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

dimoxystrobin

finalised: 10 August 2005

SUMMARY

Dimoxystrobin is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[1] the United Kingdom received an application from BASF for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2002/593/EC[2].

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State United Kingdom submitted the report of its initial evaluation of the dossier on dimoxystrobin, hereafter referred to as the draft assessment report (DAR), to the EFSA on 17 July 2003. This draft assessment report was distributed for consultation to the Member States and the notifier on 14 August 2003.

Following a quality check on the DAR, the peer review was initiated on 14 August 2003 by dispatching the DAR 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 15 January 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 April and May 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 spraying using ground base equipment to control fungal pathogens in winter wheat at application rate up to 200 g dimoxystrobin per hectare. The representative formulated product for the evaluation was “BAS 50700 F”, a suspension concentrate (SC), which contains as a second active substance epoxiconazole (a substance to be evaluated at stage

[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 192, 20.7.2002, p. 60

3, part A of the review programme under Directive 91/414/EEC). Dimoxystrobin can be used only as fungicide.

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

With respect to mammalian toxicology dimoxystrobin is rapidly and nearly completed absorbed. Dimoxystrobin is extensively metabolised to a large number of metabolites. The oral and dermal toxicity is low. However, it is harmful during inhalation, and the classification of Xn; R20 "Harmful by inhalation" is proposed. No repeated inhalation study is available. Thickening of the duodenum was the main effect observed in rats and mice. There was no evidence of genotoxicity.
Dimoxystrobin was carcinogenic in mice causing an increased incidence of adenoma and adenomacarcinoma in the duodenum at the top dose. There was also focal hyperplasia in the duodenum at the top dose, interpreted as a pre-neoplastic lesion. Based on the results, the risk phrase and classification Xn; R40 "Limited evidence of a carcinogenic effect" is proposed. There were no direct effects on reproductive performance or fertility observed up to the highest dose level. There were no indications for dimoxystrobin being neurotoxic. The metabolites 505M08[3] and 505M09[4] were considered toxicologically relevant, due to the structural similarity with dimoxystrobin.
The acceptable daily intake (ADI) and the acute reference dose (ARfD) is 0.004 mg/kg bw/day (safety factor 1000) and the acceptable operator exposure level (AOEL) is 0.02 mg/kg bw/day (safety factor 200).
The formulation, BAS 507 00F, contains two active ingredients dimoxystrobin and epoxiconazole. The studies were not performed on the representative formulation BAS 507 00F but on dimoxystrobin diluted in a solvent formulation with a similar composition of the non-active co-formulants in BAS 507 00F, an "artificial BAS 507 00F". The dermal absorption value was proposed to be 1% for both undiluted and diluted formulation. *For epoxiconazole the rapporteur Member State proposed 10%.* As the representative formulation contains two active substances the operator exposure follows a combined approach. The rapporteur Member State presented a risk assessment for each of the two active substances. For dimoxystrobin, the risk assessment is based on dimoxystrobin in the "artificial formulation BAS 507 00F". *The risk assessment for epoxiconazole, is based on the assumptions and proposals of the rapporteur Member State.* Since epoxiconazole has not yet been evaluated, but will be in the stage 3 part A of the review programme and the studies have not been peer reviewed and none of the values has been agreed on, all values should be regarded as provisional until agreed on. The proposed risk assessment is only valid when the toxicological assessment for epoxiconazole has

[3] 505M08: [*E*-*o*-(2-hydroxycarbonyl-5-methyl)phenoxymethyl]-2-methoxyimino-*N*-methylphenyl acetamide
[4] 505M09: [*E*-*o*-(5-hydroxycarbonyl-2-methyl)phenoxymethyl]-2-methoxyimino-*N*-methylphenyl acetamide

been agreed on later in the process and thus the risk assessment of BAS 507 00F can not be regarded as complete, but only indicative. The risk assessment for epoxiconazole is based on the estimated exposure calculated of the formulation Opus. The estimated exposure for dimoxystrobin is below the AOEL (13%) without any PPE in the "artificial BAS 507 00F". *The estimated operator exposure for epoxiconazole is below the AOEL in the German model without PPE (48%) and with PPE during both mixing and loading as well as during application according to the UK POEM (30%).* If, all values are agreed on and if the actual exposure should be identified as being additive, then *it might be assumed that the estimated combined exposure of dimoxystrobin and epoxiconazole is below the AOEL in the German model without PPE (61%) or with PPE during both mixing and loading as well as during application according to the UK POEM (45%) for both dimoxystrobin and epoxiconazole.*

Applied to wheat plants by foliar application dimoxystrobin itself was the major residue found at harvest in straw and in grain accounting for about 90% and 60% of the total residue, respectively. Total levels of radioactivity in grain were too low to allow further characterization of metabolites. Dimoxystrobin turned out to be persistent in soil and hence it was present in rotational crops at plant back intervals up to 365 days. However, significant residues (>0.01 mg/kg) of dimoxystrobin or other metabolites in plant parts for human consumption are not anticipated from crop rotation.

Fed to ruminants and poultry, dimoxystrobin was intensively metabolised resulting in a comparable pattern to that observed in rat metabolism, with the exception of metabolite 505M76[5], which was not specifically found in the rat. Despite the lipophilic character of dimoxystrobin there was no indication of accumulation in the body fat of the tested animal species. In a feeding study levels of relevant compounds (dimoxystrobin, metabolites 505M09 and 505M76) in edible animal matrices were all found to be below the respective LOQ.

The assessment of chronic dietary exposure of consumers to dimoxystrobin residues based on the representative GAP on cereals indicated that the most highly exposed consumer subgroup was infants at 83% of the proposed ADI. The short term exposure of all considered consumer subgroups from individual commodities, based on consumption data of UK consumers, were well within the proposed ARfD, accounting for up to 48% ARfD at a maximum from the consumption of milk by toddlers.

Since there were relevant metabolites found in ground water, a consumer risk assessment was performed, considering the sum of possible intakes of dimoxystrobin and the metabolites 505M09 and 505M76 from drinking water in addition to the intake through diet. The total intakes from diet and drinking were demonstrated to be below the ADI of dimoxystrobin for the considered consumer subgroups.

The degradation of dimoxystrobin in soil is initiated by the oxidation of methyl moieties of the phenyl ring. Metabolite 505M09 attained levels above 10 % AR in laboratory experiments and metabolite 505M08 was found at levels above 10 % of the applied parent in field trials. Maximum mineralization

[5] 505M76: (2E)-2-{2-[(5-carboxy-4-hydroxy-2-methylphenoxy)methyl]phenyl}-2-(methoxyimino)-N-methylacetamide

after 120 d was between negligible to 24 % AR. Unextractable radioactivity amounted to a maximum of 24 % after 120 d. A major photolysis metabolite 505M01[6] is identified in the soil photolysis study.
Dimoxystrobin is medium to high persistent (DT_{50} = 88 – 401 d) in soil at 20 ºC. Metabolites 505M08 and 505M09 are less persistent in soil than parent compound. Dimoxystrobin is not degraded under anaerobic conditions. Degradation of dimoxystrobin is enhanced under irradiated conditions.
Three field dissipation studies were performed in Germany, two in Spain and two in Sweden. Dimoxystrobin shows to be moderate to high persistent in field ($DT_{50\ (20\ ºC,\ pF2)}$ = 57.6 -131.6 d).
Accumulation of dimoxystrobin in soil was investigated under field conditions in two trials in S.W. Germany, following repeated annual application to cereals over three years.
Standard PEC soil (0 – 100 d) were calculated for parent and metabolite 505M01. Worst case maximum amount PEC soil for metabolite 505M01 was calculated assuming 100 % transformation from parent dimoxystrobin. The PEC soil for 505M09 values were calculated with a five compartmental model. No PEC soil was calculated for metabolite 505M08.
In the RMS calculation of potential accumulation, maximum plateau concentration was reached after 5 years (PEC soil acc = 0.046 mg/kg). Residues seen in the field accumulation trials were considered to be mostly in the range of predicted concentrations.
According batch equilibrium adsorption/desorption studies dimoxystrobin may be classified as low to medium mobile in soil, 505M01 as very high mobile, 505M08 as high to very high mobile and 505M09 as high to very high mobile.
Dimoxystrobin is stable to hydrolysis at all environmental relevant pHs. Photolysis may moderately contribute to the degradation of dimoxystrobin in water.
Degradation of dimoxystrobin in water/sediment systems was very limited. Only 10-15 % of the applied dimoxystrobin degrades after 100 d. Disappearance from the water phase is mainly attributed to partition with sediment.
Additionally an outdoor water sediment study and an outdoor mesocosm study in Germany were used to investigate the aquatic dissipation of dimoxystrobin. Photolysis and partition to sediment were considered the main routes of dissipation of dimoxystrobin from the water phase in the outdoor water sediment study. In the mesocosm study dimoxystrobin was applied in early May and a dissipation DT_{50} = 60 – 69 d was calculated for the water phase.
Only initial spray drift PECsw values were used in the surface water risk assessment presented by the RMS in the DAR. Other potential routes of surface water contamination such as run off and drainage are partially addressed in the DAR following published (run-off) and national RMS scheme (drainflow) but were not used further for the EU risk assessment. FOCUSsw calculations were not presented.
In the opinion of EFSA's Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR) related to the evaluation of dimoxystrobin[7], the PPR Panel used the DT_{50} = 63.5 d from the outdoor pond mesocosm study, as conservative but realistic value for the exposure assessment. In this opinion it is highlighted that a single exposure event applies only to exposure *via*

[6] 505M01: ((*E*)-2-(2-hydroxymethylphenyl)-2-methoxyimino-N-methyl-acetamide)
[7] 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. The EFSA Journal (2005) 178, 1-45.

the initial spray drift. Any other exposure routes as runoff and drain flow are not covered by RMS assessment. The PPR Panel noted that FOCUSsw simulations predict higher PEC values (0.15 - 3.64 µg / L) than those calculated in the DAR (1.85 µg / L) due to the fact that drainage and runoff were the major contributors to the surface water contamination for some of the selected scenarios. 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 EU risk assessment.

Concentrations of dimoxystrobin and its soil metabolites 505M08 and 505M09 in groundwater predicted with FOCUSgw for the representative uses proposed were below 0.1 µg / L trigger. However, in an outdoor lysimeter study in Germany exceedance of yearly average 0.1 µg / L trigger in the leachate was observed for metabolites 505M08 and 505M09 for all three years and in all the systems studied. By comparison of modelling and lysimeter results it was concluded that high interception was needed to reduce the potential of ground water contamination and that FOCUS modelling only covers risk assessment for application to late growth stages (crop interception 90 % or greater). Potential for groundwater contamination by 505M08 and 505M09 under vulnerable conditions needs to be assessed at MS level.

The concentration of the photodegradation product 505M01 are below the 0.1 µg/L trigger when calculated form the results of the lysimeter study.

Concentration of dimoxystrobin in air is expected to be negligible due to low volatility and short half life in air for reaction with OH radicals.

For birds and mammals EFSA provided a risk assessment according to the latest guidance document (Sanco/4145/2000 of 25 September 2002) in an addendum which however was not yet peer reviewed. The risk assessment for dimoxystrobin (technical) resulted in TER values for the acute, short term and long term risk to insectivorous birds and mammals which met the Annex VI trigger values. However, the complete risk assessment for birds and the long term risk assessment for mammals is based on the endpoints deriving from studies with the technical active substance. Since the lead formulation contains a second active substance (epoxiconazole, listed for the 3rd stage of the peer review process) it is questionable whether it is possible to extrapolate from the toxicity of the technical active substance to the formulated product. Furthermore, the acute toxicity studies with rats showed that the formulated active substance in the lead formulation is more acutely toxic than the technical active substance. A high risk was identified for birds and mammals from the uptake of contaminated drinking water in a first tier risk assessment.

EFSA is of the opinion that a high risk to birds and mammals from the application of the lead formulation cannot be excluded and additional data are required to address the risk of the lead formulation to birds and mammals.

A high risk was identified in a first tier risk assessment for all tested groups of aquatic organisms. The higher tier risk assessment for fish resulted in TER values which met the revised acute TER trigger value. No agreement was reached in the EPCO experts' meeting on ecotoxicology (EPCO 3) if the chronic risk assessment should be based on the endpoints deriving from the early life stage (ELS) test with rainbow trout (flow through test design) or on the ELS test with golden orfe (single application

and presence of sediment). Therefore, this question was forwarded to the Scientific Panel on Plant Health, Plant Protection Products and their Residues. The PPR Panel concluded that the endpoint of rainbow trout (*Oncorhynchus mykiss*) should be used. Based on this endpoint (overall NOEC of 0.316 µg a.s./L) a high risk was calculated in the addendum provided by EFSA which was not peer reviewed. Therefore the high chronic risk to fish needs to be addressed with further data. A mesocosm study was conducted as a higher tier test to address the risk to aquatic invertebrates and algae. In the EPCO experts' meeting (EPCO 3) it was agreed that a safety factor of 5 has to be applied to the TER value of 2.7 deriving from the mesocosm study. Consequently a high risk to aquatic invertebrates and algae was identified and has to be addressed with further data and risk mitigation measures are necessary.

Field studies with earthworms were conducted because a high long term risk to earthworms was identified in a first tier risk assessment. The results of the field studies led to the conclusion that the long term risk to earthworms is low.

The risk to bees, non target arthropods, soil macro-, soil micro-organisms, non target plants and biological methods of sewage treatment is considered to be low.

The risk from the metabolites 505M01, 505M08, 505M09 to the environment is low.

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

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC the United Kingdom received an application from BASF for inclusion of the active substance dimoxystrobin in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2002/593/EC.

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State United Kingdom submitted the report of its initial evaluation of the dossier on dimoxystrobin, hereafter referred to as the draft assessment report, to the EFSA on 17 July 2003. This draft assessment report was distributed for consultation to the Member States and the notifier on 14 August 2003.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives of the Member States identified and agreed in an evaluation meeting on 15 January 2004 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier was attending this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team at Federal Office for Consumer Protection and Food Safety (BVL) in Braunschweig, Germany in April and May 2004. 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 19 July 2005 leading to the conclusions as laid down in this report.

Following the consultation of technical experts a question relating to the chronic risk assessment for aquatic organisms was forwarded to the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR) which was addressed by an opinion adopted on 16 February 2005.

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

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

- the comments received
- the resulting reporting table (rev. 1-1 of 4 February 2004)
- 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. 1-2 of 9 August 2005)

Given the importance of the draft assessment report including its addendum (compiled version of July 2005 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Dimoxystrobin is the ISO common name for (*E*)-2-(methoxyimino)-*N*-methyl-2-[α-(2,5-xylyloxy)-*o*-tolyl]acetamide (IUPAC).

Dimoxystrobin belongs to the class of strobilurin fungicides. It can be used only as fungicide for the control of fungal pathogens in winter wheat. Dimoxystrobin is active against fungi on the plant surface and within the plant as mitochondrial respiration inhibitor through blockage of electron transport.

The representative formulated product for the evaluation was "BAS 50700 F", a suspension concentrate (SC), which contains as a second active substance epoxiconazole.

The representative uses evaluated comprise comprises spraying using ground base equipment to control fungal pathogens in winter wheat at application rate up to 200 g dimoxystrobin per hectare. Dimoxystrobin can be used only as fungicide.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of dimoxystrobin as manufactured should not be less than 980 g/kg. At the moment no FAO specification exists. The technical material contains no relevant impurities. The agreed technical specification (EPCO 6 experts' meeting) is given in addendum 1 to the DAR.

The main data regarding the identity of dimoxystrobin 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 dimoxystrobin 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. dimoxystrobin in food of plant and animal origin, soil, surface water and air; dimoxystrobin, 505M08[8] and 505M09[9] in ground water.
Dimoxystrobin can be determined with a multi-residue method (The German S19 method has been validated for food of plant and animal origin.) However, the applicability of the method for the determination of residue in food of animal origin has to be confirmed by the outstanding independent laboratory validation (ILV).

The submitted method for the determination of the metabolites 505M08 and 505M09 in water was not discussed in detail due to fact at the time of evaluation of the DAR the residue definition was dimoxystrobin only (a potential problem with the peak resolution is mentioned in the DAR). However, the method was accordingly validated but for the derivatisation step diazomethane is used. No validated information is given whether it is possible to substitute diazomethane by a less harmful reagent. However, as an alternative the applicant has suggested use of the commercially available reagent (trimethylsilyl)diazomethane in diethyl ether which is classified as both non-explosive and non-mutagenic (no validation data or data on the efficiency of conversion for this reagent).

In contrast to the residue definition proposed by RMS for food of animal origin EFSA considers metabolite 505M09 as more appropriate for enforcement purposes (see chapter 3.2).
However, an analytical method (incl. ILV) for the determination of metabolite 505M09 is available, but diazomethane is used as methylation agent. No detailed information is given whether it is possible to substitute diazomethane by a less harmful reagent. However, the currently validated LOQs of 0.05 mg/kg are insufficient to monitor the proposed MRLs of 0.01 mg/kg and 0.03 mg/kg, respectively. A determination without a derivatisation step and down to 0.01 mg/kg and 0.025 mg/kg, respectively, is possible by LC-MS/MS, but for this method no ILV is available. It should be noted that these methods were not discussed in detail due to fact at the time of evaluation of the DAR the residue definition was dimoxystrobin only, which can be determined with a multi-method (such as the German S19).

[8] 505M08: [*E*-*o*-(2-hydroxycarbonyl-5-methyl)phenoxymethyl]-2-methoxyimino-*N*-methylphenyl acetamide
[9] 505M09: [*E*-*o*-(5-hydroxycarbonyl-2-methyl)phenoxymethyl]-2-methoxyimino-*N*-methylphenyl acetamide

The recently submitted study, regarding the ILV of the enforcement method for the determination of residues in food of animal origin was not peer reviewed by other MS or discussed in an EPCO experts' meeting. However, the conclusion of the rapporteur Member State that this study fulfils the data gap is confirmed by EFSA (provided that the residue definition is dimoxystrobin). The assessment is presented in addendum 2 (June 2005) to the DAR.

The discussion in the experts' meeting on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material and the missing ILV for food of animal origin.

