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

fuberidazole

finalised: 14 November 2007

(version of 12 December 2007 with a minor editorial correction)

SUMMARY

Fuberidazole is one of the 79 substances of the third stage Part A of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

The United Kingdom being the designated rapporteur Member State submitted the DAR on fuberidazole in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 5 April 2005. The peer review was initiated on 20 January 2006 by dispatching the DAR for consultation of the Member States and the sole applicant Bayer CropScience. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed on during a written procedure in August – September 2006. 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 March 2007.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 25 September 2007 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 notifier which comprises seed treatment to winter-sown varieties of wheat, barley, oats, rye and triticale against Fusarium spp., bunt, smut in Northern Europe at rates up to a maximum of 34.5 g a.s./tonne seed in wheat, oats, rye and triticale and 45.0 g a.s./tonne seed in winter barley.

The representative formulated product for the evaluation was Baytan FS-094, a flowable concentrate for seed treatment (FS) containing fuberidazole, triadimenol and imazalil. Fuberidazole is used only in mixtures. In other mixed formulations fuberidazole is co-formulated with bitertanol, or with bitertanol, triazoxide and triadimenol.

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

Adequate methods are available to monitor all compounds given in the respective residue definition. Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Fuberidazole is harmful if swallowed; it is not acutely toxic via skin and inhalation routes (dermal LD50>5000 mg/kg bw and LC50 >0.4 mg/L) It is not a skin or eye irritant, but it is a skin sensitiser. Dogs were the more sensitive species. In the 90 day dog study focal fibrosis of the left ventricular fibrillary muscles was observed and the weights of some endocrine organs were increased by treatment in males and uterine weights in females. The relevant short term NOAEL was 0.72 mg/kg bw/day from the 1 year study in dog. With regard to the heart fibrosis in dogs the classification: T, R48/25? or Xn; R48/22? was proposed to be flagged to ECB. Overall, it was agreed that fuberidazole has no genotoxic potential. The relevant long term oral NOAEL in rats is 4.6 mg/kg bw/day, based on the occurrence of hepatocellular hypertrophy in males at 400 ppm (23 and 29 mg/kg bw/day in males and females, respectively) which represents the NOAEL for neoplastic effects, due to the occurrence of uterine and thyroid tumours in females at 155 mg/kg bw/day. Due to these uncertainties the meeting proposed to highlight this issue to ECB for final decision indicating "R40?" for discussion.
The relevant parental NOAEL was established to be 25 mg/kg bw/day, while the reproductive and offspring NOAELs were set at 4 mg/kg bw/day, based on reduced viability index. Thus fuberidazole was proposed for classification as R 62?", because of effects occurring without any parental toxicity.
Fuberidazole was not teratogenic either in rats or rabbits.
The ADI is 0.0072 mg/kg bw/day, based on the NOAEL of 1 year dog study with a SF of 100; the AOEL was set at 0.0036mg/kg bw/day, based on the same study and correcting by a factor of 0.5 because of biliary excretion. An acute reference dose of 0.08 mg/kg bw/day is set based on the developmental NOAEL of 8 mg/kg bw/day, SF 100. The operator exposure was estimated to be below the AOEL (31% and 17% for seed dressing and seed loading, respectively). No re-entry or bystander exposure is expected).

The main metabolic pathways of fuberidazole in wheat are similar to those observed in rats. Residues of the parent compound and its metabolites in wheat straw and grains are below limits of quantification of methods of analysis. Fuberidazole is proposed as residue definition for risk assessment and monitoring and MRLs for cereals are proposed to be set at 0.05* mg/kg (limit of quantification).
No transfer of residues from soil to rotational crop is expected.
As livestock exposure is extremely low, MRLs for animal products do not need to be set.
Consumer exposure is minimal and far below toxicological reference values.

The data available are considered sufficient to elucidate the likely route of degradation of fuberidazole in soil. The metabolites M01[2] and M11[3] will be formed (M01 up to 15.4% AR at 120

[2] M01 = 1*H*-benzimidazole-2-carboxylic acid
[3] M11 = 1-(1*H*-benzimidazole-2-yl)ethanone

days and M11 at a maximum of 5.9% AR at day 62) but these subsequently degrade, mineralising to CO_2. Mineralisation of fuberidazole to carbon dioxide accounted for 3.1-16.1% AR after 90 days. Dissipation to unextracted residues (40.5-53% AR at day 90) will also be a route of dissipation in the soil environment. In a laboratory soil photolysis study degradation was faster than in the dark control and the novel metabolite oxobutanal benzimidazole (M15[4]) was identified at up to 9.4% AR. However, for the proposed use as a seed treatment, the process of drilling seed will exclude light, so under the notified intended use conditions, photolytic breakdown at the soil surface will not occur. Fuberidazole exhibited moderate to medium persistence in soil. Dissipation was best characterised by a biphasic first order pattern with transition between initial relatively rapid dissipation to slower dissipation at 14-15 days after treatment. Metabolite M01 showed low to moderate persistence in soil. Fuberidazole exhibited low to medium mobility in soil and metabolite M01 exhibited medium mobility in soil. There was no indication that adsorption of either fuberidazole or M01 was pH dependant.

Under sterile conditions fuberidazole was relatively rapidly photolysed in water, producing 2-carboxybenzimidazole (M01; max. 11.1% AR) and two novel breakdown products: cis-oxobutenoic acid (M16[5], max. 46.3% AR) and trans-oxobutenoic acid, (M17[6]; max. 22.1% AR).

In natural sediment water systems parent fuberidazole dissipated rapidly from water by partitioning to the sediment. In the sediment it degraded to the minor metabolites 2-carboxybenzimidazole (M01) (formed at up to 7% AR) and 2-acetylbenzimidazole (M11) (formed at up to 6.2% AR). Unextracted residues were the major sink accounting for 53.5-70.1% AR at study end (100 days). Mineralisation to CO_2 also occurred, accounting for 9.4-23.5% AR at study end (100 days). The rapid partitioning to sediment seen for parent fuberidazole would minimise the possibility of significant amounts of photodegradation products being formed under actual use conditions in small edge of field water bodies. The necessary surface water and sediment exposure assessments were appropriately carried out using the agreed FOCUS scenarios approach for fuberidazole and its major metabolite M01 at steps 1-2.

The potential for groundwater exposure from the applied for intended uses above the parametric drinking water limit of 0.1µg/L by parent fuberidazole and its major soil metabolite 2-carboxybenzimidazole (M01), was concluded to be low, in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios.

The acute risk to birds and mammals was considered to be low. The long-term TER value for birds was below the Annex VI trigger but since exposure will be outside of breeding season, and of short duration due to seed germination, the risk for reproductive effects was nevertheless considered to be low. The long-term risk assessment for mammals in the DAR was based on a NOAEL of 117.7 mg a.s./kg bw/day (1250 mg a.s./kg diet) derived from a 2-generation study with rat. However lactation index was partly affected at the next lower dose of (250 mg a.s./kg diet) and a reduction in viability (15-30 % reduced survival within the first 5 days after birth) was observed in F2B generations at dose

[4] M15 = 4-(1*H*-benzimidazol-2-yl)-4-oxobutanal
[5] M16 = (2*Z*)-4-(1*H*-benzimidazol-2-yl)-4-oxobut-2-enoic acid
[6] M17 = (2*E*)-4-(1*H*-benzimidazol-2-yl)-4-oxobut-2-enoic acid

levels of 25 and 117.7 mg a.s./kg bw/day. The setting of the endpoint was discussed in the expert meeting taking into account also effects observed in developmental studies with rats and rabbits. NOELs of 8 mg/kg bw/day (skeletal effects) and 30 mg/kg bw/day (reduced foetal weights) were derived for exposure periods of day 6 to day 18 (and 19) of pregnancy. The RMS considers these developmental effects as not relevant for the long-term risk assessment of mammals. However the results indicate that relatively short exposure during critical life stages can lead to adverse developmental effects at dose rates below the originally suggested NOAEL of 117.7 mg a.s./kg bw/d. The experts on toxicology regarded the reduced viability index as a relevant effect for human risk assessment and suggest a NOAEL of 4 mg/kg bw/day. Taking all the information available into consideration EFSA proposes a precautionary approach using the endpoint of 4 mg/kg bw/day in the long-term risk assessment. The resulting TERlt would be 0.4 indicating a potential high long-term risk to mammals and the need for refinement of the exposure assessment.. Also the risk to aquatic organisms, bees, other non-target arthropods, soil organisms, non-target plants and biological methods of sewage treatment was considered to be low from exposure to fuberidazole. Since the representative formulated product contains two additional active substances, the risk from combined toxicity needs to be addressed for birds, mammals, aquatic organisms, the standard non-target arthropods *Typhlodromus pyri* and *Aphidius rhopalosiphi*, earthworms and soil micro-organisms at product authorisation.

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

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Fuberidazole is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 designating the United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, the United Kingdom submitted the report of its initial evaluation of the dossier on fuberidazole, hereafter referred to as the draft assessment report, to the EFSA on 5 April 2005. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the revised version of the draft assessment report was distributed for consultation on 20 January 2006 to the Member States and the main applicant Bayer CropScience as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed during a written procedure in August – September 2006 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level.

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 by EFSA in March 2007. 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 25 September 2007 leading to the conclusions as laid down in this report.

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

In accordance with Article 11(4) of the Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

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

- the comments received
- the resulting reporting table (rev. 1-1 of 25 October 2006)

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

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-1 of 27 September 2007)

Given the importance of the draft assessment report including its addendum (compiled version of June 2007 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

Fuberidazole is the ISO common name for 2-(2'-furyl)benzimidazole (IUPAC).

Fuberidazole belongs to the class of benzimidazole fungicides. It acts as a contact and acropetal systemic fungicide, it inhibits mitosis in fungi by interfering with the ß-tubulin assembly. After seed treatment, it penetrates into cereal grains and active concentrations of fuberidazole are translocated to the leaf tip. Fuberidazole is used as seed treatment application to control Fusarium spp., bunt, smut in cereal crops.

The representative formulated product for the evaluation was "Baytan FS 094", a flowable concentrate for seed treatment (FS), which is a co-formulation of 9 g/L fuberidazole with 75 g/L triadimenol and 10 g/L imazalil, registered under different trade names in Europe.

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide as proposed by the notifier which comprises seed treatment in cereal crops against Fusarium spp., Bunt, Smut in Northern Europe at rates up to a maximum of 34.5 g a.s./ tonne seed in wheat, oats, rye and triticale and 45.0 g a.s./tonne seed in winter barley.

The representative uses evaluated comprise seed treatment against Microdochium nivale *[Fusarium patch]*, Leptosphaeria nodorum *[Septoria]* in wheat, oats, rye and triticale, against Tilletia caries *[Common bunt, smut*] in wheat, and against Microdochium nivale in barley in Northern Europe at maximum application rates per treatment of 10.35 g as/ha (at 230 kg seed/ha) for wheat and triticale, of 8.1 g as/ha (at 180 kg seed/ha) for barley, of 7.7 g as/ha (at 170 kg seed/ha) for rye and of 8.6 g as/ha (at 190 kg seed/ha) for oats.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of fuberidazole is 970 g/kg. No FAO specifications exist.

A data gap was set by the experts of the PRAPeR 16 meeting requiring a revised technical specification listing impurity A as 3 g/kg. The revised specification provided by the notifier has been presented in addendum 6 to volume 4.

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

Adequate analytical methods are available for the determination of fuberidazole as well as for the determination of the impurities in the technical material.
Sufficient test methods and data relating to physical, chemical and technical properties are available, however data gaps were set by the experts of the PRAPeR 16 meeting requiring a new melting point study, a study for the UV spectra under acidic conditions according to GLP and the determination of suspensibility of the formulation after storage. Also adequate data are available to ensure that quality control measurements of the plant protection products are possible.

