accumulation study was carried out for five or six years in two sites of Northern Europe (Kortenaken, Belgium (5 yr) and Arras, France (6 yr)). One of the sites with acidic soil (Kortenaken, pH = 6.6) and the other with alkaline soil (Arras, pH = 7.5) and with organic carbon content of 1.2 and 1.5 % respectively. The same application practice than for the other accumulation study was employed. By one year after each

application, the concentration of fipronil in the 0-20 cm soil layer ranges from LOQ to 3 µg/kg at Arras and from 3.2 to 9.9 µg/kg at Kortenaken. The major metabolite found was MB 46136 with significant amounts of RPA 200766. Metabolite MB 45950 was also found at lower amounts. Photolysis metabolite MB 46513 remained below LOQ for both trials. Fipronil did not accumulate in any of the studies but a clear tendency for accumulation was observed for the metabolites. Experimental plateau levels were not determined since the plateau had not been reached after the five or six years of repeated applications. Kinetic analysis of the accumulation field trials was reported in a separate study. Due to the low number of data in the accumulation studies degradation rates were fixed according the estimates obtained in the new field study in northern EU (Kortenaken, Belgium) to reduce the number of parameters to be fitted. These degradation rates were normalized to reference temperature of 20 ºC based on monthly average temperatures without consideration of soil moisture. Therefore, only field formation fractions of the metabolites were derived from the field accumulation trials in this analysis. These parameters were used to extrapolate the data of the field accumulation studies in order to calculate the plateau concentrations of metabolites.

A summary of degradation parameters and formation fractions is presented in the Table 4.1.2-1

Table 4.1.2-1 Degradation parameters and formation fractions of fipronil and metabolites (in bold input parameters used for modelling ($PEC_{SW/SED}$-PEC_{GW})

Half lives in days	**Fipronil**	**MB 46136**	**MB 45950**	**RPA 200766**	**MB 46513**
Laboratory DT_{50}-$_{norm}$ (geometric mean)	32-346 (142)	265-422 (347.2)	128-337 (228.8)	160-213.6 (180.6)	66-147 (108.7)
Laboratory formation fractions (average)	Not applicable	0.35	0.21	0.51	
Field EU DT_{50}	33-120 (64.5)	147-205 (173.6)	-	264 264	-
Field USA DT_{50}	44-108 (81.8)	291-430 (371)	82-112 (95.8)	167-266 (197)	-
Field Kortenaken DT_{50}	49	**231**	**264**	**259**	-
Overall geometric mean of DT_{50} in field studies	70 (**76**)	266	134	221	
Overall arithmetic mean of formation fractions of metabolites in field studies		0.24	0.15	0.16	
Field formation fractions (based on field accumulation studies) Used for PEC_S modelling		0.45-0.67	0.06-0.11	0.22-0.28	

Half lives in days	Fipronil	MB 46136	MB 45950	RPA 200766	MB 46513
Field formation fractions (based on most recent EU field dissipation study (Kortenaken)). Used for PEC_{SW} and PEC_{GW} modelling		**0.57**	**0.13**	**0.30**	

PECs soil presented in the original dossier were not considered acceptable by the RMS since no reliable parameters for the metabolites were available. New PEC soil were provided by the applicant and summarised in Addendum 1. In this new calculation degradation parameters employed to calculate plateau levels are from the most recent field dissipation study in northern EU (Kortenaken, Belgium) for the metabolites and from the field accumulation studies for the parent compound as reported in the updated addendum. PEC soil max for the parent and metabolites was calculated taking into consideration a specific scenario for the application pattern as seed dressing in furrow. Since this deviates from the standard PEC soil calculations, experts' meeting required the RMS to provide more details on the method of calculation employed and the scenario assumed. The method has been explained in more detail in the updated addendum of (January 2006). EFSA notes that the calculation provided does not represent a worst case with respect to the parent compound (since DT_{50} employed [31 d -47.5 d] is well below field worst case DT_{50} [135 d]). Furthermore, the assumptions taken in the calculation (eg. depth of plough layer) are not well justified. Additionally specific weather data from the places where the accumulation studies where performed were used in this simulation without any assessment of how representative they were to realistic worst case EU conditions. Therefore, new data gaps are identified to provide the PEC soil max for the parent compound based on the worst case field half life and further justification of the scenario assumed for PEC soil calculations. Furthermore, calculation of the initial and 21 d TWA-PEC_S for the parent compound and soil metabolites would also be necessary to finalise the ecotoxicological risk assessment for soil micro- and macro-organisms and earthworm-eating birds and mammals respectively. Consequently, risk assessment for the EU representative uses can not be finalised with respect to the soil compartment.

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

Batch adsorption / desorption studies in five soils are available for fipronil and its metabolites MB 45950, MB 46136, MB 46513 and RPA 200766. According these studies fipronil is low to medium mobile (Koc = 427 – 1248 L / kg), MB 45950, MB 46136 are immobile to low mobile (MB 45950: Koc = 1695 – 5621 L / kg; MB 46136: Koc = 1448 – 6745 L / kg), MB 46513 is low mobile (Koc = 1150 – 1498 L / kg) and RPA 200766 is medium to high mobile (Koc = 96 – 203 L / kg).

A column leaching study with fipronil applied on the same five soils employed on the adsorption / desorption studies is available. Radioactivity in the leachate was generally low (< 0.1 % AR) except for one soil where it reached an average of 4.26 % AR (sandy loam, 77 % sand). Most of the applied radioactivity was in the upper soil layer (0-6 cm) with the sole exception of the sandy loam soil were significant amount of radioactivity was found in the 0-12 cm layer. Fipronil and minor amounts of

metabolites RPA 200766, MB 45950 and MB 46136 were found as part of the soil residue in these experiments. Composition of the leachate was not analysed.

An aged residue (dark aerobic conditions at 22 ºC for 35 d) column leaching experiment was performed with the same five soils. Recovery of radioactivity in the leachates was slightly higher than for the fresh residue but remained < 3.5 % AR. Due to the low levels the analysis of its compositions was not performed. Most of the applied radioactivity remained in the top 12 cm layer and fipronil and metabolites RPA 200766, MB 45950 and MB 46136 were also found as part of the soil residue in this experiment.

No lysimeter study is available for fipronil.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis of fipronil was investigated at 25 ºC in sterile buffered solutions at pH 5, 7 and 9. Fipronil is hydrolytically stable at pH 5 and 7, and degrades to RPA 200766 (max 52.7 % AR after 30 d) at pH 9 with a half life of 28 d. This metabolite is stable to hydrolysis under these conditions.

Hydrolysis of metabolites MB 45950, MB 46136 and MB 46513 was investigated in sterile buffered solutions at pH 4, 5, 7 and 9 at 25 ºC for 30 d and for MB 45950, MB 46136 also at 50 ºC for 5 d. These metabolites are also stable in acid and neutral conditions. MB 46136 and MB 46513 are degraded at pH 9 with half lives of 50 and 10.9 d respectively. MB 45950 is more stable at pH 9 and only degrades at 50 ºC ($DT_{50\ 50\ ºC}$ = 11 d). Therefore, hydrolysis will not contribute significantly to the degradation of fipronil in water for most relevant environmental conditions.

Photolysis of fipronil and metabolites MB 45950, MB 46136 and MB 46513 was investigated in buffered (pH 5) aqueous solutions at 25 ºC with a Xenon lamp (λ < 290 nm filtered out). Photolysis of fipronil was also investigated in natural water in a separated study. Fipronil was rapidly degraded (DT_{50} = 3.6 h) in the irradiated samples. Main metabolites formed were MB 46513 (max. 42.7 – 52.1 % AR) and RPA 104615 (max. 8.2 – 10.6 % AR). The aqueous photolysis of the metabolites is rapid (MB 45950: DT_{50} = 6 h; MB 46136: DT_{50} = 13 h; MB 46513: DT_{50} = 38.9 h, continuous irradiation) with the formation of a number of partially characterized photoproducts. As a conclusion photolysis may contribute to the degradation of fipronil and its major metabolites in water.

Fipronil is not readily biodegradable in water according the available study.

Degradation of fipronil in water / sediment was investigated in three separated studies with a total of five water / sediment systems. The systems covered a range of pH (water: pH = 5.8 – 8.2) and organic carbon (sediment: OC = 0.4 – 3.2 %). Fipronil is adsorbed on the sediment more or less rapidly (depending on the relative ratio water \ sediment and the sediment characteristics) and then degrades to MB 45950 (max. 88.72 % AR in the sediment after 120 d). In the water phase only fipronil and the major metabolite RPA 200766 (max. 20 % AR in water after 244 d) reached levels above 10 % AR. The dissipation half lives of fipronil in water ranged between 14.2 to 93.6 d and the degradation half lives in the whole system between 16.4 and 119.6 d. No decrease on the amount of the metabolites was observed in these experiments. This prevents the estimation of any reliable half life, however tentative half lives were provided by the notifier with a multicompartmental kinetic analysis performed with Top Fit. The reliability of the kinetic parameters derived for metabolite MB 45950

was discussed in the experts' meeting (DT_{50} = 2.1 d used in the PEC_{SW} calculations). Experts' meeting agreed that a reliable value should be derived and used in the new FOCUS PEC_{SW} calculations required.

A water/sediment study is available for the soil metabolite MB 46513. The degradation of this metabolite was investigated in two water /sediment systems (pH_{water} = 6.1 – 8.2; $OC_{sediment}$ = 5.1 – 5.6 %). This compound is rapidly adsorbed on the sediment and tends to persist there (amount in sediment: 57 – 61 % AR at the end of the study after 365 d).

No $PEC_{SW/SED}$ were provided in the original dossier.

New $PEC_{SW/SED}$ were provided by the applicant after the DAR was finalised (see Addendum 1). These $PEC_{SW/SED}$ were calculated using FOCUS SW models and scenarios to estimate potential surface water contamination resulting form drainage and runoff after the in furrow application. Input parameters employed were not clearly reported in the addendum and were discussed by the experts meeting. RMS clarified that for the degradation parameters in soil the values shown in bold in table 4.1.2-1 had been employed. The meeting agreed that new calculation would be needed with updated parameters following FOCUS guidance (data gap 4.8 in the evaluation table). In an updated addendum RMS confirmed that wrong input parameters have been employed for MB 45950 with respect to its degradation in water. For the other metabolites a DT_{50} in water of 1000 d has been assumed. For the seed dressing uses the CAM and DEPI values used in the $FOCUS_{SW}$ modelling performed by the notifier are in agreement with the EFSA opinion on $FOCUS_{SW}$ [18]. However, with respect to the soil degradation parameters a half life slightly longer than the field geometric mean has been employed for the parent, a half life shorter than the geometric mean has been employed for metabolite MB 46136 and worst case (or close to worst case) half lives were used for metabolites MB 45950 and RPA 200766. Formation fractions used are derived from the most recent northern EU study (Kortenaken, Belgium). These calculations need to be repeated with the parameters selected according the FOCUS recommendations. Ecotoxicological risk assessment is based on initial PEC_{SW} that are sensitive to the soil degradation parameters employed in modelling. Data requirement for new PEC_{SW} calculation is confirmed and the risk assessment with respect to aquatic organisms and fish-eating birds and mammals may not be considered completed.

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

Potential groundwater contamination by fipronil and its soil metabolites RPA 200766, MB 46136, and MB 45950 was assessed by the notifier in the original dossier with FOCUS-PRZM model and FOCUS scenarios. Application rates of 100, 50 and 25 g / ha were simulated. Fipronil did not exceed the ground water trigger of 0.1 µg / L for any scenario at any application rate. Metabolite RPA 200766 exceeds the trigger of 0.1 µg / L for at least one scenario at any of the application rates modelled (exact figures not reported in the DAR). However, these calculations were not considered reliable by the RMS since they were based on unreliable half lives for the metabolites.

[18] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS surface water scenarios. *The EFSA Journal* (2004)145, 1-31.

New PEC_{GW} were provided by the applicant after the DAR had been finalized and summarized by the RMS in Addendum 1. Only the application rate of 50 g/ha for maize has been simulated and no calculation has been provided for the lower application rate of 30 g/ha in sunflower. Results of these new calculation show that the 80th percentile of the predicted annual leachate of metabolite RPA 200766 exceeds the trigger of 0.1 µg / L for five of the seven scenarios simulated for maize (appl. rate 50 g/ha). Therefore, the metabolite RPA 200766 has been assessed for its toxicological and ecotoxicological relevance. This metabolite has been assessed to be not toxicological relevant (see 2.8) but it is considered ecotoxicological relevant (see 5.2). Levels estimated for fipronil and metabolites MB 46136 and MB 45950 were below 0.001 µg / L for the seven scenarios simulated. Input parameters in bold in **Table 4.1.2-1** were used for the simulations. Experts' meeting identified a new data gap for the applicant to justify that kinetics in field degradation studies represent degradation rather than other dissipation processes. RMS provided complementary information in the updated addendum to support the use of field derived degradation parameters for modelling. This additional information has not been peer reviewed. Furthermore, EFSA notes that kinetic parameters employed for the metabolites in the new $FOCUS_{GW}$ modelling were based on a single field study and were not selected according the criteria given by FOCUS guidance documents. Experts' meeting ask the RMS to clarify the source of the half life employed for the parent compound. Further clarification is given in the evaluation table by the RMS who indicates that the correct value for half life of fipronil to be used in the simulations should be 70 d instead of the 76 d actually used. Therefore, with respect to the soil degradation parameters a half life slightly longer than the field geometric mean has been employed for the parent, a half life shorter than the field geometric mean has been employed for metabolite MB 46136 and worst case field half lives were used for metabolites MB 45950 and RPA 200766. Due to the deviations with respect to guidelines on the input parameters selection and the need of justification for the use of field kinetic parameters the assessment of potential groundwater contamination could not be considered finalised for the EU representative uses. Data requirement for new FOCUS PEC_{GW} calculation with appropriate input parameters is therefore confirmed.

4.3. FATE AND BEHAVIOUR IN AIR

Taking into consideration the vapour pressure and the Fipronil Henry law constant ($2.3\ 10^{-7}$ $Pa \cdot m^3 \cdot mol^{-1}$) fipronil may not be considered prone to volatilization. A half life of 2.64 h for the photochemical transformation of fipronil in air has been estimated with the Atkinson method. Long range transport and deposition of fipronil may be considered negligible.

5. Ecotoxicology

Fipronil was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 27) in June 2005. Only issues related to the FS formulation EXP80415A were discussed since the formulations EXP60720A and EXP61840A were not longer supported by the applicant for the EU review process (i.e. with respect to Annex I inclusion) and no further data regarding these formulations were submitted.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to birds and mammals is calculated according to the Guidance Document on Birds and Mammals (SANCO/4145/2000). The risk from the uses as a seed treatment in maize and sunflower was extensively revised in the addendum 1 of April 2005. The risk is calculated for a herbivorous and a granivorous bird and mammal for these uses.

The EPCO experts' meeting noted that Galliformes species are the most sensitive species, and considered that the acute LD_{50} for use in the risk assessment should be the value of 11.3 mg a.s./kg bw for bobwhite quail.

A very high acute, short and long term risk to granivorous birds, with TER values far below 1, were identified in the first tier risk assessment for the representative use as a seed treatment in maize and sunflower. A refinement of these assessments is presented in the addendum 1 of April 2005 and was discussed at the EPCO experts' meeting. The Meeting agreed that the risk assessment should cover small as well as large granivorous species.

The refined acute and short term risk assessment for large granivorous birds eating treated maize seeds was based primarily on the absence of signs of toxicity in a 21 day caged field study using red-legged partridge and pheasants. The EPCO experts' meeting raised following concerns regarding this study: degree of stress prior to exposure was unclear, efficiency of drilling was unknown, availability of food other than supplemental food was unclear, no information on weight of test birds before and after exposure, high control mortality of one species. Treated maize seed was consumed less than non treated seed, but the level of consumption of untreated seed was considered to be low. In an avoidance study with grey partridge mortality was reported indicating that this species could consume sufficient treated seeds for an LD_{50} dose. The meeting concluded that mortality from consumption of treated seed cannot be excluded. The proposed GAP would involve precision drilling but no data were submitted to indicate that no seed would be exposed on the surface.

The EPCO experts' meeting agreed that the concern for small granivorous birds eating treated maize seeds was lower than for large birds but it was considered that the applicant should provide further information to confirm this.

The experts' meeting noted that lower seed loading on sunflower may result in greater exposure if this leads to lower avoidance. The same field cage study with maize, discussed above, was used to address the risk to granivorous birds in sunflower. It was concluded, apart from the remarks on the study itself (see above), that extrapolation from maize to sunflower is questionable. No indication of dehusking was observed in the avoidance studies. Small birds, e.g. finches, are likely to consume sunflower seeds. The meeting agreed that a risk assessment to quantify the risk for both large and small birds eating sunflower seeds is required.

The EPCO experts' meeting had some reservations about the proposed PT of 0.214 to refine the long term risk to birds and noted that the NOEL for reproduction is based on the top dose tested due to mortality of the parent birds. The meeting agreed that the risk to birds should focus on the acute and short term risk as there is no indication that fipronil is a reproductive toxin.

A new risk assessment for granivorous birds taking into account the concerns raised at the EPCO 27 experts' meeting, especially those regarding the cage field trial, is required. The risk to small and large granivorous birds must be quantified. The current proposed extrapolation from maize to sunflowers is not acceptable.
The risk to granivorous birds from the use of fipronil as a seed treatment in maize and sunflower can only be concluded once recently submitted data are evaluated. Nevertheless the EPCO experts' meeting agreed that the proposed labelling SPe 5 (To protect birds/wild mammals, the product must be entirely incorporated in the soil; ensure that the product is also fully incorporated at the end of the rows.) and SPe 6 (To protect birds/wild mammals remove spillages.) phrases are necessary.

The risk to herbivorous birds feeding on seedlings from treated maize and sunflower seeds is based on a measured residue concentration from a study using soil granules. The residue level of 0.27 mg a.s./kg is taken as a worst-case compared with the maximum level expected from treated seeds. The experts' meeting agreed to use a ftwa factor of 1 for the long term risk as the default factor is not applicable given the method of application as a seed treatment. The resulting TER values (54 and 18 respectively) respect the Annex VI trigger value of 10 indicating a low acute and short term risk to herbivorous birds from the representative uses of fipronil as a seed dressing. The long term TER value of 4 is below the Annex VI trigger value of 5. Nevertheless the EPCO Experts' meeting agreed that this TERlt indicates a low risk as it was calculated with a worst-case residue level from a study with soil granules and a TERlt calculated with a measured residue value from a seed treatment residue study would result in a TERlt of 5.9.

Also for granivorous mammals a high acute and long term risk, with TER values far below 1, was identified in the first tier risk assessment for the representative use as a seed treatment in maize and sunflower. A refinement of the assessment is presented in the addendum 1 of April 2005 and was discussed at the EPCO experts' meeting.
The applicant proposed a PD (proportion of different food types in the diet) of 0.264 to refine this risk assessment. This value is based on the mean percentage of seeds in the diet of wood mice living in cereal fields in April/May (from published data by Pelz (1989) and Green (1979)). It was agreed in the experts' meeting that the wood mouse is an appropriate focal species to refine this risk but considered that the PD value should be based on the 90^{th} percentile value from this data set instead of the mean. Furthermore there was also a concern regarding the appropriateness of this dataset (wood mouse living in cereal fields) to the representative uses as a seed dressing in maize and sunflower. Additionally no data is available regarding the efficiency of the precision drilling of maize/sunflower seeds.
The proposed PT (proportion of diet obtained in the treated area) value was not accepted as the data on which it is based do not indicate the active time in the field and also this was a mean value.
Furthermore the proposed AV (avoidance) factors of 0.022 (maize) and 0.093 (sunflower) were not accepted by the meeting.

The EFSA is furthermore of the opinion that a strong argumentation is necessary on the appropriateness of a refinement of the acute risk by using PT, PD and/or AV values in relation to the timeframe to observe acute effects.
The experts' meeting noted that the dehusking factor of 0.13 for sunflower, as proposed by the applicant, was taken from the guidance document SANCO/4145/2000 and relates to a study with birds having a bodyweight of less than 50 g. Therefore this value was not accepted for mammals. The meeting agreed that sunflower seeds were likely to be dehusked, but this had not been quantified.
The applicant proposed to include a seed encounter and exploitation factor (TSE) based on studies by Jones et al. (1997) and Pilipavicious (2004). The RMS could not accept this proposal as it was likely to be taken into account in the PD factor. The experts' meeting agreed that the proposed use of TSE was not appropriate.

