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

fluoxastrobin

finalised: 10 August 2005

SUMMARY

Fluoxastrobin is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[1] United Kingdom received an application from Bayer AG for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/35/EC of 10 January 2003 [2].

Following the agreement between the EU-Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State United Kingdom made the report of its initial evaluation of the dossier on fluoxastrobin, hereafter referred to as the draft assessment report (DAR), available on 2 September 2003.

The peer review was initiated on 14 October 2003 by dispatching the draft assessment report for consultation of the Member States and the notifier. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 25 May 2004. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in September and October 2004.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 20 July 2005 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 fungicide as proposed by the applicant which comprises foliar spraying to control a range of fungal diseases in wheat, rye and barley at application rate up 200 g fluoxastrobin per hectare. An Annex III dossier for a representative seed treatment containing fluoxastrobin was submitted and evaluated. However, owing to issues relating to the other active substances present in the formulation used for seed treatment, it was not possible to complete overall the risk assessment.

[1] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 70, 16.3.2005, p.1
[2] OJ No L 11, 16.01.2003, p. 52

Fluoxastrobin can be used only as fungicide. The representative formulated product for the evaluation was "HEC 5725 EC 100", an emulsifiable concentrate (EC).

Adequate methods are only available to monitor the compounds given in the respective residue definitions for food and air. 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.

In mammals, fluoxastrobin is rapidly and nearly completely absorbed and widely distributed within the body. The highest concentrations are detected in liver, kidneys and bladder as well as in the gastrointestinal tract. No accumulation in the body is observed. The major route of excretion in rats was biliary and faecal. The metabolism is extensive and 50 metabolites are identified. The acute toxicity of fluoxastrobin is low; it is not a skin or an eye irritant, nor a skin sensitiser. There is no evidence of genotoxicity or oncogenicity. Fluoxastrobin gave no evidence of reproductive toxicity or neurotoxicity.
The acceptable daily intake (ADI) is 0.015 mg/kg bw/day, the acceptable operator exposure level (AOEL) is 0.03 mg/kg bw/day, and the acute reference dose (ARfD) is 0.3 mg/kg bw with a 100-fold assessment factor applied.
The operator risk assessment has been conducted only on the representative use in cereals as a spray application. No risk assessment for the representative use as a seed treatment in cereals is available in the DAR. The estimated operator exposure for HEC 5725 EC100 is below the AOEL without personal protective equipment (PPE) (34%), according to the German model. According to calculations with the UK POEM model, gloves have to be worn when handling the concentrate. The exposure for re-entry workers and bystanders is low (<10% of the AOEL).

Applied to wheat plants by foliar application following a seed treatment fluoxastrobin itself and its *Z*-isomer was the major residue found at harvest in straw and in grain accounting for about 86% and 80% of the total residue, respectively. Some metabolites found in plants were not observed in rat metabolism. However, due to their insignificant levels (<0.01 mg/kg) they were considered being of no concern in grain, whereas in straw some non-rat metabolites, e.g. 2-chlorophenol (M82[3]) and its glycoside (M84) are expected to be present at significant levels. However, M82 was also seen in livestock metabolism studies with fluoxastrobin, but others were not and their toxicity was not tested further. Depending on the soil, fluoxastrobin was shown to be highly persistent in soil and hence it was present in rotational crops at plant back intervals up to 328 days as the major residue. Decline of fluoxastrobin residues under processing conditions does not occur.

[3] The chemical structure of the metabolites is given in appendix 3 of the conclusion.

Fed to ruminants and poultry, fluoxastrobin was intensively metabolised resulting in a comparable pattern to that observed in rat metabolism, with the exception of some metabolites, that were not specifically found in the rat, but not considered to be of concern due to insignificant levels (<0.01 mg/kg). In a feeding study levels of relevant compounds (fluoxastrobin, its *Z*-isomer and metabolite M55) in edible animal matrices were analysed, and MRLs have been proposed.
The chronic dietary exposure assessment for consumers based on the representative GAP on cereals indicated that for all consumer subgroup the intake was less then 10% of the proposed ADI. The short term exposure of all considered consumer subgroups from individual commodities, based on consumption data of UK consumers, was all below 1% of the proposed ARfD. In an assessment of possible consumer exposure and consumer risk due to intake of metabolite M48 from drinking water the margin of safety was shown to be sufficient.