2. Mammalian toxicology

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

Dimoxystrobin is rapidly and nearly completed absorbed, 80 and 60% when rats were exposed to 10 and 100 mg/kg bw, respectively. The half-life was around 11-18 h. Faecal excretion (57-82%) predominated over urinary excretion, and biliary excretion was important (34-55%). It is widely distributed in tissues and organs and radiolabel was found at highest level in the gastro-intestinal tract, liver kidney, lung, fat tissue, thyroid, pancreas, adrenals, ovaries and uterus. At the low dose, there is little potential for tissue accumulation. Dimoxystrobin is extensively metabolised to a large number of metabolites and the major route is hydroxylation, oxidation and cleavage of the ether bond.

2.2. Acute toxicity

The oral and dermal toxicity is low i.e. LD_{50} > 2000 mg/kg bw. However, it is harmful during inhalation (rats), LC_{50} was 1.3 mg/L air and **the classification of Xn; R20 "Harmful by inhalation" is proposed.** Dimoxystrobin was neither an irritant nor a sensitizer (maximisation test).

2.3. Short term toxicity

The short term effects of dimoxystrobin were studied in a 90-day dietary study in rat, the mouse, and the dog as well as 1-year in the dog. One 28-day dermal study in the rat is included in the DAR. No repeated inhalation study is available.

Thickening of the duodenum was the main effect observed in rats and mice (dose level 300 ppm i.e. 21 and 24 mg/kg bw/day in male and female rats, respectively). Diarrhoea was seen in the dog. At higher dose levels (> 1200 ppm) reduced body weight gain was observed, generally in all species. The rat was the most sensitive species.

No substance related effects were seen in the dermal study.

The relevant oral NOAEL is 50 ppm i.e. 3 mg/kg bw/day and 4 mg/kg bw/day in males and females, respectively, based on thickening of the duodenal mucosa in the 90-day rat (Mellert, 1999b).

The relevant dermal NOAEL is >1000 mg/kg bw/day.

No relevant inhalation NOAEL could be set due to lack of study.

2.4. GENOTOXICITY

In the DAR, 4 *in vitro* studies and one *in vivo* study (chromosome aberration) have been evaluated and presented. There was no evidence of genotoxicity.

2.5. LONG TERM TOXICITY

Two studies in the rat (24-month) and one in the mouse (18-month) are evaluated in the DAR. In rats, slight thickening of the duodenal mucosa at the high dose was observed but no substance related duodenal tumours. However, dimoxystrobin was carcinogenic in mice causing an increased incidence of adenoma and adenomacarcinoma in the duodenum at the top dose. There was also focal hyperplasia in the duodenum at the top dose, interpreted as a pre-neoplastic lesion. **Based on the results, the risk phrase Xn; R40 "Limited evidence of a carcinogenic effect"** is proposed.
The relevant NOAEL is 4 mg/kg bw/day (25 ppm) in male mice based on reduced body weight gain (Mellert *et al*., 2001b).

2.6. REPRODUCTIVE TOXICITY

Two studies on the rat were evaluated in the DAR in order to determine the reproductive effects of dimoxystrobin (one-, and two- generation studies). There were no direct effects on reproductive performance or fertility observed up to the highest dose level (i.e.1200 ppm).
The reproductive NOAEL is 136 mg/kg bw/day (i.e. 1200 ppm, highest dose tested) (Schilling *et al*., 2001a). The relevant parental NOAEL was set to 17 mg/kg bw/day based on slight anaemia at 500-1200 ppm (Schilling *et al*., 2001a).

In order to examine teratogenic or developmental effects of dimoxystrobin one study in rat and two studies in the rabbit were submitted in the dossier and two.
Dimoxystrobin did not seem to induce teratogenic or fetotoxic effects at the highest doses in the rats. Increased resorption rate were observed in the rabbits but at a dose that was highly toxic to the dams.
The relevant developmental NOAEL is 20 mg/kg bw/day in the rabbit based on reduced gravid uterus weight, increased resorption rate, increased post implantation loss and increased no of foetuses with variations (fused sternebrae) (Schneider *et al*., 2001). The relevant maternal NOAEL is 5 mg/kg bw/day in the rabbit based on reduced food consumption and body weight loss (Schneider *et al*., 2001).

2.7. NEUROTOXICITY

There were no indications for dimoxystrobin being neurotoxic in acute and repeat dose neurotoxicity studies.

The observed iron deficiency (see 2.8, below) might be involved in the duodenal thickening but it might also be associated with neurobehavioral deficits at levels that do not induce recognisable anaemia. It was questioned in the reporting table by a Member State if a developmental neurotoxicity study would be needed since no behavioural endpoints have been evaluated in the multigeneration

studies. This issue was discussed at the experts' meeting in May 2004 (EPCO 4) and the rapporteur Member State had prepared an addendum with summaries of scientific articles on relevance of iron deficiency in respect of disturbance of neurological development in young animals. The meeting concluded that such a study would be useful, but not essential. The safety factor was discussed and the experts agreed that an additional factor of 10, instead of 2, would be appropriate for ADI and ARfD. The utilization of iron in young animals was approximately 10-fold higher than in adults. For AOEL the proposal from rapporteur Member State was accepted. The setting of the ADI and ARfD is discussed under 2.10.

2.8. FURTHER STUDIES

Mechanistic studies

Several studies on the possible mechanism of tumour formation are presented in the DAR. The rapporteur Member State summarises that the duodenum is the main site for iron absorption. In the studies the results indicates that increased duodenal thickening is related to decreased levels of iron in serum. However, the rapporteur Members State highlights that the results in the mechanistic data is not completely consistent. Although, further mechanistic studies indicate that duodenal tumours in mice were caused by a persistent cell proliferation related to increased functional demand on the duodenum to compensate for decreased iron levels in serum.

In a 7-day screening study in adult rats, not in accordance to any guideline, GLP or QA the NOAEL was 50 ppm i.e. 4 mg/kg bw/day based on serum depression of iron.

A further study, 7-day study in young rats (Cunha *et al*., 2005), was submitted after the experts' meeting and is evaluated by the rapporteur Member State but not peer reviewed by experts' meeting The study is summarized in the Addendum from June, 2005. The rapporteur Member State concludes that there is an indication that there is a need to consider up to 5-fold greater depression in serum iron levels in young rats compared to adult rats at the effect level of 33 mg/kg bw/day. The rapporteur Member State also concludes that this does not change the proposed additional safety factor for the reference values agreed at the experts' meeting.

Metabolites

Toxicity of the numerous metabolites was considered as assessed within the rat metabolism studies (B.6.1), for 505M01 there were additional studies submitted and evaluated.

505M01[10]

M01 is a photolysis metabolite in environmental studies as well as on rotational crop and in hens. It was formed in rats and found < 1% in urine. It was of low acute toxicity i.e. LD_{50} > 2000 mg/kg bw. It was neither mutagenic (bacterial reverse mutation study) nor induced gene mutation in mammalian cells.

[10] 505M01: ((*E*)-2-(2-hydroxymethylphenyl)-2-methoxyimino-N-methyl-acetamide)

505M08 and 505M09

The two metabolites 505M08 and 505M09 were considered to have the potential to contaminate groundwater (see section Fate and behaviour). According to lysimeter studies performed with a higher application rate than representative uses the highest annual combined concentration of dimoxystrobin, 505M08 and 505M09 is 4.35 µg/L (505M08 2.35 and 505M09 1.99 µg/L, respectively) which is above the 0.1 µg/L limit set by the Drinking Water Directive (98/83 EC). Fate assessment concluded that even at the rates proposed for the representative uses the trigger of 0.1 µg/L may be exceeded (see 4.2.2). On request from the experts' meeting on fate and behaviour (EPCO 2) it was discussed whether the metabolites 505M08 and 505M09 were considered as toxicologically relevant or not.

There are no toxicological studies performed on the substances. However, they were both identified in urine and faeces after exposure of dimoxystrobin. In the DAR, the rapporteur Member State argues that the metabolites have structural similarities with parent compound (replacement of CH_3 by COOH on the phenyl ring). Thus, according to the toxicological profile of dimoxystrobin it would be reasonable to suspect that 505M08 and 505M09 are not toxic or highly toxic. In a similar way it might be assumed that they are not genotoxic since dimoxystrobin is not. However, since dimoxystrobin induces duodenal tumours and is proposed to be classified as a category 3 carcinogen (R40) and thus it might be suspected that the metabolites 505M08 and 505M09 could be regarded as potential carcinogens as well and a similar NOAEL as for dimoxystrobin be set.

This issue was discussed at the experts' meeting and the rapporteur Member State had presented reasoning and argumentation in the addendum why they should not be regarded as of concern based on risk assessment, not on hazard.

However, the MAC is according to the Drinking Water Directive 0.1 µg/L which is exceeded according to the outcome in the lysimeter study. **Therefore, the majority of the experts at the m eeting concluded that the metabolites 505M08 and 505M09 are indeed toxicologically relevant,** due to the structural similarity with dimoxystrobin, and that they should be considered in the groundwater assessment. Note: The rapporteur Member State did not agree with this conclusion.

505M76[11]

A major component of the residue in goat milk and tissues, metabolite 505M76, was not identified in the rat metabolism studies. No further toxicological studies are performed on 505M76.

Second active ingredient in the formulation BAS 507 00F; Epoxiconazole

In the formulation, epoxiconazole is a second active ingredient. The rapporteur Member State had performed a national evaluation in 1994 and presents a brief summary under B.6.13 "toxicological data on co formulants", in the DAR of dimoxystrobin.

EFSA notes that epoxiconazole has not yet been evaluated but will be in the stage 3A of the review programme (RMS: DE) and thus the studies have not been peer reviewed and none of the values has been agreed on. **All values for epoxiconazole should be regarded as provisional until agreed on.**

[11] 505M76: (2E)-2-{2-[(5-carboxy-4-hydroxy-2-methylphenoxy)methyl]phenyl}-2-(methoxyimino)-N-methylacetamide

The toxicological profile of epoxiconazole is that it of low acute toxicity. The main effects are on red blood cells, reproductive toxicity, liver tumours in the mouse, ovarian and adrenal tumours in the rat attributed to steroid hormonal balance. Epoxiconazole is a liver enzyme inducer. The relevant NOAELs for short term as well as long term exposure are in the same range as for dimoxystrobin and the rapporteur Member State proposed ADI and AOEL that were in the same range as dimoxystrobin. The rapporteur Member State proposed a dermal absorption value 10% both for concentrate and spraying solution for epoxiconazole in BAS 507 00F.

However, the classification of epoxiconazole was agreed on in 2004 at the 29th ATP which was: Carcinogenic category 3, R40 and reproduction toxic category 3, R62 and R63.

The toxicological profile of the formulation BAS 507 00F (containing both dimoxystrobin and epoxiconazole) was; acute oral and dermal LD_{50}> 2000 mg/kg bw (m) and 1421 mg/kg bw (f), acute dermal LD_{50} > 2000 mg/kg bw, inhalatory LC_{50} 1 mg/L (m) and 3.47 mg/L (f), classification **R20/22**, **"Harmful by oral intake and inhalation",** is proposed. Slight but reversible eye and skin irritation was observed but no sensitizing effects.

2.9. MEDICAL DATA

Since industrial production has not yet commenced no data on medical surveillance of the manufacturing personnel are available. No clinical cases or incidences of poisoning known.

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

ADI

Initially in the DAR the rapporteur Member State proposed an ADI of 0.02 mg/kg bw/day based on the NOAEL of 4 mg/kg bw/day from the 7-day rat study (Mellert and Deckardt, 2002) based on decreased serum iron. This was supported by the same NOAEL from the 18-month mouse study (Mellert *et al*., 2001b), based on reduced body weight gain. An additional safety factor of 2 was added due to an assumption that the variability of iron requirements amongst humans is significat. Tumours were evident and the safety margin to thyroid adenomas in rats and tumours in the duodenum in mice is ≥1000. However, the lowest dose where duodenal thickening was observed was 2 mg/kg bw/day in the 24-month rat study but this incidence was not confirmed histologically and no severe lesions or tumours were seen in the duodenum, major effects were observed at 23 mg/kg bw/day which results in a safety margin of > 1000.

The ADI, as well as ARfD values were discussed at the experts' meeting and it was agreed that they should be based on the NOAEL of 4 mg/kg bw/day as proposed by the rapporteur Member State. However, **the experts agreed to apply the safety factor of 1000** since it the iron utilisation in young animals is approximately 10-fold higher than adult animals (which is confirmed, see 2.8).

The resulting final ADI is thus 0.004 mg/kg bw/day.

AOEL

The AOEL is based, similarly to the ADI and ARfD, on the NOAEL of 4 mg/kg bw/day from the 7-day rat study (Mellert and Deckardt, 2002) supported by the same NOAEL from the 18-month mouse study (Mellert *et al*., 2001b), with a safety factor of 200 and no correction for oral absorption required.

The AOEL was discussed at the experts' meeting and the experts concluded that the safety factor of 200 was justified. It was considered at the experts' meeting that the potential for reduced availability of iron in the diet is not relevant for estimations of operator, worker and bystander exposure.

The AOEL is 0.02 mg/kg bw/day.

ARfD

Initially in the DAR, the rapporteur Member State proposed an ARfD of 0.04 mg/kg bw/day based on the NOAEL of 4 mg/kg bw/day from the 7-day rat study with rats based on decreased serum iron (Mellert and Deckardt, 2002), with a safety factor of 100.

The ARfD value was discussed at the Expert meeting and it was agreed that it should be based upon the NOAEL of 4 mg/kg bw/day as proposed by the rapporteur Member State. However, the Expert meeting agreed to apply the higher safety factor of 1000, due to the severe effects, similar to the arguments for ADI, see above.

The resulting final ARfD is thus 0.004 mg/kg bw/day.

2.11. DERMAL ABSORPTION

The formulation, BAS 507 00F, is a water soluble concentrate (SC) **containing two active ingredients** dimoxystrobin (12.5% w/w) and epoxiconazole (4.7%, w/w, of the formulation). The spray dilution will contain 0.5-1.0 g dimoxystrobin/L (0.05-0.09% w/w) and 0.19-0.38 g epoxiconazole (0.02-0.04% w/w).

A brief summary on *in vivo* and *in vitro* studies on dermal absorption is presented in B.6.1.3.3. The studies were **not performed on the representative formulation BAS 507 00F** but on dimoxystrobin diluted in a solvent formulation with a similar composition of the non-active co-formulants in BAS 507 00F, an "artificial BAS 507 00F". The highest tested concentration was comparable to approximately 25% of "artificial BAS 507 00F concentrate", the lowest equated to the spray dilution. Based on *in vivo* rat absorption of 6% and correction for a difference between human and rat skin of 15 times, the rapporteur Member State proposed in the DAR that the dermal absorption should be rounded to 1% for both undiluted and diluted formulation.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative formulation BAS 507 00F is a water soluble concentrate (SC) **containing two active substances**; 133 g dimoxystrobin/L and 50 g epoxiconazole/L. The plant protection product is applied using conventional field crop sprayers and water is intended the dilutent/carrier.

As the representative formulation contains two active substances the operator exposure follows a combined approach. In the DAR the rapporteur Member State presented a risk assessment for each of the two active substances. For dimoxystrobin, the risk assessment is based on **dimoxystrobin in the "artificial formulation BAS 507 00F".**

The risk assessment for the second active substance, epoxiconazole, is based on the assumptions and proposals of the rapporteur Member State to be discussed and agreed on during the peer review of epoxiconazole (stage 3A), see 2.8 for further details. Thus, EFSA highlights that all values for instance the dermal absorption value of 10% and the AOEL of 0.02 mg/kg bw/d for epoxiconazole should be regarded as provisional until agreed on. Attention should be paid to the reference values where a possible additional safety factor might have to be considered due to the possible severe properties of the compound (for dimoxystrobin the safety factor of 200 was applied for AOEL and 1000 for ADI and ARfD). Further on, the active substances have similar toxicological properties and eventual synergistic effects have not been completely addressed. **The proposed risk assessment is only valid when the toxicological assessment for epoxiconazole has been agreed on later in the process and thus the risk assessment of BAS 507 00F can not be regarded as complete, but only indicative.**

The risk assessment for epoxiconazole is based on the estimated exposure was calculated for: epoxiconazole in the formulation Opus (containing 125 g epoxiconazole /L).

Opus is a SC formulation, an herbicide used on wheat, barely, rye and triticale applied via ground spraying. No detailed information is presented in the DAR.

Operator exposure

The estimated operator exposure is calculated using the German model (geometric mean) and the UK POEM.

i) dimoxystrobin

The estimated exposure is below the AOEL without any PPE for dimoxystrobin in the "artificial BAS 507 00F", see table below.

ii) epoxiconazole

The estimated operator exposure for epoxiconazole is below the AOEL in the German model without PPE and with PPE during both mixing and loading as well as during application according to the UK POEM.

Combined risk assessment

If, all values are agreed on and if the actual exposure should be identified as being additive, then it might be assumed that the exposure is below the AOEL, which in this case is similar i.e. 0.02 mg/kg bw/day for both active substances, in the German model without PPE (61%) or with PPE during both

mixing and loading as well as during application according to the UK POEM (45%) for both dimoxystrobin and epoxiconazole.

Estimated operator exposure, % of AOEL for dimoxystrobin and epoxiconazole (will be peer reviewed on stage 3A, data thus provisional) respectively (in this case the same i.e. 0.02 mg/kg bw/day), according to calculations with the German model and the UK POEM.

Active substance (dermal absorption)	**Model**	**No PPE**	**With PPE gloves (M/L)**	**With PPE gloves (M/L and A)**
Dimoxystrobin (1%)	German	13	7	
	UK POEM	85	40	15
Epoxiconazole (10%)	*German*	*48*	*22*	
	UK POEM	*298*	*140*	*30*

Worker exposure

In the DAR the worker exposure was addressed by a reasoned case and by calculation of estimated exposure (based a German model by Hoernicke *et al*., 1998) of dimoxystrobin in the "artificial formulation". The outcome was 6% of the AOEL.

A similar estimation was performed for epoxiconazole (but using the 10% dermal absorption value instead). In this case the estimated worker exposure was 23% of the AOEL (for epoxiconazole).

Bystander exposure

No data was submitted in the dossier. The rapporteur Member State presented calculations (based on Lloyd and Bell, 1983) of estimated bystander exposure of both dimoxystrobin and epoxiconazole, following the assumption presented above, in the DAR which was below the AOEL (< 1%).