A revised risk assessment for granivorous mammals taking into account the concerns raised at EPCO 27 regarding the proposed refinements of PT, PD, AV and the use of a dehusking factor is required. The meeting could not accept the proposed use of Seed encounter and exploitation (TSE) factor as it was considered that this was already incorporated into PD. The availability of treated seeds for mammals (i.e. the efficiency of precision drilling and the frequency of minimum cultivation techniques for these crops) should be assessed. This latter issue should indicate whether mice consumed drilled maize and sunflower seeds.
The risk to granivorous mammals from the use of fipronil as a seed treatment in maize and sunflower can only be concluded once recently submitted data are evaluated.

The calculation of the risk for herbivorous mammals is based on the same measured residue value of 0.27 mg a.s./kg as for birds. Also for mammals the EPCO Experts' meeting did not consider it appropriate to use the default ftwa of 0.53 to assess the long term risk. The resulting TER values indicate a low risk to herbivorous mammals from the representative uses of fipronil as a seed dressing.

As the LogPow of fipronil exceeds 3 the risk from secondary poisoning for earthworm and fish eating birds was assessed (see addendum 1 of April 2005). A multi residue approach was used to assess the risk to earthworm eating birds and mammals. The EPCO experts' meeting noted that the $PEC_{plateau\text{-}min}$ in soil was used and that this should have been the plateau concentration plus an additional year. The meeting did not consider it necessary to recalculate this risk as the resulting TERlt indicates a degree of safety. The risk to earthworm eating birds and mammals is considered to be low. Also for fish eating birds and mammals a multi residue approach was used to assess the risk from secondary poisoning. The risk to fish eating birds and mammals is considered to be low for the representative uses of fipronil as a seed dressing. However there is an outstanding data requirement in the section on Fate and behaviour for a recalculation of the PECsoil and the PECsw values. PEC soil max for the parent compound based on the worst case field half life and further justification of the scenario assumed for PEC soil calculations need to be provided. It is assumed that the plateau PECsoil value for the representative uses with the FS formulation might increase. The risk to earthworm and fish

eating birds and mammals from the representative uses with the FS formulation can not be concluded as long as the recalculated PEC values in surface water and soil are not available.

The EPCO expert's meeting agreed that the risk from the plant metabolites RPA 200766, RPA 200761, RPA 105320 and MB 45897 to birds and mammals is low.

No risk assessment for birds and mammals from exposure to contaminated drinking water is considered necessary for the representative uses as a seed treatment in sunflower and maize.

In the original dossier also data for the EXP60720A, WG, and EXP61840, GB formulations, were submitted. These data were evaluated in the DAR and a risk assessment was presented. Several specific data gaps were identified by the RMS and comments were made by other MSs in the reporting table. The peer review for these products stopped after the first evaluation meeting as these formulations were not further supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion) and hence the comments were not discussed in an expert meeting. As these formulations were not longer supported new data which became available during the peer review process of the FS formulation was not discussed in relation to the EXP60720A, WG, and EXP61840, GB formulations. Nevertheless several data requirements were confirmed in the first evaluation meeting and are listed below:
- Applicant to submit residue data in seeds, seedlings and young plants (0-28 d) in maize (EXP60720A, WG and EXP61840, GB)
- Applicant to submit a realistic higher tier risk assessment for birds and mammals (e.g. palatability and avoidance tests) (EXP61840, GB)
- Applicant to submit a more documented and appropriate assessment in support of refined PD and PT values (EXP61840, GB)

5.2. RISK TO AQUATIC ORGANISMS

Fish and aquatic invertebrates are the most sensitive tested aquatic organisms to fipronil with *Mysidopsis bahia* as the most sensitive organism on an acute and chronic time-scale. The relevance of this saltwater species to the risk assessment was discussed at the experts' meeting. It was considered that the available data did not support the non-relevance of this species and if the applicant would like to pursue the argument that marine species are more sensitive than freshwater species, a more robust justification must be provided. Therefore the risk assessment for aquatic organisms is based on the most sensitive tested organisms, *M. bahia*.

Studies with the WG formulation are available. No studies with the FS and GB formulation are considered necessary given the mode of application.

A risk assessment for the representative uses as a seed treatment with the FS formulation is presented in the addendum 1 of April 2005. The risk was calculated with the maximum initial PEC values in surface water for the worst-case FOCUS Step 3 scenario, D4 (stream) for maize and D5 (stream) for

sunflower. However, there is an outstanding data requirement in the section on Fate and behaviour for a recalculation of the PECsw values and the risk to aquatic organisms can not be concluded as long as the recalculated PECsw values are not available. Based on the available provisional PECsw values a high acute and long term risk to aquatic organisms was identified for the representative use as a seed treatment in maize. The risk to aquatic organisms for the use in sunflower can be regarded as low. The EFSA would like to propose that, when agreed PECsw values are available, the risk is assessed for several FOCUS scenarios in order to identify the number of scenario's which do not meet the Annex VI trigger value. The RMS proposed to refine the long term risk by using an endpoint for *M. bahia* from a study in the presence of sediment. The EFSA considers that in order to accept this refinement option, an argumentation should be presented in line with the conclusion of the PPR Panel on dimoxystrobin[19]. The EPCO experts' meeting agreed that it might be possible to reduce the standard uncertainty factor due to the number of species tested but decided to await the opinion of the PPR panel. The EFSA would like to refer to the opinion of the PPR Panel regarding the reduction of the uncertainty due to the availability of several single species studies and proposes to take this opinion into account at MS-level.[20]

Fipronil and the metabolites MB 46136, MB 45950 and RPA 200766 were found in concentrations above 10% of the applied amount in a water/sediment study. Therefore the risk to sediment dwelling organisms from exposure to these substances needs to be addressed. A spiked water study is available for fipronil, MB 46136 and RPA 200766. Furthermore, a spiked sediment study is available for MB 45950. No further studies were considered necessary by the experts' meeting. Based on the available PECsw and PECsed values, the risk to sediment dwelling organisms from the representative uses as a FS formulation in maize and sunflower can be regarded as low. The risk to sediment dwelling organisms can only be concluded once agreed PECsw values are available (see section on fate and behaviour).

Furthermore acute toxicity studies on fish, aquatic invertebrates, algae and chronic studies on aquatic invertebrates with the metabolites MB 46136, MB 45950 and RPA 200766 are available. Based on the present PECsw values the risk from these metabolites for the representative uses as a seed treatment in maize and sunflower can be regarded as low except for the long term risk to aquatic invertebrates from MB 46136 in maize. The RMS proposes to refine this risk based on an extrapolation from the data for fipronil. For fipronil a lower chronic toxicity to *M. bahia* was observed in the presence of sediment and the RMS thinks that this is probably also the case for MB 46136. First of all the EFSA thinks an argumentation is necessary to use this sediment study with fipronil (see above) and is not convinced that this extrapolation is appropriate. Furthermore the RMS

[19] Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from EFSA related to the evaluation of dimoxystrobin. (Question N° EFSA-Q-2004-81). *The EFSA Journal* (2005) 178, 1-45.

[20] Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from EFSA related to the assessment of the acute and chronic risk to aquatic organisms with regard to the possibility of lowering the uncertainty factor if additional species were tested. (Question N° EFSA-Q-2005-042). *The EFSA Journal* (2005) 301, 1-45.

considers that the uncertainty is reduced as more species were tested. But the chronic study with *D. magna* is considered not valid so only 2 long term studies with this metabolite on aquatic invertebrates are available (*M. bahia* and *C. riparius*). The EFSA would like to refer to the opinion of the PPR Panel regarding the reduction of the uncertainty due to the availability of several single species studies and proposes to take this opinion into account at MS-level. Again, also for the metabolites, the risk to aquatic organisms can only be concluded once the revised PECsw values become available (see section on Fate and behaviour). All these metabolites are considered relevant as they show a similar or higher risk than the parent to aquatic organisms.

As fipronil is an insecticide no studies on aquatic plants are considered necessary. A study on the effects of fipronil on *Lemna gibba* is available indicating a low risk to aquatic plants from the use of fipronil as a seed treatment in maize and sunflower.

A study on bioaccumulation in fish is available as the logPow is above 3 for fipronil. The resulting BCF is 321. Elimination of the radioactive residues was nearly complete within 14 days. Therefore the risk for bioaccumulation in fish from fipronil is considered to be low. In addition the risk to fish eating birds and mammals is considered to be low based on the present provisional PEC values (see section 5.1 above) for the representative uses of fipronil as a seed dressing. The logPow of the major metabolites MB 46136, MB 45950 and RPA 200766 exceeds 3 as well. Therefore the EFSA proposes that a study on bioaccumulation in fish from these metabolites should be submitted.

In the original dossier also data for the EXP60720A, WG and EXP61840, GB formulations were submitted. These data were evaluated in the DAR and a risk assessment was presented. A specific data gap was identified by the RMS and comments were made by other MSs in the reporting table. The peer review for these products stopped after the first evaluation meeting as these formulations were not further supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion) and hence the comments were not discussed in an expert meeting. As these formulations were not longer supported new data which became available during the peer review process of the FS formulation was not discussed in relation to the EXP60720A, WG and EXP61840, GB formulations. Nevertheless the specific data requirement was confirmed in the first evaluation meeting and is listed below:

- Applicant to submit appropriate spray-drift values relative to the equipment used to apply EXP60720A by spraying in-furrow at drilling. The precision should be relevant to the level of concern (i.e. 0.001%) (EXP60720A, WG).

5.3. RISK TO BEES

A very high acute and oral toxicity of fipronil to bees was observed in the laboratory toxicity study. Furthermore the oral toxicity of the metabolites MB 46136 and RPA 200761 was tested in the laboratory, resulting in a similar oral toxicity as for fipronil in the case of MB 46136. A lower toxicity than for fipronil was observed for RPA 200761. The EPCO experts' meeting does not consider a

study with the metabolite MB 46513 necessary as the risk from this metabolite to bees is expected to be low due to the low exposure in the case of a seed treatment.

It was considered not appropriate to calculate HQ values for the representative use as a seed treatment.

Several higher tier studies were conducted to address the risk to bees from the use of fipronil as a seed treatment in maize and sunflower. Three tunnel studies, during which fipronil is applied as a seed treatment on sunflower, are considered valid. The biological part of a fourth tunnel study with treated sunflower seeds, conducted in Spain (Report nr: 2005/1006522/23), is considered valid as well but there was a contamination of some control residue samples in that study. The results of this study are not fully conclusive and should be interpreted with care as long as no solid argumentation regarding this contamination is received. Therefore the EFSA proposes a data gap for the applicant to provide such an argumentation.
No adverse effects on bee mortality and survival were observed in any of the valid tunnel studies. The Experts' meeting noted that there were problems with the lack of brood in all 3 treated tunnels in the study conducted in Spain (Report nr: 2005/1006522/23). Also absence of brood was noted in 1 of the 3 control tunnels and in the single untreated tunnel test used for residue analysis. In the same study residues were found in the bee stomachs in the single treated tunnel from which residues were sampled. The experts' meeting noted that such studies were not designed to represent brood production under field conditions. In other tunnel tests no effects on brood were reported. Overall the experts' meeting considered it is necessary to more accurately address potential effects on bee brood.

Several residue monitoring studies were conducted to measure residues of fipronil and metabolites (MB 46513, MB 45950, MB 46136 and RPA 200766) in relevant matrices, primarily pollen and nectar, from samples taken from flowering sunflowers. In the field residue programs conducted in France from 1999 to 2004 on sunflowers at flowering all measured residues were below the limit of quantification (LOQ) which varied between 0.0005-0.002 mg/kg. Furthermore, residues were measured during the tunnel studies mentioned above. Residues were below the LOQ of 0.0005 mg/kg for the tunnel study in sunflower in France (Report 2005/1006529). Residues up to 0.052 mg fipronil/kg pollen were found in the treated tunnels in the tunnel study in Spain (Report nr: 2005/1006522/23). As mentioned above, contamination of the control samples was observed during these studies which still need to be clarified (see above).
Furthermore, a field residue program was carried out to measure residues of fipronil and metabolites (MB 46513, MB 45950, MB 46136 and RPA 200766) in pollen of maize. The studies were conducted in Spain, France and Germany. No residues of fipronil or metabolites at or above the LOQ of 0.0005 mg/kg were found in residue trials. In commercial fields no residues of fipronil and metabolites were found at or above the LOQ of 0.0005 mg/kg in 8 fields. In one field a residue of 0.0023 mg fipronil/kg pollen was found and in another field a residue of 0.00079 mg fipronil/kg pollen was found. No residues of any of the metabolites were found.

The EPCO experts' meeting considered the risk to adult bees for the representative uses as a seed treatment in maize and sunflower addressed based on the low exposure situation observed in monitoring studies and the observation of no adverse effects in the tunnel studies. The risk to bees can only be concluded once recently submitted data on the risk to bee brood are evaluated. Furthermore the EFSA would like to highlight that the available monitoring studies were mainly performed in France and MS should consider the relevance of these studies for the conditions in their country.

The EPCO experts' meeting discussed the reported incidents in France. RMS noted that there was no other conclusive evidence to link the incidents to fipronil apart from a single incident which was attributable to a low coating quality of coated sunflower (which had generated important amounts of dust containing residues of fipronil at sowing). The Expert's meeting requested that MS should send any bee incidents reported to have involved the seed treatment uses of fipronil to the RMS and to the EFSA. Only a few responses were received indicating that no incidents due to the use as a seed treatment were reported.

In the original dossier also data for the EXP60720A, WG and EXP61840, GB formulations were submitted. These data were evaluated in the DAR and a risk assessment was presented. A specific data gap was identified by the RMS and comments were made by other MSs in the reporting table. The peer review for these products stopped after the first evaluation meeting as these formulations were not further supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion) and hence the comments were not discussed in an expert meeting. As these formulations were not longer supported new data which became available during the peer review process of the FS formulation was not discussed in relation to the EXP60720A, WG and EXP61840, GB formulations. Nevertheless a specific data requirement was confirmed in the first evaluation meeting and is listed below:

- Applicant to submit evidence that the analytical reports submitted in France for registration of Crocus TR are dealing with the pollen and nectar of this trial (EXP61840A, GB)

5.4. RISK TO OTHER ARTHROPOD SPECIES

Laboratory studies with *Aphidius rhopalosiphi*, *Typhlodromus pyri*, *Aleochara bilineata*, *Poecilus cupreus*, *Folsomia candida*, *Pardosa* sp. and *Coccinella septempunctata* are available to assess the risk to non-target arthropods (NTA) from the application of fipronil as a seed dressing in maize and sunflower. Some of these studies were performed with a WG formulation. A bridging study was made available to demonstrate that NTA are more sensitive to the WG formulation than to the FS formulation which is used as a seed dressing. The EPCO experts' meeting agreed that extrapolation from the WG formulation to the proposed seed treatment is acceptable.

To address the observed toxicity in the laboratory, extended laboratory studies on *A. rhopalosiphi*, *A. bilineata* and *T. pyri* are available. The toxicity to *A. rhopalosiphi* and *T. pyri* was less when tested under extended laboratory conditions (with LR_{50} values of 106 mg a.s./ha and 224 mg a.s./ha

respectively), but for *A. bilineata* still a very high toxicity was observed when tested under extended laboratory conditions.

Therefore 2 aged residue studies on *F. candida* and *A. bilineata* were conducted to address the observed toxicity. In these studies the product was applied in-furrow in the field and samples were taken at regular time intervals and tested in the laboratory. Samples were taken from soil in-furrow and at the start of the studies also the soil between furrows was sampled and tested. The final reports from these studies were not available at the moment of the EPCO experts' meeting. Impact on *A. bilineata* and *F. candida* was minimal when exposed to soil sampled between furrows. At all tested concentrations a high initial impact was observed when exposed to soil sampled in the furrow. A potential for recovery could be observed in the interim data available for the lower tested concentration at 50 g a.s/ha. For the higher test concentrations the final test results are awaited as in addition to these studies a soil residue study is available to measure the concentrations in furrow in which it was observed that total residue was still increasing. This study observed that at the start of the study 79-83% of the nominal concentrations was achieved. Also the metabolites MB 45950, MB 46136, MB 46513 and RPA 200766 were determined. The level of total residues for the metabolites was still increasing at the end of the study (30 weeks after treatment). This increase was the most pronounced at the 2 highest tested dose rates of 100 and 200 g a.s./ha. The concentrations of the metabolites did not reach or just approached the predicted initial concentrations in soil for these metabolites in the section on Fate and behaviour. The metabolites MB 45950 and MB 46136 are GABA-active metabolites and therefore it is considered important to see the final report of the extended laboratory studies.

The EPCO experts' meeting agreed that exposure of NTA off-field would be low for a seed treatment.

A non-standard in-field risk assessment for foliage dwelling NTA is presented in the addendum 1 of April 2005. The EPCO experts' meeting noted that this assessment was illustrative and agreed that the risk to NTA should be focussed on soil-dwelling species. On the basis of current practice the risk to foliar dwelling arthropods was considered to be low for the representative uses as a seed treatment in sunflower and maize.

Regarding the in-field risk to soil-dwelling species the EPCO experts' meeting agreed that the risk to NTA should be revised and based on potential effects on *A. bilineata* and *F. candida*. It was noted that aged residue studies (interim study reports see above) demonstrate potential for recolonisation but that this may not reflect potential for recovery of sensitive species in particular those with univoltine life cycles. Furthermore the meeting noted that the risk assessment should cover the plateau soil PEC for total residues (parent + metabolites). Therefore a new data gap for the applicant was identified to provide a new risk assessment for soil dwelling arthropods taking into account final results from the ongoing aged residue studies on *A. bilineata* and *F. candida*. This assessment should cover the potential for recovery of impacted species in the field. The risk to soil non-target arthropods from the representative uses with the FS formulation can only be concluded once recently submitted

studies on *A. bilineata* and *F.* candida are evaluated and the open questions for the calculation of PECsoil have been solved.

In the original dossier also data for the EXP60720A, WG and EXP61840, GB formulations were submitted. These data were evaluated in the DAR and a risk assessment was presented. A specific data gap was identified by the RMS and comments were made by other MSs in the reporting table. The peer review for these products stopped after the first evaluation meeting as these formulations were not further supported by the current applicant and hence the comments were not discussed in an expert meeting. As these formulations were not longer supported for the EU review process (i.e. with respect to Annex I inclusion), new data which became available during the peer review process of the FS formulation was not discussed in relation to the EXP60720A, WG and EXP61840, GB formulations. Nevertheless a specific data requirement was confirmed in the first evaluation meeting and is listed below:

- Applicant to submit off-crop exposure assessment (and risk assessment) for the in-furrow spray application technique. (EXP60720A, WG)

5.5. RISK TO EARTHWORMS

Studies on the acute toxicity to earthworms from fipronil, a formulation EXP61829A (0.5 % GB) and the metabolites MB 46136, MB 45950 and RPA 200766 are available. All the corresponding endpoints were corrected for the organic content of the test soil as the logPow exceeds 2 for fipronil and metabolites. The corresponding TER-values, based on the present available PEC-values (see below), do not breach the Annex VI trigger value, indicating a low acute risk to earthworms from the representative uses evaluated. However, there is an outstanding data requirement in the section on Fate and behaviour for a recalculation of the PECsoil. PEC soil max for the parent compound based on the worst case field half life and further justification of the scenario assumed for PEC soil calculations need to be provided. It is assumed that the plateau PECsoil value for the representative uses with the FS formulation might increase. The EFSA does not consider that this will change the outcome of the present risk assessment as the TER values based on the provisional PECsoil values are at least 2 orders of magnitude above the Annex VI trigger value and the revised PEC soil values are not expected to increase with that order.

The composition of the formulation EXP61829A (0.5 % GB) is not known. The EFSA proposes that a detailed description of the composition of the formulation is submitted by the applicant. The EFSA does not consider a study on earthworms with the FS formulation necessary as the TER values are at least a factor 100 above the trigger value. In line with the discussion for tolclofos-methyl (see discussion table for this substance) it could also be said in this case that there will be limited exposure to the formulation and more general exposure to the active substance as it disperses. Furthermore the FS formulation is intended to treat seeds and will not be applied to the field as such.