Adequate analytical methods are available for the determination of residues of fuberidazole in cereals, animal products (milk, meat and eggs), and environmental samples.
Most methods use GC-NPD for final analysis and differ in the extraction and/or clean-up procedures. A modification of multi-residue method DFG S19 was validated successfully for wheat grain: A GC-MSD based multi method is available for monitoring purposes in matrices of plant origin The limit of quantification (LOQ) of these methods for barley grain, green material and straw is 0.05 mg/kg.
A GC-NPD based multi-residue method is available for enforcement purposes in matrices of animal origin (LOQ: 0.01 mg/kg for milk and 0.05 mg/kg for meat and egg).
Adequate methods are available for post-registration monitoring of soil (modification of DFG S19 and using GC-MS, LOQ of 0.01 mg/kg), water, (HPLC-MS/MS, LOQ of 0.05 µg/L), air (HPLC-Fluorescence, LOQ of 0.001 mg/m^3).

2. Mammalian toxicology

Fuberidazole was discussed in a PRAPeR experts' meeting in March 2007.

Concern was raised for the comparability of batches used in the toxicological studies. The RMS summarised the information in the addendum. Analytical data were supplied for batches used in the critical assays. The levels of impurities in these batches could be considered 'worst-case' with respect

to the testing of impurities. Since the batches analysed cover most of the critical studies within the database, the data provided was considered to be sufficient. The RMS considered the batches comparable. The experts agreed on the conclusion presented by the RMS.

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

Fuberidazole is rapidly and extensively absorbed (>80%); it is widely distributed, mainly to adrenal glands and thyroid. In animal testing it did not show any potential for accumulation. Excretion is rapid with > 90% excreted after 24 hours at low doses. Fuberidazole is extensively metabolised in rats. The main metabolite in bile was the glucoside of hydroxyfuberidazole.

2.2. ACUTE TOXICITY

Fuberidazole oral LD50 is >300 <500 mg/kg bw by the acute toxic class method (classification as **R22** "Harmful if swallowed" was proposed). It is not acutely toxic via skin and inhalation routes (dermal LD50>5000 mg/kg bw and LC50 >0.4 mg/L). It is not a skin or eye irritant, but it is a skin sensitiser in a Magnusson-Kligman assay.

2.3. SHORT TERM TOXICITY

Dogs were the most sensitive species. In the 90-day dog study focal fibrosis of the left ventricular fibrillary muscles was observed and along with increased uterine weights drove the NOAEL. The weights of some endocrine organs were increased by treatment in males and uterine weights in females. The relevant NOAEL was 0.72 mg/kg bw/day from the 1 year study in dog. No treatment related effects were seen in a 21 day dermal study with fuberidazole.

The relevance of endocrine effects/tumours on the risk assessment was discussed by the experts. It was considered that at high dose levels there might be some hormonal disruption. Effects in the testes, epididymides, pancreas and thyroid occurred at dose levels 25 – 100 times higher than the NOAEL for the dog study, thus unlikely to impact on human risk assessment.

With regard to the findings in dogs the meeting agreed to highlight the concerns for heart fibrosis in dogs proposing the classification: **T, R48/25?** or **Xn; R48/22?** ("Danger of serious damage to health by prolonged exposure") to be flagged to ECB.

2.4. GENOTOXICITY

Four *in vitro* and 3 *in vivo* assays were conducted with fuberidazole.

All the *in vitro* assays were negative with the exception of the chromosomal aberration assay which produced an increase in chromosome and chromatid rearrangements at cytotoxic doses in the presence of metabolic activation. The RMS argued that based on this positive findings, another positive result would have been expected in at least one of the *in vitro* genotoxicity assays. No further indication was obtained from the carcinogenicity and reproductive/developmental toxicity data package of *in vivo* spindle inhibition effect. Lack of any micronuclei in the two micronucleus assays gave reassurance that the almost total cessation of mitosis in the chromosome aberrations assay was not likely due been to a spindle inhibition effect and that spindle inhibition was not an *in vivo* hazard.

Given the known properties of related compounds (benzimidazole spindle inhibitors), and the age of most of these studies, in the DAR the RMS recommended that an *in vitro* chromosome aberration assay and a mouse micronucleus assay to be conducted to modern standards to confirm the absence of any effects that might arise from spindle inhibition. An audited summary and results of the new *in vivo* chromosome aberration assay have been submitted and discussed at the experts' meeting. The meeting agreed with the RMS that there is no clastogenic potential in the *in vivo* studies and there is no concern for human risk assessment. The final report was submitted to the RMS 20/4/2007 – the conclusions did not change.

Overall, it was agreed that fuberidazole has no genotoxic potential.

2.5. LONG TERM TOXICITY

In the chronic toxicity/carcinogenicity studies, rats showed an increased incidence of uterine and thyroid tumours, while mice showed and increased incidence of liver adenomas.

The significance of uterine effects was discussed. At the highest dose the effects are statistically significant, but in total there is no clear dose response relationship.

At low dose levels fuberidazole has been found in the thyroid in the ADME studies. This was discussed in relation of the mechanism of tumour formation in the thyroid, which is not known. As long as the mechanism is not clear it is assumed that this is relevant for humans, the worst case assumption has to be used to perform the risk assessment. Due to these uncertainties the meeting proposed to highlight this issue to ECB for final decision indicating **R40?** ("Limited evidence of carcinogenic effect") for discussion.

The relevant long term oral NOAEL in rats is 4.6 mg/kg bw/day, based on the occurrence of hepatocellular hypertrophy in males at 400 ppm (23 and 29 mg/kg bw/day in males and females, respectively) which represents the NOAEL for neoplastic effects, due to the occurrence of uterine and thyroid tumours in females at 155 mg/kg bw/day.

The liver weight increase in mice occurs at a dose level of 25 mg/kg bw/day without histopathological changes in the chronic mouse study. It was considered that the increase in liver weight, even without histopathological findings associated, might be toxicologically relevant for the overall hepatic function. A possible trigger of 20% was mentioned also based on available experiences from other authorities. One Member State commented that the increase is significant in this study and not only an adaptive effect, and the liver necrosis occurred at the next higher dose.

It was agreed to set the LOAEL at 25 mg/kg bw/day. LOAEL 25 mg/kg bw/day (chronic mouse study)

2.6. REPRODUCTIVE TOXICITY

In a reproduction toxicity study in rats over two generations fuberidazole did not impair the general reproductive performance during the pre-mating and during the gestation period until the birth of pups. During the early lactation phase, the survival of new-born pups was slightly lower in comparison to control animals.

The experts considered that the offspring effects (viability index – survival from birth to Day 5) at the intermediate dose levels were of uncertain significance. They were not reproduced in other matings. These dose levels were not associated to any parental toxicity. Nevertheless the effects were considered adverse because of a clear dose response in the F2b generation. In the F2a generation there are similar effects but without clear dose response relationship. The relevant parental NOAEL was established to be 25 mg/kg bw/day, while the reproductive and offspring NOAELs were set at 4 mg/kg bw/day. Classification was discussed. ECB classified the substance in 2004 with R 22 only. The meeting concluded to highlight this issue to ECB and proposed **R 62?** ("Possible risk of impaired fertility"), because of effects occurring without any parental toxicity.

There were no developmental effects in the rabbit developmental toxicity study (maternal and developmental NOAEL 30 mg/kg bw/day). In the rat the developmental and maternal NOAELs were both set at 8 mg/kg bw/day, the developmental NOAEL being based on skeletal findings. There were no malformations recorded in the rat or rabbit developmental toxicity studies

2.7. NEUROTOXICITY

Fuberidazole structure does not show any relationship with compounds known to induce delayed neurotoxicity e.g. organophosphates. No studies were submitted nor required.

2.8. FURTHER STUDIES

It was not possible to clarify the mechanistic background of the cardiotoxic effects (focal heart fibrosis) seen in dogs at the end of the 1 year study. A daily dose of 200 mg/kg bw was shown to clearly exceed the metabolic capacity of the dog liver for detoxification. Fuberidazole effectively inhibited mitochondrial enzymes of the respiratory chain (mainly complex II enzymes), which may partly explain the liver toxicity seen in animals but not the cardiac effects seen in dogs

In short term tests for carcinogenicity on rat livers, fuberidazole was found to be negative for tumour initiation. The compound showed a slight tumour promoting potential but only at dose levels toxic to liver cells.

No synergistic or superadditive acute toxicity was seen in rats following simultaneous oral administration of fuberidazole with other fungicidal active ingredients such as triadimenol, bitertanol, imazalil and triazoxide.

2.9. MEDICAL DATA

No adverse health effects have been reported for workers engaged in the manufacture and formulation of fuberidazole products. No specific cases of intoxication are known for fuberidazole and epidemiological studies on the general population are not available.

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

ADI

The ADI was based on the 1 year dog NOAEL of 0.72 mg/kg bw/day (based on increased incidence of focal heart fibrosis and an increase in uterine weight). The experts agreed to apply a safety factor of 100, leading to a value of 0.0072 mg/kg bw/day.

AOEL

The NOAEL (0.72 mg/kg bw/day) from the 1 year dog study was considered the most appropriate. The need for a higher safety factor was discussed. The effects occur in the dog at 3.6 mg/kg bw/day. Therefore the meeting agreed to a safety factor of 100 because of a sufficient margin of safety. The resulting AOEL would be 0.0072 mg/kg bw/day.

The allocation of correction factor for oral absorption was discussed.

Data are not available from the dog study. Although the oral absorption observed in rat is higher than 80%, in case biliary excretion is taken into account, a correction factor of 0.5 would be appropriate, as it was not clear that the biliary component was systemically available to the target organ (heart) in the dog. This resulted in an AOEL of 0.0036mg/kg bw/day.

ARfD

The acute reference dose is based on the NOAEL from the rat developmental study. Given that the effects are not considered to adversely affect overall normal development of pups, a 100 fold assessment factor was considered sufficient. Maternal food consumption was also reduced in the first few days of dosing in this gavage study. The NOAEL for this effect was also 8 mg/kg bw/day. An acute reference dose of 0.08 mg/kg bw/day is proposed. This value is possibly conservative and might be refined if an appropriate single dose study is submitted.

2.11. DERMAL ABSORPTION

The notifier proposed the default 100 % value for dermal absorption of fuberidazole (dilution and concentrate). Subsequently, the Notifier has submitted *in vivo* and *in vitro* dermal absorption studies performed with the formulation 'Baytan FS 094'.

The RMS proposed the following values, which were agreed by the experts:

1.1% for the concentrate, rounded to 1%;

5.7% for the grain dust, rounded to 6%.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Baytan FS 094 is a seed dressing liquid containing the insecticidal active substances (a.s.) triadimenol (75 g/L product), fuberidazole (9 g/L product) and imazalil (10 g/L product). It is applied to cereal seed at a maximum rate of 0.5 l/100 kg seed. The notifier stated the only intended use of Baytan FS 094 is cereal seed treatment in professional plants. In the experts' meeting the operator exposure

assessment was discussed based on the assessment available in addendum 3. The Seed Tropex model has been used.
Based on the new AOEL value agreed during the meeting, a re-calculation of the exposure levels has been submitted by the RMS in the addendum of May 2007. New calculations are summarised below.

Operator exposure (seed dressing, worker in the plant):
Only with modifications of the models safe uses are demonstrated. Refinement was performed using alternative generic exposure data for the cleaning task and for the bagging task taking into account the amount of substance applied to the seed only. The operator is considered as wearing appropriate PPE (e.g. gloves, coverall, mask). The meeting agreed on the model calculations and on the modifications. The calculations showed exposure levels below the AOEL (31%).

Field studies were presented showing exposure levels below the ones estimated by Seed Tropex and below the AOEL (<10%), but they implied a number of assumptions. Because of the extrapolations these studies were considered only partially representative of the scenario, since they cover only some tasks for a single person. The differences in work practices at the seed treatment plants where the exposure studies were conducted reflect the differences which exist between seed treatment facilities.