Under aerobic conditions fluoxastrobin yield the major metabolite M48-*E* and 2-chlorophenol in soil. Mineralization was generally low. Metabolite M40 was identified as a potential major anaerobic metabolite in soil. *Z*-isomer of fluoxastrobin was identified as the major soil photolysis metabolite.
As a result of the cleavage of the molecule 2-chlorophenol will be released at an expected worst case maximum amount of 49.2 % (see EFSA addendum on fate and behaviour; 26 July, 2005). The microbiologically driven degradation of 2-chlorophenol in soil was supported with a number of studies from the open scientific literature.
In field trials the *Z* isomer of fluoxastrobin was measured at up to 19 % - 22 %. The EPCO experts' meeting on fate and behaviour in the environment (EPCO 12) agreed that *Z*-isomer of fluoxastrobin should be included in the residue definition in soil and assessed for their potential ecotoxicological relevance.
Persistence of fluoxastrobin in soil may be very variable. Fluoxastrobin may behave as a moderate to high persistent compound. Metabolite M48-*E* is moderate to medium persistent in soil.
Anaerobic metabolite M40 is moderately persistent in soil under aerobic conditions.
Data available from open scientific literature show that the aerobic soil metabolite 2-chlorophenol is very low to moderately persistent in soil.
PEC soil were calculated from peak concentration after four subsequent seasons with a seed treatment and two foliar applications per season. Maximum PEC for M48 provided in the DAR is based on worst case field formation of 6.3 %. Maximum PEC soil for metabolite 2-chlorophenol is provided in the EFSA addendum on fate and behaviour.
Fluoxastrobin may be classified as low to medium mobile, M48 as medium to very high mobile and M40 high to very high mobile. The rapporteur Member State identified a Koc soil pH dependence for fluoxastrobin. No adsorption / desorption data is available for metabolite 2-chlorophenol. This has been identified as a new data requirement by EFSA.
Fluoxastrobin is stable to hydrolysis at all environmental relevant pHs. Aqueous photolysis contributes to the aqueous dissipation of fluoxastrobin. The main photolysis metabolites are: *Z* isomer of fluoxastrobin, M36 and M56.
No studies on ready biodegradability are available and fluoxastrobin was proposed to be non ready biodegradable by the experts meeting.

Only metabolite M48-*E* was seen above 10 % AR in the water phase of the water / sediment systems. Concomitant formation of metabolite 2-chlorophenol at levels above 10 % cannot be excluded. Degradation of fluoxastrobin was slow in both systems. Dissipation from the water phase was mainly due to partition in to the sediment. Mineralization was very low and bound residues increased during the study to a maximum of 12.7 % AR.
Formation of the metabolite *Z*-isomer of fluoxastrobin was observed in two irradiated aerobic water sediment studies. Contribution of photodegradation to the dissipation of fluoxastrobin from the water phase in these systems is not significant, probably due to the rapid adsorption to the sediment.
PECsw and PECsed were provided by the applicant for the representative use. Spray drift initial PECsw for the metabolite M48-*E* was calculated by the rapporteur Member State. The rapporteur Member State also provided PECsw for drainage based on their national scheme. Potential loadings to surface water through run off were not considered in the assessment presented in the DAR. Due to the fact that fluoxastrobin may be high persistent in soil, potential surface water contamination through drainage and run off may not be excluded; therefore, a comprehensive assessment taking into account spray drift, run-off, drainage and effectiveness of potential mitigation measures to reduce surface water contamination is necessary to finalize the risk assessment of the EU representative uses.
PECgw of fluoxastrobin and the metabolite M48-*E* were estimated using FOCUS-PELMO 1.1.1. Calculated concentrations of Fluoxastrobin at 1 m depth were negligible. However, metabolite M48-*E* exceeds the trigger 0.1 µg /L in eight of the nine scenarios when dependence of the adsorption Koc with the soil pH is taken into account. It is noted that for six of the scenarios the level of 0.75 µg /L is also exceeded by metabolite M48-*E*. Relevance assessment has been performed for this metabolite.
Potential groundwater contamination by soil metabolite *Z*-isomer of fluoxastrobin is not addressed in the DAR, EFSA considers that the results of the exposure assessment made for fluoxastrobin may be applied to the *Z*-isomer.
Potential groundwater contamination by soil metabolite 2-chlorophenol is not addressed in the DAR and has not been discussed during the Peer Review. EFSA identified a new data requirement since potential groundwater contamination of major soil metabolite 2-chlorophenol needs to be addressed.
Concentration of fluoxastrobin in air is expected to be negligible due to low volatility and short half life in air for reaction with OH radicals.