Studies on the long term toxicity to earthworms from fipronil and the metabolite MB 46136 are available. Also these endpoints were corrected for the organic content of the test soil. The

corresponding TER-values do not breach the Annex VI trigger value, indicating a low long term risk to earthworms from the representative uses evaluated. As stated above there is an outstanding data requirement in the section on Fate and behaviour for a recalculation of the PECsoil. But also for the long term risk the EFSA does not consider that this will change the outcome of the present risk assessment

In the original dossier also data for the EXP60720A, WG and EXP61840, GB formulations were submitted. These data were evaluated in the DAR and a risk assessment was presented. The peer review for these products stopped after the first evaluation meeting as these formulations were not further supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion). As these formulations were not longer supported new data which became available during the peer review process of the FS formulation was not discussed in relation to the EXP60720A, WG and EXP61840, GB formulations.

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

The risk to collembola is discussed above under point 5.4.
Furthermore a litterbag study with the formulation EXP 60720A (WG) is available to address this annex point. EXP 60720A was applied at a rate equivalent to 0.12 mg a.s./kg soil and 0.785 mg a.s./kg soil (measured concentrations). No differences in treated samples and controls were observed at any time point in any sample. It can be concluded from this litter bag study that no adverse effects on organic matter breakdown are expected from fipronil at 0.785 mg a.s./kg soil. There is an outstanding data requirement in the section on fate and behaviour for a recalculation of the PECsoil values. The risk to soil non-target macro-organisms from the representative uses with the FS formulation can not be concluded until the open questions regarding the calculation of PEC in soil are solved.
The EFSA does not consider a litter bag study with the FS formulation necessary for the same reasons as discussed under point 5.5 (see above). Furthermore a bridging study was made available to demonstrate that NTA are more sensitive to the WG formulation than to the FS formulation which is used as a seed dressing. The EPCO Expert's meeting agreed that extrapolation from the WG formulation to the proposed seed treatment is acceptable with regard to the risk for non-target arthropods.

In the original dossier also data for the EXP60720A, WG and EXP61840, GB formulations were submitted. These data were evaluated in the DAR and a risk assessment was presented. The peer review for these products stopped after the first evaluation meeting as these formulations were not further supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion). As these formulations were not longer supported new data which became available during the peer review process of the FS formulation was not discussed in relation to the EXP60720A, WG and EXP61840, GB formulations.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of fipronil and the metabolites MB 46136, MB 45950 and RPA 200766 were tested on soil microbial respiration and nitrogen transformation. Effects were below 25% after 28 days and hence the risk can be considered as low at 0.667 mg a.s./kg soil for fipronil and 0.60, 0.133 and 0.267 mg/kg soil for MB 46136, MB 45950 and RPA 200766 respectively. There is an outstanding data requirement in the section on fate and behaviour for a recalculation of the PECsoil values. The risk to soil non-target micro-organisms from the representative uses with the FS formulation can not be concluded until the open questions regarding the calculation of PEC in soil are solved.

The EFSA does not consider a study with the FS formulation necessary as no effects were seen with the a.s. In line with the discussion for tolclofos-methyl (see discussion table for this substance) it could also be said in this case that there will be limited exposure to the formulation and more general exposure to the active substance as it disperses. Furthermore the FS formulation is intended to treat seeds and will not be applied to the field as such.

In the original dossier also data for the EXP60720A, WG and EXP61840, GB formulations were submitted. These data were evaluated in the DAR and a risk assessment was presented. The peer review for these products stopped after the first evaluation meeting as these formulations were not further supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion). As these formulations were not longer supported new data which became available during the peer review process of the FS formulation was not discussed in relation to the EXP60720A, WG and EXP61840, GB formulations.

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

A study on the effects of fipronil on the emergence of 6 plant species is evaluated and summarised in the addendum 1 of April 2005. The EC_{50} exceeds 2 mg a.s./kg dry soil (the highest tested concentration). The lowest NOEC was 0.5 mg a.s./kg dry soil for an observed reduction in plant fresh weight of oats and oilseed rape. No risk assessment was considered necessary for the use of fipronil formulated as a seed treatment in maize and sunflower as there will be no exposure of the off-crop area. This was agreed by the EPCO experts' meeting. No risk assessment is available for the use as a WG formulation (EXP60720A) in maize and a GB formulation (EXP61840A) in maize.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The NOEC for inhibition of respiration of sewage sludge micro-organisms is 1000 mg/L. Based on this study the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: fipronil, RPA 200766[21], MB 46136[22] and MB 45950[23]

Definitions for monitoring: fipronil, RPA 200766, MB 46136 and MB 45950

Member States may also wish to include the soil photolysis metabolite MB 46513[24] in the monitoring definition due to the fact that it is more acutely orally toxic than fipronil. Its inclusion may be useful when investigating possible misuse. When correctly used in line with the applied for intended uses where efficient incorporation below the soil surface represents GAP, the process of soil photolysis is precluded.

Water

Ground water

Definitions for exposure assessment: fipronil, RPA 200766, MB 46136 and MB 45950

Definitions for monitoring: fipronil and RPA 200766. Additional metabolites could eventually be added when the new modelling required is completed.

Surface water

Definitions for risk assessment: surface water: fipronil and RPA 200766

sediment: fipronil, RPA 200766 and MB 45950

Definitions for monitoring: fipronil and RPA 200766

Air

Definitions for risk assessment: fipronil

Definitions for monitoring: fipronil

Food of plant origin

Definitions for risk assessment: Sum of fipronil and sulfone metabolite (MB 46136) expressed as fipronil. (applicable to seed treatment uses only)

Definitions for monitoring Sum of fipronil and sulfone metabolite (MB 46136) expressed as fipronil. (applicable to seed treatment uses only)

Food of animal origin

Definitions for risk assessment: Sum of fipronil and sulfone metabolite (MB 46136) expressed as fipronil.

Definitions for monitoring: Sum of fipronil and sulfone metabolite (MB 46136) expressed as fipronil.

[21] RPA200766: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylsulfonyl-1H-pyrazole-3-carboxamide

[22] MB46136: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylsulfonylpyrazole-3-carbonitrile

[23] MB45950: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylthio-1H-pyrazole-3-carbonitrile

[24] MB46513: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylpyrazole-3-carbonitrile

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
fipronil	Moderate to high persistent ($DT_{50\ lab\ aerobic}$ = 32-346 d)	See 5.5, 5.6 and 5.7.
RPA 200766	High persistent ($DT_{50\ lab\ aerobic}$ = 160-213.6 d)	No conclusion possible due to outstanding data gap for non-target arthropods.
MB 46136	High persistent ($DT_{50\ lab\ aerobic}$ = 265-422 d)	No conclusion possible due to outstanding data gap for non-target arthropods.
MB 45950	High persistent ($DT_{50\ lab\ aerobic}$ = 128-337 d)	No conclusion possible due to outstanding data gap for non-target arthropods.
MB 46513	Medium to high persistent ($DT_{50\ lab\ aerobic}$ = 66-147 d) Soil photolysis metabolite, not relevant for seed treatment and incorporated uses	No data available, not considered necessary for seed treatment and incorporated uses.
RPA 104615	Soil photolysis metabolite, not relevant for seed treatment and incorporated uses	No data available, not considered necessary for seed treatment and incorporated uses.

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
fipronil	low to medium mobile (Koc = 427 – 1248 L / kg)	FOCUS: no	Yes	Yes	See 5.2.
RPA 200766	medium to high mobile (Koc = 96 – 203 L / kg)	FOCUS: yes, trigger exceeded based on provisional groundwater assessment. Concentrations RPA 200766 <0.75µg/l at this stage.	No GABA activity At least 10-fold less toxic than fipronil	No	Relevant because of the higher risk to sediment dwelling organisms than the parent.
MB 46136	immobile to low mobile (Koc = 1448 – 6745 L / kg)	FOCUS: no	Yes	Yes oral LD_{50} 184 mg/kg bw, not genotoxic in vitro, is a rat metabolite	No assessment required. Data available (fish, *D. magna*, *M. bahia*, *C. riparius*, algae). Similar toxicity than parent.
MB 45950	immobile to low mobile (Koc = 1695 – 5621 L / kg)	FOCUS: no	Yes	Yes oral LD_{50} 69 mg/kg bw, 28-d dog NOAEL 1 mg/kg bw/day, 90-d rat NOAEL 0.7 mg/kg bw/day, not genotoxic in vitro	No assessment required. Data available (fish, *D. magna*, *M. bahia*, *C. riparius*, algae). Similar or higher toxicity than parent.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Fipronil (water and sediment)	See 5.2
MB 45950 (sediment only)	Relevant because of the higher toxicity and risk to sediment dwelling organisms than the parent. Furthermore a similar/higher toxicity was observed for fish and *M. bahia*.
RPA 200766 (water and sediment)	Relevant because of the higher risk to sediment dwelling organisms than the parent.

Air

Compound (name and/or code)	Toxicology
fipronil	Toxic, LC_{50} 0.36 mg/L

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

- An analytical method for the determination of the metabolite RPA 200766 in soil (new report made available after the Evaluation Meeting February 2006 (BASF Doc ID 2005/1015065) but it has neither been evaluated or peer reviewed, data gap identified by EFSA after the residue definition was finalised, refer to chapter 1 and 6)
- An analytical method for the determination of the metabolite RPA 200766 in drinking water (date of submission unknown, data gap identified by EFSA after the residue definition was finalised, refer to chapter 1 and 6)
- A confirmatory method for the determination of the metabolite RPA 200766 in surface water (date of submission unknown, data gap identified by EFSA after the residue definition was finalised, refer to chapter 1 and 6)
- PEC soil max for the parent compound based on the worst case field half life needs to be provided (relevant for all representative uses evaluated, date of submission unknown, refer to point 4.1.2).
- Notifier to provide further justification of the scenario assumed and input parameters used for PEC soil calculations (relevant for all representative uses evaluated, date of submission unknown, refer to point 4.1.2).
- Initial (maximum) and 21 d TWA-PEC_S for the parent compound and soil metabolites is required to finalise the ecotoxicological risk assessment for soil micro- and macro-organisms and earthworm-eating birds and mammals respectively (relevant for all representative uses evaluated, date of submission unknown, refer to point 4.1.2).
- PEC_{SW} calculation with adequate input parameters are required (relevant for all uses, new report available but not evaluated (Gottesbüren 2005 BASF Doc ID2005/1027945), please refer to point 4.2.1).
- The applicant has to justify that kinetics in field degradation studies represent degradation rather than other dissipation processes (relevant for all representative uses evaluated, new report made available after the Evaluation Meeting February 2006 and not evaluated: (Platz, K. 2005 BASF Doc ID 2005/1029050), refer to point 4.2.1).
- FOCUS PEC_{GW} calculations for representative uses with appropriate input parameters are required (relevant for all representative uses evaluated, new report made available after the Evaluation Meeting February 2006 and not evaluated (Gottesbüren 2005 BASF Doc ID2005/1028924), refer to point 4.2.2).
- A new risk assessment for granivorous birds taking into account the concerns raised at EPCO 27, especially those regarding the use of the cage field trial, is required. The risk to small and large granivorous birds must be quantified. The current proposed extrapolation from maize to sunflowers is not acceptable. (relevant for the use of Regent 500 FS in maize and sunflower; submission date: 6th of December 2005, not evaluated; refer to point 5.1).
- A revised risk assessment for granivorous mammals taking into account the concerns raised at EPCO 27 regarding the proposed refinements of PT, PD, AV and the use of a dehusking factor

is required. The availability of treated seeds for mammals (i.e. the efficiency of precision drilling and the frequency of minimum cultivation techniques for these crops) should be assessed (relevant for the use of Regent 500 FS in maize and sunflower; submission date: 6th of December 2005, not evaluated; refer to point 5.1).

- If the applicant wishes to pursue the argument that marine species are more sensitive than freshwater species then a more robust justification must be provided. (relevant for all representative uses evaluated; submission date: 6th of December 2005, not evaluated; refer to point 5.2).
- An argumentation in line with the opinion of the PPR Panel on dimoxystrobin if the applicant wishes to use a study in the presence of sediment to refine the long term risk to *M. bahia*. Proposed by the EFSA, not peer reviewed. (relevant for all representative uses evaluated; date of submission unknown; refer to point 5.2).
- A study on bioaccumulation in fish from the metabolites MB 46136, MB 45950 and RPA 200766. Proposed by the EFSA, not peer reviewed. (relevant for all representative uses evaluated; date of submission unknown; refer to point 5.2).
- A solid argumentation regarding the contamination of the control residue samples in the bee tunnel study in Spain (BASF DocID 2005/1006522; Schur A. 2005 and BASF DocID 2005/1006523; Schur A. 2005) Proposed by the EFSA, not peer reviewed. (relevant for all representative uses evaluated; date of submission unknown; refer to point 5.3).
- An assessment of the potential for effects on bee brood from the proposed use of Regent 500 FS (relevant for the representative uses of Regent 500 FS; submission date: 6th of December 2005, not evaluated; refer to point 5.3).
- Final reports of the aged residue study on *Aleochara bilineata* (Report nr: 2005/1006514) and *Folsomia candida* (Report nr: 2005/1006518) and the final report of the soil residue study by Richter (Report nr: 2005/1004797) (relevant for the representative uses of Regent 500 FS; final reports submitted to the RMS, not evaluated; refer to point 5.4).
- A new risk assessment for soil dwelling arthropods taking into account final results from the ongoing aged residue studies on *A. bilineata* and *F. candida*. This assessment should cover the potential for recovery of impacted species in the field. (relevant for the representative uses of Regent 500 FS; submission date: 6th of December 2005, not evaluated; refer to point 5.4).
- The composition of the formulation EXP61829A. Proposed by the EFSA, not peer reviewed. (relevant for all representative uses evaluated; date of submission unknown; refer to point 5.5).

Requirements as far as identified for the WG- and the GB formulation (EXP60720A and EXP61840A) withdrawn by BASF for the EU peer review process (i.e. with respect to Annex I inclusion):

- Applicant to submit residue data in seeds, seedlings and young plants (0-28 d) in maize (EXP60720A, WG and EXP61840, GB)
- Applicant to submit a realistic higher tier risk assessment for birds and mammals (e.g. palatability and avoidance tests) (EXP61840, GB)

- Applicant to submit a more documented and appropriate assessment in support of refined PD and PT values (EXP61840, GB)
- Applicant to submit appropriate spray-drift values relative to the equipment used to apply EXP60720A by spraying in-furrow at drilling. The precision should be relevant to the level of concern (i.e. 0.001%) (EXP60720A, WG).
- Applicant to submit evidence that the analytical reports submitted in France for registration of Crocus TR are dealing with the pollen and nectar of this trial (EXP61840A, GB)
- Applicant to submit off-crop exposure assessment for non-target arthropods (and risk assessment) for the in-furrow spray application technique. (EXP60720A, WG)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide as proposed by the applicant which comprises seed dressing to control soil insects and wireworms in sunflower and maize at application rate up 30 g fipronil per hectare for sunflower (up to 500 g fipronil per 100 kg seeds) and up to 50 g per hectare for maize (up to 250 g per 100 kg seeds), respectively. It should be noted that due to the fact that the applicant has changed, some representative uses are not longer supported for the EU review by the new applicant. Fipronil can be used as insecticide and acaricide. It should be noted that during the peer review process the applicant stated that only the use as insecticide will be supported in the EU review programme.

The representative formulated product for the evaluation was "Regent 500FS" ("EXP80415A"), a flowable concentrate for seed treatment (FS), registered in some Member States of the EU. The WG- and the GB formulation (EXP60720A and EXP61840A, respectively) are not longer supported by the new applicant BASF for the EU review process (i.e. with respect to Annex I inclusion). However, the submitted data package was evaluated in the DAR, but the peer review was not completed.

Adequate methods to monitor all compounds given in the respective residue definition are available only for food and air. Residues in food of plant origin can be determined with a multi-residue method (The German S19 method has been validated). For the other matrices only single methods are available to determine residues of fipronil.

Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

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

Fipronil is rapidly and extensively absorbed (90%), widely distributed, readily metabolised, and slowly excreted by faeces. The long half-life (245 hours) is due to a deep compartment (fat) and a high degree of biliary recirculation. Fipronil is toxic following oral, inhalation and dermal acute exposure. It is slightly skin and eye irritating, and weakly sensitising, but not sufficiently to be

classified. The proposed classification is **T, R23/24/25 "Toxic by inhalation, in contact with skin and if swallowed"**.

Adverse effects in short term studies are observed in the central nervous system, liver and thyroid. The classification adopted by ECB is **T, R48/25 "Toxic: danger of serious damage to health by prolonged exposure if swallowed"**. This will be voted in the 30th ATP. Fipronil showed no evidence of genotoxic properties. In long term studies, high doses of fipronil induced in the rat thyroid follicular cell tumours, *via* increased thyroid hormones clearance. The experts agreed this is not relevant to humans. No evidence of developmental toxicity or teratogenic effects for foetuses is shown in rats and rabbits. In specific neurotoxicity studies, no histopathological findings are observed in the nervous system. Toxicity of fipronil metabolites or degradation products was extensively studied in rats, none of them is more toxic than fipronil.

The Acceptable Daily Intake (ADI) is 0.0002 mg/kg bw/day, the Acceptable Operator Exposure Level (AOEL) is 0.0035 mg/kg bw/day, and the Acute Reference Dose (ARfD) 0.009 mg/kg bw, with a safety factor of 100.

The operator exposure was assessed with a field study (with professional treaters and use in maize seeds), resulting in an exposure below the AOEL without PPE. Worker exposure is 89% of the AOEL without PPE, for a 8-hour working day. Bystander exposure is not likely to be an issue for seed treatments and has to be addressed at Member State level.

The metabolism of fipronil has been investigated on five different crops representative for cereals, pulses and oilseed, roots and tubers using either soil applications or seed treatment. A common metabolic pathway could be defined for the three crop groups tested and a relevant metabolite (sulfone metabolite MB 46136) was demonstrated to be present. Even though there were concerns on a highly toxic photo degradation product of fipronil, MB 46513, the experts' meeting on residues concluded that the compound is basically not relevant in relation to seed treatment uses. However, a label restriction has been proposed to ensure that treated seed remains stored in the dark to prevent photo degradation processes. In supervised residue trails no residues of fipronil and of its sulfone metabolite were observed at harvest of maize grain and sunflower seed. Trials results are suitable to propose MRLs at LOQ level.

Even though calculated animal intakes were well below the trigger of 0.1 mg/kg, there is a need to consider residues in animal products since fipronil is classified fat soluble and the ADI is very low. Based on the available livestock metabolism and feeding studies, MRLs for food of animal origin were proposed.

In a consumer risk assessment the TMDI was demonstrated to exceed the ADI for toddlers and infants, mainly due to the fact that milk consumption accounted for the most significant contribution of pesticide intake in terms of the total dietary assessment. However, in a refined chronic dietary risk assessment the IEDI/NEDI was below the ADI for all considered consumer groups (adults, toddles, infants) and thus, it is unlikely that exposure to fipronil and fipronil sulfone residues from seed treatment will pose a high chronic risk to consumers. In an acute dietary risk assessment the estimated exposure of all considered consumer groups was well below the proposed ARfD.

Use pattern as soil application, band application & incorporation at sowing / planting for maize at 100 g/ha has not been addressed in the fate section and should be labelled in grey in the table of representative uses. Maximum application rate partially addressed in the fate and behaviour in the environment is 50 g / ha applied in furrow at drilling of maize with subsequent incorporation or as seed treatment. For sunflower seed treatment at application rates of 30 g/ha has been also partially addressed. However, data gaps have been identified also for these use patterns and therefore they have been labelled in grey.

Under laboratory aerobic conditions at 20 or 25 ºC fipronil is moderate to high persistent in soil (DT_{50} = 32 – 346 d). Main degradation processes were hydrolysis to the amide RPA 200766 (max. 38.4 % AR after 219 d), oxidation to the sulphone MB 46136 (max. 34.3 % AR after 162 d) and reduction to the sulphide MB 45950 (max 17 % AR after 91 d). Mineralization was very low and bound residues were formed at amounts up to 15.1 % AR after 336 d. No new metabolites were identified in the study performed under anaerobic conditions.