Operator exposure (loading/sowing):
The Seed Tropex model was used. The results exceed the AOEL (277%). However, taking into account the field studies, which in this case were considered appropriate to the task of loading treated seed into a hopper of a drilling machine (this is regarded as the task contributing most to the exposure), an exposure level of 17% of the AOEL was estimated.

Task – Seed Tropex	% of the AOEL
Seed dressing	31*
Seed loading/sowing	17°

* operator wearing gloves, coverall

° operator wearing standard protective garment i.e. coverall

Worker exposure
No re-entry activity is expected.

Bystander exposure:
The bystander exposure is unlikely to occur from seed treatment plants and the meeting considered the exposure for bystanders negligible.

3. Residues

Fuberidazole was discussed at the PRAPeR experts' meeting on residues in food (PRAPeR 20) in March 2007.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of fuberidazole was investigated in winter wheat after application as seed treatment. Total Radioactive Residues (TRR) at 1N application rate in straw and grains at harvest time were extremely low, amounting to 0.02 and 0.002 mg/kg, respectively. The main metabolic reactions involve opening of the furane ring and oxidation, as well as hydroxylation of the phenyl moiety. The resulting metabolites are subsequently conjugated. Wheat metabolism of fuberidazole is similar to rat metabolism.

In straw 3 compounds were identified, unchanged fuberidazole (4 % of the TRR), metabolites **M09**[7] and 2-carboxybenzimidazole (**M01**[8]) (8 and 13 % of the TRR respectively). The extremely low residue levels did not allow the investigation of the residue pattern in grains.

Therefore, the residue definition for monitoring and risk assessment is proposed to consist per default in parent compound only.

A sufficient number of supervised residue trials were conducted and confirmed the expectation from the metabolism study. Residues of fuberidazole in all cereal forage, straw and grain samples were consistently below the Limit of Quantification (LOQ) of 0.05 mg/kg.

These results are supported by storage stability studies demonstrating that fuberidazole is stable for at least 24 months under deep-freeze conditions.

Studies on the effect of processing on the nature and level of residues were not performed given the extremely low residue levels in raw cereal grains.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

A confined rotational crop study has been submitted. This study showed that TRR were below 0.01 mg/kg in rotational crops grown 30 days after application of fuberidazole at normal rate of application. A concern was raised on the validity of this study because the substance was allowed to age on soil surface instead of being incorporated, what could have caused a faster degradation of the compound due to its photolytic sensitivity. Opinion on this was asked to the expert meeting on environmental fate and behaviour which indicated that fuberidazole residue levels found in soil in this study were in the range of what could be expected from the available degradation studies. Therefore it was concluded that significant residues (above 0.01 mg/kg) were not expected in edible parts of rotational plant, not only on the basis of the confined rotational crop study, but also on the ground of the metabolism study in wheat after seed treatment, showing TRR not exceeding 0.02 mg/kg in straw. Indeed, wheat straw most generally reflects a worst case situation for uptake of soil residues.

[7] M09: 4-(1*H*-benzimidazol-2-yl)-4-hydroxybutanoic acid
[8] M01: 1*H*-benzimidazole-2-carboxylic acid

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Fuberidazole do not show any accumulation potential in rodents. Due to the extremely low exposure rate of livestock, metabolism of fuberidazole in lactating goats and laying hens was therefore not investigated. No MRL is needed in animal products.

3.3. CONSUMER RISK ASSESSMENT

No risk for the consumer resulting from the use of fuberidazole according to the representative use as seed treatment in cereals is expected.

Chronic and acute exposure assessments were carried out in accordance with the WHO calculation models. For these assessments, residues in cereal grains were considered to be present at the level of the proposed MRL (0.05 mg/kg). This constitutes a clear overestimation of the actual residue level, considering that the metabolism study in wheat showed TRR in grains to be one order of magnitude lower. Nevertheless, under these conditions, calculated potential exposure following UK national and WHO European cluster diets were largely below chronic and acute toxicological reference values.

3.4. PROPOSED MRLS

Given the results of supervised residue trials, the MRL proposed for wheat, rye, triticale, barley and oats grain is 0.05* mg/kg.

4. Environmental fate and behaviour

Fuberidazole was discussed at the PRAPeR experts' meeting on environmental fate and behaviour (PRAPeR 17) in March 2007.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The aerobic route of degradation of phenyl-^{14}C fuberidazole under dark conditions was investigated in four soils for 120 days at 20 ºC and 50% of the maximum water holding capacity (MWHC). The soils covered a range of pH values (5.9-7.6), clay contents (5.0-12.3%) and organic carbon contents (0.28-2.11%).

The major (>10% AR) metabolite **2-carboxybenzimidazole** (M01) was formed in amounts up to 15.4% AR at 120 days in the sand soil. A minor metabolite (< 6% AR) was identified as 2-acetylbenzimidazole (**M11**[9]). During the PRAPeR experts' meeting on fate and behaviour, it was noted that in some of the degradation studies the maximum formation of this metabolite was not reached at the end. Therefore the experts discussed the need for further assessment of metabolite M11, with the aim of quantitatively or qualitatively assessing its ability to contaminate groundwater (see section 4.2.2). Other metabolites were not identified, but the sum of these never accounted for > 8.3% AR at any sampling point. At day 90, mineralisation represented 3.1-16.1% AR and unextracted

[9] M11: 1-(1*H*-benzimidazole-2-yl)ethanone

radioactivity accounted for 40.5-53% AR. No further characterisation of unextracted residues was performed. An additional aerobic degradation study was performed with [phenyl-UL-^{14}C]2-carboxybenzimidazole (M01) in three soils at 20 ºC and 50% MWHC. During the entire study period of 120 days, fuberidazole-2-carboxybenzimidazole underwent intense mineralization yielding amounts of $^{14}CO_2$ up to 72.7% AR in the silt loam. Maximum levels of bound residues reached between 7 d and 91 d, ranging from 28% to 37% of AR. None of the detected degradates exceeded the amount of 5% AR.

An aerobic/anaerobic laboratory soil metabolism was performed with the same silt soil used in the aerobic study. The results of the study demonstrated that the route of degradation was not different under anaerobic conditions as compared to the aerobic conditions, although mineralisation to CO_2 was minimal (1% AR after 91 days, study end). The metabolites formed during the degradation process were 2-carboxybenzimidazole (M01) as major metabolite (max. 14.7% AR at 80d) and 2-acetylbenzimidazole (M11) as minor degradation product (< 6% AR).

Although for the proposed use as a seed treatment the process of drilling seed will exclude light, a soil photolysis degradation study was performed. In the irradiated samples, the major degradate was identified as 2-carboxybenzimidazole (M01) (maximum 30.5% AR on day 5). A new metabolite, oxobutanal benzimidazole (**M15**)[10] was identified up to 9.4% AR after 1 day. No single degradate comprised > 6% AR in the dark controls. Degradation was faster in light exposed sample than in dark soil control samples.

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

Degradation rate of fuberidazole was investigated in the same degradation studies used to establish the soil metabolism. For all soils, the degradation was biphasic, with the point of inflection at the 14 or 15 day. The calculated first order half-life by nonlinear regression for phase I (0- to 14- or 15-day data) ranged from 5.8 days to 14.7 days, and for phase II (14- or 15- to 120-day data) from 86.6 days to 136 days. During the peer review process, concerns raised on the overall DT_{90} values calculated from the biphasic analysis. In order to address the trigger for a litterbag study in the ecotoxicology section, the degradation rates for parent fuberidazole calculated according to single first order kinetics by non-linear regression over 120 days were provided in addendum 2. DT_{50} and DT_{90} values normalised to 20ºC and pF2 were in the range 6.3-56.5 days and 20.8-187.7 days, respectively. The MS experts agreed that the value for use the triggering a litter bag test is the longest overall biphasic DT_{90} of 289 days at FOCUS reference conditions.

The appropriate degradation kinetics of fuberidazole for modelling purpose was also discussed at the PRAPeR meeting on fate and behaviour. The experts confirmed that the dissipation pattern is biphasic, and that, on the basis of a simple visual assessment, first order kinetics do not fit the data acceptably. The use of first order DT_{50} values in groundwater modelling will underestimate the

[10] M15 = 4-(1*H*-benzimidazol-2-yl)-4-oxobutanal

groundwater exposure assessment to fuberidazole. However, for Member States who wish to conduct groundwater modelling with single first order DT_{50} the available data are reported in the list of endpoints (Annex I).

The rate of degradation of the major soil metabolite 2-carboxybenzimidazole (M01) measured in the laboratory with 3 soils, resulted in a simple first order DT_{50} value ranging from 6.3 to 19.5 days.

Under anaerobic conditions a half-life of 96.3 days ($r^2 = 0.45$) could be estimated.

In line with Annex II data requirements, field dissipation studies were not provided. Use of laboratory data is considered likely to result in a more conservative exposure assessment than might have been produced had field studies been available. The soil DT_{90} for fuberidazole would indicate that the potential for residues in following crops needs to be assessed (see section. 3.1.2), however this is not a fate data requirement as such.

Predicted environmental concentrations in soil (PECsoil) for fuberidazole were calculated using the longest dissipation from the laboratory data, where biphasic first order kinetic was observed (first phase DT_{50} = 14.7 days, inflection point at 15 days, second phase DT_{50} = 136 days). Maximum PECsoil was also estimated for metabolite M01.

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

A batch equilibrium adsorption/desorption study was carried out with unlabelled fuberidazole in three soils and another test was conducted on a silt soil investigating [phenyl-UL-^{14}C]fuberidazole. The adsorption constants appeared to correlate with the organic carbon content of the soils tested. K_{foc} ranged from 420 to 698 mL/g. The mean 1/n value was 0.82 (from a range of 0.76 – 0.87). On the basis of the results obtained it appears that fuberidazole has a low to medium potential soil mobility.

Again in guideline laboratory batch adsorption studies the major soil degradation product 2-carboxybenzimidazole (M01) was moderately adsorbed to all three soils tested. The mean K_{foc} value was 278 mL/g (from a range 257 – 308 mL/g), indicating that M01 is medium mobile in soil.

No column leaching studies were provided.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

In buffered aqueous solutions at pH 4, 7 and 9, maintained in the dark at 50 ºC, fuberidazole resulted stable to hydrolysis. Only minor degradates were detected, making up less than 3% AR at various times of the study.

In an aqueous photolysis study [^{14}C]fuberidazole was irradiated with artificial light at 25ºC. Fuberidazole degraded photolytically to 2-carboxybenzimidazole (M01, max. 11.1% AR), cis-oxobutenoic acid (**M16**[11], max. 46.3% AR) and trans-oxobutenoic acid (**M17**[12], 22.1% AR). First order DT_{50} values for fuberidazole and photolytic breakdown products were estimated by non linear regression using a 5 compartment model. Further detail on this model (fuberidazole and the three

[11] M16 = (2*Z*)-4-(1*H*-benzimidazol-2-yl)-4-oxobut-2-enoic acid

[12] M17 = (2*E*)-4-(1*H*-benzimidazol-2-yl)-4-oxobut-2-enoic acid

identified minor degradates) was presented in Addendum 2. The MS experts in the PRAPeR meeting 17 agreed that aqueous photolysis of fuberidazole is unlikely to be an important route of degradation in the environment. The DT_{50} value (1st order DT_{50} = 10.5 June days at Phoenix Arizona USA, ca. 34ºN in the irradiated samples) calculated for the parent is reliable, whilst no reliable photodegradation rate for metabolites could be determined.

The quantum yield of direct photodegradation of fuberidazole was determined according to the ECETOC method in polychromatic light and was calculated to be $\Phi = 0.00131$. The estimates based on the GC-SOLAR model resulted in environmental direct photolysis half-lives for the 0-1 cm top layer of a pure water column at 50ºN to be 1.2-9.4 days at the time a spring cereal crop is drilled and 0.9-15 days at the time a winter cereal crop is drilled (using the calculation method of Frank and Klöpffer).

In the absence of data on readily biodegradability, fuberidazole is considered to be not readily biodegradable.

