



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

fipronil

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SUMMARY

Fipronil is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000¹, as amended by Commission Regulation (EC) No 1490/2002². 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 to 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



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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 trials 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, toddlers, 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 200766³, the sulphone MB 46136⁴ and the sulphide MB 45950⁵. Mineralization is very low.

Under dark aerobic conditions at metabolite RPA 200766 is high persistent, RPA 200761⁶ moderate to high persistent, MB 45950 medium to high persistent, MB 46136 high persistent and MB 46513⁷ 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 104615⁸.

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 PEC_{sw}-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 PEC_{sw} values. Based on the available provisional PEC_{sw} 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 PEC_{sw} 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 PEC_{soil} have been solved.



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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