A new study to investigate the degradation of metabolites RPA 200766, RPA 200761, MB 45950, MB 46136 and MB 46513 (photolysis metabolite) under dark aerobic conditions at 27 ºC was provided by the applicant after the DAR was finalized. In this study RPA 200766 shows to be high persistent (DT_{50} = 107 – 149 d), RPA 200761 moderate to high persistent (DT_{50} = 43.5 – 139 d), MB 45950 medium to high persistent (DT_{50} = 89 – 224 d), MB 46136 high persistent (DT_{50} = 185 – 280.5 d) and MB 46513 moderate to medium persistent (DT_{50} = 46.5 – 98 d). Experts' meeting noted that most of these half lives are longer than the duration of the studies and therefore uncertain.

Photolysis may contribute slightly to the environmental dissipation of fipronil in soil. Two main metabolites, not previously detected in the aerobic degradation studies, were identified as MB 46513 (max. 6.9 % AR after 30 d) and RPA 104615 (max. 7.2 % AR after 21d).

Two field dissipation studies in six sites of South of Europe are available. Fipronil and metabolites RPA 200766, MB 46136, MB 45950 and MB 46513 (photolysis metabolite only detected in Sevilla and Bologna when product was applied on bare soil and not incorporated) are found as soil residue components in these studies. Additionally, a field study performed in four USA sites where fipronil was incorporated to soil has been provided. Fipronil and metabolites RPA 200766, MB 46136, MB 45950 are found as soil residue components in these experiments.

Available field studies confirmed that fipronil is medium to high persistent in soil (DT_{50} = 96 – 135 d). In the field studies performed under conditions where photodegradation could occur (Bologna and Seville) a faster degradation was observed (DT_{50} = 5.6 – 22.2 d).

A new kinetic analysis of the eight field studies was provided after the DAR had been finalised (see Addendum 1) to reduce the scattering of data due to sampling heterogeneity. Half lives of fipronil (DT_{50} = 33 – 120 d) and metabolites MB 46136 (DT_{50} = 147 – 430 d), MB 45950 (DT_{50} = 82 – 112 d, only data from two USA sites) and RPA 200766 (DT_{50} = 167 – 266 d) were obtained in this way. However, environmental modelling of metabolites was finally based on the parameters derived from the most recent field study in northern EU (Kortenaken, Belgium). This new field study was provided by the applicant after the DAR had been finalised (see Addendum 1). In this study, a wettable granule formulation (EXP60720A) was homogeneously sprayed and then incorporated prior to planting maize seeds. A multicompartmental model was used to estimate the firs order half lives of fipronil (DT_{50} =

49 d) and metabolites MB 46136 (DT_{50} = 231 d), MB 45950 (DT_{50} = 264 d) and RPA 200766 (DT_{50} = 259 d).

Since DT_{90} of fipronil was above one year in some studies, two field accumulation studies were presented by the applicant (see Addendum 1). One of the studies was carried out for six years in two sites of Southern EU and the other in two sites of Northern EU. Fipronil was sprayed and then incorporated at 200 g a.s. / ha, prior to planting maize seeds. Fipronil did not accumulate in any of the studies but a clear tendency for accumulation was observed for the metabolites. Experimental plateau levels were not determined since the plateau had not been reached after the five or six years of repeated applications. Kinetic analysis of the accumulation field trials was reported in a separate study, but in this analysis only was possible to derive field formation fractions of the metabolites.

New PEC soil were provided by the applicant (see updated addendum for complete report). In this new calculation degradation parameters employed to calculate plateau levels are from the new field dissipation study in northern EU (Kortenaken, Belgium) for the metabolites and from the field accumulation studies for the parent compound. The calculation provided does not represents a worst case with respect to the parent compound, since DT_{50} employed is well below field worst case DT_{50}. Furthermore, the assumptions taken in the calculation (depth of plough layer, climatic data) are not well justified. Therefore, new data requirements are identified to provide the PEC soil max for the parent compound based on the worst case field half life and to provide further justification of the scenario assumed and input parameters used for PEC soil calculations. Furthermore, calculation of the initial and 21 d TWA-PEC_S for the parent compound and soil metabolites would also be necessary to finalise the ecotoxicological risk assessment for soil micro- and macro-organisms and earthworm-eating birds and mammals respectively. Consequently, risk assessment for the EU representative uses can not be finalised with respect to the soil compartment.

According adsorption / desorption studies fipronil is low to medium mobile (Koc = 427 – 1248 L / kg), MB 45950, MB 46136 are immobile to low mobile (MB 45950: Koc = 1695 – 5621 L / kg; MB 46136: Koc = 1448 – 6745 L / kg), MB 46513 is low mobile (Koc = 1150 – 1498 L / kg) and RPA 200766 is medium to high mobile (Koc = 96 – 203 L / kg).

A column leaching and an aged residue column leaching experiments with five soils were provided. No lysimeter study is available for fipronil.

Hydrolysis will not contribute significantly to the degradation of fipronil for most relevant environmental conditions. However, photolysis may contribute to the degradation of fipronil and its major metabolites in water. Fipronil is not readily biodegradable in water.

In water / sediment system fipronil is adsorbed on the sediment more or less rapidly and then degrades to MB 45950 (max. 88.72 % AR in the sediment after 120 d). In the water phase only fipronil and the major metabolite RPA 200766 reached levels above 10 % AR. The dissipation half lives of fipronil ranged between 14.2 to 93.6 d in water and from 16.4 to 119.6 d in whole system. No reliable half lives could be derived for metabolites in these experiments.

$PEC_{SW/SED}$ were provided by the applicant after the DAR was finalised (see Addendum 1). These $PEC_{SW/SED}$ were calculated using FOCUS SW models and scenarios to estimate potential surface water contamination resulting from drainage and runoff after the treated seeds applied in furrow. The expert's meeting agreed that new calculation would be needed with updated parameters following

FOCUS guidance. Data requirement for new PEC_{SW} calculation is confirmed and the risk assessment with respect to aquatic organisms and fish-eating birds and mammals may not be considered completed.
New PEC_{GW} were provided by the applicant after the DAR had been finalized (see Addendum 1). Only the application rate of 50 g/ha for maize has been simulated. Results of these new calculation show that the 80th percentile of the predicted annual leachate of metabolite RPA 200766 exceeds the trigger of 0.1 µg / L for five of the seven scenarios simulated for maize (appl. rate 50 g/ha). This metabolite has been assessed to be not toxicological relevant (see 2.8) but it is considered ecotoxicological relevant (see 5.2). Experts' meeting identified a new data gap for the applicant to justify that kinetics in field degradation studies represent degradation rather than other dissipation processes. RMS provided complementary information in the updated addendum to support the use of field derived degradation parameters for modelling. This additional information has not been peer reviewed. Due to the deviations with respect to guidelines on the input parameters selection and the need of justification for the use of field kinetic parameters the assessment of potential groundwater contamination could not be considered finalised for the EU representative uses. Data requirement for new FOCUS PEC_{GW} calculation with appropriate input parameters is therefore confirmed.
Taking into consideration the vapour pressure, the Henry law constant and the photochemical transformation estimated with the Atkinson method, long range transport and deposition of fipronil may be considered negligible.

Regarding the section on ecotoxicology only issues related to the FS formulation EXP80415A are discussed. In the original dossier also data for the EXP60720A, WG and EXP61840, GB formulations were submitted. These data were evaluated in the DAR and a risk assessment was presented. The peer review for these products stopped after the first evaluation meeting as these formulations were not further supported by the current applicant for the EU review process (i.e. with respect to Annex I inclusion). As these formulations were not longer supported new data which became available during the peer review process of the FS formulation was not discussed in relation to the EXP60720A, WG and EXP61840, GB formulations.

A high acute, short and long term risk to granivorous birds, with TER values far below 1, were identified in the first tier risk assessment for the representative use as a seed treatment in maize and sunflower. The EPCO experts' meeting agreed that the risk to birds should focus on the acute and short term risk as there is no indication that fipronil is a reproductive toxin. A refined risk assessment was submitted and discussed in the EPCO experts' meeting. A new risk assessment for granivorous birds taking into account the concerns raised at the EPCO 27 experts' meeting, especially those regarding the cage field trial, is required. The risk to small and large granivorous birds must be quantified. The current proposed extrapolation from maize to sunflowers is not acceptable.
Also for granivorous mammals a high acute and long term risk, with TER values far below 1, were identified in the first tier risk assessment for the representative use as a seed treatment in maize and sunflower. A revised risk assessment for granivorous mammals taking into account the concerns raised at EPCO 27 regarding the proposed refinements of PT, PD, AV and the use of a dehusking

factor is required. The meeting could not accept the proposed use of seed encounter and exploitation (TSE) factor as it was considered that this was already incorporated into PD. The availability of treated seeds for mammals should be assessed to indicate whether mice consumed drilled maize and sunflower seeds.
The risk to granivorous birds and mammals from the use of fipronil as a seed treatment in maize and sunflower can only be concluded once recently submitted data are evaluated.
The risk to herbivorous birds and mammals from the representative uses of fipronil as a seed dressing is considered to be low.
The risk to earthworm and fish-eating birds and mammals can be considered low based on the currently available PECs and PECsw-values. The risk to earthworm and fish eating birds and mammals from the representative uses with the FS formulation can not be concluded due to still open questions regarding the calculation of PEC in surface water and soil.

The risk to aquatic organisms is based on the most sensitive species, *Mysidopsis bahia*. If the applicant would like to pursue the argument that marine species are more sensitive than freshwater species then a more robust justification must be provided. The risk to aquatic organisms from the representative uses with the FS formulation can not be concluded due to still open questions regarding PECsw values. Based on the available provisional PECsw values a high acute and long term risk to aquatic organisms was identified for the representative use as a seed treatment in maize. The risk to aquatic organisms for the representative use in sunflower can be regarded as low. The RMS proposed to refine the long term risk by using an endpoint for *M. bahia* from a study in the presence of sediment. The EFSA considers that in order to accept this refinement option, an assessment in line with the conclusion of the PPR Panel on dimoxystrobin should be presented. The EPCO experts' meeting agreed that it might be possible to reduce the standard uncertainty factor due to the number of species tested. The EFSA would like to refer to the opinion of the PPR Panel regarding the reduction of the uncertainty due to the availability of several single species studies and proposes to take this opinion into account at MS-level. Based on the present PECsw values the risk from the metabolites MB 46136, MB 45950 and RPA 200766 for the representative uses as a seed treatment in maize and sunflower can be regarded as low except for the long term risk to aquatic invertebrates from MB 46136 in maize. Also for the refinement of this risk the EFSA would like to refer to the opinion of the PPR Panel on the lowering of aquatic trigger values.
The risk for bioaccumulation in fish from fipronil is considered to be low. The EFSA proposes that a study on bioaccumulation in fish from the metabolites MB 46136, MB 45950 and RPA 200766 should be submitted as the Log Pow of these metabolites exceeds 3.

A very high acute contact and oral toxicity of fipronil to bees were observed in the laboratory toxicity studies. The metabolite MB 46136 showed a similar toxicity to bees as fipronil and the metabolite RPA 200761 showed a lower toxicity to bees than fipronil. The EPCO experts' meeting considered the risk to adult bees for the representative uses as a seed treatment in maize and sunflower addressed based on the low exposure situation observed in monitoring studies and the observation of no adverse effects in the tunnel studies. The risk to bees can only be concluded once recently submitted data on

the risk to bee brood are evaluated. Furthermore the EFSA would like to highlight that the available monitoring studies were mainly performed in France and MS should consider the relevance of these studies for the conditions in their country.

A high toxicity to NTA was observed in the laboratory. Extended laboratory studies are available to address this risk. The EPCO Experts' meeting identified the need for a new risk assessment for soil dwelling arthropods taking into account final results from the ongoing aged residue studies on *A. bilineata* and *F. candida*. This assessment should cover the potential for recovery of impacted species in the field. Furthermore the meeting noted that the risk assessment should cover the plateau soil PEC for total residues (parent + metabolites). The risk to non-target arthropods from the representative uses with the FS formulation can only be concluded once recently submitted studies on *A. bilineata* and *F.* candida are evaluated and the open questions for the calculation of PECsoil have been solved.

The risk to soil macro-organisms can be considered low at a concentration of 0.785 mg a.s./kg soil and the risk to soil micro-organisms can be considered as low at a concentration of 0.667 mg a.s./kg soil for fipronil and 0.60, 0.133 and 0.267 mg/kg soil for MB 46136, MB 45950 and RPA 200766 respectively. The risk to soil non-target macro- and micro-organisms from the representative uses with the FS formulation can not be concluded due to still open questions regarding the calculation of PECsoil.

The risk to earthworms, non-target plants and biological methods for sewage treatment is considered to be low.

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

- To prevent photo degradation of fipronil into the very toxic metabolite MB 46513, treated seed must be kept in the dark prior to use. Therefore, a label restriction is considered necessary to ensure that treated seed remains in sealed bags to keep treated seed stored in the dark. If the use is to be extended for soil treatment with soil incorporation it will be necessary to consider whether a label statement to ensure that the soil is incorporated straight after application of the pesticide is needed. (refer to point 3.1.1).
- Photolysis on the soil surface results in the formation of a very acutely toxic to terrestrial vertebrates by oral ingestion metabolite (MB 46513). The current fate and behaviour assessment only addresses uses where the active substance is efficiently incorporated below the soil surface such that the soil photolysis is precluded.
- Potential for ground water contamination should be assessed employing the appropriate input parameters.
- The risk to granivorous birds from the use of fipronil as a seed treatment in maize and sunflower can only be concluded once recently submitted data are evaluated. Nevertheless the EPCO experts' meeting agreed that the proposed labelling SPe 5 (To protect birds/wild mammals, the product must be entirely incorporated in the soil; ensure that the product is also

fully incorporated at the end of the rows) and SPe 6 (To protect birds/wild mammals remove spillages.) phrases are necessary (refer to point 5.1).

Critical areas of concern

- No validated enforcement methods are available to monitor metabolite RPA 200766 ~~in soil~~ and water (ground and surface)
- Toxic if swallowed, in contact with skin and by inhalation
- The operator risk assessment has been performed for the treatment of maize seeds in factories, with FS formulation. Other uses/formulations should be considered at Member State level.
- The currently proposed residue definition in plants and the consumer risk assessment is applicable to seed treatment uses only (representative use). For uses with a different mode of application, such as foliar treatment, attention should be paid to the formation of the very toxic photo metabolite MB 46513.
- Potential for groundwater contamination by the ecotoxicological relevant metabolite RPA 200766 under vulnerable situations has been identified with available information.
- A high acute and short term risk to granivorous birds and a high acute risk to mammals from the use of fipronil as a seed treatment were identified. Further data was submitted by the applicant but not evaluated or peer reviewed. The risk to granivorous birds and mammals from the use of fipronil as a seed treatment in maize and sunflower can only be concluded once recently submitted data is evaluated. The risk to earthworm and fish eating birds and mammals from the representative uses with the FS formulation can not be concluded due to still open questions regarding the calculation of PEC in surface water and soil.
- Based on the available provisional PECsw values a high acute and long term risk to aquatic organisms was identified from fipronil and a long term risk to aquatic invertebrates from MB 46136 for the representative use as a seed treatment in maize. There is an outstanding data requirement in the section on fate and behaviour for a recalculation of the PECsw values. The risk to aquatic organisms from the representative uses with the FS formulation can not be concluded as long as the recalculated PECsw values are not available. The EFSA would like to refer to the opinion of the PPR Panel regarding the reduction of the uncertainty due to the availability of several single species studies and proposes to take this opinion into account at MS-level to refine this risk.
- The risk to bees can only be concluded once recently submitted data on the risk to bee brood are evaluated.
- The risk to soil non-target macro- and micro-organisms from the representative uses with the FS formulation can not be concluded due to still open questions regarding the calculation of PECsoil.
- A high risk to NTA was identified in the laboratory. Data to address these risks is still awaited. The risk to NTA from the use of fipronil as a seed treatment in maize and sunflower can only be concluded once recently submitted studies on *A. bilineata* and *F.* candida are evaluated and the open questions for the calculation of PECsoil have been solved

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

(Abbreviations used in this list are explained in appendix 2, explanations of compound codes are listed in appendix 3)

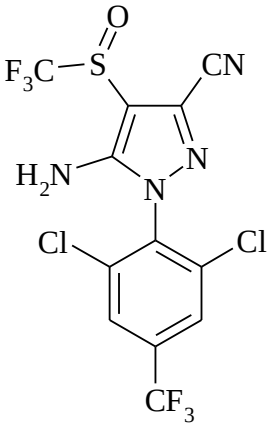
Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Fipronil
Function (e.g. fungicide)	Insecticide, acaricide
Rapporteur Member State	France

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(±)-5-amino-1-(2,6-dichloro-α,α,α-trifluoro-para-tolyl)-4-trifluoromethylsulfinyl-pyrazole-3-carbonitrile
Chemical name (CA) ‡	5-amino-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(1*R*,*S*)- (trifluoromethyl)sulfinyl]-1*H*-pyrazole-3-carbonitrile
CIPAC No ‡	581
CAS No ‡	120068-37-3
EEC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification ‡ (including year of publication)	950 g/kg ±25 g/kg [581/TC/S/F (1998)]
Minimum purity of the active substance as manufactured ‡ (g/kg)	950 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	none
Molecular formula ‡	$C_{12}H_4Cl_2F_6N_4OS$
Molecular mass ‡	437.15

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

Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	203 °C (99.3%)
Boiling point (state purity) ‡	No boiling point before decomposition
Temperature of decomposition	230 °C (99.3 %)
Appearance (state purity) ‡	White Powder (96.6% and 97.4 %)
Relative density (state purity) ‡	1.705 (99.4%)
Surface tension	72.5 mN/m at 20°C (96.2%) (2 mg/L)
Vapour pressure (in Pa, state temperature) ‡	$2x10^{-6}$ at 25°C; $3.5x10^{-5}$ at 50 °C (99.4%)
Henry's law constant (Pa m^3 mol^{-1}) ‡	2.31 10^{-4} Pa m^3 mol^{-1} at 25 °C
Solubility in water ‡ (g/l or mg/l, state temperature)	pH 6.58: 3.78 mg/l, 20°C (99.4%)
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	Purity: 96.7% Hexane: 28 mg/ L Acetone: 545.9 g/ L Toluene: 3 g/ L Ethyl acetate: 264.9 g/ L Methylene chloride: 22.3 g/L 1-Octanol: 12.2 g/L Methanol: 137.5 g/L
Partition co-efficient (log POW) ‡ (state pH and temperature)	log Pow: 3.5-4.0 at 20 °C (99.3% – 99.9%) pH:not studied as fipronil is not ionisable in water
Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	Stable at 25 °C, pH 5 Stable at 25 °C, pH 7 DT_{50} 28 days at 25 °C, pH 9
Dissociation constant ‡	No dissociation constant determinable

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

UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	ε = 48385 L/mol ∗ cm (λ = 203 nm) ε = 7281 L/mol ∗ cm (λ = 286 nm) Molar extinction coefficient at a wavelength above 290 nm: ε = 6008 L/mol ∗ cm (λ = 291 nm)
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	0.33 day (pH 5, 25 °C)
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	1.99 x 10^{-1} mole/Einstein
Flammability ‡	Not highly flammable
Explosive properties ‡	Fipronil does not present a danger of explosion and has no oxidizing properties (96.1% and 96.2%)

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

List of representative uses evaluated* (fipronil)

Crop and/or situation	Member State or Country	Product Name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
					Type	Conc. of a.s.	method, kind	growth stage & season	number (range)	interval between applications (minimum)	kg a.s./hl (range)	water l/ha (range)	kg a.s./ha (range)		
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)					(l)	(m)
Use Pattern: Seed treatment															
Sunflower	SP S FR N/S IT S	EXP80415 A	F	Soil insects and wireworms	FS	500g/l	Seed dressing	BBCH 00	1	-			0.015-0.030	140 Days	0.25-0.5 kg as/100kg seeds 6kg seeds/ha=1UU=75000 grains [1] [2]
Maize	GR S IT S SP S FR N/S NL/BLG N	EXP80415 A	F	Soil insects and wireworms	FS	500g/l	Seed dressing	BBCH 00	1	-			0.045-0.05	80-120 (silage) 120-140D (S) 150-180 D (N)	0.25kg as/100kg seeds 18-20 kg seeds /ha (GR-SP:20kg seeds /ha) (BLG: 40.8g/50000 seeds) (Swiss: 50 g/100 Kg seeds 18-30kg/seeds /ha) [1] [2]
Use Pattern: Soil application, band application & incorporation at sowing / planting															
Maize	SP S FR N/S NL/BLG N	EXP60720 A	F	Soil insects and wireworms	WG	800 g/kg	In furrow spraying at drilling, incorporated	At drilling S in March or in June as 2nd crop-N in May	1		0.02-0.05	200-500	0.1	#	#Silage at BBCH 73; #Harvest at BBCH 79-87 [3]

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

Crop and/or situation	Member State or Country	Product Name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
					Type	Conc. of a.s.	method, kind	growth stage & season	number (range)	interval between applications (minimum)	kg a.s./hl (range)	water l/ha (range)	kg a.s./ha (range)		
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)					(l)	(m)
Use Pattern: Bait application (in furrow)															
Maize	FR N/S IT S ESP S POR	EXP61840 A	F	Soil insects and wireworms	GB	0.5%	in furrow application at drilling incorporated	At drilling	1			N/A	0.025		Silage at BBCH 73-75 Harvest BBCH 87-89 (grain) [3]

[1] The risk assessment was not completed since data gaps have been revealed in sections 4 and 5.
[2] The risk assessment has revealed a risk (exceedance of relevant threshold) in section 5.
[3] The risk assessment was not completed since the new applicant does not support this use for the review at EU level.