In the reliable sediment/water study, [phenyl-UL-^{14}C]fuberidazole was investigated in two systems at 20 ºC in the dark. Results showed that fuberidazole dissipated rapidly from water by partitioning to the sediment with first order $DT_{50\ water}$ of 0.34-0.83 days. In the sediment fuberidazole degraded to the minor metabolites 2-carboxybenzimidazole (M01) (formed up to 7% AR) and 2-acetylbenzimidazole (M11) (formed at up to 6.2% AR). Unextracted residues were the major sink accounting for 64.7-70.1% AR at 66-100 days. First order DT_{50} values for parent fuberidazole in the sediment alone were calculated to be 21.7 and 31.5 days. First order DT_{50} values for 2-carboxybenzimidazole (M01) were calculated to be 41 and 78 days for the whole system (geometric mean 56.7 days).

The rapid partitioning to sediment in these studies seen for parent fuberidazole would minimise the possibility of significant amounts of photodegradation products being formed under actual use conditions in small edge of field water bodies. It is therefore concluded that exposure assessment are not required for aqueous photodegradates cis-oxobutenoic acid (M16) and trans-oxobutenoic acid (M17) and that the appropriate DT_{50} values for use in surface water exposure assessment are those derived from the 2 satisfactorily submitted dark laboratory aerobic sediment water studies.

For the supported use, assuming a single application of 10.35 g/ha and a geometric mean soil DT_{50} of 9.4 days for fuberidazole, global maximum surface water and sediment PEC calculated using FOCUS surface water step 2 calculation methods resulting from residues moving out of the soil into surface water were 0.71 µg/L and 4.3 µg/kg dry sediment respectively. These values for 2-carboxybenzimidazole (M01) were 0.13 µg/L and 0.37 µg/kg dry sediment respectively.

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

The leaching behaviour of fuberidazole and its major metabolite 2-carboxybenzimidazole (M01) was estimated using the simulation model FOCUS PRZM 2.4.1 and the associated standard FOCUS groundwater scenarios. The calculations were based on a maximum application rate of 12 g/ha. Half lives used in the modelling were derived from aerobic laboratory experiments in the dark at 20ºC and 50% MWHC. The values were not normalised to field capacity moisture content before calculating

the mean as required by FOCUS guidance. However the input values used were more conservative (longer geometric mean DT_{50}) than would result from following the FOCUS normalisation procedure. The results for all 9 FOCUS scenarios for winter cereals resulted in predicted 80th % annual average concentrations (as defined by FOCUS) < 0.001 µg/L for both parent fuberidazole and 2-carboxybenzimidazole (M01). At the meeting of experts it was agreed that first order DT_{50} values are not the optimum value to use for modelling groundwater exposure (see section 4.1.2) and that in the case for fuberidazole it was straightforward to parameterise PRZM model for biphasic kinetics as the hinge point was comparable for all the four soils tested.

Therefore, for the intended use, based on the results from first tier FOCUS groundwater modelling, contamination of vulnerable shallow groundwater above 0.1 µg/L would not be expected for parent fuberidazole or its soil metabolite 2-carboxybenzimidazole (M01).

The need for an assessment of the potential for groundwater contamination from soil degradation product 2-acetylbenzimidazole (M11) was discussed during the PRAPeR meeting 17. The experts agreed an assessment was necessary as the maximum formation of the metabolite was not reached at the end of some of the soil metabolism studies. However, it was noted that M11 was formed in lower amounts relative to the major metabolite M01 and also that the mobility potential of M11 might be expected to be lower than M01 which is a carboxylic acid. It was then concluded that the available groundwater assessment for M01 would be expected to cover the leaching potential of M11, in relation to the notified intended use conditions as a seed treatment. Nevertheless, following the proposal of the experts on mammalian toxicology to classify fuberidazole as R40? (see section 2.5), in the absence of convincing evidence of the contrary, metabolite M11 should be considered relevant in accordance with the Guidance document on the relevance of metabolites in groundwater[13]. Therefore, Member States might need to request the necessary information (e.g. DT_{50}, $K_{oc,}$ 1/n and formation fraction) for M11 in order to finalise the groundwater risk assessment, should uses be requested with higher application rates where the risk of groundwater contamination is increased.

4.3. FATE AND BEHAVIOUR IN AIR

Fuberidazole has a low vapour pressure 9 x 10^{-7} Pa at 20ºC and a Henry's Law constant of 2 x 10^{-6} Pa m^3 / mol (dimensionless Henry's Law coefficient at 20ºC, 8.2 x 10^{-10}) indicating volatilisation losses from water/soil water will be minimal. The fact the product is a seed treatment (applied just below the soil surface) also minimises the potential for emissions to the atmosphere. Any minimal amount that was released to the atmosphere would be degraded in the troposphere by hydroxyl radical mediated indirect photolysis (half life estimated using the method of Atkinson 1 hour). The potential for long range transport of fuberidazole via the air compartment is therefore considered to be extremely limited.

[13] Guidance document on the assessment of the relevance of metabolites in groundwater of substance regulated under Council Directive 91/414/ECC (Sanco/221/2000).

5. Ecotoxicology

Fuberidazole was discussed in the experts' meeting for ecotoxicology (PRAPeR 18) in March 2007.

5.1. RISK TO TERRESTRIAL VERTEBRATES

Birds and mammals may be exposed to fuberidazole by intake of treated seeds and young seedlings since fuberidazole is considered to be systemic.

The risk to generic species, representing granivorous birds and mammals was assessed according to SANCO/ 4145/2000 for the use of 45 mg fuberidazole per kg seed and a maximum seed drilling rate of 230 kg seed/ha. The acute and short-term TER values for birds are well above the Annex VI triggers in the first tier assessment, hence indicating a low risk. The long-term TER value for granivorous birds is 4.5 as presented in Addendum 2 of March 2007 and thus is below the Annex VI trigger of 5 indicating the need further concern. The long-term risk was discussed by Member State experts and it was agreed that since exposure to treated seeds would only occur outside of the breeding season for birds (winter cereals), the risk for long-term/reproductive effects to birds can be considered as low. It was noted that no residue data in cereal shoots are available for the growth stages that would be grazed by herbivorous birds and mammals. However, the concentration in plants is unlikely to exceed the concentration on the treated seed. Residue data for later growth stages showed concentrations below the limit of quantification. The meeting considered that the margin of safety was acceptable for the acute and short-term and since exposure would not occur during breeding season there was no further concern for long-term effects.

The acute risk to granivorous mammals was concluded to be low. The long-term risk assessment for mammals in the DAR was based on a NOAEL of 117.7 mg a.s./kg bw/day (1250 mg a.s./kg diet) derived from a 2-generation study with rat. However lactation index was partly affected at the next lower dose of in females (250 mg a.s./kg diet). A clear reduction in viability (15-30 % reduced survival within the first 5 days after birth) was observed in F2B generations at dose levels of 25 and 117.7 mg a.s./kg bw/day. The RMS proposed these effects to be dependent on long duration of exposure. The setting of the endpoint was discussed in the expert meeting taking into account also effects observed in developmental studies with rats and rabbits. NOELs of 8 mg/kg bw/day (skeletal effects) and 30 mg/kg bw/day (reduced foetal weights) were derived for exposure periods of day 6 to day 18 (and 19) of pregnancy. The RMS considers these developmental effects may not be revlevant for the long-term risk assessment of mammals. However the results indicate that relatively short exposure during critical life stages can lead to adverse developmental effects at dose rates below the originally suggested NOAEL of 117.7 mg a.s./kg bw/d. The expert meeting on ecotoxicology did not conclude on a NOAEL for mammals since there was also some concern regarding possible endocrine effects and decided to await the outcome of the meeting on human toxicology. Endocrine effects were observed at dose rates 25-100 times higher than the NOAEL in the dog study suggesting that potential endocrine disrupting effects would be covered by the endpoints from developmental and reproduction studies. The experts on toxicology regarded the reduced viability index as a relevant effect for human risk assessment and suggest a NOAEL of 4 mg/kg bw/day. Taking all the information available into

consideration EFSA proposes a precautionary approach using the endpoint of 4 mg/kg bw/day in the long-term risk assessment. The resulting TERlt would be 0.4 indicating a potential high long-term risk to mammals and the need for refinement of the exposure assessment. The RMS proposes that the toxicity endpoint may be further refined taking into account that exposure in the field would be shorter than in the reproduction studies and that the effects observed in the developmental studies may not be relevant in relation to population effects. EFSA agrees to the opinion of the RMS. However a refinement of the toxicity endpoint as suggested by the RMS is not a standard risk refinement option and it would need to be peer reviewed and agreed among Member State experts.

Since the $logP_{ow}$ for fuberidazole and the soil metabolite 2-carboxybenzimidazole is below 3 the potential for bioaccumulation is considered as low and no further consideration is necessary according to SANCO/4145/2000.

It was noted that no information was available on the toxicity to birds of the formulation Baytan FS 094, which contains two additional active substances (triadimenol and imazalil). Acute toxicity to mammals was low. Before concluding on a safe use of the product, the possible combined effects of the active substances in the product need to be addressed.

5.2. RISK TO AQUATIC ORGANISMS

Fuberidazole is proposed to be classified as very toxic to aquatic organisms (lowest LC_{50} = 0.91 mg/L for fish). Based on the intended use as seed treatment, corresponding to an application rate of 10.35 g/ha at 230 kg seed/ha, the acute TER values for fuberidazole are at least 12 times the Annex VI trigger based on FOCUS step 2 PEC_{sw}, hence indicating a low risk. Also the long-term risk to aquatic organisms is considered low based on toxicity of fuberidazole to *Daphnia*, while the chronic toxicity to fish has not been tested since fuberidazole dissipates fast from surface water. During the peer review the issue of potential endocrine effects of fuberidazole was raised. However, for the evaluated use concentrations would be very low in surface water and the experts' meeting agreed that no further studies were required.

Fuberidazole partitions into sediment, and was found in amounts up to 64% of applied in the water/sediment studies. However, since the NOEC for *Daphnia* is 0.12 mg/L, which is >0.1 mg/L, a study with sediment dwelling organisms is not required according to SANCO/3268/2001.

The log P_{ow} for fuberidazole is <3 and therefore the potential for bioconcentration is considered as low.

No major metabolites (≥10%) were detected in the water/sediment study. However, M01 is a major metabolite in soil, where it has a DT_{50} of up to 12 days. It is therefore possible that it will reach surface water through runoff and/or drain flow events. If it is assumed that the metabolite is 10 times more toxic than fuberidazol the acute TER values will be 128 and 662 for fish and aquatic invertebrates, respectively, based on PEC_{sw} from FOCUS step 2 calculations and hence the risk to

aquatic organisms is considered to be low. Three metabolites were identified at > 10% in the aqueous photolysis study. However photolysis was considered as not being an important route of degradation of fuberidazole in the environment and hence the photolysis metabolites are not expected to be found in relevant quantities under the intended use conditions.

Since no studies with the formulation were submitted the risk posed by the use of Baytan FS 094 cannot be concluded. Even if the formulated product would not reach surface water as such, the three active substances may have combined toxic effects which need to be addressed.

5.3. RISK TO BEES

No exposure of bees to fuberidazole is expected from the intended use as a seed treatment. However, fuberidazole is systemic and it cannot be excluded that bees may be exposed to residues in contaminated food e.g. honey dew. No data are available for whole plant residues levels at the time when bees are likely to be foraging on honey dew. A worst case assessment was presented in the DAR assuming that the maximum amount likely to be found in a seed would be translocated throughout the plant and the corresponding concentration is the same in honey dew. Assuming a bee consumes 20 µl/day, this will result in 0.9 µg fuberidazole/day. As the oral toxicity is 187.2 µg fuberidazole/bee, the risk is considered low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Laboratory studies with the two standard species *Typhlodromus pyri* and *Aphidius rhopalosiphi* did not show mortality above the Annex VI trigger of 30% at test concentration of 10.35 g a.s/ha. Additional studies are available with Baytan FS 094 treated seeds with *Poecilius cupreus*, *Bembidion tetracolum*, *Aleochara bilineata* and *Pardosa* sp. at rates close to the intended sowing rate. No effects on mortality or reproduction above 30% were observed.