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The metabolism in plants was studied in wheat after foliar treatment, by applying dimoxystrobin radiolabelled in two positions. Dimoxystrobin was the major component of the total radioactivity (TRR) in wheat forage (>90%), straw (*ca* 90%) and grain samples (*ca* 60%) and accounted for almost the entire extracted radioactivity. The remaining, unextracted radioactivity in forage and straw was found to be associated with bioploymers such as protein, lignin, cellulose and starch. In grain, total levels of radioactivity were too low to allow further characterization.

In order to investigate effects of industrial or household processing on the nature of the residue a study simulating normal processing practice by applying representative hydrolytic conditions to a test solution was conducted. The study indicated that dimoxystrobin remained unchanged during the tests. Thus, the residue of concern is defined as dimoxystrobin for risk assessment and monitoring purposes. Due to the fact, that the investigation of the metabolic behaviour of dimoxystrobin is limited to cereals only, a final residue definition for plants in general can not be proposed.

The magnitude of dimoxystrobin residues in grain and straw was determined in a total of 35 cereal field residue trials (16 in barley and 19 in wheat) conducted over three growing seasons in Northern and Southern European regions. It is noted that for all trials two applications at the proposed application rate were made instead of the intended one application per crop with a formulation containing also epoxiconazole. All samples were analyzed with validated methods. Dimoxystrobin was the residue determined at a limit of quantification (LOQ) of 0.05 mg/kg. At harvest ($\geq$ 40 days after the last application) no residues above LOQ were found in any of the wheat grain samples; in barley grain the residues accounted up to 0.11 mg/kg. Dimoxystrobin residues in straw ranged between 0.1 and 6.1 mg/kg at harvest. Residues of the second active substance in the formulation, epoxiconazole, have been presented by RMS, but are not peer reviewed. These data need to be assessed in terms of consumer safety when epoxiconazole that is listed for the 3rd stage of the review process has been evaluated.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

The metabolism and distribution of radio labelled dimoxystrobin was studied in the rotational crops wheat, radish and lettuce grown in soil treated at an application rate 3fold critical GAP. A decrease of incorporation of soil residues into the crops due to ageing of soil was not observed for the investigated plant back intervals of 30, 120 and 365 days, as for the respective crops the total radioactivity after harvest was similar for all planting intervals. This corresponds with the observed DT_{90} values in soil > 500 days (see 4.1.2).

In lettuce, radish leaves and roots and wheat grain unchanged dimoxystrobin was present but not always as the major component. The metabolite profile in rotational crops was much more complex compared to that found in the primary wheat metabolism. There were several identified and unknown metabolites but none of these individually were present at levels above 0.01 mg/kg.

In wheat straw dimoxystrobin was the major individual component (up to 14% TRR). Glucosides or malonyl glucosides metabolites (further 8%) have been found besides a number of unidentified metabolites. Considering the increased rate applied all of these unidentified metabolites would be present at <0.01 mg/kg. Up to 44% of total radioactivity in straw was associated with biopolymers such as cellulose, lignin, hemicelluloses, pectin and other cell wall material.

Generally, the metabolic pathway of dimoxystrobin in rotational crops is adequately understood. From use in accordance with GAP, significant residue levels of dimoxystrobin or other metabolites are not expected to be present in rotational crops.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Because significant amounts of dimoxystrobin residues were found in potential feeding stuff at the time of harvest and dimoxystrobin is deemed to be fat-soluble (log Pow 3.6) metabolism studies in livestock are necessary. Studies on the metabolism of radio labelled dimoxystrobin in lactating goats and laying hens were carried out with exaggerated doses compared to the expected exposure of the animals from cereal grains and straw. The majority of the administered radioactivity (*ca* 86-99%) was excreted by both species. Additional *ca* 1 -7 % were recovered in the Gastro intestinal tract. The sum of residues in edible tissues, organs, milk and eggs, respectively, was found to be less than 1% of the total administered dose.

Dimoxystrobin was extensively metabolised by both species. The major components in liver, kidney and milk of goats were the carboxylic acid metabolite 505M09 and the hydroxyl acid metabolite 505M76 (both up to *ca* 20% TRR), whereas dimoxystrobin accounted for less than 10% TRR in all three matrices. Attempts for identification of residues were also made in eggs, fat and liver of hens. Dimoxystrobin accounted for up to 15% TRR in hen fat, equivalent to 0.001-0.002 mg/kg, and was the only identified compound in eggs. Major metabolite in liver and fat were 505M02[12] (up to 33% TRR) and 505M78[13] (up to 23% TRR). None of the metabolites found in goats or poultry were considered to be of greater toxicological significance than dimoxystrobin. However, metabolite 505M09 forms a significant portion of the total residues in all edible animal matrices and, moreover, was considered as possibly toxicological relevant. Metabolite 505M76 was not specifically found in the rat. (See 2.8) Thus, the residue definition for risk assessment purposes includes dimoxystrobin and the metabolites carboxylic acid metabolite 505M09 and the hydroxyl acid metabolite 505M76. In terms of MRLs and post approval monitoring of animal products, dimoxystrobin or metabolite 505M09 would be adequate markers. Both have been found to be suitable for analysing with multi-residue methods. (See 1.) In the evaluation meeting Member States agreed with the RMS proposal, that for monitoring purposes the residue should preferably be defined as dimoxystrobin. However, in terms of the possible toxicological relevance of 505M09 and it's quantity in animal matrices compared to that of dimoxystrobin EFSA considers metabolite 505M09 as more appropriate for post approval monitoring of animal products.

In a livestock feeding study on cows dosed with dimoxystrobin (30 days; 2.5, 7.5 and 25 mg/kg feed DM) samples were analysed for residues of dimoxystrobin and the metabolites 505M09 and 505M76. Residues in milk samples from the animals of all dose levels were individually all below the LOQ of 0.01 mg/kg. Residues in samples of muscle, liver, kidney and fat from all dose groups were also all individually below the LOQ of 0.025 mg/kg. A feeding study for poultry has not been provided but is not required because intake of residues by poultry from the consumption of cereal grain is insignificant.

[12] 505M02: (E)-o-(2,5-dimethyl-4-hydroxy phenoxymethyl)-2-methoxyimino-N-methylphenylacetamide

[13] 505M78: 4-({2-[(1*E*)-*N*-methoxy-2-(methylamino)-2-oxoethanimidoyl] benzyl}oxy)-2,5-dimethylphenyl glucopyranosiduronic acid

3.3. CONSUMER RISK ASSESSMENT

The long term total dietary intake for dimoxystrobin (and relevant metabolites for animal products) has been carried out using consumption data for UK consumers (NEDI, UK Rees/Day Model). Total intakes for all consumer groups were all well within the proposed ADI of 0.004 mg/kg bw/day, accounting for 13-83% of the proposed ADI. The total intake (TMDI) for an adult based on the WHO/GEMS Food Standard European Diet was 20% of the proposed ADI.

In groundwater the level of 0.1 µg /L is expected to be exceeded by the metabolites 505M08 and 505M09 (refer to 4.2.2). Moreover, both metabolites are considered toxicologically relevant (refer to 2.8.). Therefore, a consumer risk assessment was performed, considering the sum of possible intakes of the two metabolites and dimoxystrobin from drinking water in addition to the intake through diet. Intake estimates with the highest annual average concentration of dimoxystrobin, 505M08 and 505M09 were submitted by RMS in an addendum. The estimates are based on the default assumptions laid down in the WHO Guidelines of drinking water quality and on values from lysimeter studies performed at twice the intended application rate. For the considered consumer subgroups of infants, toddlers and adults the estimated intakes from drinking water are *ca* 16%, 11% and 4% of the ADI of dimoxystrobin, respectively. The total intake from diet and drinking water is accounting for up to *ca* 99% of the ADI of dimoxystrobin for infants.

A short term exposure risk assessment indicated that the National estimated Short Term Intake (NESTI), using the UK model for adults and toddlers, is accounting for up to *ca* 48% of the ARfD from the consumption of milk by toddlers. An acute risk due to the intake of dimoxystrobin and metabolites 505M08 and 505M09 from drinking water is not expected.

However, it is noted that no toxicological studies were performed on the metabolites. Assumptions on their toxicological properties are based on their high structural similarity with dimoxystrobin (refer to 2.8.).

3.4. PROPOSED MRLS

It is proposed to set the maximum residue level (MRL) in barley grain to 0.1 mg/kg and in wheat grain to the limit of quantification (LOQ) of the analytical method of 0.05 mg/kg, resulting in an MRL of 0.05* mg/kg. Further on MRLs for meat, kidney, liver and fat are proposed at the LOQ of 0.03* mg/kg and for milk at the LOQ of 0.01* mg/kg. The proposals are based on the LOQ of the LC-MS/MS method and are applicable for both options of either dimoxystrobin or metabolite 505M09 as the defined residue for post approval monitoring.

Currently, no Codex MRLs have been established or proposed yet and need to be considered.

4. Environmental fate and behaviour

Dimoxistrobin was discussed in the experts' meeting on the fate and behaviour in the environment EPCO 2 (April 2004).

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of dimoxystrobin in soil was investigated under dark aerobic conditions at 20 ºC and 45 % maximum water holding capacity (MWC, 44 g water/100g dry soil) in one study with sandy loam soil (pH 7.5, 2 % oc). Active ingredient labelled at the phenyl or the benzyl rings was employed in this study. Formation of the main metabolites was also investigated in another study with four soils under various conditions of temperature and humidity (T= 5 ºC, 20 ºC and 30 ºC, 20-40 % MWC, pH 5.8 – 7.7, 0.6-3 % oc) using the active ingredient labelled at the benzyl ring.

Dimoxistrobin (pure *E* isomer) used in the fate and behaviour studies was contaminated with different levels of the Z-isomer (2-12 % AR). The percentage of Z-isomer is constant or decreases slightly during the studies. It is noted that the amount of Z-isomer in the product employed for the soil degradation studies is about 10 to 50 times higher of what would be expected from the technical specifications. For the kinetic analysis the amount of isomer was added up to the amount of parent dimoxistrobin. Since the ether of oxyme is not directly involved in the first degradation steps of dimoxystrobin, this approach is found scientifically acceptable. The degradation of dimoxystrobin in soil is initiated by the oxidation of methyl moieties in positions *orto* or *meta* of the phenyl ring yielding various metabolites. Of these metabolites, only metabolite **505M09** (maximum 13 % AR after 90 d) attained levels above 10 % AR in some of the laboratory experiments. However, in field studies also metabolite **505M08** was found at levels above 10 % (corrected for molecular weight) of the applied parent which corresponds to measured levels slightly above the LOQ in the corresponding studies. Metabolite 505M01 was found in field studies but at levels below 7 % of the applied parent. Maximum mineralization after 120 d was 24 % AR for the phenyl labelled moiety and 14 % AR for the benzyl labelled moiety in the first route study, but was below to measurable levels in the second study performed with benzyl labelled dimoxystrobin. Unextractable radioactivity amounted to a maximum of 24 % after 120 d and 32 % AR after 1 year.

An anaerobic degradation study in soil (sandy loam, pH 7.5, 2% oc) at 20 ºC under dark conditions shows that dimoxystrobin is not degraded under anaerobic conditions. The soil photolysis study shows that degradation of dimoxistrobin is enhanced under irradiated conditions. Due to the analytical method employed it was not possible to differentiate dimoxystrobin from its Z isomer. Therefore, potential photoisomerization was not tested and may not be excluded for this class of compounds. A major photolysis metabolite **505M01** (maximum 10.78 % AR after 15 d, end of the study) is identified in the soil photolysis study.

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

Rate of degradation of dimoxystrobin in soil was investigated in six soils (20 ºC, 40 % MWC) as part of the same studies used to investigate the route of degradation. Dimoxystrobin is medium to high persistent (DT_{50} = 88 – 401 d) in soil at 20 ºC. The rate of degradation of metabolites 505M08 and 505M09 was investigated in the same six soils fitting data to a multicompartmental model by ModelMaker (505M08: DT_{50} = 14 – 61 d; 505M09: DT_{50} = 15 – 69 d).

Three field dissipation studies were performed in Germany, two in Spain and two in Sweden. These field studies do not fully represent the cropping situation of the representative uses since the product is applied to bare soil whereas in the proposed use the product must be applied when the crop is near to fully development. Results of these studies were analyzed with a Model Maker. The degradation of dimoxystrobin could not be satisfactory described by simple first order models in these field trials. A three compartment model that assumes equilibrium between a protected and an unprotected compartment is used to describe and explain the initial fast dissipation in the German trials. Slightly different 3-compartment models were proposed for the Spanish and Swedish trials. Field dissipation DT_{50} was also calculated by the Rapporteur using the Timme and Frehse best fit approach. These calculations show that dissipation of dimoxystrobin in soil is in some instances initially rapid (DT_{50} = 8 – 120 d) but then slowed significantly (DT_{90} > 500 d). However, given the limited data points in the trials, the models are considered to have underestimated the DT_{50} and overestimated the DT_{90}. Approximately 14.3 % - 16.5 % of the initial soil core parent residue remained 1 yr after application in the German and Spanish trials. In the Swedish trial as much as 44 % of the initial soil core parent residue remained after 1 yr. Disregarding the first soil core sampling, but accepting all the rest does have a substantial impact on some of the DT_{50} values. An additional first order calculation was provided excluding the first data point (potentially affected by photolysis) and the results of the Spanish trials (due to the dryness of the field soil according Dutch CTB standards) and the results were standardized to reference temperature and moisture conditions. Under these assumptions dimoxystrobin shows to be moderate to high persistent in field ($DT_{50\ (20\,°C,\ pF2)}$ = 57.6 -131.6 d).

As the field DT_{90} of dimoxystrobin was greater than 1 year, accumulation of dimoxystrobin in soil was investigated under field conditions in two trials in S.W. Germany, following repeated annual application to cereals over three years. The residues were not measured immediately after each application and only 5 time points were analysed over the whole period of three years. Results seem to indicate that residues decline below the limit of quantification (LOQ = 0.01 mg / kg) between applications but some accumulation may not be completely excluded. Metabolites 505M01, 505M08 and 505M09 were found only at LOQ, except for one detection of 505M09 at 0.0103 mg/kg.

Standard PEC soil (0 – 100 d) were calculated for parent and metabolite 505M01. Worst case field half lives standardised to 20 ºC (DT_{50} = 131.6 d) were corrected to 15 ºC (DT_{50} = 195.2 d). Worst case maximum amount PEC soil for metabolite 505M01 was calculated assuming 100 % transformation from parent dimoxystrobin. The PEC soil for 505M09 were calculated with a five compartmental model. Half life of 38 d was used (from phenyl labelled study instead of worst case from benzyl labelled study were half life is 61 d). Maximum amount obtained in this modellization exercise was 12.8 % (experimentally observed 13%). PEC soil after the maximum concentration were calculated. No PEC soil was calculated for metabolite 505M08.

Potential for accumulation of dimoxystrobin in soil was evaluated by calculating plateau PEC soil after annual application over 26 years using FOCUS-PEARL and the EU scenarios Jokioinen, Hamburg and Sevilla. Average field half life standardised to 20 ºC of 82.5 d was proposed in the calculation provided by the notifier. RMS repeated the modelling exercise using the longest field half life standardised to 10 ºC (DT_{50} = 289.5 d). In the RMS calculation maximum plateau concentration was reached after 5 years (PEC soil acc = 0.046 mg/kg). However, a different method of calculation

was used in the ecotoxicology section resulting in a predicted concentration of 0.04 mg/kg for immediately after the second application in the organic matter breakdown study (litter bag test). This is considered reasonably close to the worst case peak plateau concentration of 0.046 mg/kg. Residues seen in the field accumulation trials were considered to be mostly in the range of predicted concentrations.

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

Two batch equilibrium adsorption/desorption studies with a total of seven soils were conducted for dimoxystrobin and one batch adsorption/desorption study with seven soils was conducted for each of the metabolites 505M01, 505M08 and 505M09.

According these studies dimoxystrobin may be classified as low to medium mobile in soil (Koc = 196 – 935 mL / g), 505M01 as very high mobile (2 – 35.5 mL / g), 505M08 as high to very high mobile (7.8 – 133.0 mL / g) and 505M09 as high to very high mobile (9.0 – 119 mL / g).

Column and aged column leaching studies are available. A maximum of 2.5 % AR is found in the leachate, this was not identified but is claimed not to be parent dimoxystrobin.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

The hydrolytic stability of dimoxystrobin was studied in sterile aqueous buffer solutions (pH 4, 5, 7, and 9) at 25 ºC and 50 ºC. Dimoxystrobin is stable at all environmental relevant pHs. Photolysis in water was investigated in two different studies. Photolysis may moderately contribute to the degradation of dimoxystrobin in water. Measured half life under continuous irradiation under laboratory conditions was 14.1 d (pond water) and 64.8 d (sterile buffer pH 7, extrapolated).

Distribution and degradation of dimoxystrobin (benzyl and phenyl radiolabels) was further investigated using two natural water sediment systems, incubated in the dark at 20 ºC for 100 d. Sediment (2-2.5 cm) and water (6 cm) were similar in properties in both systems (sediment organic carbon content 1-1.23 %, pH 7.5-7.6 for sediment and pH 8.2-8.5 for water). Degradation of dimoxystrobin in both systems was very limited. Little if any mineralization occurred until after 61 d, then reaching a maximum of 2.1 % AR by day 100. Unextractable residue in sediment was also low, rising to 6.3 – 10 % AR by day 100. Only 10-15 % of the applied dimoxystrobin degrades after 100 d (extrapolated DT_{50} for the whole system 302 – 520 d). Disappearance from the water phase is mainly attributed to partition with sediment. Fitting to first order degradation kinetics was not possible because once the equilibrium between phases is reached dissipation turns to be much slower. Fitting data to a two compartment biphasic model a DT_{50} = 15 – 27 d and a DT_{90} = 136 d - > 200 d were obtained for each system.

Additionally an outdoor water sediment study and an outdoor mesocosm study in Germany were used to investigate the aquatic dissipation of dimoxystrobin. Photolysis and partition to sediment was considered the main routes of dissipation of dimoxystrobin from the water phase in the outdoor water sediment study. Levels of dimoxystrobin remaining in the water phase after 100 d were slightly lower (9.6 % – 10.7 % AR) than in the laboratory studies. A first order water phase $DT_{50water}$ = 15.3 d was

calculated using only 0-58 d data. Whole system first order $DT_{50whole}$ = 26.9 d was calculated using only 0-58 d data. Almost no degradation was observed for day 58 onwards due to lower irradiation on September and November.