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

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

Appendix 1.2: Methods of Analysis

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

Technical as (principle of method)	HPLC / UV
Impurities in technical as (principle of method)	HPLC / UV
Plant protection product (principle of method)	HPLC / UV

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 or MSD; Analyte: fipronil MB 46136, MB 45950, MB 46513 LOQ = 0.002 mg/kg in Maize, peach, potato, bean, sunflower seeds (for each analyte), Additonal data with LOQ = 0.001-0.002 mg/kg in banana, sugar beet, wheat and rice commodities
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	GC / ECD or MSD; Analyte: fipronil MB 46136, MB 45950, MB 46513 LOQ = 0.002 mg/kg in in bovine (muscle, milk, fat), poultry muscle and fat, chicken eggs (for each analyte)
Soil (principle of method and LOQ)	GC / ECD or MSD; LOQ = 0.002 mg/kg (for each analyte) Analyte: fipronil MB 46136, MB 45950, MB 46513 A LC-MS-MS method is available for the metabolite RPA 200766 but it has not been evaluated or peer reviewed.
Water (principle of method and LOQ)	GC / ECD or MSD; LOQ = 0.004 µg/L (drinking water and surface water) for fipronil and metabolites (MB 45950, MB 46513). For metabolite MB 46136, LOQ = 0.004 µg/L in drinking water and 0.04 µg/L in surface water. No sufficiently validated methods are available for the metabolite RPA 200766 (surface and drinking water).
Air (principle of method and LOQ)	GC / ECD; LOQ = 50 ng/m^3 (fipronil)
Body fluids and tissues (principle of method and LOQ)	GC / ECD; LOQ = 1 ng/ml in blood plasma (fipronil)

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	No classification

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapid and extensive at 4mg/kg (blood Tmax @ *ca* 5.5 h, >80% absorbed based on urinary and biliary excretion and tissue concentration), slower at higher dose level
Distribution ‡	Widely distributed in the tissues with predominance in fatty tissues.
Potential for accumulation ‡	Log P = 3.5-4 ; Terminal elimination half-lives of *ca* 183 h (male rat) and 245 h (female rat) Fat:blood 20:1 at high dose and ~70-90:1 at low dose.
Rate and extent of excretion ‡	After low dose: via faeces: 46-61% in 7 days; via urine: <6-16% in 7 days; via bile: 7-18% in 72 hours.
Metabolism in animals ‡	Extensive and rapid; major residue in tissues is MB 46136 (sulphone derivative)
Toxicologically significant compounds ‡ (animals, plants and environment)	Fipronil MB 46136, MB 45950 and MB 46513 (metabolites)

Acute toxicity (Annex IIA, point 5.2)

Rat LD50 oral ‡	92 mg/kg	**T, R25**
Rat LD50 dermal ‡	Rat: > 2000 mg/kg bw Rabbit: 354 mg/kg	 **T, R24**
Rat LC50 inhalation ‡	0.36 mg/L	**T, R23**
Skin irritation ‡	Not irritant	
Eye irritation ‡	Not irritant	
Skin sensitization ‡ (test method used and result)	Not a sensitiser (M&K, Buehler)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Neurotoxicity with clinical signs (all species tested), liver and thyroid (rats)
Lowest relevant oral NOAEL / NOEL ‡	Overall 0.35 mg/kg/day in 90-day rat and 90-day/1-year study in dogs
Lowest relevant dermal NOAEL / NOEL ‡	5 mg/kg bw/day (21-d rabbit study)
Lowest relevant inhalation NOAEL / NOEL ‡	Not determined

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

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	No genotoxic potential

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

Target/critical effect ‡	Neurotoxicity with clinical signs / Liver (rats and mice).
Lowest relevant NOAEL / NOEL ‡	0.02 mg/kg bw/day (2-y rat study)
Carcinogenicity ‡	The induction of thyroid follicular cell tumors at high dose levels is specific to the rat and not considered to be relevant to humans.

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Delayed development and clinical signs of neurotoxicity in the presence of significant parental toxicity. Reductions in mating performance and litter size.
Lowest relevant reproductive NOAEL / NOEL ‡	Parental: 0.25 mg/kg bw/day Developmental: 2.53 mg/kg bw/day
Developmental target / critical effect ‡	No evidence of developmental toxicity. Reduced maternal body weight gain.
Lowest relevant developmental NOAEL / NOEL ‡	Maternal: rabbit: 0.2 mg/kg bw/day Developmental: rabbit: 1.0 mg/kg/day (highest dose tested)

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

.....	• Acute oral NOEL in rats = 2.5 mg/kg bw (reduced hind limb leg splay) • Subchronic oral in rats: - neurotoxic NOEL 8.9 mg/kg bw/day (highest dose tested) - systemic NOAEL 0.3 mg/kg bw/day (reduced body weight gain) • Developmental neurotoxicity in rats: - neurotoxic NOEL (maternal, offspring) 0.9 mg/kg bw/day - systemic NOEL 0.05 mg/kg bw/day (body weight changes in the offspring)

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

Other toxicological studies ‡ (Annex IIA, point 5.8)

Mechanistic studies	Fipronil increases the clearance of thyroid hormones. The mechanism of thyroid toxicity is a threshold effect specific to the rat.

Toxicity of metabolites

MB 45950

Rat LD_{50} oral	69 mg/kg bw
Rat LD_{50} dermal	> 500 < 4000 mg/kg bw
Skin irritation	Not irritant
Eye irritation	Not irritant
Oral 28-day toxicity dog	Critical effect: body weight/ food consumption NOEL: 1 mg/kg bw/day
Oral 90-day toxicity rat	Target: thyroid. NOEL = 0.69 mg/kg bw/day (M)
Genotoxicity	No mutagenic activity

MB 46136

Rat LD_{50} oral	184 mg/kg bw
Rat LD_{50} dermal	> 2000 mg/kg bw
Skin irritation	Not irritant
Eye irritation	Not irritant
Genotoxicity	No mutagenic activity

MB 46513

Rat LD_{50} oral	15 mg/kg bw
Rat LD_{50} dermal	> 2000 mg/kg bw
Skin irritation	Not irritant
Eye irritation	Not irritant
Oral 28-day toxicity	Critical effect: neurotoxicity Rat: NOEL: 0.23 mg/kg bw/day (M) Dog: NOEL > 1 mg/kg bw/day
Oral 90 -day toxicity	Critical effect: neurotoxicity (rat, dog), liver (mouse) Rat: NOEL = 0.177 mg/kg bw/day (M) Dog: NOEL = 0.27 mg/kg bw/day (M) Mouse: NOEL = 0.32 mg/kg bw/day (M)
Genotoxicity	No mutagenic activity (in vitro-in vivo)

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

Carcinogenicity (rat)	Critical effect: Neurotoxicity NOEL 0.025 mg/kg bw/day (M)
Reproductive toxicity (rat)	Maternal toxicity: NOEL 0.2 mg/kg bw/day Developmental toxicity: NOEL 1 mg/kg bw/day
Acute oral Neurotoxicity	Rat: NOEL 2 mg/kg bw.

RPA 200766

Rat LD50 oral	> 2000 mg/kg bw
Oral 28-day toxicity	Critical effect: liver, adrenals Rat: NOAEL 3.8 mg/kg bw/day
Genotoxicity	No mutagenic activity (in vitro/in vivo)

RPA 200761

Rat LD_{50} oral	> 2000 mg/kg bw
Genotoxicity	Negative in vitro

Medical data ‡ (Annex IIA, point 5.9)

.....	No known human intoxications during production, transportation, formulation and packaging. Reports of suicidal attempts involving fipronil intake include one death preceded by severe neurological symptoms and further non-lethal cases with general and neurological clinical signs.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.0002 mg/kg bw/day	Long term study in rats	100
AOEL ‡	0.0035 mg/kg bw/day	90-d oral study in rat and 90-d/1-y dog	100
ARfD ‡ (acute reference dose)	0.009 mg/kg bw	Developmental neurotoxicity study in rats	100

Dermal absorption (Annex IIIA, point 7.3)

SC formulation (equivalent to FS formulation)	1% for concentrate and 11% for dilution from in vitro human and rat

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

Acceptable exposure scenarios (including method of calculation)

formulated product EXP80415A (FS formulation)

Operator	Based on a specific operator exposure study, exposure is 63% of the AOEL with PPE.
Workers	Exposure is 89% of AOEL in the absence of gloves (Seed Tropex model, 8h exposure)
Bystanders	Bystander exposure is not likely to be an issue for seed treatment. However, for maize and sunflower exposure exposure may occur, depending on the sowing technology used. This issue is to be addressed at a Member State level.

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T;	toxic
	R 23/24/25	Toxic by inhalation, in contact with skin and if swallowed
	R 48/25	Toxic, danger of serious damage to health by prolonged exposure if swallowed

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

Appendix 1.4: Residues

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

Plant groups covered	Cereals (maize, wheat) pulses/oilseed (sunfllower, cotton) root/tuber (sugarbeet)
Rotational crops	Lettuce, radish, carrot, sorghum and wheat
Plant residue definition for monitoring	Fipronil and its metabolite sulfone MB 46136 expressed as fipronil (definition valid for seed treatment use only)
Plant residue definition for risk assessment	Fipronil and its metabolite sulfone MB 46136 expressed as fipronil (definition valid for seed treatment use only)
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	Dairy goats and laying hens
Animal residue definition for monitoring	Fipronil and its metabolite sulfone MB 46136 expressed as fipronil
Animal residue definition for risk assessment	Fipronil and its metabolite sulfone MB 46136 expressed as fipronil
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes: Log P_{ow} = 3.5 - 4.0 for fipronil Log P_{ow} = 3.8 for sulfone (MB 46136)

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

.....	Residues of concern in succeeding crop and following seed treatment uses only: fipronil and sulfone metabolite MB 46136. Following seed treatment uses, residues are not expected to be significant in succeeding crops.

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

Maize (grain, forage, fodder, silage) and processed fractions (oil, meal, starch)	Residues of fipronil and metabolites including MB 46136 stable up to 12 months at about –10°C.

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

Cotton seed and processed fractions (hull, meal, crude oil, refined oil)	Residues of fipronil and metabolites including MB 46136 stable up to 12 months at about –20°C.
Potato	Residues of fipronil and metabolites including MB 46136 stable up to 24 months at –20°C.
Lettuce	Residues of fipronil and metabolites including MB 46136 stable up to 12 months at –20°C.
Beef: milk, liver, kidney, muscle, fat Poultry: egg, liver, muscle, skin with fat	Residues of fipronil and metabolites including MB 46136 stable up to 3 months at –10°C.

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: no[#]	Poultry: no[#]	Pig: no[#]
Muscle	0.005*	0.005*	0.005*
Liver	0.005*	0.005*	0.005*
Kidney	0.005*	0.005*	0.005*
Fat	0.010	0.010	0.010
Milk (whole)	0.002		
Milk fat	0.010		
Eggs		0.010	

Estimated daily dietary burden, 0.0029, 0.0029, 0.0019 and 0.0018 mg/kg DM/day for the dairy, beef cattles, poultry and pig, respectively.
* LOQ

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

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)		Recommendation/comments	MRL (mg/kg)	STMR (b)
Maize grain	2 N/12 S	Seed treatment (cGAP: 50 g/ha) Representative Use	50 g/ha: 5x <0.004 mg/kg 75 g/ha: 6x <0.004 mg/kg 300 g/ha 3x <0.010 mg/kg Residue expressed as "sum fipronil+sulfone".	Aditional data: - Spray application: 188-200 g/ha: 14x <0.004; 1x 0.005 mg - Granule application: 153-200 g/ha 4x <0.004 mg/kg 240-420 g/ha 4x <0.004 mg/kg	0.005* maize grain and sweet corn	0.002
Maize silage	3 N/4 S	Seed treatment (cGAP: 50 g/ha) Representative Use	50 g/ha: 4x <0.0010, 0.0011, 0.0018 and 0.0044 mg/kg	Additional data over a second growing season requested	/	0.001
Sunflower	3 N/6 S	Seed treatment (cGAP: 30 g/ha) Representative Use	22.5 g/ha: 6x <0.004 mg/kg 60 g/ha: 3x <0.004 mg/kg	Aditional data: - Seed treatment 90 g/ha: 3x <0.020 mg/kg - Granule application: 206 g/ha 1x <0.020 mg/kg	0.005*	0.002

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

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

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

ADI	0.0002 mg/kg bw/day
TMDI (European Diet) (% ADI)	WHO/FAO: 20% (adult) UK/PSD: 22% (adult), 125% (infant), 81% (toddler) French: 24% (adult), 136% (infant), 124% (toddler)
IEDI (% ADI)	WHO/FAO: 3% (adult) UK/PSD: 3% (adult), 17% (infant), 12% (toddler) French: 4% (adult), 18% (infant), 18% (toddler)
Factors included in IEDI	STMR values for maize, sunflower and animal products
ARfD	0.009 mg/kg bw/day
Acute exposure (% ARfD)	Maximum NESTI: 2% (adult) and 4% (toddler) from sweet corn, calculation based on the UK/PSD 97.5th percentile consumption data.

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Maize grain into: Grit, Meal, Flour, Oil (crude/refined) and Grain dust	1	Not calculated as no residues above LOQ in grains RAC	No residues in processed fractions when residue in RAC <LOQ No transfer factor could be calculated.
Sunflower seed into: Oil and pressed cake	3		
Whole milk/fat milk	1	14	

* 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)

Maize	0.005* mg/kg
Sweet corn	0.005* mg/kg
Sunflower	0.005* mg/kg

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

Milk	0.002 mg/kg
Eggs, milk fat, animal fat	0.010 mg/kg
Muscle, liver, kidney	0.005* mg/kg

*) LOQ

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

Appendix 1.5: Fate and Behaviour in the Environment

2 representative uses evaluated: seed treatment of Sunflower (15 – 30 g/ha) and Maize (45 – 50 g/ha)

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

Mineralization after 100 days ‡	<1%AR after 149 days (2 soils, 25°C) <1%AR after 91 days (4 soils, 20°C)
Non-extractable residues after 100 days ‡	6-10%AR after 149 days (2 soils, 25°C) 4.2-10.7%AR at 91 days(4soils, 20°C)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	Major metabolites and their highest %AR levels – 6 soils Amide RPA 200766 (38.4%AR after 219 days) Sulfone MB 46136 (34.3%AR after 162 days) Sulfide MB 45950 (17%AR after 91 days-major in 1soil only)

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

Anaerobic degradation ‡	MB 45950 (36.5% after 365 days)
Soil photolysis ‡	Same metabolites as with biodegradation but in smaller amounts and desulfinyl MB 46513 (6.9% after 30 days.

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

Method of calculation	First order kinetics - linear
Laboratory studies ‡ (range or median, with n value, with r2 value) mean, arithmetic (if not specified), or geometric‡	DT_{50lab} (20°C, aerobic): ‡ Fipronil: 32-346 days (6 soils, r^2 0.80-0.98) mean 142 d (geom.) Metabolites: study performed at 27 °C (3 soils) ; values normalized at 20°C - pF2, are reported. MB 46136: 265.3, 373.9, 422.0 d (r^2 0.57 – 0.88) mean 347.2 d(geo) MB 45950: 127.8, 277.7, 337.3 d (r^2 0.68 – 0.79) mean 229 d(geo) RPA 200766: 160.4, 171.8, 213.6 d mean 180.6 d(geo) RPA 200761: 65.4, 71.4, 207.8 d mean 99 d(geo) MB 46513: 66.6, 131.8 d, 146.8 d mean 108.7 (geo) (r^2 0.91 – 0.98)
	DT_{90lab} (20°C, aerobic): ‡ Due to the slow degradation, could only be extrapolated.(for fipronil and metabolites)

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

	DT_{50lab} (10°C, aerobic): ‡ 515-747 days – 2 soils, R^2 0.5-0.73
	DT_{50lab} (25°C, anaerobic): ‡ Fipronil 166 days – 1 soil, R^2 0.99
	DT_{50lab} (25°C, photodegradation): 34 days
degradation in the saturated zone: ‡ Not available	
Field studies ‡ (state location, range or median with n value)	DT_{50f}: ‡ Estimation without normalization 4 sites (2 France, 1 Italy, 1 Spain) – in furrow application, 2 year study: Fipronil: 96-135 days without normalization (linear 1st order). Total residues 195-342 days; indicates slower degradation of the metabolites. 2 sites (Italy, Spain)-surface application, 18 months study, product exposed to photolysis DT_{50} fipronil: 5.6-22.2 d Estimation with normalization (20 ºC, pF2)-Overall geomean. ▪In furrow application at 4 sites in Europe (24 months) and 4 sites in USA (18 months): Normalised values (20°C, pF2) (PERSIST) – "scaling procedure" proposed by NOT to reduce the heterogeneity - SFO + ModelMaker. In ( ), number of estimated values. ▪Broadcast application on soil and immediate incorporation at 1 site, Kortenaken, north EU (34 months): SFO + ModelMaker ; no scaling Fipronil: 33 – 120 d (9 values) mean 70 (geo) Metabolites: MB 46136: 147–430 d (6) mean 266 d (geo) MB 45950: 82–264 d (3) mean 134 d(geo) RPA 200766: 167–266 d (5) mean 221 d (geo)
	DT_{90f}: ‡ same 4 sites in furrow application Fipronil 10.5-14.8 months. Accumulation studies in the field are required.

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

Soil accumulation and plateau concentration ‡	Experiments in progress, at 4 sites: Belgium, France north, 2 Europe south. Final report after 6 years summarized in addendum. Broadcast application and immediate incorporation (5 to 6 years study): significant amounts of MB 46136 and RPA 200766 are formed. Problem of variability of experimental results, to be further assessed.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	5 soils, pH 5.6-8.2, OC 0.5-4.9%, batch sorption data. Freundlich isotherms calculated → Kfoc values (l/kg): Fipronil: 427-1248 (mean 727, 1/n 0.94-0.97) RPA 200766: 96-203 (mean 167, 1/n 0.89-0.94) MB 46136: 1448-6745 (mean 4209, 1/n 0.94-1.14) MB 45950: 1695-5621 (mean 3911, 1/n 0.93-1.04) MB 46513: 1150- 1498(mean 1290, 1/n 0.92-0.94) No pH dependance

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

Column leaching ‡	5 soils (pH 6.1-6.9, OC 0.3-4.3%). Elution with 508 mm calcium chloride, over a period of 2-7 days. <1% AR recovered in the leachates, except for 1 soil with 4.3% AR; no radiochemical analysis of the leachate. Most of AR in the top 6 cm layer.
Aged residues leaching ‡	Same 5 soils, 35 day aged columns at 22°C. <3.5% AR recovered in the leachate; no radiochemical analysis of the leachate. Most of the AR in the top 12 cm layer; minor amounts of RPA 200766, MB 46136, MB 45950 in soil segments.
Lysimeter/ field leaching studies ‡	Not available ; not required

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

PEC (soil) (Annex IIIA, point 9.1.3)

This PECs soil are only maintained for illustrative purposes. New calculations are required with appropriate input parameters. Worst case fipronil half life has not been used in these calculations.