Since no data are available on toxicity of the formulation Baytan FS 094 to the standard species, no conclusion on risk from use of Baytan FS 094 can be drawn at this stage.

5.5. RISK TO EARTHWORMS

The acute toxicity of fuberidazole to earthworms is low and the TER value calculated based on initial PEC_{soil} is more than 3000 times above the Annex VI trigger. The chronic risk was addressed in studies with seeds treated with the formulation Baytan FS 094. Since a soil with 5% organic matter was used no correction of the NOEC value was done. No effects on body weight or reproduction were observed at the highest concentration tested (1150 kg seed/ha, treated with 500 ml formulation/100 kg seed). If the NOEC is divided by the maximum application rate of 230 kg seeds/ha a TER of 5 is obtained. This is just at the Annex VI trigger and therefore no further studies are considered necessary.

A significant effect on reproduction was observed at one dose level in a chronic study with the major soil metabolite M01. However, there was no dose response and the effect was not considered to be treatment related. Since no data are available on effects to earthworms from soil metabolites deriving from the other active substances (especially triadimenol) in the formulation, no conclusion on risk to earthworms from use of Baytan FS 094 can be drawn at this stage.

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

Studies on *Folsomia candida* with the formulation Baytan FS094 and the soil metabolite M01 are available. The NOEC values from these studies were compared to maximum PEC_{soil}. The TER values are well above the Annex VI trigger and hence the risk is considered to be low.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects on soil respiration and nitrification were tested with fuberidazole. Effects on nitrogen turnover were also tested with the metabolite M01. No deviation >25% from the control was observed. No studies are available with the lead formulation Baytan FS 094 and therefore no conclusion on the risk from combined toxicity of the three active substances to soil micro-organisms can be drawn.

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

No exposure of non-target plants off-field is expected from the use of fuberidazol as a seed treatment. However, a phytotoxicity test is available in which no effects were observed at an application rate of 30 g fuberidazole per hectare.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Data from a test with fuberidazole on effects on activated sludge respiration rate are available and indicate that the risk to biological methods of sewage treatment is low.

6. Residue definitions

Soil

Definitions for risk assessment: fuberidazole, 2-carboxybenzimidazole (metabolite M01[14])

Definitions for monitoring: fuberidazole

Water

Ground water

Definitions for exposure assessment: fuberidazole, metabolite M01

[14] M01: 1*H*-benzimidazole-2-carboxylic acid

Should uses be requested with higher application rates at Member States level, metabolite M11[15] might be included.
Definitions for monitoring: fuberidazole

Surface water
Definitions for risk assessment: fuberidazole, metabolite M01
Definitions for monitoring: fuberidazole

Air
Definitions for risk assessment: fuberidazole
Definitions for monitoring: fuberidazole

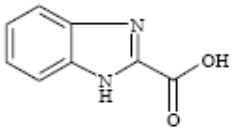
Food of plant origin
Definitions for risk assessment: fuberidazole
Definitions for monitoring: fuberidazole

Food of animal origin
Definitions for risk assessment: not required
Definitions for monitoring: not required

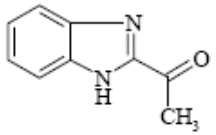
[15] M11: 1-(1*H*-benzimidazole-2-yl)ethanone

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
fuberidazole	Moderate to medium persistence $DT_{50\ lab}$ according to biphasic (hockey stick) 1st order = 5.8-14.7 d (1st phase); 87-136 d (2nd phase); breakpoint = 14/15 d (20°C, 50% MWHC) Overall biphasic 1st order DT_{90} = 133-309 d (20°C, 50% MWHC)	The risk to soil organisms is low.
M01 (2-carboxybenzimidazole) 	Low to moderate persistence Single first order $DT_{50\ lab}$ = 6.3-19.5 d (20°C, 50% MWHC)	The risk to soil organisms is low.

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
Fuberidazole	Low to medium mobility (Kfoc = 420-698 mL/g)	FOCUS PRZM (v. 2.4.1): no	Yes	Yes	Relevant
M01 (2-carboxybenzimidazole)	Medium mobility (Kfoc = 257-308 mL/g)	FOCUS PRZM (v. 2.4.1): no	No data available No data required	No data available	Low risk to aquatic organisms
M11 (2-acetylbenzimidazole) 	No data, not required for the notified intended use conditions	This would only be of potential concern at member state level should uses be requested with higher application rates.	No data available No data required	No data available	No data available. No data required for the representative use evaluated.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Fuberidazole (water and sediment)	The risk to aquatic organisms is low.
M01 (2-carboxybenzimidazole) (water and sediment)	The risk to aquatic organisms is low.

Air

Compound (name and/or code)	Toxicology
Fuberidazole	Not acutely toxic by inhalation. No data available on repeated inhalation exposure, not required.

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

- Data gap identified by the meeting of experts (PRAPeR 16) to submit a new melting point study, a study for the UV spectra under acidic conditions according to GLP (relevant for all representative uses evaluated, submitted in August 2007, but not peer reviewed) and the suspensibility of the formulation after storage (relevant for all representative uses evaluated, proposed submission date April 2009).
- Member States might need to request at national level the necessary information (e.g. DT_{50}, K_{oc}, 1/n and formation fraction) for metabolite M11 (2-acetylbenzimidazole) in order to finalise the groundwater assessment, should uses be requested with higher application rates, where the risk of groundwater contamination is increased (not essential to conclude the EU level risk assessment for the supported use; requirement identified during the PRAPeR meeting 17 on fate and behaviour; refer to point 4.2.2)
- The long-term risk assessment for mammals needs to be refined (relevant for all representative uses evaluated; data gap identified by EFSA; no submission date proposed; refer to point 5.1)
- The combined toxicity of the active substances in the formulation Baytan FS 094, which besides fuberidazole contains two additional active substances (triadimenol and imazalil) needs to be addressed for birds, mammals, aquatic organisms, the standard non-target arthropods *Typhlodromus pyri* and *Aphidius rhopalosiphi*, earthworms and soil micro-organisms (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to points 5.1, 5.2, 5.4, 5.5, 5.7)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as proposed by the applicant which comprises seed treatment against Microdochium nivale *[Fusarium patch]*, Leptosphaeria nodorum *[Septoria]* in wheat, oats, rye and triticale, against Tilletia caries *[Common bunt, smut*] in wheat, and against Microdochium nivale in barley in Northern Europe at maximum application rates per treatment of 10.35 g as/ha (at 230 kg seed/ha) for wheat and triticale, of 8.1 g as/ha (at 180 kg seed/ha) for barley, of 7.7 g as/ha (at 170 kg seed/ha) for rye and of 8.6 g as/ha (at 190 kg seed/ha) for oats.

The representative formulated product for the evaluation was "Baytan FS 094", a flowable concentrate for seed treatment (FS), which is a co-formulation of 9 g/L fuberidazole with 75 g/L triadimenol and 10 g/L imazalil.

Adequate analytical methods are available for the determination of residues of fuberidazole in cereals, animal products (milk, meat and eggs), and environmental samples.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.

Fuberidazole is harmful if swallowed; it is not acutely toxic via skin and inhalation routes It is not a skin or eye irritant, but it is a skin sensitiser. The relevant short term NOAEL was 0.72 mg/kg bw/day (based on heart fibrosis in the 1 year study in dogs, for which the classification: T, R48/25? or Xn; R48/22? was proposed). Overall, fuberidazole has no genotoxic potential. The relevant long term oral NOAEL in rats is 4.6 mg/kg bw/day, while 400 ppm (23 and 29 mg/kg bw/day in males and females, respectively) represents the NOAEL for neoplastic effects, due to the occurrence of uterine and thyroid tumours in females at 155 mg/kg bw/day ("R40?" proposed). The relevant parental NOAEL was established to be 25 mg/kg bw/day, while the reproductive and offspring NOAELs were set at 4 mg/kg bw/day, based on reduced viability index. Thus fuberidazole was proposed for classification as R 62?", because of effects occurring without any parental toxicity. Fuberidazole was not teratogenic either in rats or rabbits. The ADI is 0.0072 mg/kg bw/day, the AOEL is set at 0.0036 mg/kg bw/day, the ARfD is 0.08 mg/kg bw/day. The operator exposure was estimated to be below the AOEL (31% and 17% for seed dressing and seed loading, respectively). No re-entry or bystander exposure is expected).

The main metabolic pathways of fuberidazole in wheat are similar to those observed in rats. Residues of the parent compound and its metabolites in wheat straw and grains are below limits of quantification of methods of analysis. Fuberidazole is proposed as residue definition for risk assessment and monitoring and MRLs for cereals are proposed to be set at 0.05* mg/kg (limit of quantification).
No transfer of residues from soil to rotational crop is expected.
As livestock exposure is extremely low, MRLs for animal products do not need to be set.
Consumer exposure is minimal and far below toxicological reference values.

Sufficient satisfactory information on the fate and behaviour of fuberidazole in environmental matrices is available to complete an appropriate EU level environmental exposure assessment. For the applied for intended uses, the potential for groundwater exposure by fuberidazole or its soil metabolite M01 (2-carboxybenzimidazole) above the parametric drinking water limit of 0.1 µg/L, is low. Member States might need to require the necessary information (degradation and sorption) for metabolite M11 (2-acetylbenzimidazole) to finalise the groundwater assessment, should uses be requested with higher application rates at national level.

The acute risk to birds and mammals was considered to be low. The long-term TER value for birds was below the Annex VI trigger but since exposure will be outside of breeding season, and of short duration due to seed germination, the risk for reproductive effects was nevertheless considered to be low. The long-term risk assessment for mammals in the DAR was based on a NOAEL of 117.7 mg a.s./kg bw/day (1250 mg a.s./kg diet) derived from a 2-generation study with rat. However lactation

index was partly affected at the next lower dose of in females (250 mg a.s./kg diet) and a reduction in viability (15-30 % reduced survival within the first 5 days after birth) was observed in F2B generations at dose levels of 25 and 117.7 mg a.s./kg bw/day. The setting of the endpoint was discussed in the expert meeting taking into account also effects observed in developmental studies with rats and rabbits. NOELs of 8 mg/kg bw/day (skeletal effects) and 30 mg/kg bw/day (reduced foetal weights) were derived for exposure periods of day 6 to day 18 (and 19) of pregnancy. The RMS considers these developmental effects as not relevant for the long-term risk assessment of mammals. However the results indicate that relatively short exposure during critical life stages can lead to adverse developmental effects at dose rates below the originally suggested NOAEL of 117.7 mg a.s./kg bw/d. The experts on toxicology regarded the reduced viability index as a relevant effect for human risk assessment and suggest a NOAEL of 4 mg/kg bw/day. Taking all the information available into consideration EFSA proposes a precautionary approach using the endpoint of 4 mg/kg bw/day in the long-term risk assessment. The resulting TERlt would be 0.4 indicating a potential high long-term risk to mammals and the need for refinement of the exposure assessment. The risk to aquatic organisms, bees, other non-target arthropods, soil organisms, non-target plants and biological methods of sewage treatment was considered to be low from exposure to fuberidazole. Since the representative formulated product contains two additional active substances, the risk from combined toxicity needs to be addressed for birds, mammals, aquatic organisms, the standard non-target arthropods *Typhlodromus pyri* and *Aphisius rhopalosiphi*, earthworms and soil micro-organisms at product authorisation.

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

- Use of PPE to reduce operator exposure at levels below the AOEL

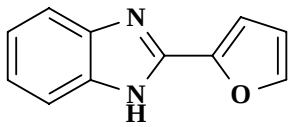
Critical areas of concern

- The risk assessment for the formulation Baytan FS 094, which is a combi product (triadimenol 75 g/L, fuberidazole 9 g/L and imazalil 10 g/L), should be regarded as inconclusive for both mammalian toxicology and ecotoxicology section.
- Long-term risk to mammals needs further refinement.