In the section on ecotoxicology only the risk to non-target organisms from the representative use in cereals as a spray application was assessed. No risk assessment for the representative use as a seed treatment in cereals is available in the DAR.

It should be noted that the assessment in the DAR is based on a pilot plant production. Since then the production process has been modified and optimised. Therefore, a new material accountability study and a new five batch analysis have been performed. The new resultant specification was supported by additional toxicological data, which have been peer-reviewed and accepted. An appropriate assessment with respect to ecotoxicology is still outstanding.

The risk to bees, non-target terrestrial plants and biological methods for sewage treatment is low with respect to fluoxastrobin and the metabolites for the representative use of fluoxastrobin as a spray application.

The risk to herbivorous birds and mammals can be regarded as low for the representative use of fluoxastrobin as a spray application if the risk was calculated using residue data as outlined in EPPO (1992). EFSA made a risk assessment available according to the latest guidance document on birds and mammals (SANCO/4145/2000). According to this assessment (see EFSA's addendum on ecotoxicology) the risk to mammals can be regarded as low and also the acute, short and long term risk for insectivorous and herbivorous birds as well as the acute and short term risk to granivorous birds from the representative uses evaluated can be regarded as low. But a long term risk to granivorous birds is observed (TER= 1.79 according to SANCO/4145/2000). Therefore EFSA proposes a data requirement for the notifier to submit a refinement of the long term risk to granivorous birds for the use as a seed treatment in cereals if the risk is assessed according to the latest guidance document (SANCO/4145/2000).

A high risk is identified to aquatic organisms. A bufferzone of 15 metres is needed to respect the Annex VI trigger value for the long term risk for the use of fluoxastrobin as a spray application in cereals. It was noted by the EPCO experts' meeting on ecotoxicology (EPCO 13) that additional chronic invertebrate data are available. The meeting agreed that some lowering of the chronic uncertainty would be acceptable in this case and that these additional data may be used to refine the risk assessment at MS level. Furthermore the meeting decided to address a generic question on lowering the uncertainty factor by using additional chronic species sensitivity data to EFSA's Panel on Plant Health, Plant Protection and their Residues (PPR). This generic question was forwarded to the PPR Panel by EFSA; the opinion of the Panel is still pending. The risk of the metabolite M48 to aquatic organisms is considered to be low. The experts' meeting on ecotoxicology decided that based on biological screening data, data on Daphnia and some mammalian data that it is unlikely that the *Z*-isomer is of greater toxicity than the *E*-isomer. It is noted by EFSA that also the metabolite 2-chlorophenol is considered as a major metabolite by the section on fate and behaviour. No studies with this metabolite are available and therefore EFSA proposes that a study or at least a solid argumentation regarding the effects of the metabolite 2-chlorophenol on aquatic organisms should be made available. The need for this data was not discussed at an EPCO experts meeting.

The risk to non-target arthropods was discussed at the EPCO experts' meeting. The meeting decided that based on the available data, population recovery/recolonisation in-field would be possible within one year. Therefore the meeting agreed that the risk to non-target arthropods is addressed for the representative use of fluoxastrobin as a spray application.

The risk to soil micro- and macro-organisms, including earthworms is low with respect to fluoxastrobin and the metabolites M48 and M40 for the use of fluoxastrobin as a spray application in cereals. The experts' meeting decided that it is unlikely that the *Z*-isomer is of greater toxicity than the *E*-isomer (see above). It is noted by EFSA that also the metabolite 2-chlorophenol is considered as a major metabolite by the section on Fate and behaviour. No studies with this metabolite are available and therefore EFSA proposes that a study or at least a solid argumentation regarding the

effects of the metabolite 2-chlorophenol on earthworms and soil micro-organisms should be made available. The need for this data was not discussed at an EPCO experts' meeting.

Key words: fluoxastrobin, peer review, risk assessment, pesticide, fungicide