May 2005

Method of calculation	PECini is estimated in the furrows, for fipronil and metabolites considering the accumulation plateau+single application. PEC at the plateau concentration (plateau min), assuming that the soil is mixed in the upper 20 cm soil layer.
Application rate	2 uses evaluated: - Maize: 50 g/ha - treated seed applied in furrows (10 cm deep and 5 cm wide) distant from 75 cm, corresponding to 6.3% of the plot area. - Sunflower: 30 g/ha – treated seed in furrows (10 cm deep and 5 cm wide) distant from 45 cm, corresponding to 10% of the plot area.

Degradation rate constants and DT_{50} values (standardized 20°C, pF2)used in the calculations

		Fipronil		MB 46136		MB 45950		RPA 200766	
		k_{ij}ref [1/d]	DT_{50} [d]	k_{ij}ref [1/d]	DT_{50} [d]	k_{ij}ref [1/d]	DT_{50} [d]	k_{ij}ref [1/d]	DT_{50} [d]
North EU	Arras	0.0170	40.8	0.0030	231.0	0.0026	266.6	0.0027	256.7
	Kortenaken	0.0146	47.5						
South EU	Saulce	0.0146	47.5						
	Bologna	0.0223	31.1						

Formation fractions of metabolites used in the calculations

Field site		MB 46136	MB 45950	RPA 20076
North EU	Arras	0.65	0.11	0.24
	Kortenaken	0.64	0.08	0.28
South EU	Saulce	0.67	0.09	0.23
	Bologna	0.45 (1)	0.06 (1)	0.22 (1)

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

PEC ini (mg/kg) in the furrows (higher concentration after a single application)

Site		Fipronil		MB 46136		MB 45950		RPA 200766	
		Maize	Sunflower	Maize	Sunflower	Maize	Sunflower	Maize	Sunflower
		$PEC_{s,ini}$ [mg/kg]							
North EU	Arras	0.500	0.180	0.337	0.121	0.053	0.019	0.125	0.045
	Kortenaken	0.500	0.180	0.332	0.119	0.039	0.014	0.146	0.052
South EU	Saulce	0.500	0.180	0.347	0.125	0.043	0.016	0.120	0.043
	Bologna	0.500	0.180	0.238	0.086	0.029	0.010	0.115	0.041

PEC plateau mini (mg/kg) –soil and residues mixed on 20 cm depth,; homogenization in the whole field.

Site		Fipronil		MB 46136		MB 45950		RPA 200766	
		Maize	Sunflower	Maize	Sunflower	Maize	Sunflower	Maize	Sunflower
		$PEC_{s,ini}$ [mg/kg]							
North EU	Arras	0.001	0.001	0.018	0.011	0.004	0.002	0.008	0.005
	Kortenaken	0.001	0.001	0.017	0.010	0.003	0.002	0.008	0.005
South EU	Saulce	0.000	0.000	0.011	0.007	0.002	0.001	0.004	0.003
	Bologna	0.000	0.000	0.007	0.004	0.001	0.001	0.004	0.002

Note: PEC max are obtained by adding the corresponding PEC plateau mini to the PEC ini.

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)	pH_5_: Fipronil and metabolites are stable pH_7_: Fipronil and metabolites are stable pH_9_: Degradation is observed (DT_{50}, metabolite formed) for fipronil (28 days, RPA 200766), MB 46136 (50 days, RPA 105320), MB 46513 (10.9 days, MB 46400), for MB 45950 (slow degradation at 25°C – estimated DT_{50} at 50°C 11days, MB 46126)
Photolytic degradation of active substance and relevant metabolites ‡	Fipronil and metabolites are rapidly photodegraded (DT_{50} in hours of artificial irradiation) – fipronil (3.6 h), MB 46136 (13 h), MB 46513 (38.9 h), MB 45950 (3.6 h).
Readily biodegradable (yes/no)	No

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

Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	5 water/sediment systems (pH 5.8-8.2, OC0.4-3.2%) – linear 1st order. DT_{50} water:14.2-93.6 days DT_{50} whole system:16.4-119.6 days
Mineralization	<1%AR after 93 or 112 days
Non-extractable residues	2.1-4.3%AR after 93 or 112 days
Distribution in water / sediment systems (active substance) ‡	Fipronil: max and final concentration in 4 sediments Max. 16.4%AR after 7 d (n d at 121 d study end) Max. 40.7% AR after 14 d (11.4% at 121 d study end) Max. 18.1% AR at 17 d (8.6% at 244 d study end) Max. 31.1 at 10 d (11.3 at 112 d) The dissipation of fipronil from water is rather fast ; fipronil is adsorbed on the sediment and degraded to MB 45950, which degrades slowly ; DT_{50} of MB 45950 estimated with TopFit2.0: 50.2-78.8 d in whole system
Distribution in water / sediment systems (metabolites) ‡	Metabolites of fipronil in water/sediment systems, maximum amount: -RPA 200766: 20% in water at 244 d, 11% in sediment at 60 d. -MB 45950: 8.9% in water at 93 d, 80% in sediment at 120 d. MB 46136: 2.3% in water at 244 d, 4.9% in sediment at 244 d. 1 study for MB 46513 – 2 sediments MB 46513 dissipates from water (DT_{50} 4.2-9.9days), it is adsorbed on the sediment (max. 57.4 and 69.5%AR at 125d) and is slowly degraded: 61% AR remaining in the whole system at 365 d study end.

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

This PECs surface water are only maintained for illustrative purposes. New calculations are required with appropriate input parameters

PECsw estimated according to FOCUS surface water group recommendations.
Drainage and runoff considered. No spray drift (treated seeds incorporated in the soil).

Step 1, 2 and 3 calculations for fipronil, MB 46136, MB 45950, RPA 200766.

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

Values of compound parameters for calculations in step 2, 3

Parameters	Fipronil	MB 46136	MB 45950	RPA 20766
MW (g/mol)	437.2	453.2	421.2	455.2
Water solubility (mg/L)	2.3	0.16	1.1	16.4
Formation fraction	-	0.57	0.13	0.3
DT_{50} soil (d) (1)	76	231	264	259
DT_{50} water (d)	32.8	1000	2.1	1000
DT_{50} sediment (d)	76	1000	1000	1000
Mean Koc	727	4209	3911	167
1/n	0.95	1.0	0.98	0.91

(1) normalised to 20°C and FC ; mean field values for fipronil ; values from Kortenaken (broadcast application + incorporation) field dissipation study for Fipronil metabolites

1) Maize 50g/ha once a year

PECsw max for Maize

FOCUS Step / Location	Type of water body	Fipronil [µg/L]	MB 46136 [µg/L]	MB 45950 [µg/L]	RPA 200766 [µg/L]
Step 1	Static 30 cm	8.463	1.489	0.336	4.258
Step 2 / North	Static 30 cm	1.632	0.294	0.067	0.843
Step 2 / South	Static 30 cm	3.264	0.589	0.133	1.685
Step 3 / D3	Ditch	<0.00001	<0.00001	<0.00001	0.017
Step 3 / D4	Pond	0.00077	0.00026	0.00007	0.093
	Stream	0.00300	0.00092	0.00035	0.096
Step 3 / D5	Pond	0.00039	0.00031	0.00003	0.019
	Stream	0.00106	0.00060	0.00011	0.023
Step 3 / D6	Ditch	0.00066	0.00088	0.00017	0.018
Step 3 / R1	Stream	< 0.0001	< 0.0001	< 0.0001	< 0.0001
	Pond	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Step 3 / R2	Stream	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Step 3 / R3	Stream	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Step 3 / R4	Stream	< 0.0001	< 0.0001	< 0.0001	< 0.0001

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

PECsw (fipronil) at different times in drainage scenario D4 and D5 - Maize

	D4				D5			
Days (after Global max)	Pond		Stream		Pond		Stream	
	PEC_{sw} [µg/L]		PEC_{sw} [µg/L]		PEC_{sw} [µg/L]		PEC_{sw} [µg/L]	
	Actual	Max TWA	Actual	Max TWA	Actual	Max TWA	Actual	Max TWA
Global max	0.001		0.003		0.000		0.001	
1	0.001	0.001	0.000	0.001	0.000	0.000	0.001	0.001
2	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.000
4	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.000
7	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.000
14	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.000
21	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.000
28	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000
42	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000
50	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000
100	0.000	0.001	0.000	0.000	*	0.000	0.000	0.000

2) Sunflower 30g/ha once a year

PECsw max for Sunflower

FOCUS Step / Location	Type of water body	Fipronil [µg/L]	MB 46136 [µg/L]	MB 45950 [µg/L]	RPA 200766 [µg/L]
Step 1	Static 30 cm	5.0779	0.8936	0.2015	2.5547
Step 2 / North	Static 30 cm	0.9792	0.1766	0.0399	0.5055
Step 2 / South	Static 30 cm	1.9584	0.3532	0.0798	1.0110
Step 3 / D5	pond	0.00021	0.00017	0.00002	0.012
	stream	0.00057	0.00035	0.00006	0.012
Step 3 / R1	stream	<0.00001	<0.00001	<0.00001	<0.00001
	pond	<0.00001	<0.00001	<0.00001	<0.00001
Step 3 / R3	stream	<0.00001	<0.00001	<0.00001	<0.00001
Step 3 / R4	stream	<0.00001	<0.00001	<0.00001	<0.00001

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

PECsw (fipronil and RPA 200766) at different times in drainage scenario D5 - Sunflower

	BAS 350 I - Fipronil				RPA 200766			
Days (after Global max)	Pond		Pond		Pond		Pond	
	PEC_{sw} [µg/L]		PEC_{sw} [µg/L]		PEC_{sw} [µg/L]		PEC_{sw} [µg/L]	
	Actual	Max TWA	Actual	Max TWA	Actual	Max TWA	Actual	Max TWA
Global max	< 0.001 (0.00021)		0.001 (0.00057)		0.012		0.012	
1	< 0.001	< 0.001	< 0.001	< 0.001	0.012	0.012	0.010	0.009
2	< 0.001	< 0.001	< 0.001	< 0.001	0.012	0.012	0.008	0.008
4	< 0.001	< 0.001	< 0.001	< 0.001	0.012	0.012	0.005	0.008
7	< 0.001	< 0.001	< 0.001	< 0.001	0.011	0.012	0.003	0.007
14	< 0.001	< 0.001	< 0.001	< 0.001	0.011	0.011	0.002	0.005
21	< 0.001	< 0.001	< 0.001	< 0.001	0.011	0.011	0.001	0.004
28	< 0.001	< 0.001	< 0.001	< 0.001	0.01	0.011	0.001	0.004
42	< 0.001	< 0.001	< 0.001	< 0.001	0.01	0.011	0.002	0.003
50	< 0.001	< 0.001	< 0.001	< 0.001	0.009	0.011	0.002	0.003
100	< 0.001	< 0.001	< 0.001	< 0.001	*	0.009	*	0.002

PEC (sediment)

Parent, Metabolite

May 2005

PECsediment max for Maize

FOCUS Step / Location	Type of water body	Fipronil [µg/kg]	MB 46136 [µg/kg]	MB 45950 [µg/kg]	RPA 200766 [µg/kg]
Step 1	Static 30 cm	61.527	62.687	13.136	7.111
Step 2 / North	Static 30 cm	11.865	12.388	2.600	1.407
Step 2 / South	Static 30 cm	23.729	24.776	5.200	2.8139
Step 3 / D3	ditch	<0.001	<0.001	<0.001	0.139
Step 3 / D4	pond	0.005	0.003	<0.001	0.448
	stream	0.002	0.001	<0.001	0.166
Step 3 / D5	pond	0.002	0.004	<0.001	0.084
	stream	0.001	0.001	<0.001	0.039
Step 3 / D6	ditch	0.001	0.001	<0.001	0.014

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

FOCUS Step / Location	Type of water body	Fipronil [µg/kg]	MB 46136 [µg/kg]	MB 45950 [µg/kg]	RPA 200766 [µg/kg]
Step 3 / R1	stream	< 0.001	< 0.001	< 0.001	< 0.001
	pond	< 0.001	< 0.001	< 0.001	< 0.001
Step 3 / R2	stream	< 0.001	< 0.001	< 0.001	< 0.001
Step 3 / R3	stream	< 0.001	< 0.001	< 0.001	< 0.001
Step 3 / R4	stream	< 0.001	< 0.001	< 0.001	< 0.001

PECsediment max for Sunflower

FOCUS Step / Location	Type of water body	Fipronil [µg/kg]	MB 46136 [µg/kg]	MB 45950 [µg/kg]	RPA 200766 [µg/kg]
Step 1	Static 30 cm	36.916	37.612	7.882	4.266
Step 2 / North	Static 30 cm	7.119	7.433	1.560	0.844
Step 2 / South	Static 30 cm	14.237	14.865	3.120	1.688
Step 3 / D5	pond	0.001	0.002	<0.001	0.062
	stream	< 0.001	0.001	<0.001	0.015
Step 3 / R1	stream	< 0.001	< 0.001	< 0.001	< 0.001
	pond	< 0.001	< 0.001	< 0.001	< 0.001
Step 3 / R3	stream	< 0.001	< 0.001	< 0.001	< 0.001
Step 3 / R4	stream	< 0.001	< 0.001	< 0.001	< 0.001

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

These PEC ground water are only maintained for illustrative purposes. New calculations are required with appropriate input parameters

May 2005

Simulation of PECgw with FOCUS-PELMO 3.3.2 – Application to maize (50 g/ha).

Values of parameters used for simulations.

	DT_{50} (1) (days)	Koc (2)	1/n (2)	Formation fraction
Fipronil	76	727	0.95	
MB 46136	231	4209	1.0	0.57
MB 45950	264	3911	0.13	0.13

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

	DT_{50} [1] (days)	Koc [2]	1/n [2]	Formation fraction
RPA 200766	259	167	0.3	0.3

[1] normalised to 20°C and FC ; mean field values for fipronil ; values from Kortenaken field dissipation study for Fipronil metabolites.
[2] mean value

80th percentile annual concentration of fipronil and its metabolites

Scenario	BAS 350 I fipronil [µg/L]	Metabolite MB 46136 [µg/L]	Metabolite MB 45950 [µg/L]	Metabolite RPA 200766 [µg/L]
Châteaudun	<0.001	<0.001	<0.001	0.186
Hamburg	<0.001	<0.001	<0.001	0.378
Kremsmünster	<0.001	<0.001	<0.001	0.206
Okehampton	<0.001	<0.001	<0.001	0.281
Piacenza	<0.001	<0.001	<0.001	0.527
Porto	<0.001	<0.001	<0.001	0.002
Sevilla	<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 measured, not required
Quantum yield of direct phototransformation	Not measured, not required
Photochemical oxidative degradation in air ‡	Latitude: ..... Season: ..... DT_{50} 0.11 d for 12 h of sunlight (model AOPWIN)
Volatilization ‡	from plant surfaces: ‡ Not available nor required
	from soil: ‡ Not available nor required

PEC (air)

Method of calculation	Fipronil is not expected to volatilise to any significant extent, considering its vapour pressure and the GAP. However, the emission of dust from seed coatings, at time of sowing, if pneumatic sowing equipment is used, is possible ; this risk should be assessed at Member State level.

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

PEC$_{(a)}$

Maximum concentration	Not calculate, not required.

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	**Soil** Definitions for risk assessment: fipronil, RPA 200766[25], MB 46136[26] and MB 45950[27] Definitions for monitoring: fipronil, RPA 200766, MB 46136 and MB 45950 Member States may also wish to include the soil photolysis metabolite MB 46513[28] in the monitoring definition due to its potential higher toxicity than fipronil. Only when correctly used in line with the representative uses evaluated, i.e. with efficient incorporation below the soil surface, the process of soil photolysis is precluded. **Water** **Ground water** Definitions for exposure assessment: fipronil, RPA 200766, MB 46136 and MB 45950 Definitions for monitoring: fipronil and RPA 200766. Additional metabolites could be eventually added when new modeling required is completed. **Surface water** Definitions for risk assessment: surface water: fipronil and RPA 200766 sediment: fipronil, RPA 200766 and MB 45950 Definitions for monitoring: fipronil and RPA 200766 **Air** Definitions for risk assessment: fipronil Definitions for monitoring: fipronil

[25] RPA200766: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylsulfonyl-1H-pyrazole-3-carboxamide

[26] MB46136: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-p-tolyl)-4-trifluoro-methylsulfonylpyrazole-3-carbonitrile

[27] MB45950: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylthio-1H-pyrazole-3-carbonitrile

[28] MB46513: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylpyrazole-3-carbonitrile

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

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)	France: monitoring of groundwater (wells). Trigger concentrations not exceeded, but sampling scheme is not exposed. Moreover, the history of fipronil use in the monitored regions was not clarified.
Air (indicate location and type of study)	Not available

Classification and proposed labelling (Annex IIA, point 10)

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

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

Appendix 1.6: Effects on non-target Species

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

Acute toxicity to mammals	Fipronil: LD_{50} = 92 mg/kg bw (rat, male)
Reproductive toxicity to mammals	Fipronil: NOEL = 2.53 mg/kg bw (rat, male)
Acute toxicity to birds	Fipronil: LD_{50} = 11.3 mg/kg bw (Bobwhite quail) MB 46136: LD_{50} = 41 mg/kg bw (Bobwhite quail) MB 46513: LD_{50} = 5.4 mg/kg bw (Bobwhite quail)
Dietary toxicity to birds	Fipronil: 5-d NOEL[1] = 3.77 mg/kg bw/d (Bobwhite quail) MB 46136: 5-d NOEL[1] = 7.83 mg/kg bw/d (Bobwhite quail) MB 46513: 5-d NOEL[1] = 7.12 mg/kg bw/d (Bobwhite quail) MB 45950: 5-d NOEL[1] = 6.98 mg/kg bw/d (Bobwhite quail)
Reproductive toxicity to birds	Fipronil: NOEL = 0.88 mg/kg bw/d (Bobwhite quail)

[1] endpoint based on the NOEC due to a reduced feed consumption observed at the LC_{50}

Eight avoidance studies and one cage study were considered for the treated seeds.

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

TER for the use of EXP80415A (FS 500 g/L, seed treatments) (amended)

Herbivorous birds

Exposure assessment for fipronil concerning herbivorous birds

Exposure via emerging shoots	Crop stage	Indicator species	Daily intake (fresh) related to body weight *)	Category	C [mg a.s./kg diet]	PT	PD	AV	ftwa	MAF	ETE [mg/kg b.w.]
Acute	Early	Partridge Pigeon	0.76	Seedlings / young plants	0.27	1	1	1	1	1	0.21
Short-term	Early	Partridge Pigeon	0.76	Seedlings / young plants	0.27	1	1	1	1	1	0.21
Repro-duction	Early	Partridge Pigeon	0.76	Seedlings / young plants	0.27	1	1	1	1	1	0.21

*) Daily intake (fresh) related to body weight calculated based on Crocker et al. (2002).

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

Toxicity / exposure ratios for fipronil concerning herbivorous birds (Tier 1)

Crop stage	Indicator species	Food type	TER
Acute			
Early	Partridge Pigeon	Seedlings / young plants	TER_a = 11.3 / 0.21 = 54
Short-term			
Early	Partridge Pigeon	Seedlings / young plants	TER_{st} = 3.77 / 0.21 = 18
Reproduction			
Early	Partridge Pigeon	Seedlings / young plants	TERlt = 0.88 / 0.21 = 4.0

Granivorous birds

Exposure assessment for fipronil concerning granivorous birds (Tier 1)

Scenario	Indicator species	FIR (fresh) / body weight	Food type	PD	PT	AV	Nominal seed treatment rate [mg a.s./kg]	ETE [mg a.s./kg]
Acute	Linnet	0.38	Treated maize seeds	1	1	1	2 500	950
	Linnet	0.38	Treated sunflower seeds	1	1	1	5 000	1 900
Repro-duction	Linnet	0.38	Treated maize seeds	1	1	1	2 500	950
	Linnet	0.38	Treated sunflower seeds	1	1	1	5 000	1 900

Toxicity / exposure ratios for fipronil concerning granivorous birds (Tier 1)

Scenario	Indicator species	Food type	TER
Acute	Linnet	Treated maize seeds	TER_a = 11.3 / 950 = **0.012**
		Treated sunflower seeds	TER_a = 11.3 / 1 900 = **0.006**

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

Scenario	Indicator species	Food type	TER
Short-term	Linnet	Treated maize seed	TER_{st} = 3.77 / 950 = **0.004**
		Treated sunflower seeds	TER_{st} = 3.77 / 1 900 = **0.002**
Repro-duction (note)	Linnet	Treated maize seed	$TER_{Reproduction}$ = 0.88 / 950 = **0.0009**
		Treated sunflower seeds	$TER_{Reproduction}$ = 0.88 / 1 900 = **0.0005**

Note: Meeting (EPCO 27) agreed that the risk to birds should focus on the acute and short term risk as there is no indication that fipronil is a reproductive toxin.