In the mesocosm study dimoxystrobin was applied in early May and a water phase DT_{50} = 60 – 69 d was calculated.

RMS surface water risk assessment was based on outdoor water sediment study and spray drift loadings to surface water. Time dependent PECsw were calculated ($DT_{50water}$ = 15.3 d from outdoor water sediment study), but only initial PECsw were finally used in the assessment. Other potential routes of surface water contamination such as run off and drainage are partially addressed in the DAR following published (run-off)[14] and national RMS scheme (drainflow)[15] but were not used further for the EU risk assessment by the RMS. FOCUSsw calculations were not presented.

In the EFSA Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues related to the evaluation of dimoxystrobin;[16] exposure regime in the golden orfe ELS study was compared with FOCUS surface water estimates for some selected scenarios. For its exposure calculations with FOCUSsw scenarios the PPR Panel used the DT_{50} = 63.5 d from the outdoor pond mesocosm study, as conservative but realistic and therefore the most relevant value for the exposure assessment. In this opinion it is highlighted that assuming a single exposure event (as per the assessment presented in the DAR) applies only to exposure *via* the initial spray drift even. Any other exposure routes as runoff and drain flow which occur with delay and may occur repeatedly after application are not covered by RMS assessment. The exposure assessment at EU level aims to allow an EU-wide decision by using a range of scenarios which together are representative for the variety of agro-climatic conditions. In the EU aquatic risk assessment procedure, the exposure in major agricultural regions across the EU is assessed with FOCUSsw Step 3 scenarios. These scenarios include ponds, ditches and streams showing a very large variability with respect to the course of concentration with time. The FOCUSsw PEC calculations made by the PPR panel provided concentration profiles for the selected scenarios as well as information on which route of exposure (spray drift, runoff or drainage) provided most of the load. As a result of the FOCUSsw modelling exercise, the PPR Panel noted that even spray drift deposition is lower in the FOCUSsw modelling than in the DAR (1.72 % *versus* 2.77 %) FOCUSsw simulations predict higher PEC values (0.15 - 3.64 µg / L) than those calculated in the DAR (1.85 µg / L). Contributions of the different loading routes were analysed by the Panel finding that drainage and runoff were the major contributors to the surface water contamination for some of the selected scenarios. The run off and drainage PECsw

[14] Kloskowski, R. *et al.* (1999), Draft guidance on the calculation of predicted environmental concentration values of plant protection products for soil, groundwater, surface water and sediment.-in human and environmental exposure to xenobiotics. Proceedings of the XI symposium Pesticide Chemistry, Sept 11-15, 1999. Cremona Italia, 835-850.

[15] PSD Data requirements handbook, Chapter 6.5, pp 32-35. PSD, Mallard House, Kings Pool, 3 Peasholme Green, York, YO107OX.
http://www.pesticides.gov.uk/psd_pdfs/registration_guides/data_reqs_handbook/datareqhandbook.pdf

[16] 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.

estimations presented in the DAR were also considered by the PPR Panel. With respect to the runoff the PPR Panel found that some of the FOCUSsw scenarios predict a PECsw peak about 30 times higher and runoff concentrations about 10 higher than those run off estimations provided in the DAR. With respect to the drainage the PPR Panel found that some of the FOCUSsw scenarios predict a PECsw peak about 4 times higher and drain flow concentrations about 10 higher than drainflow estimations provided in the DAR.

A complete FOCUSsw assessment is necessary to characterize the risk in the major agricultural regions across the EU. An illustrative risk assessment based only on spray drift loadings is presented by EFSA in an addendum. The need for risk mitigation measures is already identified. However, 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 EU risk assessment.

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

Concentrations of dimoxystrobin and its soil metabolites 505M08 and 505M09 in groundwater resulting form the representative uses were predicted with FOCUSgw scenarios in conjunction with the model FOCUS- PEARL 1.1.1. and FOCUS-MACRO 2.2.1 (Chateaudun). Predicted 80 th percentile annual leachate concentrations were below 0.1 µg / L trigger for dimoxystrobin and metabolites 505M08 and 505M09 for all the situations modelled when average field DT_{50} = 82.5 d was used as input parameter.

An outdoor lysimeter study in Germany is available. Three lysimeter vessels filled with different soils were investigated after two applications of 500 g of ^{14}C-dimoxystrobin the first year in two vessels and the first and second year in the other one. Exceedance of yearly average 0.1 µg / L trigger in the leachate was observed for metabolites 505M08 and 505M09 for all three years in all the systems studied. These results were discussed during the experts meeting on fate and behaviour in the environment (EPCO 2, April 2004). Linear reduction of these results based on the lower rate proposed for the representative uses still result in levels of metabolites just above the trigger of 0.1 µg / L. By comparison of modelling and lysimeter results the meeting concluded that high interception was needed to reduce the potential of ground water contamination and that uses may need to be restricted to late growth stages, such us the ones proposed for the representative uses (max appl. 0.2 kg / ha, cereals GS49 , crop interception 90 % or greater). The meeting agreed that assessment of relevance of metabolites 505M08 and 505M09 had to be performed before finalising the EU risk assessment. Result of this relevance assessment is summarized in the table found in the section 6 for the residue definition. Potential for groundwater contamination by 505M08 and 505M09 under vulnerable conditions needs to be assessed at MS level.

The results of the lysismeter study were also used to calculate PECgw values for the photolysis metabolite 505M01 applying adjusting factors to account for lower amounts of substance reaching the soil in the representative uses and the fact that the application rate was higher than the proposed in the lysimeter study. Even without the application of these adjustment factor the concentration of the photodegradation product 505M01 are below the 0.1 µg / L trigger.

4.3. FATE AND BEHAVIOUR IN AIR

Concentrations of dimoxystrobin in air are expected to be negligible due to low volatility and short half life in air for reaction with OH radicals.

5. Ecotoxicology

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk assessment for birds and mammals was conducted by the RMS according to the EPPO vertebrate risk assessment scheme. The acute, short term and long term risk of dimoxystrobin to insectivorous birds and the acute and long term risk to mammals was assessed to be low since the TER values were well above the Annex VI trigger values.

For birds and mammals EFSA provided a risk assessment according to the latest guidance document (Sanco/4145/2000 of 25 September 2002) in an addendum which however was not yet peer reviewed. The TER values for the acute, short term and long term risk to insectivorous birds and mammals were above the Annex VI trigger values. However, the long term TER values of 6 (birds) and 7.5 (mammals) did not extensively exceed the relevant trigger value of 5.

It should be taken into account that the complete risk assessment for birds and the long term risk assessment for mammals is based on the endpoints deriving from studies with the technical active substance. Since the lead formulation contains a second active substance (epoxiconazole, listed for the 3rd stage of the peer review process) it is questionable whether it is possible to extrapolate from the toxicity of the technical active substance to the formulated product. Additionally, the acute studies with rats showed that the formulated active substance in the lead formulation is more acutely toxic than the technical active substance.

The first tier risk assessment for the uptake of contaminated drinking water revealed a high acute and long-term risk for mammals and a high short-term and long-term risk for birds. Further refinement steps are necessary to address the risk to birds and mammals via this exposure route.

EFSA is of the opinion that a high acute, short term and chronic risk to birds and a high chronic risk to mammals cannot be excluded if the lead formulation is applied according to the GAP. Consequently, a new data requirement is proposed by EFSA: The notifier is asked to address the risk of the formulated active substance to birds and mammals.

5.2. RISK TO AQUATIC ORGANISMS

The first tier risk assessment for fish, invertebrates and algae resulted in TER values below the relevant Annex VI trigger values. The TER values were calculated with a PECsw value taking into account only spray drift and a buffer zone of 1 metre.

Additional fish species were tested to reduce the uncertainty deriving from interspecies variability. The technical active substance was of lower acute toxicity compared to the formulated active substance. Therefore five different fish species were tested with the lead formulation BAS 507 00F. The most sensible species was *Pimephales promelas* with an acute LC50 (96 h) of 0.15 mg product/L and a TER value of 10.7. The EPCO 3 Expert meeting (28-29 April 2004) agreed that it is appropriate to follow the approach of the HARAP workshop and to apply the maximum possible reduction of the Annex VI trigger value from 100 to 10 since the sensitivity of the tested species to dimoxystrobin was similar (within a range of 0.0434 – 0.052 mg a.s./L and 0.15 – 0.61 mg formulation/L). Consequently, the acute TER value for fish is slightly above the revised acute TER trigger value of 10.

No agreement was reached in the EPCO 3 Expert meeting (28-29 April 2004) if the chronic risk assessment should be based on the endpoints deriving from the early life stage (ELS) test with rainbow trout (flow through test design) or on the ELS test with golden orfe (single application and presence of sediment). Therefore this question was forwarded to the Scientific Panel on Plant Health, Plant Protection Products and their Residues. The panel concluded that the endpoint of rainbow trout (*Oncorhynchus mykiss*) should be used[17]. The panel concluded on an overall NOEC of 0.316 µg a.s./L based on body length as the most sensitive endpoint.

EFSA provided a risk assessment based on the above mentioned endpoint in an addendum which was not peer reviewed. Since the toxicity data on dimoxystrobin suggest a rather acutely than chronically toxicity it cannot be excluded that a short exposure to dimoxystrobin exceeding the NOEC value could lead to adverse effects. Therefore it was considered as appropriate to compare the NOEC from the ELS rainbow trout study with the peak concentration in surface water. The PECsw calculations in the DAR were based on spray drift resulting in an initial PECsw of 1.85 µg a.s./L. Using the initial PECsw from the DAR the chronic TER value for fish is calculated as 0.17. The TER value of 0.17 is markedly below the Annex VI trigger value of 10 indicating a high chronic risk to fish. A very large buffer zone of 75 m would be required to achieve a TER value of 11.9 to meet the Annex VI trigger.

A mesocosm study was conducted to address the risk to invertebrates and algae. The mesocosm study was discussed at the EPCO 3 Expert meeting (28-29 April 2004). The meeting agreed on the endpoint of 0.005 mg a.s./L from the mesocosm study resulting in a TER of 2.7 at a buffer zone of 1 metre. Furthermore the meeting agreed on a safety factor of 5, taking into account the uncertainty deriving from the low abundance of benthic crustaceans in the mesocosms. The TER trigger of 5 for the risk to aquatic invertebrates and algae would be exceeded at a buffer zone of 5 m. Therefore risk mitigation measures like buffer zones or drift reducing nozzles are required to reduce the risk to aquatic invertebrates and algae.

[17] 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.

It should be taken into account that the PPR panel provided FOCUSsw calculations for selected scenarios where drainage and run-off were identified as main contributors to surface water contamination. Some of the scenarios resulted in peak PECsw values higher than the initial PECsw of 1.85 µg a.s./L (from spray drift). Therefore it is questionable whether buffer zones are sufficient as risk mitigation measures especially with regard to the very high chronic risk to fish. A comprehensive risk assessment taking into account spray drift, run-off, drainage and the effectiveness of potential risk mitigation measures is required.

No major metabolites were detected in the water/sediment study. The metabolites 505M01, 505M08, 505M09 were present in the lysimeter leachates and were tested with fish, daphnia and algae. Their toxicity was 600 times less than that of dimoxystrobin. Therefore the risk from theses metabolites to aquatic organisms is considered to be low.

The risk of bioaccumulation was assessed as low because the BCF for the whole fish was calculated to be 48 which are below the Annex VI trigger value of 100. In the list of endpoints a BCF of 84 was given. This was a typo and amended by EFSA.

The proposal for classification and labelling for dimoxystrobin is: N – dangerous to the environment, R50, R53.

5.3. RISK TO BEES

The effects of the technical active substance and the formulation BAS507007F were examined in acute oral and acute contact tests with bees. The HQ values for the acute oral and acute contact exposure were well below the Annex VI trigger value of 50 indicating a very low risk to bees.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Apart from the two standard species *Aphidius rhopalosiphi* and *Typhlodromus pyri* also *Chrysoperla carnea, Poecilus cupreus, Aleochara bilineata* and a lycosid spider *Pardosa sp*. were tested. The formulated product BAS 507 00F was of low toxicity at the recommended dose level of 200 g a.s./ha and the the Annex VI trigger value of 30% was not exceeded. Hence, the risk for harmful effects on populations of non-target arthropods in the field can be regarded as low for the representative use of dimoxystrobin

5.5. RISK TO EARTHWORMS

Studies on the acute and chronic toxicity to earthworms from the technical active substance, the lead formulation BAS 507 00F and the "solo formulation" BAS 507 01F were available. Short-term and long-term TER values were calculated on the basis of a single application in one year and also on the basis of a worst case peak plateau concentration PECsoil of 0.046 mg a.s./kg after 5 years. Both TER calculations indicated a high long term risk to earthworms.

Therefore five earthworm field studies were conducted. Three studies were of 12 month duration (two with the "solo" formulation BAS 507 01F and one with the lead formulation BAS 507 00F). The other two studies were conducted with the "solo" formulation BAS 507 01F, one of 18 month duration and one of three years duration. Three of the studies with BAS 507 01F (two twelve month and one 18 month) included two applications at the proposed dose of 200 g a.s./ha. Each of these studies showed an initial adverse effect on earthworm numbers and biomass but partial or full recovery to levels comparable to the untreated control by the end of the study. The same pattern was observed in the study with BAS 507 00F.

In the three year study BAS 507 01F was applied once a year. Fluctuations in earthworm numbers and biomass were observed but not clearly related to the treatment. Earthworm number and biomass were identical to those in untreated areas at the end of the study.

The level of dimoxystrobin was not measured in the soil in these studies, but calculations of dimoxystrobin concentration in the soil (based on 90% crop interception, worst case soil half life of 289.5 days and an average soil half life of 181.5 days) conducted by the RMS lead to the conclusion that the concentration levels in the field studies were comparable to the worst case soil plateau levels.

The soil metabolites 505M01, 505M08, 505M09 were clearly less toxic than dimoxystrobin. The 14 day LC50 and NOEC values were >1000 mg/kg for each metabolite. Thus even if 100% conversion of the parent to each metabolite was to occur, the acute risk from each of these metabolites is low.

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

Testing with soil non-target macro organisms was required since the field and laboratory DT90 values for dimoxystrobin in soil were greater than one year. A laboratory reproduction study with the collembola *Folsomia candida* was conducted. The EC50 for reproduction was calculated to be 395 mg BAS 505 00F/kg substrate. A NOEC (reproduction) of 125 mg BAS 505 00F/kg substrate (equivalent to 16.6 mg a.s./kg) was observed. Since the initial and plateau PECs are only 0.027 and 0.046 mg a.s./kg the risk to collembola is considered to be low.

A litterbag study was conducted. No difference in litter degradation was observed in treated and untreated plots. The litterbag study was discussed at the EPCO 3 Expert meeting (28-29 April 2004) because no toxic standard was applied and the bags were removed for 5 weeks between the two applications. The meeting agreed that it is not necessary to ask for a new litterbag study since these points were considered as minor shortcomings of the study and a low risk was noted for collembola and soil micro-organisms.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

Studies were available on the effects of dimoxystrobin, BAS 507 00F and the soil metabolites 505M01, 505M08, 505M09 on soil microbial respiration and nitrogen transformation. Neither respiration nor mineralization of treated soils differed by greater than 25% (=Annex VI trigger value)

from untreated soils at the maximum recommended application rate. Therefore the risk to soil micro organisms is considered to be low.

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

Two glasshouse screening studies with six crop plants were conducted with the lead formulation BAS 505 00F and the "solo" formulation BAS 505 01F. It was observed in the studies that crop damage could occur at the proposed dose of 200 g a.s./ha. Since PEC values for dimoxystrobin would be only 2.77 % of the applied dose at a drift distance of 1 metre, the risk to non-target plants is considered to be low.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The application of 1000 mg a.s./L (technical dimoxystrobin, purity 97.4 %) to activated sludge led to an inhibition of respiration of 5% compared to controls. The EC50 was therefore >1000 mg a.s./L. The risk for biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: dimoxystrobin, 505M09[18], 505M08[19], 505M01[20].
Definitions for monitoring: dimoxystrobin

Water

Ground water

Definitions for risk assessment: dimoxystrobin, 505M09, 505M08, 505M01
Definitions for monitoring: dimoxystrobin, 505M09, 505M08

Surface water

Definitions for risk assessment: dimoxystrobin
Definitions for monitoring: dimoxystrobin

Air

Definitions for risk assessment: dimoxystrobin
Definitions for monitoring: dimoxystrobin

Food of plant origin

Definitions for risk assessment: dimoxystrobin (use on cereals only)
Definitions for monitoring: dimoxystrobin (use on cereals only)

[18]505M09: (E)-o-[(5-hydroxycarbonyl-2-methyl) phenoxymethyl]-2-methoxyimino-N-methylphenylacetamide
[19] 505M08: [*E*-*o*-(2-hydroxycarbonyl-5-methyl)phenoxymethyl]-2-methoxyimino-*N*-methylphenyl acetamide
[20] 505M01: ((*E*)-2-(2-hydroxymethylphenyl)-2-methoxyimino-N-methyl-acetamide)

Food of animal origin

Definitions for risk assessment: sum of dimoxystrobin plus metabolites 505M09 and 505M76[21], expressed as dimoxystrobin

Definitions for monitoring: dimoxystrobin

or alternatively metabolite 505M09, expressed as dimoxystrobin (See 3.2)

[21]505M76: (2E)-2-{2-[(5-carboxy-4-hydroxy-2-methylphenoxy)methyl]phenyl}-2-(methoxyimino)-N-methylacetamide

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
dimoxystrobin	medium to high persistent ($DT_{50\ lab\ (20\ °C)}$ = 88 – 401 d)	See 5.5, 5.6, 5.7
505M09	moderately to medium persistent $DT_{50\ lab\ (20\ °C)}$ = 15 – 69 d	Not relevant The TER values meet the Annex VI triggers and the risk is lower than that of dimoxystrobin
505M08 (> 10 % in field studies)	moderately persistent $DT_{50\ lab\ (20\ °C)}$ = 14 – 61 d	Not relevant The TER values meet the Annex VI triggers and the risk is lower than that of dimoxystrobin
505M01 (photolysis in soil metabolite)	Risk assessment based on worst case maximum formation assuming 100 % transformation from parent compound.	Not relevant The TER values meet the Annex VI triggers and the risk is lower than that of dimoxystrobin

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
dimoxystrobin	medium mobile (Koc = 196 – 935 mL / g)	FOCUS gw: No Lysimeter: No	Yes	Yes	Yes
505M09	high to very high mobile (Koc = 9.0 – 119 mL / g)	FOCUS gw: No Lysimeter: Yes	No[1]	No data available Toxicologically relevant Due to structural similarities with dimoxystrobin it can be assumed that 505M09 is of low toxicity. However, since dimoxystrobin has carcinogenic properties this might also be the case for 505M09.	Ecotoxicologically not relevant The risk to aquatic organisms is considered to be low. The metabolite does not appear as a major metabolite in the water/sediment study but was present in the lysimeter leachates which were 600 times less toxic than dimoxystrobin.
505M08	high to very high mobile (Koc = 7.8 – 133.0 mL / g)	FOCUS gw: No Lysimeter: Yes	No[1]	No data available Toxicologically relevant Due to structural similarities with dimoxystrobin it can be assumed that 505M08 is of low toxicity. However,	Ecotoxicologically not relevant The risk to aquatic organisms is considered to be low. The metabolite does not appear as a major metabolite in the water/sediment study but

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
				since dimoxystrobin has carcinogenic properties this might also be the case for 505M08.	was present in the lysimeter leachates which were 600 times less toxic than dimoxystrobin
505M01	very high mobile (Koc = 2 – 35.5 mL / g)	No (based on lysimeter study)	No data required No data available	Not toxicologically relevant LD_{50} > 2000 mg/kg bw/day Negative in genotoxicity tests	Ecotoxicologically not relevant The risk to aquatic organisms is considered to be low. The metabolite does not appear as a major metabolite in the water/sediment study but was present in the lysimeter leachates which were 600 times less toxic than dimoxystrobin

1 Data on the biological acitivity of 505M08 and 505M09 against four different fungi species was presented in the addendum of June 2005. The pesticidal activity of the metabolites 505M08 and 505M09 was assessed by the RMS to be less than 50% of that of dimoxystrobin. The addendum was not peer reviewed.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Dimoxystrobin (water and sediment)	See 5.2

Air

Compound (name and/or code)	Toxicology
Dimoxystrobin	Harmful (**R20**) by acute inhalation, no study on repeated exposure available (see 2.1, 2.2 and critical areas of concern).