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) ‡	Fuberidazole (ISO, no synonyms)
Function (e.g. fungicide)	Fungicide
Rapporteur Member State	United Kingdom
Co-rapporteur Member State	None
Identity (Annex IIA, point 1)	
Chemical name (IUPAC) ‡	2-(2'-furyl)benzimidazole
Chemical name (CA) ‡	2-(2-furanyl)-1*H*-benzimidazole
CIPAC No ‡	525
CAS No ‡	3878-19-1
EC No (EINECS or ELINCS) ‡	223-4.4-0
FAO Specification (including year of publication) ‡	None exists
Minimum purity of the active substance as manufactured ‡	970 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_{11}H_8N_2O$
Molecular mass ‡	184.2 g/mol
Structural formula ‡	

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

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	Open
Boiling point (state purity) ‡	Not measureable
Temperature of decomposition (state purity)	DTA-measurement: Exothermic reaction above 390°C (99.9%) TGA-measurement: A weight loss was observed above 170°C (99.9%) Fuberidazole is thermally stable at ambient temperature under air.
Appearance (state purity) ‡	Active substance, pure (99.9%): colourless crystals Technical active substance (96.7%): light brown powder
Vapour pressure (state temperature, state purity) ‡	9 · 10-7 Pa at 20 °C, purity 99.9% (extrapolated) 2 · 10-6 Pa at 25 °C, purity 99.9% (extrapolated)
Henry's law constant ‡	Henry's law constant at 20 °C (calculated): 2 x 10-6 Pa m3 mol-1
Solubility in water (state temperature, state purity and pH) ‡	pH 7: 0.071 g/L at 20°C, purity 99.9%
	pH 4: 0.22 g/L at 20°C above pH 7: 0.07 g/L at 20 °C
Solubility in organic solvents ‡ (state temperature, state purity)	n-hexane < 0.1g/L at 20 °C (99.9%) toluene 0.35g/L at 20 °C (99.9%) acetonitrile 3.9g/L at 20 °C (99.9%) dichloromethane 6.6g/L at 20 °C (99.9%) acetone 14g/L at 20 °C (99.9%) 2-propanol 31g/L at 20 °C (99.9%) 1-octanol 36g/L at 20 °C (99.9%) polyethylene glycol (PEG) 62g/L at 20 °C (99.9%) PEG + ethanol (1:1) 71g/L at 20 °C (99.9%) dimethylformamide > 200g/L at 20 °C (99.9%) dimethylsulfoxide > 200g/L at 20 °C (99.9%) ethyl acetate 7.9g/L at 20 ºC (99.9%)
Surface tension ‡ (state concentration and temperature, state purity)	72.35 mN/m at 20 °C (conc. 63.4 mg/L, 90% sat.)
Partition co-efficient ‡ (state temperature, pH and purity)	log PO/W = 2.71 at 20 °C (unbuffered) log PO/W = 0.78-2.51 at 20 °C (pH 2.8-5.0) log PO/W = 2.78 at 20 °C (pH 7) log PO/W = 2.79 at 20 °C (pH 9)
Dissociation constant (state purity) ‡	pKa approx 4. (99.9%)

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

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	At neutral pH: ε at 298.7nm = 26651 1000cm^2/mol ε at 306.3nm = 33982 1000cm^2/mol ε at 321.5nm = 26243 1000cm^2/mol
Flammability ‡ (state purity)	Not highly flammable. Does not spontaneously combust. (96.9%)
Explosive properties ‡ (state purity)	Not sensitive to heat, shock or friction (96.9%)
Oxidising properties ‡ (state purity)	Does not have oxidizing properties as defined by the test procedure (98.4%)

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

Summary of representative uses evaluated *

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Winter wheat, triticale	EU North **only**	Baytan FS-094	F	Fusarium spp., Bunt, Smut	FS	9g/L[fu] 75g/L[tr] 10g/L[i m]	seed treat-ment	pre sowing	1	n.a. (0)	-	500 ml	10.35 g as/ha at 230 kg seed / ha	n.a.	[1]
Winter barley	EU North **only**	Baytan FS-094	F	Fusarium spp., Bunt, Smut	FS	9g/L[fu] 75g/L[tr] 10g/L[i m]	seed treat-ment	pre sowing	1	n.a. (0)	-	500 ml	8.1 g as/ha at 180 kg seed / ha	n.a.	[1]
Winter rye	EU North **only**	Baytan FS-094	F	Fusarium spp., Bunt, Smut	FS	9g/L[fu] 75g/L[tr] 10g/L[i m]	seed treat-ment	pre sowing	1	n.a. (0)	-	503 ml	7.7 g as/ha at 170 kg seed / ha	n.a.	[1]
Winter oat	EU North **only**	Baytan FS-094	F	Fusarium spp., Bunt, Smut	FS	9g/L[fu] 75g/L[tr] 10g/L[i m]	seed treat-ment	pre sowing	1	n.a. (0)	-	503 ml	8.6 g as/ha at 190 kg seed / ha	n.a.	[1]

[1] The risk assessment for the lead formulation Baytan FS 094 is inconclusive for mammalian toxicology and ecotoxicology.

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

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s). (a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure) (b) Outdoor or field use (F), greenhouse 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. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).** (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) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

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

Appendix 1.2: Methods of Analysis

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

Technical as (analytical technique)	Isocratic HPLC with UV (DAD) detection
Impurities in technical as (analytical technique)	Organic impurities: isocratic HPLC with UV and LC/MS detection; headspace GC with FID; water: Karl-Fischer titration; Inorganic impurities: acid digestion (sulphated ash)
Plant protection product (analytical technique)	GC-FID Method validated for all 3 active substances.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Parent fuberidazole only
Food of animal origin		Not applicable
Soil		Parent fuberidazole only
Water	surface	Parent fuberidazole only
	drinking/ground	Parent fuberidazole only
Air		Parent fuberidazole only

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	DFG S19 (extraction module E2 combined with GPC). Analysis by GC-MSD detection LOQ: 0.05mg/kg (grain)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Animal intakes indicate that neither a residue definition nor an MRL will be needed for feedstuffs or food products of animal origin.
Soil (analytical technique and LOQ)	DFG S19 (extraction module ASE; GPC clean-up) with analysis by GC-MSD. LOQ: 0.01mg/kg
Water (analytical technique and LOQ)	HPLC-MS/MS Validated for surface water. LOQ: 0.05µg/litre
Air (analytical technique and LOQ)	Extraction using Tenax or XAD-2 sorbents. Analysis by gradient HPLC-fluorescence/DAD LOQ: 0.001mg a. s/m^3

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

Body fluids and tissues (analytical technique and LOQ)	Not submitted and not required.

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	Unclassified

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Rapid (< 1 h) absorption, ≈45% excreted via urine, >80% when bile is included (rat study)
Distribution ‡	Widely distributed, highest concentrations in adrenal gland and thyroid.
Potential for accumulation ‡	No evidence.
Rate and extent of excretion ‡	Excretion was rapid with >80-90% excretion after 24 hours at low dose,
Metabolism in animals ‡	Extensively metabolised, initial step via hydroxylation.
Toxicologically relevant compounds ‡ (animals and plants)	Parent only
Toxicologically relevant compounds ‡ (environment)	Parent only

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	>300-500 mg/kg bw	**R22**
Rat LD_{50} dermal ‡	>5000 mg/kg bw	
Rat LC_{50} inhalation ‡	>0.458 mg/L (4 hrs, nose only, highest obtainable conc.	
Skin irritation ‡	Not irritating	
Eye irritation ‡	Not irritating	
Skin sensitisation ‡	Sensitising (M+K)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Increase incidence of focal heart fibrosis and an increase in uterine weight in dogs.	
Relevant oral NOAEL ‡	0.72 mg/kg bw/day	**T; R48/25?** **Xn; R48/22?**
Relevant dermal NOAEL ‡	>250 mg/kg bw (top dose)	
Relevant inhalation NOAEL ‡	No data available – not required.	

Genotoxicity ‡ (Annex IIA, point 5.4)

……..	Clastogenic in vitro; negative in vivo, no aneugenicity was observed. No concern for human risk assessment.	

‡ Endpoints identified by 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 ‡	Hepatocellular hypertrophy in male rats.	
Relevant NOAEL ‡	4.6 mg/kg bw/day (rat)	
Carcinogenicity ‡	Uterine adencarcinomas and follicular cell adenoma in thyroid (rats). Hepatocellular adenomas (mice). Clear NOAELs derived for all tumours.	**R40?**

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

target / critical effect ‡	Parental: liver hypertrophy	
	Reproductive: Decreased viability in F2b animals	
	Offspring: Decreased viability in F2b animals	
Relevant parental NOAEL ‡	25 mg/kg bw/day	
Relevant reproductive NOAEL ‡	4 mg/kg bw/day	**R 62?**
Relevant offspring NOAEL ‡	4 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Skeletal effects at maternally toxic dose (reduced bodyweight gain) in rats. Reduced foetal weights at maternally toxic dose (reduced feed consumption) in rabbits.	
Relevant maternal NOAEL ‡	Rat: 8 mg/kg bw/day Rabbit: 30 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 8 mg/kg bw/day Rabbit: 30 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data, not required.	
Repeated neurotoxicity ‡	No data, not required.	
Delayed neurotoxicity ‡	No data, not required.	

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

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Dogs: heart toxicity investigated and confirmed. Liver: indications of weak promoting activity; no initiating activity. No additive acute toxicity was seen in rats following simultaneous oral administration of fuberidazole with other fungicidal active ingredients such as triadimenol, bitertanol, imazalil and triazoxide.
Studies performed on metabolites or impurities ‡	No data available – not required

Medical data ‡ (Annex IIA, point 5.9)

No adverse effects for workers or public reported.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.0072	1 year dog study	100
AOEL ‡ (long and short term)	0.0036	1 year dog study,	100, correction factor of 0.5 for limited enteral absorption
ARfD ‡	0.08	Rat developmental toxicity study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation:- "Baytan FS 094" FS containing 0.9% fuberidazole, 7.3% triadimenol and 1.0% imazalil	Concentrate: 1% Grain dust from treated seed: 6% Rat *in vivo* and comparative *in vitro* (human/rat skin)

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

Exposure scenarios (Annex IIIA, point 7.2)

Operator (seed dressing)	Seed Tropex model: 0.0066 mg/kg bw/day Seed Tropex model (modified): 0.0011 mg/kg bw/day. 31% of the AOEL (operator wearing gloves, coverall, mask). Field studies: supplementary information indicated exposure below the AOEL. (systemic exposure <1% - 8% of the systemic AOEL)
Operator (seed loading/sowing)	Seed Tropex model: 0.0062 mg/kg bw/day. Field study (generic data): 0.0006 mg/kg bw/day. 17% of the AOEL (operator wearing long sleeved shirt and long trousers)
Workers	No re-entry exposure expected
Bystanders	No exposure expected from static treatment plants.