Worm eating birds

BIRD / MULTIRESIDUE	fipronil	MB 46136	MB 45950	RPA 200766
log Pow	4	3.8	3.7	3.4
Kow	10000	6309.57	5011.87	2511.89
foc	0.02	0.02	0.02	0.02
Mean Koc	727	4209	3911	167
BCF worm	6.94	0.76	0.65	7.77
PEC plateau min (mg/kg soil)	0.001	0.02	0.004	0.009
PEC worm (mg/kg worm)	0.007	0.015	0.003	0.070
Molecular weight ratio	1	1.036	0.963	1.041
Dietary 5 d-NOED ratio	1	2.6	2.4	(10)
PEC worm as fipronil equ. (mg/kg worm)	0.007	0.006	0.001	0.007
sum of the residues (mg/kg worm)	0.021			
RDI	1.13			
ETE worm (mg/kg bw/d)	0.024			
Long-term bird NOEL (mg/kg bw/d)	0.88			
TERlt	36.54			

Fish eating birds

BIRD / MULTIRESIDUE	fipronil	MB 46136	MB 45950	RPA 200766
log Pow	4	3.8	3.7	3.4
BCF fish	321	321	321	321
PECsw (max, mg/L)	0.00000327	0.00000092	0.00000035	0.000096

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

BIRD / MULTIRESIDUE	fipronil	MB 46136	MB 45950	RPA 200766
PEC fish (mg/kg fish)	0.001050	0.000295	0.000112	0.030816
Molecular weight ratio	1	1.036	0.963	1.041
Dietary 5 d-NOED ratio	1	2.6	2.4	10
PEC fish fipronil equ (mg/kg fish)	0.001	0.00011767	4.508E-05	0.00320795
Sum of the residues (mg/kg fish)	0.004			
RDI	0.21			
ETE fish (mg/kg bw/d)	0.001			
Long-term bird NOEL (mg/kg bw/d)	0.88			
TERlt	199			

Herbivorous mammals

Exposure assessment for fipronil concerning herbivorous mammals

Exposure via emerging shoots	Crop stage	Indicator species	Daily intake (fresh) related to body weight *)	Category	C [mg a.s./kg diet]	PT	PD	AV	ftwa	MAF	ETE [mg/kg b.w.]
Acute	Early	Vole	1.39	Seedlings / young plants	0.27	1	1	1	1	1	0.38
Repro-duction	Early	Vole	1.39	Seedlings / young plants	0.27	1	1	1	1	1	0.38

*) Daily intake (fresh) related to body weight calculated based on Crocker et al. (2002).

Toxicity / exposure ratios for fipronil concerning herbivorous mammals (Tier 1)

Crop stage	Indicator species	Food type	TER
Early	Vole	Seedlings / young plants	TER_a = 92 / 0.38 = 242
Early	Vole	Seedlings / young plants	TER_{lt} = 2.53 / 0.38 = 6.7

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

Granivorous mammals

Exposure assessment for fipronil concerning granivorous mammals (Tier 1)

Scenario	Indicator species	FIR (fresh) / body weight	Food type	PD	PT	AV	Nominal seed treatment rate [mg a.s./kg]	ETE [mg a.s./kg]
Acute	Wood mouse	0.23	Treated maize seeds	1	1	1	2 500	575
	Wood mouse	0.23	Treated sunflower seeds	1	1	1	5 000	1 150
Repro-duction	Wood mouse	0.23	Treated maize seeds	1	1	1	2 500	575
	Wood mouse	0.23	Treated sunflower seeds	1	1	1	5 000	1 150

Toxicity / exposure ratios for fipronil concerning granivorous mammals (Tier 1)

Scenario	Indicator species	Food type	TER
Acute	Wood mouse	Treated maize seeds	TER_a = 92 / 575 = **0.16**
		Treated sunflower seeds	TER_a = 92 / 1 150 = **0.08**
Repro-duction	Wood mouse	Treated maize seed	$TER_{reproduction}$ = 2.53 / 575 = **0.0044**
		Treated sunflower seeds	$TER_{reproduction}$ = 2.53 / 1 150 = **0.0022**

Worms eating mammals

MAMMALS / MULTIRESIDUE	fipronil	MB 46136	MB 45950	RPA 200766
log Pow	4	3.8	3.7	3.4
Kow	10000	6309.57	5011.87	2511.89
foc	0.02	0.02	0.02	0.02
Mean Koc	727	4209	3911	167
BCF worm	6.94	0.76	0.65	7.77
PEC plateau min (mg/kg soil)	0.001	0.02	0.004	0.009

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

MAMMALS / MULTIRESIDUE	fipronil	MB 46136	MB 45950	RPA 200766
PEC worm (mg/kg worm)	0.007	0.015	0.003	0.070
Molecular weight ratio	1	1.036	0.963	1.041
acute LD50 ratio	1	2.4	0.9	21
PEC worm as fipronil equ. (mg/kg worm)	0.007	0.0066	0.0028	0.0035
sum of the residues (mg/kg worm)	0.020			
RDI	1.4			
ETE worm (mg/kg bw/d)	0.028			
Long-term mammal NOEL (mg/kg bw/d)	2.53			
TERlt	91.51			

Fish eating mammals

MAMMALS / MULTIRESIDUES	fipronil	MB 46136	MB 45950	RPA 200766
log Pow	4	3.8	3.7	3.4
BCF fish	321	321	321	321
PECsw (max, mg/L)	0.00000327	0.00000092	0.00000035	0.000096
PEC fish (mg/kg fish)	0.001050	0.000295	0.000112	0.030816
Molecular weight ratio	1	1.036	0.963	1.041
acute LD50 ratio	1	2.4	0.9	21
PEC fish fipronil equ (mg/kg fish)	0.001	0.00012748	0.00012021	0.00152759
Sum of the residues (mg/kg fish)	0.003			
RDI	0.13			
ETE fish (mg/kg bw/d)	0.0004			
Long-term mammal NOEL (mg/kg bw/d)	2.53			
TERlt	896			

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

Laboratory tests
abbreviations used in tables: F: flow-through, S: static, SS: semi-static, mmc: mean measured concentration, nc-: nominal concentration with no analytical verification, nc+: nominal concentration with analytical verification, imc: initial measured concentration

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

Data in fish (laboratory)				
Group / Species	Test item	Time-scale (condition)	Endpoint	Toxicity value (mg test item /L)
Oncorhynchus mykiss	fipronil	Acute (96 h F)	LC50 mmc	0.248
Oncorhynchus mykiss	EXP60720A (WG 80%)	Acute (96 h S)	LC50 mmc	0.291 0.229 (a.s.)
Lepomis macrochirus	fipronil	Acute (96 h F)	LC50 mmc	0.0852
Cyprinus carpio	fipronil	Acute (96 h F)	LC50 mmc	0.430
Ictalurus punctatus	fipronil	Acute (96 h F)	LC50 mmc	0.560
Cyprinodon variegatus	fipronil	Acute (96 h F)	LC50 mmc	0.130
Oncorhynchus mykiss	MB 45950	Acute (96 h F)	LC50 mmc	0.0295
Oncorhynchus mykiss	MB 46136	Acute (96 h F)	LC50 mmc	0.039
Lepomis macrochirus	MB 46136	Acute (96 h F)	LC50 mmc	0.025
Oncorhynchus mykiss	MB 46513	Acute (96 h SS)	LC50 mmc	0.031
Lepomis macrochirus	MB 46513	Acute (96 h SS)	LC50 mmc	0.020
Oncorhynchus mykiss	RPA 104615	Acute (96 h SS)	LC50 nc- NOEC nc-	>100 100
Oncorhynchus mykiss	RPA 200761	Acute (96 h SS)	LC50 nc+ NOEC nc+	>100 100
Oncorhynchus mykiss	RPA 200766	Acute (96 h SS)	LC50 mmc NOEC mmc	>17 7.9
Oncorhynchus mykiss	fipronil	Chronic (ELS test 90 d F)	NOEC mmc	0.015
Cyprinodon variegatus	fipronil	Chronic (ELS test 35 d F)	NOEC mmc	0.0029
Cyprinodon variegatus	fipronil	Chronic (LC test 110 d F0 + 28 d F1, F)	NOEC mmc	0.006

Data in aquatic invertebrates (laboratory)				
Group / Species	Test item	Time-scale (condition)	Endpoint	Toxicity value (mg test item /L)
Daphnia magna	fipronil	Acute (48 h F)	EC50 mmc	0.190
Daphnia magna	fipronil	Acute (96 h F)	EC50 mmc	0.0129
Daphnia magna	EXP60720A (WG 80%)	Acute (48 h S)	EC50 mmc	0.223 0.175 (a.s.)
Crassostrea virginica	fipronil	Acute (96 h F)	EC50 mmc	0.770

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

Data in aquatic invertebrates (laboratory)				
Group / Species	Test item	Time-scale (condition)	Endpoint	Toxicity value (mg test item /L)
Mysidopsis bahia	fipronil	Acute (96 h S)	EC50 mmc	0.000140
Hexagenia sp.	fipronil	Acute (96 h SS)	LC50 mmc	0.00044
Hydropsyche instabilis	fipronil	Acute (96 h S)	LC50 mmc	0.00154
Lumbriculus variegatus	fipronil	Acute (96 h SS)	LC50 mmc	> 1.9
Corbicula fluminea	fipronil	Acute (96 h SS)	LC50 mmc	> 2
Daphnia magna	MB 45950	Acute (48 h F)	EC50 mmc	0.100
Mysidopsis bahia	MB 45950	Acute (96 h F)	EC50 mmc	0.000077
Daphnia magna	MB 46136	Acute (48 h F)	EC50 mmc	0.029
Mysidopsis bahia	MB 46136	Acute (96 h S)	EC50 mmc	0.000056
Mysidopsis bahia	MB 46513	Acute (96 h S)	EC50 mmc	0.001500
Daphnia magna	RPA 104615	Acute (48 h S)	EC50 nc- NOEC nc-	> 100 22
Daphnia magna	RPA 200761	Acute (48 h S)	EC50 nc+ NOEC nc+	>100 100
Daphnia magna	RPA 200766	Acute (48 h S)	EC50 mmc NOEC	> 20 2.4
Chironomus riparius 1st instar larvae	RPA 200766	Acute (48 h S)	LC50 mmc NOECmmc	0.25 0.008
Daphnia magna	fipronil	Chronic (21 d F)	NOEC mmc	0.0098
Chironomus riparius 1st instar larvae	fipronil	Chronic (28 d S) Spiked-water	NOEC imc NOEC mc after 7 d	0.000117 mg/L 0.000193 mg/kg sediment
Mysidopsis bahia	fipronil	Chronic (28 d F	NOEC mmc	0.0000077
Mysidopsis bahia	fipronil	Chronic (28 d S plus sediment)	NOEC nc+	0.00006
Daphnia magna	MB 45950	Chronic (21 d F)	NOEC mmc	0.013
Mysidopsis bahia	MB 45950	Chronic (28 d F)	NOEC mmc	0.0000046
Chironomus riparius 1st instar larvae	MB 45950	Chronic (28 d S) Spiked-sediment	NOEC mc NOEC mc	0.0011 mg/kg sediment 0.000008 mg/L
Daphnia magna	MB 46513	Chronic (21 d SS)	NOEC mmc	0.041

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

Data in aquatic invertebrates (laboratory)				
Group / Species	Test item	Time-scale (condition)	Endpoint	Toxicity value (mg test item /L)
Daphnia magna	MB 46136	Chronic (21 d F)	NOEC mmc	Not valid study
Mysidopsis bahia	MB 46136	Chronic (28 d F)	NOEC mmc	0.0000051
Chironomus riparius 1st instar larvae	MB 46136	Chronic (28 d S) Spiked-water	NOEC imc NOEC mc after 7 d	0.000069 mg/L 0.000165 mg/kg sediment
Chironomus riparius 1st instar larvae	RPA 200766	Chronic (28 d S) Spiked-water	NOEC imc NOEC mmc	0.00358 mg/L 0.00543 mg/kg sediment

Data in algae and aquatic plants (laboratory)				
Group / Species	Test item	Time-scale (condition)	Endpoint	Toxicity value (mg test item /L)
Scenedesmus subspicatus	fipronil	(96 h S)	EbC50 nc+	0.068
Scenedesmus subspicatus	EXP60720A (WG 80%)	(72 h S)	EbC50 mmc	0.211 0.166 (a.s.)
Selenastrum capricornutum	fipronil	(120 h S)	EC50 mmc	> 0.140 (= NOEC)
Anabaena flos-aquae	fipronil	(120 h S)	EC50 mmc	> 0.170 (= NOEC)
Naviculla pelliculosa	fipronil	(120 h S)	EC50 mmc	> 0.120 (= NOEC)
Skeletonema costatum	fipronil	(120 h S)	EC50 mmc	> 0.140 (= NOEC)
Lemna gibba	fipronil	(14 d S)	EC50 imc	> 0.160 (= NOEC)
Scenedesmus subspicatus	MB 45950	(72 h S)	EbC50 mmc	0.45
Scenedesmus subspicatus	MB 46136	(72 h S)	EbC50 imc	> 0.92 (= NOEC)
Selenastrum capricornutum	MB 46513	(72 h S)	EC50 mmc	0.065
Scenedesmus subspicatus	RPA 200761	(72 h S)	EbC50/NOEC nc+	> 100 / 56
Scenedesmus subspicatus	RPA 200766	(72 h S)	EbC50 imc	> 10 (= NOEC)

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

Microcosm or mesocosm tests/Higher Tier Tests
No data

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

Acute and chronic TER calculations for fish based on initial PEC values in surface water for the maize scenario (50 g a.s./ha)

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./L)	Exposure value (µg a.s./L)	TER
Acute risk					
Fipronil	*Lepomis macrochirus*	LC_{50}	85.2	0.0030	28 400
Fipronil	*Cyprinodon variegatus*	LC_{50}	130	0.0030	43 333
MB 45950	*Oncorhynchus mykiss*	LC_{50}	29.5	0.00035	84 286
MB 46136	*Lepomis macrochirus*	LC_{50}	25	0.00092	27 174
RPA 200766	*Oncorhynchus mykiss*	LC_{50}	> 17 000	0.096	> 177 083
Chronic risk					
Fipronil	*Oncorhynchus mykiss*	NOEC	15	0.0030	5 000
Fipronil	*Cyprinodon variegatus*	NOEC	6	0.0030	2 000

TER calculations for aquatic invertebrates based on maximum initial PEC values in surface water for the worst case (D4, steam) maize scenario (50 g a.s./ha)

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./L)	Exposure value [a] (µg a.s./L)	TER
Acute endpoints					
Fipronil	*Corbicula fluminea*	LC_{50}	> 2 000	0.0030	> 666 667
Fipronil	*Lumbriculus variegatus*	LC_{50}	> 1 900	0.0030	> 633 333
Fipronil	*Daphnia magna*	LC_{50}	12.9	0.0030	4 300
Fipronil	*Hydropsyche instabilis*	LC_{50}	1.54	0.0030	513
Fipronil	*Hexagenia sp.*	LC_{50}	0.44	0.0030	147
Fipronil	*Mysidopsis bahia*	LC_{50}	0.14	0.0030	46.7
MB 45950	*Daphnia magna*	LC_{50}	100	0.00035	285 714
MB 45950	*Mysidopsis bahia*	LC_{50}	0.077	0.00035	200
MB 46136	*Daphnia magna*	LC_{50}	29	0.00092	31 522

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

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./L)	Exposure value [a] (µg a.s./L)	TER
MB 46136	*Mysidopsis bahia*	LC_{50}	0.056	0.00092	61
RPA 200766	*Daphnia magna*	EC_{50}	>20 000	0.096	> 208 333
RPA 200766	*Chironomus riparius*	LC_{50}	250	0.096	2 604
RPA 200766	*Mysidopsis bahia*	LC_{50}	No data	0.096	-
Chronic endpoints					
Fipronil	*Daphnia magna*	NOEC	9.8	0.0030	3 267
Fipronil	*Chironomus riparius*	NOEC	0.117	0.0030	39
Fipronil	*Mysidopsis bahia*	NOEC water/sed	0.060	0.0030	20
Fipronil	*Mysidopsis bahia*	NOEC water	0.0077	0.0030	2.5
MB 45950	*Daphnia magna*	NOEC	13	0.00035	37 143
MB 45950	*Chironomus riparius*	NOEC	0.008 [b]	0.00035	23
MB 45950	*Mysidopsis bahia*	NOEC water	0.0046	0.00035	13
MB 46136	*Daphnia magna*	NOEC	Not valid	0.00092	Expected to be > 10
MB 46136	*Chironomus riparius*	NOEC	0.069	0.00092	75
MB 46136	*Mysidopsis bahia*	NOEC water	0.0051	0.00092	5.5
RPA 200766	*Chironomus riparius*	NOEC	3.58	0.096	37
RPA 200766	*Mysidopsis bahia*	NOEC water	No data	0.096	-

a As a worst case assumption, the global maximum peak concentrations have been used as PEC-values.
b Results derived from 28 d study with *Chironomus riparius* performed according to OECD-guidelines with spiked sediment; water concentrations are based on measured overlying water concentrations, which represents a worst-case assumption with respect to aquatic toxicity of this metabolite.

Chronic TER calculations for sediment-dwelling aquatic invertebrates based on initial PEC values in sediments for the worst-case ('D4, pond') maize scenario (50 g a.s./ha)

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./kg)	Exposure value (µg a.s./kg)	TER
Fipronil	*Chironomus riparius*[b]	NOEC	0.193	0.005	39
MB 45950	*Chironomus riparius*[a]	NOEC	1.1	< 0.001	> 1100
MB 46136	*Chironomus riparius*[b]	NOEC	0.165	0.003	55
RPA 200766	*Chironomus riparius*[b]	NOEC	5.43	0.448	12

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

[a] Results based on 28 d study with *Chironomus riparius* according to OECD draft guideline with spiked sediment.
[b] Results based on 28 d study with *Chironomus riparius* according to OECD draft guideline with spiked water, NOEC estimates based on measured sediment concentrations must be considered as worst case assumption.

TER calculations for algae and aquatic plants based on maximum initial PEC values in surface water for the worst-case ('D4, stream') maize scenario (50 g a.s./ha)

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./L)	Exposure value (µg a.s./L)	TER
Fipronil	*Scenedesmus subspicatus*	EbC50	68	0.0030	22 667
MB 45950	*Scenedesmus subspicatus*	EbC50	450	0.00035	1 285 714
MB 46136	*Scenedesmus subspicatus*	EbC50	> 920	0.00092	> 1 000 000
RPA 200766	*Scenedesmus subspicatus*	EbC50	> 10 000	0.096	> 104 166
Fipronil	*Lemna gibba*	EbC50	> 160	0.0030	> 53 333

Acute and chronic TER calculations for fish based on maximum initial PEC values in surface water for the worst case ('D5, stream') sunflower scenario (30 g a.s./ha)

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./L)	Exposure value (µg a.s./L)	TER
Acute risk					
Fipronil	*Lepomis macrochirus*	LC_{50}	85.2	0.00057	149 474
Fipronil	*Cyprinodon variegatus*	LC_{50}	130	0.00057	228 070
MB 45950	*Oncorhynchus mykiss*	LC_{50}	29.5	0.00006	491 667
MB 46136	*Lepomis macrochirus*	LC_{50}	25	0.00035	71 429
RPA 200766	*Oncorhynchus mykiss*	LC_{50}	>17 000	0.012	> 1 416 667
Chronic risk					
Fipronil	*Oncorhynchus mykiss*	NOEC	15	0.00057	26 316
Fipronil	*Cyprinodon variegatus*	NOEC	6	0.00057	10 526

TER calculations for aquatic invertebrates based on maximum initial PEC values in surface water for the worst case ('D5, stream') sunflower scenario (30 g a.s./ha)

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./L)	Exposure value [a] (µg a.s./L)	TER
Acute endpoints					
Fipronil	*Mysidopsis bahia*	LC_{50}	0.14	0.00057	246
MB 45950	*Mysidopsis bahia*	LC_{50}	0.077	0.00006	1 283

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

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./L)	Exposure value [a] (µg a.s./L)	TER
MB 46136	*Mysidopsis bahia*	LC_{50}	0.056	0.00035	160
RPA 200766	*Chironomus riparius*	LC_{50}	250	0.012	20 833
Chronic endpoints					
Fipronil	*Chironomus riparius*	NOEC	0.117	0.00057	205
Fipronil	*Mysidopsis bahia*	NOEC water/sed	0.060	0.00057	105
Fipronil	*Mysidopsis bahia*	NOEC water	0.0077	0.00057	13.5
MB 45950	*Chironomus riparius*	NOEC	0.008 [b]	0.00006	133
MB 45950	*Mysidopsis bahia*	NOEC	0.0046	0.00006	77
MB 46136	*Chironomus riparius*	NOEC	0.069	0.00035	197
MB 46136	*Mysidopsis bahia*	NOEC	0.0051	0.00035	14.6
RPA 200766	*Chironomus riparius*	NOEC	3.58	0.012	298

[a] As a worst case assumption, the global maximum peak concentrations have been used as PEC-values.
[b] Results derived from 28 d study with *Chironomus riparius* performed according to OECD-guidelines with spiked sediment; water concentrations are based on measured overlying water concentrations, which represents a worst-case assumption with respect to aquatic toxicity of this metabolite.