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

- ILV (independent laboratory validation) for the method to determine residue in food of animal origin (relevant for all representative uses evaluated; submission date proposed by the applicant: September 2004; refer to chapter 1).
  In the meantime this study has become available. The assessment of the RMS is confirmed by EFSA.
  In case the residue definition turns out to be 505M09 further validation data maybe required (refer to chapter 1 and 3.2).
- A high acute, short term and chronic risk to birds and a high chronic risk to mammals cannot be excluded if the lead formulation is applied according to the GAP. Consequently, a new data requirement is proposed by EFSA: The notifier is asked to address the risk of the formulated active substance to birds and mammals.
- A high risk to aquatic invertebrates, algae and in particular a very high chronic risk to fish was identified in the risk assessment. EFSA proposes a data requirement for the notifier to address the high chronic risk to fish.
- It is questionable whether buffer zones are sufficient as risk mitigation measures since the FOCUSsw calculations provided by the PPR panel showed that run-off and drainage are major entry routes into surface water for dimoxystrobin. EFSA proposes that a comprehensive aquatic risk assessment taking into account spray drift, run-off, drainage and the effectiveness of potential risk mitigation measures should be conducted.

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide as proposed by the applicant which comprises spraying using ground base equipment to control fungal pathogens in winter wheat at application rate up to 200 g dimoxystrobin per hectare. The representative formulated product for the evaluation was “BAS 50700 F”, a suspension concentrate (SC), which contains as a second active substance epoxiconazole. Dimoxystrobin can be used only as fungicide.

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

Dimoxystrobin is rapidly and nearly completed absorbed. It is widely distributed in tissues and organs and dimoxystrobin were found in the gastro-intestinal tract, liver kidney, lung, fat tissue, thyroid, pancreas, adrenals, ovaries and uterus but no potential for tissue accumulation. Dimoxystrobin is extensively metabolised to a large number of metabolites. The oral and dermal toxicity is low i.e. LD_{50} > 2000 mg/kg bw. However, it is harmful during inhalation, LC_{50} 1.3 mg/L **and the classification of Xn; R20 "Harmful by inhalation" is proposed**. No repeated inhalation study is available. Thickening of the duodenum was the main effect observed in rats and mice. The relevant oral NOAEL is 3 mg/kg bw/day and 4 mg/kg bw/day in males and females, respectively, based on reduced body weight gain, altered haematological and chemical parameters and thickening of the duodenal mucosa in the rat.

There was no evidence of genotoxicity. Dimoxystrobin was carcinogenic in mice causing an increased incidence of adenoma and adenomacarcinoma in the duodenum at the top dose. There was also focal hyperplasia in the duodenum at the top dose, interpreted as a pre-neoplastic lesion. **Based on the results, the risk phrase Xn; R40 "Limited evidence of a carcinogenic effect"** is proposed. The relevant NOAEL is 4 mg/kg bw/day in male mice based on reduced body weight gain.

There were no direct effects on reproductive performance or fertility observed up to the highest dose level based on impaired body weight gain, and food consumption. Dimoxystrobin did not induce teratogenic or fetotoxic effects. The reproductive NOAEL is 136 mg/kg bw/day, developmental NOAEL is 20 mg/kg bw/day and parental NOAEL was 5 mg/kg bw/day.

There were no indications for dimoxystrobin being neurotoxic. The metabolites 505M08 and 505M09 were found to be toxicologically relevant, due to the structural similarity with dimoxystrobin.

The ADI and the ARfD is 0.004 mg/kg bw/day (safety factor 1000) and the AOEL is 0.02 mg/kg bw/day (safety factor 200). The representative formulation, BAS 507 00F, contains two active substances dimoxystrobin and epoxiconazole. The studies were not performed on the representative formulation BAS 507 00F but on dimoxystrobin diluted in a solvent formulation with a similar composition of the non-active co-formulants in BAS 507 00F, an "artificial BAS 507 00F". The dermal absorption value is 1% for both undiluted and diluted formulation. *For epoxiconazole the rapporteur Member State proposed 10%.*

The rapporteur Member State had performed a national evaluation on epoxiconazole in 1994 and presents proposals in the toxicological evaluation. Since epoxiconazole has not yet been evaluated but will be in the stage 3A of the review programme the studies have not been peer reviewed and none of the values has been agreed on. All values for epoxiconazole should be regarded as provisional until agreed on.

As the representative formulation contains two active substances the operator exposure follows a combined approach. In the DAR the rapporteur Member State presented a risk assessment for each of the two active substances. For dimoxystrobin, the risk assessment is based on dimoxystrobin in the "artificial formulation BAS 507 00F". The risk assessment for the second active substance, epoxiconazole, is based on the assumptions and proposals of the rapporteur Member State to be discussed and agreed on during the peer review of epoxiconazole (stage 3A). **The proposed risk assessment is only valid when the toxicological assessment for epoxiconazole has been agreed on**

later in the process and thus the risk assessment of BAS 507 00F can not be regarded as complete, but only indicative.

The risk assessment for epoxiconazole is based on the estimated exposure calculated of the formulation Opus. The estimated exposure for dimoxystrobin is below the AOEL without any PPE in the "artificial BAS 507 00F" (13%). *The estimated operator exposure for epoxiconazole is below the AOEL in the German model (48%) without PPE and with PPE during both mixing and loading as well as during application according to the UK POEM (30%).* If, all values are agreed on and if the actual exposure should be identified as being additive, then *it might be assumed that the estimated combined exposure is below the AOEL in the German model without PPE (61%) or with PPE during both mixing and loading as well as during application according to the UK POEM (45%) for both dimoxystrobin and epoxiconazole.*

Applied to wheat plants by foliar application dimoxystrobin itself was the major residue found at harvest in straw and in grain accounting for about 90% and 60% of the total residue, respectively. Total levels of radioactivity in grain were too low to allow further characterization of metabolites. Dimoxystrobin turned out to be persistent in soil and hence it was present in rotational crops at plant back intervals up to 365 days. However, significant residues (>0.01 mg/kg) of dimoxystrobin or other metabolites in plant parts for human consumption are not anticipated from crop rotation.

Fed to ruminants and poultry, dimoxystrobin was intensively metabolised resulting in a comparable pattern to that observed in rat metabolism, with the exception of metabolite 505M76, which was not specifically found in the rat. Despite the lipophilic character of dimoxystrobin there was no indication of accumulation in the body fat of the tested animal species. In a feeding study levels of relevant compounds (dimoxystrobin, metabolites 505M09 and 505M76) in edible animal matrices were all found to be below the respective LOQ.

The chronic dietary exposure assessment for consumers based on the representative GAP on cereals indicated that the most highly exposed consumer subgroup was infants at 83% of the proposed ADI. The short term exposure of all considered consumer subgroups from individual commodities, based on consumption data of UK consumers, were well within the proposed ARfD, accounting for up to 48% ARfD at a maximum from the consumption of milk by toddlers.

Since there were relevant metabolites found in ground water, a consumer risk assessment was performed, considering the sum of possible intakes of dimoxystrobin and the metabolites 505M09 and 505M76 from drinking water in addition to the intake through diet. The total intakes from diet and drinking were demonstrated to be below the ADI of dimoxystrobin for the considered consumer subgroups.

The degradation of dimoxystrobin in soil is initiated by the oxidation of methyl moieties of the phenyl ring. Only metabolite 505M09 attained levels above 10 % AR in laboratory experiments. However, in field studies also metabolite 505M08 was found at levels above 10 % (corrected for molecular weight) of the applied parent. Maximum mineralization after 120 d was between negligible to 24 % AR. Unextractable radioactivity amounted to a maximum of 24 % after 120 d. A major photolysis metabolite 505M01 is identified in the soil photolysis study.

Dimoxystrobin is medium to high persistent (DT_{50} = 88 – 401 d) in soil at 20 ºC. Metabolites 505M08 and 505M09 are less persistent in soil than parent compound. Dimoxystrobin is not degraded under anaerobic conditions. Degradation of dimoxistrobin is enhanced under irradiated conditions.

Three field dissipation studies were performed in Germany, two in Spain and two in Sweden. Dissipation of dimoxystrobin in soil is in some instances initially rapid (DT_{50} = 8 – 120 d) but then slowed significantly (DT_{90} > 500 d). First order calculation excluding the first data point (potentially affected by photolysis) and the results of the Spanish trials (due to the dryness of the field soil according Dutch CTB standards) standardized to reference temperature and moisture conditions were calculated. Under these assumptions dimoxystrobin shows to be moderate to high persistent in field ($DT_{50\ (20\ ºC,\ pF2)}$ = 57.6 -131.6 d).

Accumulation of dimoxystrobin in soil was investigated under field conditions in two trials in S.W. Germany, following repeated annual application to cereals over three years.

Standard PEC soil (0 – 100 d) were calculated for parent and metabolite 505M01. Worst case field half lives standardised to 20 ºC (DT_{50} = 131.6 d) were corrected to 15 ºC (DT50 = 195.2 d). Worst case maximum amount PEC soil for metabolite 505M01 was calculated assuming 100 % transformation from parent dimoxystrobin. The PEC soil for 505M09 were calculated with a five compartmental model. No PEC soil were calculated for metabolite 505M08.

In the RMS calculation of potential accumulation, maximum plateau concentration was reached after 5 years (PEC soil acc = 0.046 mg/kg). Residues seen in the field accumulation trials were considered to be mostly in the range of predicted concentrations.

According batch equilibrium adsorption/desorption studies dimoxystrobin may be classified as low to medium mobile in soil (Koc = 196 – 935 mL / g), 505M01 as very high mobile (2 – 35.5 mL / g), 505M08 as high to very high mobile (7.8 – 133.0 mL / g) and 505M09 as high to very high mobile (9.0 – 119 mL / g).

Dimoxystrobin is stable to hydrolysis at all environmental relevant pHs. Photolysis may moderately contribute to the degradation of dimoxystrobin in water.

Degradation of dimoxystrobin in water /sediment systems was very limited. Very little mineralization was observed (2.1 % AR by day 100). Unextractable residue in sediment was also low (6.3 – 10 % AR by day 100). Only 10-15 % of the applied dimoxystrobin degrades after 100 d. Disappearance from the water phase is mainly attributed to partition with sediment.

Additionally an outdoor water sediment study and an outdoor mesocosm study in Germany were used to investigate the aquatic dissipation of dimoxystrobin. Photolysis and partition to sediment was considered the main routes of dissipation of dimoxystrobin from the water phase in the outdoor water sediment study. A first order water phase $DT_{50water}$ = 15.3 d was calculated using only 0-58 d data. Almost no degradation was observed for day 58 onwards due to lower irradiation on September and November. In the mesocosm study dimoxystrobin was applied in early May and dissipation DT_{50} = 60 – 69 d was calculated for the water phase.

Only initial spray drift PECsw were used in the surface water risk assessment presented by the RMS in the DAR. Other potential routes of surface water contamination such as run off and drainage are partially addressed in the DAR following published (run-off) and national RMS scheme (drainflow) but were not used further for the EU risk assessment. FOCUSsw calculations were not presented.

In the Opinion of EFSA's Scientific Panel on Plant Health, Plant protection products and their Residues (PPR) related to the evaluation of dimoxystrobin, the PPR Panel used the DT_{50} = 63.5 d from the outdoor pond mesocosm study, as conservative but realistic value for the exposure assessment. In this opinion it is highlighted that a single exposure event applies only to exposure *via* the initial spray drift. Any other exposure routes as runoff and drain flow are not covered by RMS assessment. The FOCUSsw PEC calculations made by the PPR panel provided concentration profiles for the selected scenarios as well as information on which route of exposure (spray drift, runoff or drainage) provided most of the load. The PPR Panel noted that FOCUSsw simulations predict higher PEC values (0.15 - 3.64 µg / L) than those calculated in the DAR (1.85 µg / L) due to the fact that drainage and runoff were the major contributors to the surface water contamination for some of the selected scenarios. A complete FOCUSsw assessment is necessary to characterize the risk in the major agricultural regions across the EU. An illustrative risk assessment based only on spray drift loadings is presented by EFSA in an addendum. The need for risk mitigation measures is already identified. However, 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 EU risk assessment.

Concentrations of dimoxystrobin and its soil metabolites 505M08 and 505M09 in groundwater predicted with FOCUSgw for the representative uses proposed were below 0.1 µg / L trigger. However, in an outdoor lysimeter study in Germany where three lysimeter vessels were investigated exceedance of yearly average 0.1 µg / L trigger in the leachate was observed for metabolites 505M08 and 505M09 for all three years and in all the systems studied. Linear reduction of these results, based on the lower rate proposed for the representative uses, still result in levels of metabolites just above the trigger of 0.1 µg / L. By comparison of modelling and lysimeter results it was concluded that high interception was needed to reduce the potential of ground water contamination and that FOCUS modelling only covers risk assessment for application to late growth stages, such us the ones proposed for the representative uses (crop interception 90 % or greater). Potential for groundwater contamination by 505M08 and 505M09 under vulnerable conditions needs to be assessed at MS level.

The results of the lysimeter study were also used to calculate PECgw values for the photolysis metabolite 505M01. The concentration of the photodegradation product 505M01 are below the 0.1 µg/L trigger.

Concentration of dimoxystrobin in air are expected to be negligible due to low volatility and short half life in air for reaction with OH radicals.

For birds and mammals EFSA provided a risk assessment according to the latest guidance document (Sanco/4145/2000 of 25 September 2002) in an addendum which however was not yet peer reviewed. The addendum was not peer reviewed. The risk assessment for dimoxystrobin (technical) resulted in TER values for the acute, short term and long term risk to insectivorous birds and mammals which met the Annex VI trigger values. However, the complete risk assessment for birds and the long term risk assessment for mammals is based on the endpoints deriving from studies with the technical active substance. Since the lead formulation contains a second active substance (epoxiconazole, listed for the 3rd stage of the peer review process) it is questionable whether it is possible to extrapolate from the

toxicity of the technical active substance to the formulated product. Furthermore, the acute toxicity studies with rats showed that the formulated active substance in the lead formulation is more acutely toxic than the technical active substance. A high risk was identified for birds and mammals in a first tier risk assessment from the uptake of contaminated drinking water.

EFSA is of the opinion that a high risk to birds and mammals from the application of the lead formulation cannot be excluded and additional data are required to address the risk of the lead formulation to birds and mammals.

A high risk was identified in a first tier risk assessment for all tested groups of aquatic organisms. The higher tier risk assessment for fish resulted in TER values which met the revised acute TER trigger value. However the high chronic risk to fish remains and needs to be addressed with further data. A mesocosm study was conducted as a higher tier test to address the risk to aquatic invertebrates and algae. In the EPCO 3 Expert meeting (28-29 April 2004) it was agreed that a safety factor of 5 has to be applied to the TER value of 2.7 deriving from the mesocosm study. Consequently a high risk to aquatic invertebrates and algae was identified and has to be addressed with further data and risk mitigation measures are necessary.

Field studies with earthworms were conducted because a high long term risk to earthworms was identified in a first tier risk assessment. The results of the field studies led to the conclusion that the long term risk to earthworms is low.

The risk to bees, non target arthropods, soil macro-, soil micro-organisms, non target plants and biological methods of sewage treatment is considered to be low.

The risk from the metabolites 505M01, 505M08, 505M09 to the environment is low.

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

- The second active substance in the formulation, epoxiconazole, has not been discussed within the process and the critical values for as for instance dermal absorption as well as AOEL have not been agreed on. The ones that the risk assessment is based on proposals from the rapporteur Member State and are thus regarded as provisional.
- Ground water risk assessment is based on representative use with application at a late growing stage, resulting in a high mitigation through crop interception (90 % interception or more). Application of the products at early growing stages may need reassessment of the ground water contamination potential by MS paying special attention to metabolites 505M08 and 505M09.