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Substance classified (fuberidazole)	Harmful; irritant R22 Harmful if swallowed. R43 May cause sensitisation by skin contact. R40? R48/25? or R48/22? to be discussed R 62? ("Possible risk of impaired fertility"),

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

Appendix 1.4: Residues

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

Plant groups covered	Cereals (wheat) Seed treatment.
Rotational crops	No significant residues >0.01mg/kg for all crops (wheat (forage, hay, straw, grain), swiss chard, turnip (leaves and roots))
Metabolism in rotational crops similar to metabolism in primary crops?	Comparison is not possible. There was no identification in the rotational crop study because of low TRR.
Processed commodities	Cereal grains. Studies are not required due to low residues in grain (< 0.1 mg/kg)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Studies are not required due to low residues in grain (< 0.1 mg/kg)
Plant residue definition for monitoring	Parent fuberidazole only
Plant residue definition for risk assessment	Parent fuberidazole only
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	None submitted: none required
Time needed to reach a plateau concentration in milk and eggs	Not applicable
Animal residue definition for monitoring	Not applicable
Animal residue definition for risk assessment	Not applicable
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Not applicable
Fat soluble residue: (yes/no)	Not applicable

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

……..	No significant residues >0.01mg/kg for all crops (wheat (forage, hay, straw, grain), swiss chard, turnip (leaves and roots))

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

……..	Demonstrated for fuberidazole in wheat grain, straw and green material for storage time of 24 months

‡ Endpoints identified by 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)

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No	No	No
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)			
	Feeding studies Residue levels in matrices : Mean (max) mg/kg		
Muscle Liver Kidney Fat Milk Eggs	None submitted, none required.		

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

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Spring wheat	N.E.	3 x <0.05	1 x <0.05 (additional non-GAP trial)	0.05*	<0.05	<0.05
Winter wheat	N.E.	2 x <0.05	2 x <0.05 (additional non-GAP trial)	0.05*	<0.05	<0.05
Spring barley	N.E.	4 x <0.05	3 x <0.05 (additional non-GAP trials)	0.05*	<0.05	<0.05
Winter barley	N.E.	1 x <0.05	None	0.05*	<0.05	<0.05
Winter rye	N.E.	2 x <0.05	1 x <0.05 (additional non-GAP trials)	0.05*	<0.05	<0.05
Oat	N.E.	None	2 x <0.05 (additional non-GAP trials)	0.05*	<0.05	<0.05

(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 representative use
(c) Highest residue

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

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

ADI	0.0072 mg/kg bw/d
TMDI (% ADI) according to WHO European diet	See NEDI
TMDI (% ADI) according to national (to be specified) diets	See NEDI
IEDI (WHO European Diet) (% ADI)	7.2% for 76kg adult (wheat) based on WHO / GEMS Food Consumption Cluster Diets B,D,E and F.
NEDI (specify diet) (% ADI)	Three worst-case consumer groups: toddlers, 4-6 yr old, 7-10 yr old (14%, 13%, 11% of ADI respectively), based on UK consumption data for oats, barley, wheat and rye using Rees / Day model and residue of 0.05mg/kg.
Factors included in IEDI and NEDI	None
ARfD	0.08 mg/kg bw/d
IESTI (% ARfD)	See NESTI estimate.
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Worst case: 0.9 % of ARfD (4-6 yr olds) for UK consumption data (wheat) using Rees / Day model and residue of 0.05 mg/kg.
Factors included in IESTI and NESTI	None

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
No data submitted, none required.				

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

Wheat, barley, rye, oat and triticale	0.05*mg/kg

* LOQ

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	3.1-16.1% AR at day 90 (uniformly phenyl ring labelled) (n=4).
Non-extractable residues after 100 days ‡	40.5-53%AR at day 90 (n=4).
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	M01 at up to 15.4% AR at 120 days (n=4).

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

Anaerobic degradation ‡	Aerobic/anaerobic study, duration 121 days, included an initial 30 day aerobic phase
Mineralization after 100 days	Mineralisation 1%AR after 121 days, (n=1) (study end)
Non-extractable residues after 100 days	Non-extractable residues 57%AR at 110 days, 54.5%AR after 121 days (n=1) (study end)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Minimal degradation of parent fuberidazole under anaerobic conditions (no DT50 estimated). M01 at up to 14.7%AR at 110 days (n=1)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Not of relevance for a seed treatment. However data submitted: mineralisation minimal, non extracted residues 27%AR after 10 days (n=1). No major (>10%AR) metabolites formed except M01, (maximum 30.5%AR at 5 days (n=1)). First order DT50 10.5 June days at 34°N (dark control 17 days).

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

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

Laboratory studies ‡

Parent	**Aerobic conditions** NOTE values presented for information for MS in order that GW modelling may be conducted with SFO DT50.						
Soil type	X*	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Silt		7.6	20˚C/50% MWHC	6.3 / 20.8	6.3 / 20.8	0.858	Single 1st order kinetics
Sandy loam		7.2	20˚C/50% MWHC	51.5 / 171.2	48.0 / 159.7	0.744	Single 1st order kinetics
Silt loam		7.4	20˚C/50% MWHC	27.8 / 92.5	21.6 / 72.0	0.760	Single 1st order kinetics
Sand		5.9	20˚C/50% MWHC	56.5 / 187.7	56.5 / 187.7	0.749	Single 1st order kinetics
Geometric mean				26.7 / 88.7	24.6 / 81.8		

*) X This column is reserved for any other property that is considered to have a particular impact on the degradation rate

Parent	Aerobic conditions DT_{50} according to biphasic (hockey stick) 1st order, used for PECsoil.										
Soil type	Org. C. (%)	pH (H_2O)	t. °C / % MWHC	DT_{50} (d) 1st phase	DT_{50} (d) 20 °C pF2/10kPa 1st phase	r^2	DT_{50} (d) 2nd phase	DT_{50} (d) 20 °C pF2/10kPa 2nd phase	r^2	Overall DT_{90} (un-normalised)	Method of calculation
Silt	2.11	7.6	20˚C/50 % MWHC	5.8	5.8	0.96	105	105	0.68	133	Biphasic (hockey stick) Breakpoint = 15 d
Sandy loam	1.02	7.2	20˚C/50 % MWHC	14.7	13.7	0.96	136	126.8	0.76	309*	Biphasic (hockey stick) Breakpoint = 15 d
Silt loam	0.83	7.4	20˚C/50 % MWHC	9	7	0.95	87	67.5	0.93	179*	Biphasic (hockey stick) Breakpoint = 14 d

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

Parent	Aerobic conditions DT_{50} according to biphasic (hockey stick) 1st order, used for PECsoil.										
Sand	0.28	5.9	20˚C/50 % MWHC	13.8	13.8	0.94	112	112	0.92	281*	Biphasic (hockey stick) Breakpoint = 14 d
Geometric mean				10.1	9.4	-	108.6	100.2	-	-	

*extrapolated beyond study duration

Met M01	Aerobic conditions, lab study with metabolite as starting material							
Soil type	X*	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		6.9	20˚C/50% MWHC	18.2 / 60.5		17.0	0.97	SFO
Silt loam		7.6	20˚C/50% MWHC	19.5 / 64.8		15.2	0.99	SFO
Silt		6.8	20˚C/50% MWHC	6.3 / 20.9		6.3	0.98	SFO
Geometric mean/median						11.8 / 39.2		

*) X This column is reserved for any other property that is considered to have a particular impact on the degradation rate

Field studies ‡
None submitted, none required

pH dependence ‡ (yes / no) (if yes type of dependence)	None observed
Soil accumulation and plateau concentration ‡	No data submitted, none required

Parent	**Anaerobic conditions**						
Soil type	X[16]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Silt		7.6	Not applicable	97 days	-	0.45	SFO

[16] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sand	0.95	5.6			6.24	657	0.866
Loamy sand	2.42	5.4			16.89	698	0.852
Sandy loam	1.14	5.8			7.35	645	0.759
Silt	2.11	7.6			8.86	420	0.811
Arithmetic mean					9.84	605	0.82
pH dependence, Yes or No			None observed				

Metabolite M01 ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	1.47	6.9			4.53	308	0.777
Silt loam	0.88	7.6			2.26	257	0.772
Silt	1.56	6.8			4.2	269	0.793
Arithmetic mean/median						278	0.78
pH dependence (yes or no)			None observed				

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

Column leaching ‡	None submitted, no data required
Aged residues leaching ‡	None submitted, no data required

Lysimeter/ field leaching studies ‡	None submitted, no data required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	Biphasic first order kinetics, 1st phase DT50 14.7 days inflection point 15 days, second phase DT50 136 days longest from lab studies. Even incorporation over top 5cm, soil density 1.5g/cm^3. Metabolite M01 15.4%AR formation from parent and molecular weight correction (162/184)
Application data	Crop: wheat, Pre-emergence (seed treatment) therefore no crop interception 10.35g/ha (calculated assuming a cereal seed drilling rate of 230kg seed /ha).

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

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
		Parent fuberidazole		Metabolite M01	
Initial		0.014	0.014	0.0019	0.0019
Short term	24h	0.013	0.013	-	-
	2d	0.013	0.013	-	-
	4d	0.011	0.013	-	-
Long term	7d	0.10	0.012	-	-
	28d	0.006	0.008	-	-
	50d	0.006	0.007	-	-
	100d	0.004	0.006	-	-
Plateau concentration		Not relevant, not expected to accumulate			

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	50 °C, pH 4, essentially stable to hydrolysis 50 °C, pH 7 essentially stable to hydrolysis 50 °C, pH 9 essentially stable to hydrolysis
Photolytic degradation of active substance and metabolites above 10 % ‡	Midsummer sunlight 40°N Parent DT50 0.15 days (first order r^2=0.99) M01 11.1 %AR; M16 46.3%AR; M17 22.1%AR Dark control: no degradation of parent, no metabolites evident M16 = cis-oxobutenoic acid or (2Z,5E)-6-(2-aminophenyl)-6-aza-5-methyl-4-oxohexa-2,5-dienoic acid M17 = trans-oxobutenoic acid or (2E,5E)-6-(2-aminophenyl)-6-aza-5-methyl-4-oxohexa-2,5-dienoic acid) No reliable metabolite photolysis DT50 values could be determined. Aqueous photolysis unlikely to be significant in the environment.

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

Quantum yield of direct phototransformation in water at Σ > 290 nm	Φ = 0.00131
Readily biodegradable ‡ (yes/no)	No data submitted, substance considered not ready biodegradable.

Degradation in water / sediment

Parent	Distribution (Max. sed 58.1 – 64% AR after 3 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Anglersee	6.9 – 8.1	6.6	20	12.4 / 41.4	0.9	0.83 - <3	0.9	21.7 / 71.9	0.9	1st order
Hönniger Weiher	5.8 – 7.2	5.0	20	17.8 / 59.0	0.96	0.34 / <2	0.96	31.5 / 104.7	0.96	1st order
Geometric mean				14.8 / 49.4		0.53 / -		26.1 / 86.8		

Metabolite M01	Distribution (not found in water. Max. sed 4.7 – 7.0% AR after 31 - 66 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Anglersee	6.9 – 8.1	6.6	20	41.1 / 136.7	0.974	-		-		1st order
Hönniger Weiher	5.8 – 7.2	5.0	20	78.1 / 259.6	0.969	-		-		1st order
Geometric mean/median				56.6 / 188.4						

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Anglersee	6.9 – 8.1	6.6	23.5% at 100 d	64.7% at 66 d	53.5% at 100 d
Hönniger Weiher	5.8 – 7.2	5.0	9.4% at 100 d	70.6% at 100 d	70.6% at 100 d

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

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

Parent	FOCUS step 2 calculator version 1.1.
Parameters used in FOCUSsw step 1 and 2	Whole system geometric mean first order DT_{50} used. Fuberidazole soil: 9.4 days sediment water 13.4 days Kfoc 605 ml/g M01 soil: 11.8 days sediment water 56.7 days Kfoc 278 ml/g formation fraction from parent 15.4%
Parameters used in FOCUSsw step 3 (if performed)	--
Application rate	Crop: wheat, Pre-emergence (seed treatment) therefore no crop interception 10.35g/ha (calculated assuming a cereal seed drilling rate of 230kg seed /ha). Northern Europe, Oct - Feb

$PEC_{(sw)}$ (µg / L)		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
		Parent fuberidazole		M01	
Initial		0.7109	0.7109	0.1349	0.1349
Short term	24h	0.6751	0.6930	0.1332	0.1341
	2d	0.6410	0.6755	0.1316	0.1333
	4d	0.5780	0.6423	0.1284	0.1316
Long term	7d	0.4949	0.5966	0.1238	0.1293
	14d	0.3446	0.5059	0.1137	0.1240
	21d	0.2399	0.4337	0.1043	0.1190
	28d	0.1670	0.3756	0.0958	0.1142
	42d	0.0810	0.2900	0.0807	0.1055

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

PEC$_{(sed)}$ (µg / kg dry sediment)		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
		Parent fuberidazole		M01	
Initial		4.3010	4.3010	0.3750	0.3750
Short term	24h	4.0842	4.1926	0.3704	0.3727
	2d	3.8783	4.0869	0.3659	0.3704
	4d	3.4971	3.8861	0.3571	0.3660
Long term	7d	2.9944	3.6092	0.3442	0.3594
	14d	2.0842	3.0610	0.3160	0.3446
	21d	1.4515	2.6238	0.2901	0.3307
	28d	1.0105	2.2723	0.2663	0.3175
	42d	0.4898	1.7546	0.2244	0.2933

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUSPRZM 2.4.1		
	DT_{50} (days)	Parent fuberidazole 1st phase 10.1, 2nd phase 103.8 (un-normalised geomean DT_{50} values) Inflection time 14 days Formation fraction of M01 from parent 100% Note that DT_{50} used for parent are slightly higher than listed earlier in end points. The correct normalised geomean DT_{50} values would be 1st phase 9.4 d, 2nd phase 100.2 d (break point 14 d)	M01 13.1
	Koc (ml/g)	605	278
	1/n	0.82	0.78
Application rate	12g a.s./ha to winter cereals (no crop interception as is a seed treatment) application date as specified for drilling at each scenario. Soil incorporation depth 3cm/CAM 5.		