Chronic TER calculations for sediment-dwelling aquatic invertebrates based on initial PEC values in sediments for the worst-case ('D5, pond') sunflower scenario (30 g a.s./ha)

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./kg)	Exposure value (µg a.s./kg)	TER
Fipronil	*Chironomus riparius*[b]	NOEC	0.193	0.001	193
MB 45950	*Chironomus riparius*[a]	NOEC	1.1	<0.001	> 1 100
MB 46136	*Chironomus riparius*[b]	NOEC	0.165	0.002	83
RPA 200766	*Chironomus riparius*[b]	NOEC	5.43	0.062	88

[a] Results based on 28 d study with *Chironomus riparius* according to OECD draft guideline with spiked sediment.
[b] Results based on 28 d study with *Chironomus riparius* according to OECD draft guideline with spiked water, NOEC estimates based on measured sediment concentrations must be considered as worst case assumption.

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

TER calculations for algae and aquatic plants based on maximum initial PEC values in surface water for the worst-case ('D5, stream') sunflower scenario (30 g a.s./ha)

Substance	Species	Toxicity endpoint	Toxicity value (µg a.s./L)	Exposure value (µg a.s./L)	TER
Fipronil	*Scenedesmus subspicatus*	EbC50	68	0.00057	119 298
MB 45950	*Scenedesmus subspicatus*	EbC50	450	0.00006	7 500 000
MB 46136	*Scenedesmus subspicatus*	EbC50	> 920	0.00035	> 2 628 571
RPA 200766	*Scenedesmus subspicatus*	EbC50	>10 000	0.012	> 833 333
Fipronil	*Lemna gibba*	EbC50	> 160	0.00057	> 280 702

Bioconcentration

Bioconcentration factor (BCF) ‡	321
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	Approx. 3 days Approx 7 days
Level of residues (%) in organisms after the 14 day depuration phase	< 1 % left (clearance > 99%)

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

Acute oral toxicity ‡	Fipronil: LD_{50} = 0.00417 µg/bee equivalent to LC_{50} = 0.160 mg/kg diet MB 46136: LD_{50} = 0.0064 µg/bee equivalent to LC_{50} = 0.269 mg/kg diet RPA 200761: NOEC = 10.3 mg/kg diet equivalent to 0.29 µg/bee
Acute contact toxicity ‡	Fipronil: LD_{50} = 0.00593 µg/bee

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

No HQ is calculated since this approach is inappropriate for soil and seed treatments.

Risk assessment for sunflowers (seed treatment with EXP80415A = Regent 500FS)

Exposure in bee relevant matrices

Residues of fipronil and metabolites in samples from sunflower plots or fields treated with fipronil products applied to soil. Descriptive statistics for residues of fipronil assuming residues <LOQ to be equal to the LOQ value. For details regarding the residue values: see addendum 1 of April 2005.

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

Field or semi-field tests/ High tier studies
One field study and three tunnel studies were conducted for the three preparations with sunflower. Of the higher tier studies included and evaluated in the DAR of April 2004, the RMS considered as valid two tunnel studies (C019707 and C013759). In these two studies, no differences were found between bees tested in control and fipronil-treated plots, thus no lethal or sublethal effects linked to fipronil were reported. Similar results (lack of effects) have been obtained in two new tunnel trials conducted in 2004. The study conducted in France by ACTA (2005/1006529) has provided conclusive results based on biological observations and residue results in pollen and nectar while the results of the work in Spain by GAB (2005/1006522 and 2005/1006523) are not conclusive at this time because residues of fipronil and metabolites were found in samples from the control samples. In summary, results for at least three valid higher tier studies with honeybees in sunflowers found no adverse effects on honeybees in plots treated with Regent 500FS.

Risk assessment for maize (seed treatment with EXP80415A = Regent 500FS)

Exposure in bee relevant matrices

Residues of fipronil and metabolites in samples from maize plots or fields treated with Regent 500FS. Descriptive statistics for residues of fipronil assuming residues <LOQ to be equal to the LOQ value. For details regarding the residue values: see addendum 1 of April 2005.

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests data obtained with EXP60720A = WG 80%)						
Aphidius rhopalosiphi	adults	Fipronil as EXP60720 A		LR50	0.010 g a.s./ha	
Typhlodromus pyri	Nymphs & adults	Fipronil as EXP60720 A		LR50	0.101 g a.s./ha	
Aleochara bilineata	Adults & larvae	Fipronil as EXP60720 A		EC50repro	0.078 mg a.s./kg equ. 7.81 g a.s./ha in furrow	
Poecilus cupreus	adults	Fipronil as EXP60720 A		LC50	< 0.34 mg a.s./kg (1) equ. 38 g a.s./ha in furrow	

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Folsomia candida	Adults & offspring	Fipronil as EXP60720 A		EC50repro	0.32 mg a.s./kg equ. 32 g a.s./ha in furrow	
Pardosa	adults	Fipronil as EXP60720 A	100 g a.s./ha 25 g a.s./ha	mortality	70.5% 54.5%	
Coccinella septempunctata	Larvae & nymphs	Fipronil as EXP60720 A	100 g a.s./ha 25 g a.s./ha	mortality	100% 100%	

1) no consistent dose response between 0.069 and 0.2 mg/kg, sublethal effects prior to death were observed during the study but none of the surviving beetle was affected at the end of the study.

Extended laboratory tests (data obtained with EXP60720A = WG 80%)

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect
Aphidius rhopalosiphi	adults	Fipronil as EXP60720 A	38 mg a.s./ha 68 mg a.s./ha 121 mg a.s./ha	Mortality / parasitism LR50	13.3 / 40.6 % 26.7 / 78.9 % 40.0 / 75.3 % 106 mg a.s./ha
Typhlodromus pyri	Nymphs & adults	Fipronil as EXP60720 A	39 mg a.s./ha 118 mg a.s./ha 355 mg a.s./ha	Mortality / reproduction LR50	14.0 / 5.5 % 28.1 / 14.3 % 64.9 / 22.0 % 224 mg a.s./ha

Test species Substrate	Rate [g/ha]	Rate [g a.s./ha]	Concen-tration in Substrate [mg a.s./kg]	Effects lethal [%]	Effects sublethal [%]
Aleochara bilineata[4)] Natural soil, field furrow application – aged residue	Exposure in-furrow				
	62.5 DAT0	50.0	0.625	--	58.3
	WAT4	50.0	0.625	--	41.1
	WAT10	50.0	0.625	--	33.8
	WAT15	50.0	0.625	--	22.7
	125.0 DAT0	100.0	1.250	--	97.0

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

Test species Substrate	Rate [g/ha]	Rate [g a.s./ha]	Concen-tration in Substrate [mg a.s./kg]	Effects lethal [%]	Effects sublethal [%]
	WAT4	100.0	1.250	--	98.8
	WAT10	100.0	1.250	--	80.9
	WAT15	100.0	1.250	--	67.3
	WAT20	100.0	1.250	--	34.1
	250.0 DAT0	200.0	2.500	--	99.9
	WAT4	200.0	2.500	--	100.0
	WAT10	200.0	2.500	--	100.0
	WAT15	200.0	2.500	--	98.9
	WAT20	200.0	2.500	--	69.1
Aleochara bilineata[4)] Natural soil, field furrow application – aged residue	Exposure between-furrow				
	62.5 DAT0	50.0	--	--	3.2
	125.0 DAT0	100.0	--	--	-3.6
	250.0 DAT0	200.0	--	--	1.9
Folsomia candida Natural soil, field furrow application – aged residue	Exposure in-furrow				
	62.5 DAT0	50.0	0.625	n.r.	53
	WAT4	50.0	0.625	n.r.	43
	WAT10	50.0	0.625	n.r.	3
	125.0 DAT0	100.0	1.250	n.r.	78
	WAT4	100.0	1.250	n.r.	58
	WAT10	100.0	1.250	n.r.	37
	WAT15	100.0	1.250	n.r.	34
	WAT20	100.0	1.250	n.r.	29
	WAT25	100.0	1.250	n.r.	35
	WAT30	100.0	1.250	n.r.	32
	250.0 DAT0	200.0	2.500	n.r.	94
	WAT4	200.0	2.500	n.r.	93
	WAT10	200.0	2.500	n.r.	75

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

Test species Substrate	Rate [g/ha]	Rate [g a.s./ha]	Concen-tration in Substrate [mg a.s./kg]	Effects lethal [%]	Effects sublethal [%]
	WAT15	200.0	2.500	n.r.	81
	WAT20	200.0	2.500	n.r.	60
	WAT25	200.0	2.500	n.r.	66
	WAT30	200.0	2.500	n.r.	72
	Exposure between-furrow				
	62.5 DAT0	50.0	--	n.r.	4
	125.0 DAT0	100.0	--	n.r.	45
	250.0 DAT0	200.0	--	n.r.	5

DAT = Days After Treatment; WAT = Weeks After Treatment
n.r. = not relevant for evaluation of this study

Laboratory tests (data obtained with treated maize seeds with EXP80415A = FS 500 g/L)

Species	Stage	Test substance	Dose (g as/ha)	Endpoint	Effect
Aleochara bilineata	Adults & larvae	Treated maize seed	397 g a.s./ha	mortality reproduction	91.6 % 99.7 %
Poecilus cupreus	adults	Treated maize seed	349.8 g a.s./ha	mortality predation behaviour	10 % 23 % < 8%

Extended laboratory tests (data obtained with treated maize seeds with EXP80415A = FS 500 g/L)

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect
Aleochara bilineata	Adults & larvae	Treated maize seed	75 g a.s./ha	repro	89%

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

Test species Substrate	Rate [g/ha]	Rate [g a.s./ha]	Concen-tration in Substrate [mg a.s./kg]	Effects lethal [%]	Effects sublethal [%]	Reference
For this study also bigger exposure units were used (surface area: 1891 cm²). The first three rates were applied as maize seeds treated with the Regent 500FS, the second three rates were applied into furrows with the Regent 800WG.						
Aleochara bilineata[1)] *Natural soil*	-- -- -- -- -- --	29.6 58.2 117.4 25 50 100	-- -- -- -- -- --	-- -- -- -- -- --	8.8 17.9 21.5 27.4 39.2 32.0	2004/1015005 B.9.5.1.24

Field or semi-field tests
No data

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

Acute toxicity ‡	Fipronil LC50 > 1000 mg/kg soil ; LC50corr > 500 mg/kg soil (1) MB 46136 LC50 > 1000 mg/kg soil ; LC50corr > 500 mg/kg soil (2) MB 45950 LC50 > 1000 mg/kg soil ; LC50corr > 500 mg/kg soil (3) RPA 200766LC50 > 1000 mg/kg soil ; LC50corr > 500 mg/kg soil (4) EXP61829A LC50 > 1000 mg/kg soil
Reproductive toxicity ‡	Fipronil NOEC = 1000 mg/kg soil ; NOECcorr = 500 mg/kg soil (1) MB 46136 NOEC = 1000 mg/kg soil ; NOECcorr = 500 mg/kg soil (2)

(1) log Pow = 4; (2) log Pow = 3.8; (3) log Pow = 3.7; (4) log Pow = 3.4

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

Acute TER for EXP80415A (FS 500 g/L, 50 g a.s./ha in maize)

Substance	Time-scale	Toxicity value (corrected)	Initial PEC (in furrow)	TER_{acute}
Fipronil	Acute	> 500 mg a.s./kg soil	0.500 mg a.s./kg soil	> 1000
Fipronil	Chronic	500 mg a.s./kg soil	0.500 mg a.s./kg soil	1000
MB 46136	Acute	> 500 mg/kg soil	0.325 mg a.s./kg soil	> 1539
MB 46136	Chronic	500 mg/kg soil	0.325 mg a.s./kg soil	1539

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

Substance	Time-scale	Toxicity value (corrected)	Initial PEC (in furrow)	TER_{acute}
MB 45950	acute	> 500 mg/kg soil	0.055 mg a.s./kg soil	> 9091
RPA 200766	acute	> 500 mg/kg soil	0.140 mg a.s./kg soil	> 3571

Acute TER for EXP80415 (FS 500 g/L, 30 g a.s./ha in sunflower)

Substance	Time-scale	Toxicity value (corrected)	Initial PEC (in furrow)	TER_{acute}
Fipronil	acute	> 500 mg a.s./kg soil	0.180 mg a.s./kg soil	> 2778
Fipronil	chronic	500 mg a.s./kg soil	0.180 mg a.s./kg soil	2778
MB 46136	acute	> 500 mg/kg soil	0.117 mg a.s./kg soil	> 4274
MB 46136	chronic	500 mg/kg soil	0.117 mg a.s./kg soil	4274
MB 45950	acute	> 500 mg/kg soil	0.020 mg a.s./kg soil	> 25000
RPA 200766	acute	> 500 mg/kg soil	0.050 mg a.s./kg soil	> 10000

Long-term TER for EXP80415A (FS 500 g/L, 50 g a.s./ha in maize)

Substance	Time-scale	Toxicity value (corrected)	Long-term PEC (in furrow)	$TER_{long-term}$
Fipronil	Chronic, NOEC	500 mg a.s./kg soil	0.501 mg a.s./kg soil	998
MB 46136	Chronic, NOEC	500 mg/kg soil	0.357 mg a.s./kg soil	1401
MB 45950	Acute, NOEC	278 mg/kg soil	0.057 mg a.s./kg soil	4877
RPA 200766	Acute, NOEC	500 mg/kg soil	0.155 mg a.s./kg soil	3226

Long-term TER for EXP80415 (FS 500 g/L, 30 g a.s./ha in sunflower)

Substance	Time-scale	Toxicity value (corrected)	Long-term PEC (in furrow)	$TER_{long-term}$
Fipronil	Chronic, NOEC	500 mg a.s./kg soil	0.181 mg a.s./kg soil	2762
MB 46136	Chronic, NOEC	500 mg/kg soil	0.133 mg a.s./kg soil	3759
MB 45950	Acute, NOEC	278 mg/kg soil	0.021 mg a.s./kg soil	13238
RPA 200766	Acute, NOEC	500 mg/kg soil	0.058 mg a.s./kg soil	8621

No treatment related effects on the organic matter breakdown under field conditions (0.12 and 0.785 mg a.s./kg).

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

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

Nitrogen mineralization ‡	Fipronil Effects< 25% at 0.667 mg a.s./kg soil after 28 days MB 046136Effects< 25% at 0.600 mg /kg soil after 28 days MB 045950Effects< 25% at 0.133 mg /kg soil after 28 days RPA 200766 Effects< 25% at 0.267 mg /kg soil after 28 days
Carbon mineralization ‡	Fipronil Effects< 25% at 0.667 mg a.s./kg soil after 28 d MB 046136Effects< 25% at 0.600 mg /kg soil after 28 days MB 045950Effects< 25% at 0.133 mg /kg soil after 28 days RPA 200766 Effects< 25% at 0.267 mg /kg soil after 28 days

Respiration of **activated sludge**: NOEC = 1000 mg a.s./L

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N; Harmful R50/53 Very toxic to aquatic organisms, may cause long-term adverse effect in the aquatic environment (Fipronil, MB 46136, MB 45950, MB 46513, RPA 200766)

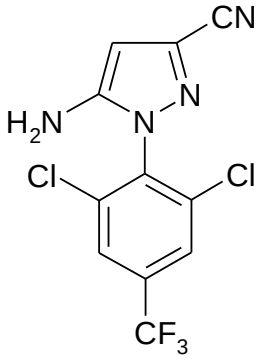
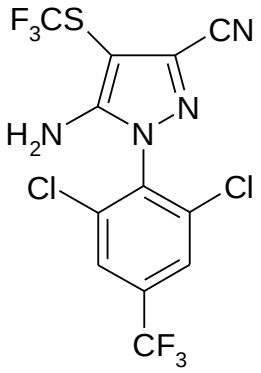
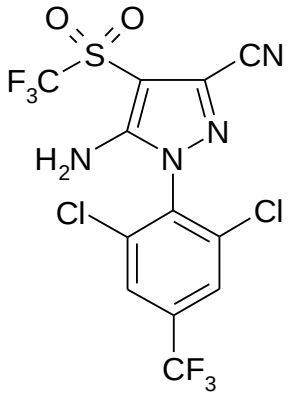
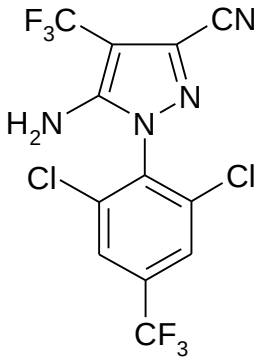
‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

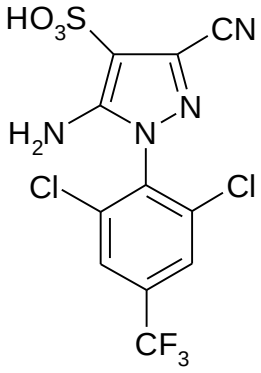
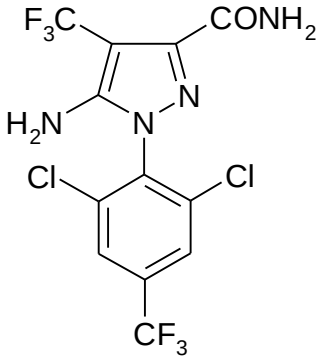
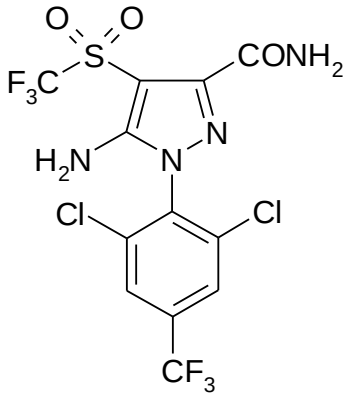
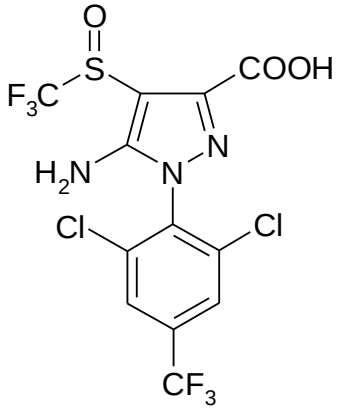
APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
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)
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

APPENDIX 3 – USED COMPOUND CODES

Code/Trivial name	Chemical name	Structural formula
MB 45897:	5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-1H-pyrazole-3-carbonitrile	
MB 45950:	5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylthio-1-pyrazole-3-carbonitrile	
MB 46136:	5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylsulfonylpyrazole-3-carbonitrile	
MB 46513:	5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoro-methylpyrazole-3-carbonitrile	

RPA 104615:	5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl) pyrazole-4-sulfonic acid, potassium salt	
RPA 105048:	1-(2,6-dichloro-4-trifluoromethylphenyl)-3-amino-5-amino-4-trifluoromethylsulfonylpyrazole	
RPA 105320:	5-amino-3-carbamyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonylpyrazole	
RPA 200761:	5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonylpyrazole-3-carboxylic acid	

RPA 200766:	5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-trifluoromethylsulfonyl-1H-pyrazole-3-carboxamide