Critical areas of concern

- No repeated inhalation study was submitted. Since dimoxystrobin was moderately toxic during acute exposure (proposed classification **R22 "Harmful by inhalation"**) there is a possible need

for a new study to be submitted. Further consideration should be given at Member State level in case of national application especially if dimoxystrobin is intended for indoor use e.g. in greenhouses.

- The dermal absorption study is not performed on the representative formulation BAS 507 00F, but solely dimoxystrobin diluted in a solvent formulation with a similar composition of the non-active co-formulants in BAS 507 00F. **Therefore, the dermal absorption value for the representative formulation can not be set.**
- The second active ingredient in the representative formulation BAS 507 00F (epoxiconazole) has not been discussed within the process and the studies have not been peer reviewed (will be reviewed at stage 3A). Thus, the dermal absorption value or AOEL (including safety factor) are not agreed on.
- Possible synergistic effects between dimoxystrobin and epoxiconazole as well as relevant AOEL (and possible additional safety factor) have to be considered for the formulation BAS 507 00F when data for epoxiconazole has been agreed on.
- Potential ground water contamination by toxicological relevant metabolites 505M08 and 505M09.
- A high risk to birds and mammals from the application of the lead formulation cannot be excluded and additional data are required to address the risk of the lead formulation to birds and mammals.
- A high risk to aquatic invertebrates, algae and a high chronic risk to fish were identified. Risk mitigation measures such as buffer zones up to 75 m are required. However, FOCUSsw calculations, provided in the opinion of the PPR panel, indicate that run-off and drainage are major entry routes for dimoxystrobin to surface water. The peak concentrations in some of the selected scenarios were higher than the initial PECsw from spray drift (= 1.85 µg/L) which was used for the TER calculations. Therefore it is not possible to conclude that buffer zones are sufficient as risk mitigation measures. A comprehensive risk assessment taking into account spray drift, run-off, drainage and the effectiveness of potential risk mitigation measures is required.

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

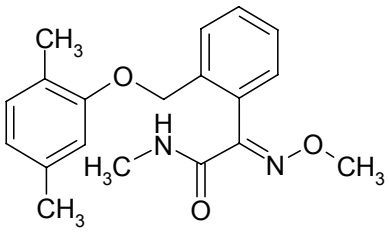
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Dimoxystrobin (proposed)
Function (e.g. fungicide)	Fungicide

Rapporteur Member State	UK
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(*E*)-*o*-(2,5-dimethylphenoxymethyl)-2-methoxyimino-N-methylphenylacetamide
Chemical name (CA) ‡	(*E*)-2-[(2,5-dimethylphenoxy)methyl]-2-(methoxyimino)-N-methylbenzeneacetamide
CIPAC No ‡	739
CAS No ‡	149961-52-4
EEC No (EINECS or ELINCS) ‡	Not assigned
FAO Specification ‡ (including year of publication)	None
Minimum purity of the active substance as manufactured ‡ (g/kg)	980
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	C_{19} H_{22} N_2 O_3
Molecular mass ‡	326.39
Structural formula ‡	

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

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	138.1-139.7 °C, (purity 99.9%)
Boiling point (state purity) ‡	No boiling point up to decomposition at 300 °C, (99.9 %)
Temperature of decomposition	300 °C, (99.9 %)
Appearance (state purity) ‡	White crystalline solid, (99.9%); beige fine powder (97.9%)
Relative density (state purity) ‡	1.235 at 20 °C, (99.9%)
Surface tension	64.3 mN/m at 20 °C and 0.5% w/w in water 63.0 mN/m at 20 °C and 1.0% w/w in water, (97.9%)
Vapour pressure (in Pa, state temperature) ‡	6.0×10^{-9}, 20 °C, (99.9 %)
Henry's law constant (Pa m^3 mol^{-1}) ‡	4.554×10^{-8}
Solubility in water ‡ (g/l or mg/l, state temperature)	pH 5.7: 4.3 mg/l, 20 °C, (99.9%) pH 8.0: 3.5 mg/l, 20 °C, (99.9%)
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	Dichloromethane > 250 g/l; DMF 200-250 g/l; acetone 67-80 g/l; acetonitrile 50-57 g/l; ethylacetate 33-40 g/l; toluene & methanol 20-25 g/l; 2-propanol < 10 g/l; *n*-heptane < 10 g/l; 1-octanol < 10 g/l; olive oil < 10 g/l.
	All at 20 °C, (99.7%)
Partition co-efficient (log POW) ‡ (state pH and temperature)	pH 6.5: 3.59, at 22 °C, (99.9%)
Hydrolytic stability (DT50) ‡ (state pH and temperature)	pH 4, 7 and 9: dimoxystrobin was stable in the aqueous solution at 25 and 50 °C. No DT_{50} values were determined because no significant degradation occurred
Dissociation constant ‡	No indication of dissociation of dimoxystrobin in water
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	3.0×10^4 at 205 nm 4.8×10^3 at 254 nm 2.9×10^2 at 290 nm, [l mol^{-1} cm^{-1}] No absorbance maximum >290nm, (99.9%)

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

Photostability (DT50) ‡ (aqueous, sunlight, state pH)	at pH 7: DT_{50} of > 30 d was determined (mean Value of both labels: benzyl and phenyl label)
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	1.29×10^{-3} DT_{50}: 64.8 test system days (continuous irradiation); value extrapolated beyond 15 day study duration.
Flammability ‡	Not considered highly flammable
Explosive properties ‡	No potential for explosivity as evident from the structural formula and the calculated oxygen balance (–224).

Classification and proposed labelling (Annex IIA, point 10)

With regard to physical/chemical data	No classification, it is non-explosive, non-oxidising and not highly flammable

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

List of representative uses evaluated*

Crop and/ or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max	(l)	(m)
Wheat (TRZAX)	United Kingdom	BAS 507 00 F	F	Fusarium sp. Septoria sp. Puccinia sp.	SC	133* (+ 50**) g/l	SP	49 69 latest	1	-		200-400	0.2* + 0.075**	35	-
Wheat (TRZAX)	Netherlands	BAS 507 00 F	F	Fusarium sp. Septoria sp. Puccinia sp.	SC	133* (+ 50**) g/l	SP	49 69 latest	1	-		200-400	0.2* + 0.075**	35	-
Wheat (TRZAX)	Belgium	BAS 507 00 F	F	Fusarium sp. Septoria sp. Puccinia sp.	SC	133* (+ 50**) g/l	SP	49 69 latest	1	-		200-400	0.2* + 0.075**	35	-
Wheat (TRZAX)	France	BAS 507 00 F	F	Fusarium sp. Septoria sp. Puccinia sp.	SC	133* (+ 50**) g/l	SP	49 69 latest	1	-		200-400	0.2* + 0.075**	35	-
Wheat (TRZAX)	Germany	BAS 507 00 F	F	Fusarium sp. Septoria sp. Puccinia sp.	SC	133* (+ 50**) g/l	SP	49 69 latest	1	-		200-400	0.2* + 0.075**	35	-
Wheat (TRZAX)	Ireland	BAS 507 00 F	F	Fusarium sp. Septoria sp. Puccinia sp.	SC	133* (+ 50**) g/l	SP	49 69 latest	1	-		200-400	0.2* + 0.075**	35	-

*BAS 505 F, ** epoxiconazole

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

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

Appendix 1.2: Methods of Analysis

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

Methods for the technical material and the formulated product are capable of distinguishing dimoxystrobin from its *Z*-isomer.

Technical as (principle of method)	HPLC, UV detection
Impurities in technical as (principle of method)	HPLC, UV detection; GC, FID and MS detection; LOQ: 0.05 % for each impurity
Plant protection product (principle of method)	GC, FID detection

Analytical methods for residues (Annex IIA, point 4.2)

None of the residue methods have been specifically assessed to determine whether they would distinguish dimoxystrobin from its *Z*-isomer.

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	GC/MS or GC/ECD, LOQ grain 0.05 mg/kg (dimoxystrobin) Additional method: HPLC-MS/MS, LOQ: 0.05 mg/kg for grain and straw (dimoxystrobin)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	GC/MS or GC/ECD; LOQ:0.01 mg/kg (milk, meat) 0.02 mg/kg (egg, fat) (both for dimoxystrobin) LOQ:0.05 mg/kg (milk, meat, liver, kidney, egg) (for 505M09) Additional/alternative method: LC-MS/MS; LOQ:0.01 mg/kg (milk) 0.025 mg/kg (fat, liver, kidney, muscle) (LOQ refers separately to dimoxystrobin, 505M09[22] and 505M76)[23]
Soil (principle of method and LOQ)	GC-MS; LOQ: 0.01 mg/kg (dimoxystrobin)
Water (principle of method and LOQ)	GC-MS; LOQ:0.05 µg/kg (validated for tap and surface water) (LOQ refers separately to dimoxystrobin, 505M08[24] and 505M09)
Air (principle of method and LOQ)	GC-MS; LOQ:0.0009 µg/l (dimoxystrobin)

[22] 505M09: [*E*-*o*-(5-hydroxycarbonyl-2-methyl)phenoxymethyl]-2-methoxyimino-*N*-methylphenyl acetamide
[23] 505M76: (2*E*)-2-{2-[(5-carboxy-4-hydroxy-2-methylphenoxy)methyl]phenyl}-2-(methoxyimino)-*N*-methylacetamide
[24] 505M08: [*E*-*o*-(2-hydroxycarbonyl-5-methyl)phenoxymethyl]-2-methoxyimino-*N*-methylphenyl acetamide

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

Body fluids and tissues (principle of method and LOQ)	No method required as dimoxystrobin is not classified as toxic or highly toxic.

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	85-90% within 5d at 10 mg/kg bw
Distribution ‡	Extensive: highest levels in gut, liver, kidney, lung, fat, thyroid, pancreas, adrenals, ovaries, uterus
Potential for accumulation ‡	Very little potential for accumulation at 10 mg/kg bw
Rate and extent of excretion ‡	65-83% (mainly in faeces) within 24h at 10 mg/kg bw
Metabolism in animals ‡	Extensive. 45 identified metabolites in rats.
Toxicologically significant compounds ‡ (animals, plants and environment)	Dimoxystrobin. The metabolites 505M08 and 505M09 are considered as toxicologically relevant.

Acute toxicity (Annex IIA, point 5.2)

Rat LD50 oral ‡	>5000 mg/kg bw
Rat LD50 dermal ‡	>2000 mg/kg bw
Rat LC50 inhalation ‡	1.3 mg/L **R20**
Skin irritation ‡	Non irritant
Eye irritation ‡	Non irritant
Skin sensitization ‡ (test method used and result)	Non-sensitizer (Magnusson and Kligman)

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Duodenal (mucosal) thickening
Lowest relevant oral NOAEL / NOEL ‡	3 mg/kg bw/day, 90-day rat
Lowest relevant dermal NOAEL / NOEL ‡	> 1000 mg/kg bw/day
Lowest relevant inhalation NOAEL / NOEL ‡	No data available

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	No genotoxic potential

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

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

Target/critical effect ‡	Reduced body weight gain and/or increased duodenal thickening. Duodenal tumours in mice and thyroid adenomas in rats.
Lowest relevant NOAEL / NOEL ‡	4 mg/kg bw/d, 18-month mouse
Carcinogenicity ‡	Non-genotoxic mechanism proposed **R40** (increased proliferation of duodenal mucosa to increase surface area for absorption of iron in response to reduced serum iron levels)

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	No adverse effects on reproductive performance. Developmental toxicity (slight microcytic hypochromic anaemia, reduced body weight gain, reduced thymus weight, discoloured liver, cardiomegaly) in presence of parental toxicity (slight microcytic hypochromic anaemia)
Lowest relevant reproductive NOAEL / NOEL ‡	Reproductive performance: 136 mg/kg bw/day Parental: 17 mg/kg bw/day
Developmental target / critical effect ‡	Increased incidence of skeletal variation at maternally toxic dose, only in rabbits
Lowest relevant developmental NOAEL / NOEL ‡	Maternal toxicity: 5 mg/kg bw/day Developmental effects: 20 mg/kg bw/day

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

.....	Not neurotoxic in acute and repeat-dose neurotoxicity studies in rats

Other toxicological studies ‡ (Annex IIA, point 5.8)

Mechanistic studies	Dimoxystrobin (1000 ppm) caused increased cell proliferation, but no apoptosis, in mouse duodenal epithelium; the effect was fully reversible Dimoxystrobin (4500 ppm) reduced serum iron concentration in rats, the effect was reversible. Co-administration of additional iron and dimoxystrobin to rats provided some evidence that increased duodenal thickness could be due to decreased serum iron.

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

	In vitro evidence indicates dimoxystrobin forms complexes with Fe3+ ions. Exposure to dimoxystrobin reduced serum ion levels to a greater extent in young rats than in adult rats.
7-day study in adult rats	4 mg/kg bw/day based on decreased serum levels.
Metabolites	505M01 Acute oral LD50 > 2000 mg/kg bw Negative results obtained in three in vitro genotoxicity assays. 505M08 and 505M08 No toxicological data. Due to structural similarity with dimoxystrobin a similar toxicity profile is assumed.

Medical data ‡ (Annex IIA, point 5.9)

.....	No evidence of adverse effects in personnel exposed to dimoxystrobin during its development.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.004 mg/kg bw/day	Rat, 7-day study	1000
AOEL ‡	0.02 mg/kg bw/day	7-day rat study, supported by the 18-month mouse	200
ARfD ‡ (acute reference dose)	0.004 mg/kg bw	Rat, 7-day study	1000

Dermal absorption (Annex IIIA, point 7.3)

"BAS 507 00F" Based on an artificial formulation containing dimoxystrobin only (12.5%) diluted in a solvent solution with a similar composition of the non-active co-formulants in the representative formulation BAS 50700F.	1% for concentrate and in-use dilution based on in vivo and correction (15) based on in vitro studies, justified only for dimoxystrobin

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

Acceptable exposure scenarios (including method of calculation)

Operator	The representative formulation BAS 507 00F (SC) contains two active substances, dimoxystrobin (133 g /L) and epoxiconazole (50 g/L). The peer review on epoxiconazole is not yet finalised (is on stage 3A). *Thus, the proposed (by RMS) dermal absorption value of 10% as well as AOEL of 0.02 mg/kg bw/day has not been agreed on within the EU-process. The estimations of exposure for epoxiconazole are based on the formulation Opus SC containing 125 g epoxiconazole/L.* Until epoxiconazole has been peer reviewed all values must be recognized as provisional, furthermore a harmonised procedure of performing combined risk assessments must be agreed on. A proposal for combined risk assessment for BAS 507 00F is based on several assumptions. Separate risk assessments for dimoxystrobin and epoxiconazole are performed and then added. <u>i) Dermal absorption values</u> dimoxystrobin 1% in BAS 507 00F *epoxiconazole 10% Opus, not agreed* No studies on the combined dermal absorption for BAS 507 00F are submitted <u>ii) AOEL</u> dimoxystrobin 0.02 mg/kg bw/day *epoxiconazole 0.02 mg/kg bw/day, not agreed* Since the proposed AOEL for epoxiconazole is the same as for dimoxystrobin, this value is used in the calculations. <u>iii) Combined effects</u> It is assumed that it is appropriate to add the systemic exposure for each active substance and that no synergistic (or antagonistic) effects occur and that no additional safety factor is needed.

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

	Estimated exposure, % of AOEL (0.02 mg/kg bw/day) Model: German UK-POEM Dimoxystrobin, no PPE 13% 85% with PPE* 15% *Epoxiconazole,* *no PPE 48% 298%* *with PPE* 30%* *Combined,* *no PPE 61% 393%* *with PPE 45%*
Workers	In the DAR the worker exposure was addressed by a reasoned case and by calculation of estimated exposure (based a German model by Hoernicke et al., 1998) of dimoxystrobin in the "artificial formulation". The outcome was 6% of the AOEL. A similar estimation was performed for epoxiconazole (but using the 10% dermal absorption value instead). In this case the estimated worker exposure was 23% of the AOEL (for epoxiconazole)
Bystanders	No data was submitted in the dossier. The rapporteur Member State presented calculations (based on Lloyd and Bell, 1983) of estimated bystander exposure of both dimoxystrobin and epoxiconazole, following the assumptions on combined approach presented above, which was below the AOEL (< 1%).

* PPE gloves during mixing and loading as well as during application.

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	Xn; R20: Harmful by inhalation; Carc cat 3: R40: Limited evidence of a carcinogenic effect

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

Appendix 1.4: Residues

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

Plant groups covered	Wheat (cereals)
Rotational crops	Wheat, lettuce, radish (replant intervals: 30, 120 and 365 days)
Plant residue definition for monitoring	Dimoxystrobin
Plant residue definition for risk assessment	Dimoxystrobin
Conversion factor (monitoring to risk assessment)	Not applicable

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

Animals covered	Goat, poultry
Animal residue definition for monitoring	Dimoxystrobin *or alternatively* metabolite 505M09
Animal residue definition for risk assessment	The sum of dimoxystrobin plus the metabolites 505M09 and 505M76 expressed as dimoxystrobin.
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Yes. (cleavage of the molecule occurs in rats but not goats).
Fat soluble residue: (yes/no)	Yes

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

Confined study (radiolabelled)	Not required. The rotational crops study (direct soil application, 3N rate) indicated TRR in lettuce and radish 0.01-0.05 mg/kg with parent and metabolites individually present at up to 0.01 mg/kg. Parent and metabolites in grain were <0.01 mg/kg. In straw, parent was up to 0.15 mg/kg and related conjugates totalled *ca* 0.13 mg/kg. Significant residues of parent or metabolites not expected in practice.

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

Metabolism and residue studies	Residues of dimoxystrobin were stable in wheat plant, grain and straw, oilseed rape, sugar beet roots, white cabbage, peas and peach for up to 720 days at –20 °C.

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

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: yes	Poultry: no	Pig: no
Muscle	<0.075mg/kg*	no hen feeding study conducted metabolism results indicated that the residues will not be significant (<0.01 mg/kg (LOQ	no pig feeding study conducted or required.;
Liver	<0.075mg/kg*		
Kidney	<0.075mg/kg*		
Fat	<0.075mg/kg*		
Milk	<0.03 mg/kg**		
Eggs	-		

* sum of dimoxystrobin and the metabolites **505M09** ([E-o-(5-hydroxycarbonyl-2-methyl)phenoxymethyl]-2-methoxyimino-N-methylphenyl acetamide) and **505M76** ((2E)-2-{2-[(5-carboxy-4-hydroxy-2-methylphenoxy)methyl]phenyl}-2-(methoxyimino)-N-methylacetamide), each with a reporting limit of 0.025 mg/kg
** sum of dimoxystrobin and the metabolites 505M09 and 505M76, each with a reporting limit of 0.01 mg/kg

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/ comments	MRL	STMR (b)
Wheat	Northern	Grain: 15 x <0.05 mg/kg Straw: 0.5-6.1 mg/kg	-	0.05	<0.05 mg/kg 1.0 mg/kg
Wheat	Mediterranean	Grain: 4 x < 0.05 mg/kg Straw: 0.12-2.51 mg/kg	-	0.05	<0.05 mg/kg 1.3 mg/kg

(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

‡ Endpoint identified by the 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	0.004 mg/kg/bw/d
TMDI (% ADI)	20% Total adult intake (WHO standard EU diet)[25] 15-83 % for various consumer groups (UK model)[26]
IEDI (European Diet) (% ADI)	Not necessary due to low TMDI
Factors included in IEDI	Not necessary
ARfD	0.004 mg/kg bw/day
Acute exposure (% ARfD)	UK model/data: up to 50% for individual commodities.

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

Crop/processed crop	Number of studies	Transfer factor	% Transference [a]
Wheat	Dimoxystrobin stable under the hydrolysis conditions used to simulate pasteurisation, brewing and boiling. Further studies not required due to low residues in grain (<0.1 mg/kg)	not applicable	

[a] 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)

Wheat grain:	0.05* mg/kg
Milk	0.01* mg/kg
Meat, fat, liver, kidney (except poultry)	0.03** mg/kg

(*) At the LOQ; milk: applicable for both alternatives, dimoxystrobin *or* 505M09
(**) LOQ = 0.025 mg/kg, applicable for both alternatives, dimoxystrobin *or* 505M09

[25] intake of dimoxystrobin, 505M08 and 505M09 through drinking water not included; estimated *ca* 4% ADI of dimoxystrobin for adults, based on a study at twice the intended application rate
[26] intake of dimoxystrobin, 505M08 and 505M09 through drinking water not included; estimated *ca* 16% ADI of dimoxystrobin for most critical consumer group infants, based on a study at twice the intended application rate

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	At 20°C: 10.7-15% after 87-119 d, [^{14}C-benzyl]-label (1 soil) 16.8-25% after 90-122 d, [^{14}C-phenyl]-label (1 soil) Under sterile conditions: material balance proposed to be CO_2 only decreased to 93.3-88.2% after 90-120 days (1 soil, [^{14}C-benzyl]-label).
Non-extractable residues after 100 days ‡	At 20°C: 6.3-24.1% after 87-125 d, [^{14}C-benzyl]-label (6 soils) 19.2-24.6% after 90-122 days, [^{14}C-phenyl]-label (1 soil) Under sterile conditions: 1.8-1.5%AR after 90-120 d, [^{14}C-benzyl]-label (1 soil)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	<u>In laboratory soil studies:</u> Only **505M09** ([E-o-(5-hydroxycarbonyl-2-methyl)phenoxymethyl]-2-methoxyimino-N-methylphenyl acetamide) was >10%AR at max. 13% at 90 d, [^{14}C-phenyl]-label (1 soil) max. 12.2% at 57 d, [^{14}C-benzyl]-label (1 soil) <u>In field dissipation studies:</u> **505M08** ([E-o-(2-hydroxycarbonyl-5-methyl)phenoxymethyl]-2-methoxyimino-N-methylphenyl acetamide) & **505M09** ([E-o-(5-hydroxycarbonyl-2-methyl)phenoxymethyl]-2-methoxyimino-N-methylphenyl acetamide) were detected at max. ≤0.011 mg/kg. Converted to percentage of highest residues of parent detected & corrected for molecular weight this was equivalent to max. <12.1%. <u>In soil photolysis study:</u> Only **505M01** ((E)-2-(2-hydroxymethylphenyl)-2-methoxyimino-N-methyl-acetamide) was >10%AR with max. 10.8% after 15 d, [^{14}C-benzyl]-label (1 soil).

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

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

Anaerobic degradation ‡	At 20°C with [^{14}C-phenyl]-label only: No mineralisation to CO_2 occurred during study (120 d). Non-extractable residues were 7.2-9.7 % after 90-120 d. No major metabolites were formed during study (120 d)
Soil photolysis ‡	At 22°C with both radiolabels: Mineralisation to CO_2 was 0.57 & 1.82% [^{14}C-benzyl]-& [^{14}C-phenyl]-labels respectively, at 15 days. After 15 days non-extractable residues were 8.12 & 8.61% [^{14}C-benzyl]- & [^{14}C-phenyl]-labels. (Unextracted residues peaked after 7 days at 8.7-8.8%). The major photolysis metabolite was 505M01 or ((E)-2-(2-hydroxymethylphenyl)-2-methoxyimino-N-methyl-acetamide), which reached a max. 10.8% after 15 d in the [^{14}C-benzyl]-label only.

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

Method of calculation	Laboratory studies: 1st order kinetics (Rates of degradation were calculated using ModelMaker v. 3.0.3/ 3.0.4 , Cherwell Scientific Publishing Limited, Marquardt-Newton, least square method and 5-compartment model). Some were extrapolated beyond the study duration. Field studies: Field dissipation did not follow 1st order kinetics. DT_{50f} values according to 1st order kinetics were calculated using ModelMaker v. 3.0.3/ 3.0.4 , Cherwell Scientific Publishing Limited, Marquardt-Newton, least square method and a 3-compartment model).

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

Laboratory studies ‡ (range or median, with n value, with r^2 value)	DT_{50lab} (20°C, aerobic) for '**dimoxystrobin + Z-isomer'**: [^{14}C-benzyl]-label: 88 d (1 soil, r^2=0.99) 262 - 401 d* (5 soils, r^2=0.89-0.97). [^{14}C-phenyl]-label: 92 d (1 soil, r^2=0.98). * extrapolated beyond study duration of 120-125 d. DT_{50lab} (20°C, 20% MWC, aerobic) for '**dimoxystrobin + Z-isomer'**: [^{14}C-benzyl]-label: 296 d (1 soil, r^2=0.96). DT_{50lab} (20°C, sterile, aerobic) for '**dimoxystrobin + Z-isomer':** [^{14}C-benzyl]-label: 733 d (1 soil, r^2=0.37) <u>Metabolites:</u> DT_{50lab} (20°C, aerobic) for **505M08**: [^{14}C-benzyl]-label: 14-61 d (5 soils, r^2=0.97-0.99) [^{14}C-phenyl]-label: 27 d (1 soil, r^2=0.99) DT_{50lab} (20°C, 20% MWC, aerobic) for **505M08** [^{14}C-benzyl]-label: 44 d (1 soil, r^2=0.96). DT_{50lab} (20°C, aerobic) for **505M09**: [^{14}C-benzyl]-label: 15-69 d (5 soils, r^2=0.90-0.99) [^{14}C-phenyl]-label: 38 d (1 soil, r^2=0.99) DT_{50lab} (20°C, 20% MWC, aerobic) for **505M09**: [^{14}C-benzyl]-label: 20 d (1 soil, r^2=0.96)
	DT_{90lab} (20°C, aerobic): not calculated
	DT_{50lab} (5°C, aerobic) for **'dimoxystrobin + Z-isomer'**: [^{14}C-benzyl]-label: 1203 d (1 soil, r^2=0.68) DT_{50lab} (5°C, aerobic) for **505M08 & 505M09**: Not calculated.
	DT_{50lab} (30°C, aerobic) for **'dimoxystrobin + Z-isomer'**: [^{14}C-benzyl]-label: 200 d (1 soil, r^2=0.97). DT_{50lab} (30°C, aerobic) for **505M08 & 505M09**: [^{14}C-benzyl]-label: 21 d & 27 d respectively (1 soil, r^2=0.97).
	DT_{50lab} (20°C, anaerobic) for **'dimoxystrobin + Z-isomer'** with [^{14}C-phenyl]-label.: stable (93.2% remained at 120 d)
	Degradation in the saturated zone: No data.

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

Field studies ‡ (state location, range or median with n value)	DT_{50f}: 6 sites (4 North & 2 South EU) at application rate approximately 250 g a.s./ha to bare soil. (Field dissipation did not follow 1st order kinetics. DT_{50f} were determined using Modelmaker and a 3-compartment model and taken as 'graphical estimations from the degradation curves'): N. & S.W Germany: 16- 39 d (3 trials, r^2= 0.97-1.0) Spain: 2- 3 d (2 trials, r^2=0.99) Sweden: 34 d (1 trial, r^2=0.95)
	Q_{10} factor of 2.2 used to standardise DT_{50f} to 20, 15 & 10°C, for use in probabilistic models): DT_{50f} from Spanish trials of 2-3 d were excluded and DT_{50f} from the 4 N. EU trials of 16-39 d were standardised to: <u>20°C:</u> DT_{50f} range of 16-39 d was standardised to 57.6 - 131.6 d at 20°C. Average = 82.5 d at 20°C. <u>15°C</u>: Longest DT_{50f} (at 20°C) of 131.6 d was standardised to 195.2 d at 15°C. Average DT_{50f} (at 20°C) of 82.5 d was standardised to 122 d at 15°C. PEC_{soil} calculation for dimoxystrobin used DT_{50f} (15°C) of 195.2 d. <u>10°C:</u> Longest DT_{50f} (at 20°C) of 131.6 d was standardised to 289.5 d (at 10°C). Average DT_{50f} (20°C) of 82.5 d was standardised to 181.5 d at 10°C. $PEC_{soil, accumulation}$ calculation for dimoxystrobin used DT_{50f} (10°C) of 289.5 d.

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

	DT_{90f}: 6 bare soil sites (4 North & 2 South EU) at application rate approx. 250 g a.s./ha to bare soil. (Field dissipation did not follow 1st order kinetics. DT_{90f} determined using Modelmaker and 3-compartment model, taken as 'graphical estimations from the degradation curves': N. & S.W. Germany: 23- >1 year* (n=3, r^2= 0.97-1.0) Spain: 354 d (n=2, r^2=0.99); Sweden: >1 year* (n=1, r^2=0.95). * extrapolated beyond study duration of up to 360 d.
Soil accumulation and plateau concentration ‡	2 x 3-year field studies (S.W. Germany). Total annual dose approximately 200 g a.s/ha to wheat and oats (BBCH growth stage 31-33). Assuming an application rate of 200 g a.s./ha per annum, evenly distributed over 5 cm topsoil, with 90% crop interception at growth stage 49-69, & longest DT_{50f} (10°C) of 289.5 d: Peak plateau concentration was estimated to be achieved after 5 years with 0.046 mg/kg.

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	Koc: **parent** [^{14}C-benzyl]-label: 195.8 - 935.3 ml/g (mean Koc 486.2 ml/g, 1/n = 0.894 - 0.942, mean 0.92, 7 soils) **505M01** [^{14}C-phenyl]-label: 2 - 35.5 ml/g (mean Koc 13.1 ml/g, 1/n = 0.736 - 0.933, mean 0.87, 7 soils) **505M08** [^{14}C-phenyl]-label: 7.8 - 133 ml/g (mean Koc 38.8 ml/g, 1/n = 0.913 – 0.986, mean 0.95, 6 soils) **505M09** [^{14}C-phenyl]-label: 9 - 119 ml/g (mean Koc 46 ml/g, 1/n = 0.808 - 0.915, mean 0.86, 7 soils). Kf: **parent** 0.58 - 18.62 ml/g (mean 8.18 ml/g, 7 soils) **505M01** 0.023 - 1.208 ml/g (mean 0.243 ml/g, 7 soils) **505M08** 0.086 - 0.688 ml/g (mean 0.351 ml/g, 6 soils) **505M09** 0.135 - 1.771 ml/g (mean 0.651 ml/g, 7 soils) No dependence for parent or metabolites.

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

Column leaching ‡	BBA part IV 4-2 & SETAC guidelines with [^{14}C-benzyl]-label only. Precipitation: 200 mm (393 ml $CaCl_2$) Time period: eluted over 2 d Leachate: <1% total radioactivity in leachate 86-97% total radioactivity retained mostly in top 18 cm (not characterised).

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

Aged residues leaching ‡	BBA part IV 4-2 & SETAC guidelines with [^{14}C-benzyl]-label only. Precipitation: 200 mm (393 ml $CaCl_2$) Time period: eluted over 2 d, incubated 31 d Leachate: <2.5% total radioactivity in leachate 94.2-103.3% total radioactivity retained mostly in top 18 cm (not characterised).
Lysimeter/ field leaching studie ‡	3 lysimeters in Germany, Schmallenburg, each run for: (i) 2 years, (ii) 3 years, (iii) 3 years. Application rates of: (i) year 1 only - 2 x 250 g a.s./ha (ii) year 1 only - 2 x 250 g a.s/ha (iii) year 1 - 2 x 250 g a.s./ha and year 2 - 2 x 200 g a.s/ha. Average annual rainfall: 855, 1318, 1107 mm. Average annual leachate volume: 690, 1106, 792 mm. Max. ≤5.7% radioactivity in leachate /year 1 Max. ≤6.8% radioactivity in leachate /year 2 Max. 1.9 % radioactivity in leachate /year 3 Peak annual average concentrations: dimoxystrobin 0.01 µg/l 505M01 0.09 µg/l 505M08 2.35 µg/l 505M09 1.99 µg/l

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	DT_{50} 195.2 days First order Kinetics Longest DT_{50f} (standardised to 20°C) of 131.6 days using Q_{10} factor 2.2), further standardised to 15°C gave a first order DT_{50f} (15°C) of 195.2 d for use in the PEC_{soil} calculation. (15°C was justified on basis of being a representative air temperature for 100 days after application in the EU).
Application rate	Single application of 200 g a.s/ha to wheat, at BBCH growth stage 49-69 with 90% crop interception (i.e. 10% reaches soil = 0.02 kg as/ha).

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

PECsoil **Dimoxystrobin**	DAT [d]	$PEC_{s,act}$ [mg/kg]	$PEC_{s,twa}$ [mg/kg]
Initial	0	0.027	0.027
Short-term	1	0.027	0.027
	2	0.026	0.027
	3	0.026	0.027
	4	0.026	0.026
Long-term	7	0.026	0.026
	14	0.025	0.026
	21	0.025	0.026
	28	0.024	0.025
	50	0.022	0.024
	100	0.019	0.022

Metabolites

Metabolite 505M01 (Photolysis) Method of calculation	Assumptions: No degradation and 100% formation of metabolite 505M01; soil bulk density is 1.5 kg/dm^3 and depth of soil layer is 5 cm.
Application rate	Single application of 0.2 kg as/ha to cereals with 10% (0.02 kg as/ha) reaching soil. 100 % formation of 505M01 assumed. From the laboratory soil photolysis study, a max. concentration of 11%AR after 15 days is assumed. Correction factor of 0.681 for molecular weight is applied (MW metabolite / MW parent).

PECsoil **505M01**	DAT [d]	$PEC_{s,act}$ [mg/kg]	$PEC_{s,twa}$ [mg/kg]
Initial, short term and long term	0 - 100	0.018	0.018

505M09 (soil) Method of calculation	A 5-Compartment model established with ModelMaker with parallel formation and degradation (formation rate $k_{BAS\ 505\ F\ ->\ BF\ 505\text{-}8}$ = 0.00492 [1/d]; degradation $k_{deg.\ 505M09}$ =0.0183 [1/d], equal to a half-life of 38 days from laboratory aerobic metabolism study).

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

Application rate	Single application of 0.2 kg as/ha to cereals with 10% (0.02 kg as/ha) reaching soil. 505M09 assumed to be formed as in laboratory metabolism study with a max. fitted concentration of 12.8 % applied a.s. after 78 days. Correction factor of 1.092 applied for molecular weight (MW metabolite / MW parent).

PECsoil **505M09**	DAMC* [d]	$PEC_{s,act}$ [mg/kg]	$PEC_{s,twa}$ [mg/kg]
Initial	0	0.0037	0.0037
Short-term	1	0.0037	0.0037
	2	0.0037	0.0037
	3	0.0037	0.0037
	4	0.0037	0.0037
Long-term	7	0.0037	0.0037
	14	0.0037	0.0037
	21	0.0037	0.0037
	28	0.0036	0.0037
	50	0.0034	0.0036
	100	0.0028	0.0033

* DAMC = days after maximum simulated concentration

PEC (soil, accu)

Dimoxystrobin	
Method of calculation	Longest DT_{50f} (standardised to 20°C) of 131.6 days, further standardised to 10°C to give 289.5 days. Single application/year of 200 g a.s./ha with 10% (0.02 kg as/ha) reaching the soil. Worst case peak plateau concentration of 0.046 m/kg reached after 5 years.

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 4, at 50°C : no significant degradation of a.s. detected over 5 d. pH 5, at 25°C : no significant degradation of a.s. detected over 30 d. pH 7, at 25°C & 50°C : no significant degradation of a.s. detected over 30 d and 5 d respectively.
	pH 9, at 25°C & 50°C: no significant degradation of a.s. detected over 30 d and 5 d respectively.

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

Photolytic degradation of active substance and relevant metabolites ‡	1. Standard sterile aqueous photolysis study: With both radiolabels and continuous irradiation ≡ clear April/May day ca. 36°N. No major metabolites formed. Dimoxystrobin+Z-isomer accounted for 83 – 85% AR after 15 d. First order DT50 value estimated using ModelMaker v. 4, and Marquardt-Newton least squares method. (r2 =0.81) DT50 of 65 'test system' days (assuming continuous irradiation), extrapolated beyond study end of 15 d. 2. Aqueous photolysis (lab) using natural surface water: With non-labelled dimoxystrobin and continuous irradiation ≡ clear April/May day ca. 36°N. Dimoxystrobin accounted for 47% AR after 15 d. Linear regression analysis was used to estimate a first order DT50 of 14 'test system' days (assuming continuous irradiation), r2= 0.98.
Readily biodegradable (yes/no)	Data submitted. Not readily biodegradable.
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡	Aerobic water-sediment study (laboratory -dark): With both radiolabels and water: sediment depth ratio of 6 : 2-2.5 cm. 'Statistical best fit graphical' $DT_{50/90}$ calculated using ModelMaker v.3.04, Marquardt-Newton least squares method and a 2-compartment model: System A: 27 d system B: 15 d system A: > 200 d system B: 136 d
- DT_{50} sediment ‡ - DT_{90} sediment	$DT_{50/90\ sed}$ could not be calculated.
- DT_{50} whole system ‡	First order non linear regression. System A: 520 d (r^2=0.92) System B:302 d(r^2=0.94) Both extrapolated beyond the study duration.
Mineralization	System A: 0.8%AR (at 100 d study end, n=1) System B: 2.1%AR (at 100 d study end, n= 1)
Non-extractable residues	System A: max. 6.3 % (at 100 d study end, n=1) System B: max. 10.7% (at 100 d study end, n=1)

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

Distribution in water / sediment systems (active substance) ‡	Dimoxystrobin+Z-isomer accounted for: System A: max. 58.1% in sediment after 100 d. System B: max. 63.6% in sediment after 62 d.
Distribution in water / sediment systems (metabolites) ‡	505M09 accounted for max. 5% in water after 100 d. No metabolites were formed in sediment.
Degradation in water/sediment under outdoor conditions - DT50 water - DT50 sediment - DT50 whole system - DT90 whole system	1. Outdoor water-sediment study (natural light): 15.3 d 9.1 d 26.9d (r2=0.99) 89.4d Outdoor study in Germany, application with [14C-benzyl]-label only made on 5 July, to water: sediment depth ratio of 20: 2 cm (same water and sediment source as laboratory 'system A'). Separate water and sediment first order DT_{50} for 'dimoxystrobin+Z-isomer' estimated using ModelMaker v.4, Marquardt-Newton least squares method, and a 5-compartment model (r2= 0.99 for model). Whole system DT50/90 was first order non linear regression. 2. Outdoor mesocosm study (natural light) Mesocosm study in S.W. Germany, with water: sediment depth ratio of 100 : 10 cm. Linear regression used to calculate a mean first order DT50 of 63 d and DT_{90} of 212 d in water (n= 4 concentrations).
Mineralisation	Outdoor aerobic study (natural light): The amount of CO_2 formed was calculated from the material balance difference to be approximately 20% after 58 d.
Non-extractable residues	Outdoor aerobic study (natural light): about 24% after 120 days
Distribution in outdoor water / sediment system (active substance)	Outdoor aerobic study (natural light): water: 97% at 0 d decreased to 11% after 120 d sediment:max. 16% at 14 d decreased to 10-12% after 100 d

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

Distribution in outdoor water / sediment system (metabolites >10%)	Outdoor aerobic study (natural light): No metabolites were formed > 10%. Numerous photolytical transformation and breakdown products (n>20), especially in water.

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

Parent

Method of calculation	**Static water body:** Overall 90th percentile drift values at 1, 5 and 10m. Assumed a first order DT_{50} of 15.3 d from the outdoor water-sediment study. (Justification for use of this study over the standard sterile aqueous photolysis study was it represented the same water and sediment as the worst case laboratory 'system A', but under natural light conditions. There was evidence that photolysis contributed to degradation of dimoxystrobin. The 20 cm water depth was closer to the standard static water body assumption of 30 cm, than the outdoor mesocosm study with 100 cm water depth).
Application rate	Single application of 0.2 kg as/ha to cereals. Depth of water body assumed: 30 cm
Main routes of entry	**Spray Drift (static):** 2.77% drift from 1 m, 0.57% drift from 5 m, 0.29% drift from 10 m (90th percentiles for field crops). Spray drift loading is worst case for distance of 1 m.

2.77% spray drift, 1 m distance; static water body

	Time	$PEC_{sw,initia;}$	$PEC_{sw,twa}$
	[d]	[µg/l]	[µg/l]
Initial	0	1.85	1.85
Short-term	1	1.77	1.81
	2	1.69	1.77
	3	1.62	1.73
	4	1.54	1.69
Long-term	7	1.35	1.58
	14	0.98	1.37
	21	0.71	1.19

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

	Time	$PEC_{sw,initia;}$	$PEC_{sw,twa}$
	[d]	[µg/l]	[µg/l]
	28	0.52	1.05
	42	0.28	0.83

Metabolite 505M01 (photolysis) Method of calculation	505M01: A compartment model established with ModelMaker with parallel formation and degradation and partitioning between water and sediment. Depth of the static water layer assumed as 30 cm.
Application rate	Single application of 0.2 kg as/ha to cereals, (assumed that 505M01 is formed as in the outdoor water-sediment study with a maximum fitted concentration of 7.84 % of applied a.s. after 13 d and a first order DT_{50} of 5.7 d. Correction factor applied for molecular weight of 0.681.
Main routes of entry	Spray Drift (static): 2.77% drift from 1 m, 0.57% drift from 5 m, 0.29% drift from 10 m (90th percentiles for field crops). Spray drift loading is worst case for distance of 1 m.

2.77% spray drift, 1 m distance; static water body

PECsw, act and PECsw, twa		**505M01**	
	Time	$PEC_{sw,act}$	$PEC_{sw,twa}$
	[days after max concentration]	[µg/l]	[µg/l]
Initial	0	0.099	0.099
Short-term	1	0.098	0.098
	2	0.098	0.098
	3	0.095	0.097
	4	0.089	0.095
Long-term	7	0.072	0.088
	14	0.056	0.080
	21	0.042	0.072
	28	0.023	0.059
	42	0.016	0.053
	100	0.002	0.030

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

PEC (sediment)

Dimoxystrobin Method of calculation	Single application to cereals. Max. 15.9% partitioning to top 5 cm of sediment after 14 d, (10-12% partitioned to sediment after 120 d). Spray drift values, with same assumptions as for PEC_{sw}, pattern of decline reflecting that measured in the outdoor water sediment study.
Application rate	Single application rate of 0.2 kg as/ha to cereals

PECsed,actual

Time	Dimoxystrobin	
	Overspray	drift: 1 m buffer
[d]	[mg/kg]	[mg/kg]
maximum PECsed at day 14	**0.048**	**0.0012**
120 days, study end	**0.036**	**0.0012**

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

Dimoxystrobin, 505M08, 505M09 Method of calculation and type of study	Modelling using FOCUS-PEARLv.2.2.2 for all nine EU scenarios and for a 26 year run. Soil and climate scenarios as defined by FOCUS 2000 (Chateaudun, Hamburg, Joioinen, Kremsmuster, Okehampton, Piacenza, Porto, Sevilla, Thiva). Application of 0.2 kg as/ha to winter cereals, with 90% crop interception for BBCH growth stage 49-69. Soil moisture standardised to pF 2. <u>Dimoxystrobin:</u> Average DT_{50f} (20°C) of 82.5 d (4 field trials); Average K_{F_OM} of 282 dm³/kg, 1/n of 0.918 (n=7) <u>505M08:</u> formation fraction of 0.276 average laboratory half-life of 19 d (at 20° C, normalised first order to soil moisture pF2, n=2); K_{F_OM} of 22.5 dm³/kg, 1/n of 0.945. <u>505M09:</u> formation fraction of 0.724 average laboratory half-life of 35 d (at 20° C, normalised first order to soil moisture pF2, n=2); K_{F_OM} of 27 dm³/kg, 1/n of 0.856.

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

Application rate	Single application of 0.2 kg as/ ha to cereals in late spring March-May, with 90 % interception.
Maximum annual concentration	Predicted 80th percentile year concentration in all nine EU scenarios of. Dimoxystrobin: <0.001 µg/l 505M08: ≤0.016 µG/l 505M09 ≤0.031 µg/l .

PEC(gw) - FOCUS modelling results

	Scenario	Parent (µg/l) dimoxystrobin	Metabolite (µg/l)	
			505M08	505M09
PEARL2.2.2/winter cereals	Chateaudun	<0.001	0.002	0.001
	Hamburg	<0.001	0.012	0.019
	Jokioinen	<0.001	0.005	0.002
	Kremsmunster	<0.001	0.007	0.014
	Okehampton	<0.001	0.014	0.020
	Piacenza	<0.001	0.016	0.031
	Porto	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001
	Thiva	<0.001	0.002	0.002

Metabolite 505M01 (photolysis), 505M08 and 505M09 Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Results from lysimeter study with higher application rates of a.s. and earlier crop growth stage than proposed GAP were standardised to rates and timing representative of GAP, using adjustment factors. These were 0.133 for lysimeters receiving 2 x 250 g a.s./ha and 0.148 for the lysimeter receiving 2 x 250 + 2 x 200 g a.s./ha).
Application rate	Single application of 0.2 kg as/ha to cereals in late spring with 90 % interception
$PEC_{(gw)}$ **505M01**	
Maximum annual concentration	0.01 µg/L
$PEC_{(gw)}$ **505M08**	
Annual average concentrations	0.34 µg/L (maximum annual average concentration found the first year)
$PEC_{(gw)}$ **505M09**	
Annual average concentrations	0.29 µg/L (maximum annual average concentration found the second year)

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

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

Direct photolysis in air ‡	see below (photochemical oxidative degradation)
Quantum yield of direct phototransformation	1.29 x 10^{-3}
Photochemical oxidative degradation in air ‡	DT_{50} of <5 hours derived by the Atkinson method of calculation.
Volatilization ‡	from plant surfaces about 3% in 24 hours (BBA guideline Part IV, 6-1, 1990) from soil surfaces about 2% in 24 hours (BBA guideline Part IV, 6-1, 1990)

PEC (air)

Method of calculation	Assessment by RMS, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	Negligible

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	**Soil** Definitions for risk assessment: dimoxystrobin, 505M09[27], 505M08[28], 505M01[29]. Definitions for monitoring: dimoxystrobin **Water** **Ground water** Definitions for risk assessment: dimoxystrobin, 505M09, 505M08, 505M01 Definitions for monitoring: dimoxystrobin, 505M09, 505M08 **Surface water** Definitions for risk assessment: dimoxystrobin Definitions for monitoring: dimoxystrobin **Air** Definitions for risk assessment: dimoxystrobin Definitions for monitoring: dimoxystrobin

[27] 505M09: (E)-o-[(5-hydroxycarbonyl-2-methyl) phenoxymethyl]-2-methoxyimino-N-methylphenylacetamide
[28] 505M08: [*E*-*o*-(2-hydroxycarbonyl-5-methyl)phenoxymethyl]-2-methoxyimino-*N*-methylphenyl acetamide
[29] 505M01: ((*E*)-2-(2-hydroxymethylphenyl)-2-methoxyimino-N-methyl-acetamide)

‡ Endpoint identified by the 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 (new substance)
Surface water (indicate location and type of study)	Not available (new substance)
Ground water (indicate location and type of study)	Not available (new substance)
Air (indicate location and type of study)	Not available (new substance)

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Nothing proposed

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

Appendix 1.6: Effects on non-target Species

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

Acute toxicity to mammals ‡	LD_{50}: >5000 mg a.s./kg bw rat (technical a.s.) LD_{50}: 188.9 mg a.s./kg bw rat (formulation; chosen by EFSA, not peer reviewed)
Dietary toxicity to mammals‡	LC_{50}: 50 ppm (5mg/kg bw/d) rat (MG)
Acute toxicity to birds ‡	LD_{50}: >2000 mg a.s./kg bw (*C. virginianus*)
Dietary toxicity to birds ‡	LC_{50}: >5000 ppm (>1043 mg/kg bw/d) *C. virginianus* LC_{50}: >5000 ppm (>232 mg/kg bw/d) *A. platyrhynchos*)
Reproductive toxicity to birds ‡	NOEC 300 ppm (36 mg/kg bw/d) *A. platyrhynchos* NOEC 1000 ppm (77 mg/kg bw/d) *C. virginianus*

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

Application rate (kg as/ha)	Crop	Category (e.g. insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.2	winter wheat	Insectivorous bird	Acute	>479, >185*	10
		Insectivorous bird	Short-term	>862, >232*	10
		Insectivorous bird	Long-term	52, 6*	5
		Insectivorous mammal	Acute	>12860, 107*	10
		Insectivorous mammal	Long-term	93, 7.8*	5

Short-term risk to mammals not calculated since long-term risks acceptable.
* TER values calculated by EFSA according to (SANCO/4145/2000), not peer reviewed

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests ‡				
Oncorhynchus mykiss	active substance	96 hr	LC_{50}	0.0434
Oncorhynchus mykiss	505M08	96 hr	LC_{50}	>100
Oncorhynchus mykiss	505M09	96 hr	LC_{50}	>100
Lepomis macrochirus	active substance	96 hr	LC_{50}	0.0512
Daphnia magna	active substance	48 hr	EC_{50}	0.0394

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Daphnia magna	505M08	48 hr	EC_{50}	>100
Daphnia magna	505M09	48 hr	EC_{50}	>100
Pseudokirchneriella subcapitata	active substance	96 hr	EbC_{50}	0.017
Pseudokirchneriella subcapitata	505M08	72 hr	EbC_{50}	>100
Pseudokirchneriella subcapitata	505M09	72 hr	EbC_{50}	>100
Oncorhynchus mykiss	BAS 507 00F	96 hr	LC_{50}	0.178
Lepomis macrochirus	BAS 507 00F	96 hr	LC_{50}	0.61
Cyprinus carpio	BAS 507 00F	96 hr	LC_{50}	0.408
Danio rerio	BAS 507 00F	96 hr	LC_{50}	0.21
Pimephales promelas	BAS 507 00F	96 hr	LC_{50}	0.15
Daphnia magna	BAS 507 00F	48 hr	EC_{50}	0.42
Pseudokirchneriella subcapitata	BAS 507 00F	72 hr	EbC_{50}	0.084
Leusiscus idus	BAS 505 01F	96 hr	LC_{50}	0.147
Oncorhynchus mykiss	active substance	28 day	NOEC	0.01
Oncorhynchus mykiss	active substance	97 day ELS	NOEC	0.316 µg/l
Pimephales promelas	active substance	36 day ELS	NOEC	0.016
Daphnia magna	active substance	21 day	NOEC	0.0125
Chironomus riparius	active substance	28 day	NOEC	0.01
Leusiscus idus	BAS 505 01F	66 day ELS	NOEC	0.015
Microcosm or mesocosm tests: EAC derived from the mesocosm study was 0.005 mg a.s./L				

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.2	winter wheat	*Oncorhynchus mykiss*	acute	1	23.5	100
		Leusiscus idus	acute	1	13.3	100
		Pimephales promelas	acute	1	10.7	10 [1]

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
		Daphnia magna	acute	1	21.3	100
		Pseudokirchneriella subcapitata	acute	1	6.0	10
		EAC from mesocosm	acute and chronic	1	2.7	-
		Oncorhynchus mykiss	chronic	1	0.5	10
		Pimephales promelas	chronic	1	8.7	10
		Oncorhynchus mykiss (ELS)	chronic	1	**0.17**[2]	10
		Leusiscus idus	chronic	1	8.1	10
		Leusiscus idus	chronic	5	39	10
		Daphnia magna	chronic	1	6.8	10
		Chironomus riparius	chronic	1	5.4	10

Appropriate risk mitigation measures should be considered at Member State level.
[1] Reduced trigger value used as data submitted on five fish species (HARAP). (*P. promelas* the most sensitive)
[2] TER value calculated by EFSA, not peer reviewed

Bioconcentration

Bioconcentration factor (BCF) ‡	48
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT50) (CT90)	0.5 1.6
Level of residues (%) in organisms after the 14 day depuration phase	< 2.5%

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

Acute oral toxicity ‡	Active substance: >79.4 µg a.s./bee BAS 507 00 F: >882 µg a.s./bee
Acute contact toxicity ‡	Active substance: >100 µg a.s./bee BAS 507 00 F: >1093 µg a.s./bee

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

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.2	winter wheat	oral	<2.52	50
		contact	<2.0	50
BAS 507 00 F (0.2 kg a.s./ha)		oral	<1.7	50
		contact	<1.38	50
Field or semi-field tests None				

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 ‡						
Typhlodromus pyri	adults	BAS 507 00 F	0.2	Mortality Repro	<30% <30%	>30%
Aphidius rhopalosiphi	adults	BAS 507 00 F	0.2	Mortality Repro	<30% <30%	>30%
Chrysoperla carnea	larvae	BAS 507 00 F	0.2	Mortality Repro	<30% <30%	>30%
Poecilus cupreus	adults	BAS 507 00 F	0.2	Mortality Feeding	<30% <30%	>30%
Aleochara bilineata	adults	BAS 507 00 F	0.2	Repro	<30%	>30%
Pardosa sp.	adults	BAS 507 00 F	0.2	Mortality Feeding	<30% <30%	>30%
Field or semi-field tests None						

Appropriate risk mitigation measures should be considered at Member State level.

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

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

Acute toxicity ‡	LC50 14-day 23.65 mg a.s./kg soil # LC50 14-day 3.35 mg a.s./kg soil (BAS 507 00 F) # LC50 14-day 5.78 mg a.s./kg soil (BAS 505 01 F) #
Reproductive toxicity ‡	NOEC 56-day <0.0887 mg a.s./kg soil (BAS 507 00 F) # NOEC 56-day <0.11 mg a.s./kg soil (BAS 505 01 F) #

Allowing for a reduction of the test LC_{50}/NOEC value by a factor of two, to allow for the relatively high organic matter content of the artificial test soil.

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
Use in a single year				
0.2	winter wheat	acute (a.s.)	876	10
		acute (formulation)	124	10
		long-term	<3.3	5
Repeated use (plateau level)				
0.2	winter wheat	acute (a.s.)	514	10
		acute (formulation)	73	10
		long-term	<1.9	5
Field or semi-field tests In field studies where BAS 507 00 F or BAS 505 01 F was applied at up to twice the proposed dose of active substance, initial reductions in earthworm numbers and biomass were seen followed by partial or full recovery to untreated levels by study end. The majority of field studies were carried out at soil concentrations which were representative of worst case soil plateau levels.				

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

Nitrogen mineralization ‡	<25% after 28 days at 2.0 kg a.s./ha
Carbon mineralization ‡	<25% after 28 days at 2.0 kg a.s./ha

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N; Dangerous to the environment R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects on the aquatic environment S60: This material and its container must be disposed as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/safety data sheet

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

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

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

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