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

$PEC_{(gw)}$

Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Annual average concentrations (80^{th} percentile) passed 1m depth according to FOCUS guidance <0.001µg/L for all 9 FOCUS scenarios for both parent fuberidazole and the major soil metabolite M01.

$PEC_{(gw)}$ From lysimeter / field studies

Not applicable

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	Active substance: 0.00131
Photochemical oxidative degradation in air ‡	First order DT50 of 1 hour derived by the Atkinson method of calculation AOPWIN (version 1.87) assuming a concentration of $1.5x10^6$ OH radicals/cm^3.
Volatilisation ‡	From plant surfaces: ‡ Not studied, no data requested, not applicable for a seed treatment.
	from soil surfaces (BBA guideline): Not studied, no data requested.
Metabolites	None

PEC (air)

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

$PEC_{(a)}$

Maximum concentration	Negligible

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

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: fuberidazole and metabolite M01 Surface Water: fuberidazole and metabolite M01 Sediment: fuberidazole and metabolite M01 Ground water: fuberidazole and metabolite M01 and M11[17] Air: fuberidazole

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	No data provided: none requested
Surface water (indicate location and type of study)	No data provided: none requested
Ground water (indicate location and type of study)	No data provided: none requested
Air (indicate location and type of study)	No data provided: none requested

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Possibly a candidate for R53

[17] Should uses be requested with higher application rates at Member States level (see section 4.2.2)

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

Appendix 1.6: Effects on non-target Species

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Coturnix coturnix japonica	a.s.	Acute	LD_{50}: > 750 mg a.s./kg bw	-
Coturnix coturnix japonica	a.s.	Short-term	Daily dose: >930 mg a.s./kg bw/day	LC_{50}: > 5000 mg a.s./kg diet
Colinus virginianus	a.s.	Long-term	Daily dose: 76.9 mg a.s./kg bw/day	NOEC: 500 mg a.s./kg diet
Mammals ‡				
Rat	a.s.	Acute	LD_{50}: > 300 mg a.s./kg bw	-
Rat	'Baytan FS 094'	Acute	LD_{50}: > 5000 mg formulation/kg bw	-
Rat	a.s.	Long-term	4 mg a.s./kg bw/d 1	50 mg a.s./kg diet 1
Additional higher tier studies ‡				
None required.				

[1] No agreed endpoint from the PRAPeR expert meeting on ecotoxicology. EFSA proposes a precautionary NOAEL of 4 mg a.s./kg bw/d (50 mg a.s./kg diet) taking into consideration reduced viability at dose rates of 25 and 117.7 mg a.s./kg bw/d in F2B generation.(see point 5.1. in the EFSA conclusion)

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

Winter wheat at 10.35 g a.s./ha (seed loading 45 mg fuberidazole/kg seeds)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Granivorous birds	Acute	17.10	43.86	10
	Short-term	17.10	54.4	10
	Long-term	17.10	4.5	5
Tier 1 (Mammals)				
Granivorous mammal	Acute	10.35	30	10
	Long-term	10.35	0.4[2]	5

[2)] No agreed endpoint from the PRAPeR expert meeting on ecotoxicology. The TER of 0.4 is based on a precautionary NOAEL of 4 mg a.s./kg bw/d (50 mg a.s./kg diet) proposed by EFSA see point 5.1. in the EFSA conclusion)

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

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 (Test type)	End point	Toxicity[1] (mg a.s./L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	a.s.	96 hr	Mortality, $_{nom}LC_{50}$	0.91 mg/L
Lepomis macrochirus	a.s.	96 hr	Mortality, $_{nom}LC_{50}$	4.3 mg/L
Aquatic invertebrate				
Daphnia magna	a.s.	48 h (static)	Immobility, $_{mm}EC_{50}$	4.7 mg/L
Daphnia magna	a.s.	21-day (semi-static)	$_{mm}NOEC$[3]	0.12 mg/L
Algae				
Pseudokirchneriella subcapitata	a.s.	72 h (static)	Biomass: $_{mm}E_bC_{50}$	1.4 mg/L[2]
			Growth rate: $_{mm}E_rC_{50}$	12.1 mg/L
Microcosm or mesocosm tests				
Not required.				

[1] nominal ($_{nom}$) or mean measured concentrations ($_{mm}$).
[2] Based on 96-hour exposure.
[3] Based on differences in the mean number of off-spring compared to the control.

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

Winter wheat at 10.35 g a.s./ha (seed loading 45 mg fuberidazole/kg seeds)

Application Rate (g as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
fuberidazole						
10.35	W. wheat seed	Fish	Acute	1 m	1282	100
10.35	W. wheat seed	Aquatic invertebrate	Acute	1 m	6620	100
10.35	W. wheat seed	Algae	Acute	1 m	1972	10
10.35	W. wheat seed	Aquatic invertebrate	Chronic	1 m	169	10

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

Application Rate (g as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
Metabolite M01 (2-carboxybenzimidazole)						
10.35	W. wheat seed	Fish	Acute	1 m	128.2[1]	100
10.35	W. wheat seed	Aquatic invertebrate	Acute	1 m	662[1]	100
10.35	W. wheat seed	Algae	Acute	1 m	197.2[1]	10
10.35	W. wheat seed	Aquatic invertebrate	Chronic	1 m	16.9[1]	10

[1] Calculated assuming toxicity of M01 is ten times more toxic than the parent.

Bioconcentration	
	fuberidazole
$logP_{O/W}$	<3
Bioconcentration factor (BCF)[1] ‡	Not required.
Annex VI Trigger for the bioconcentration factor	Not required.
Clearance time (days) (CT_{50})	Not required.
(CT_{90})	Not required.
Level and nature of residues (%) in organisms after the 14 day depuration phase	Not required.

[1] only required if log $P_{O/W}$ >3.
* based on total ^{14}C or on specific compounds

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	> 187.2 µg a.s./bee	> 200 µg a.s./bee
Formulation: 'Baytan FS 094'*	298 µg formulation/bee	>2232 µg formulation/bee
Field or semi-field tests		
Not required.		

*FS formulaion containing 75g triadimenol, 9 g/L fuberidazole and 10 g/L imazalil

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

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

Winter wheat at 10.35 g a.s./ha (seed loading 45 mg fuberidazole/kg seeds)

Test substance	Route	TER*	Annex VI Trigger
fuberidazole	oral	> 200 µg a.s./bee	50

* this is a TER and not a HQ value based on a comparison of the amount of a.s. on a seed and the amount of liquid a bee could consume.

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

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
‡*T. pyri*	Adult	Glass plate	26 g a.s./ha	Mortality: Fecundity:	8.9% 87.8% of control	30%
‡*A. rhopalosiphi*	Adult	Glass plate	26 g a.s./ha	Mortality: Fecundity:	0.0% 63.1% of control	30%
‡*P. cupreus*	Adult	Sandy soil	500 ml product/dt seed (261 kg seed/ha) 11.75g a.s./ha	Mortality:	7.5%	30%
‡*B. tetracolum*	Adult	Quartz sand	500 ml product/dt seed (210 kg seed/ha) 9.45g a.s./ha	Mortality: Feeding:	3.3% 87.5% of control	30%
‡*A. bilineata*	Adult	Sandy soil	500 ml product/dt seed (210 kg seed/ha) 9.45g a.s./ha	Mortality: Fecundity:	3.3% 76% of control	30%
‡*Pardosa* spp	Adult	Sandy soil	12.47 g a.s./ha	Mortality: Feeding:	0.0% 97% of control	30%

Field or semi-field tests
None required.

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

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point[1]
Earthworms			
	a.s. ‡	Acute 14 days	LC50: > 1000 mg a.s./kg d.w. soil LC_{50CORR} >500 mg a.s./kg d.w.soil
	'Baytan FS 094'	Acute 14 days	LC_{50} >1000 mg formulation/kg d.w.soil[3]
	'Baytan FS 094'	Chronic (56-day reproduction)	NOEC: 1150 kg treated seed/ha[3] (FS formulation containing 75.1 g/L triadimenol, 8.3 g/L fuberidazole & 11.5 g/L imazalil)
	M01 (2-carboxybenzimidazole)	Chronic (56-day reproduction)	NOEC: ≥ 1000 mg/kg d.w. soil
Other soil macro-organisms			
Collembola			
Folsomia candida	'Baytan FS 094'	Chronic	NOEC: 260.3 mg product./kg d.w. soil (tested as 'Baytan FS 094') $NOEC_{CORR}$ 130.15 mg a.s./kg d.w.soil
Folsomia candida	Metabolite M01	Chronic	NOEC: 1000 mg fuberidazole-2-carboxybenzimidazole/kg d.w. soil
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡	28 day study	No effects at 72.13 µg a.s./kg d.w. soil
Carbon mineralisation	a.s. ‡	28 day study	No effects at 72.13 µg a.s./kg d.w. soil
Nitrogen mineralisation	M01 (2-carboxybenzimidazol	28-day study	No effects at 61 µg metabolite/kg d.w. soil
Field studies			
None required.			

[1)] end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[3)] Correction not required (Section B.9.6.2 of the DAR) study was conducted in soil with 5% organic matter content, which is similar to the organic carbon content of agricultural soil.

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

Toxicity/exposure ratios for soil organisms

Winter wheat at 10.35 g a.s./ha (seed loading 45 mg fuberidazole/kg seeds)

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s. ‡	Acute	0.014mg/kg soil	>35714	10
	'Baytan FS 094'	Acute	0.0019 mg/kg soil	>526315	10
	'Baytan FS 094'	Chronic	230 kg seeds/ha	5	5
	M01 (2-carboxybenzimidazole)	Chronic	0.0019 mg/kg d.w. soil	526315	5
Other soil macro-organisms					
Collembola (*Folsomia candida*)	'Baytan FS 094'	Chronic	1.63 mg formulation/kg d.w. soil	79.8	5
Collembola (*Folsomia candida*)	Metabolite M01	Chronic	1.63 mg formulation/kg d.w. soil	526315	5

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Preliminary screening data

None submitted. None required for seed treatments

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha) vegetative vigour	ER_{50} (g/ha) emergence	Exposure $(g/ha)^2$	TER	Trigger
None submitted. None required for seed treatments						

Additional studies (e.g. semi-field or field studies)

None submitted. None required for seed treatments

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	Endpoint
Activated sludge	EC_{50} 1640 mg a.s./L
Pseudomonas sp	--

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

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Parent (fuberidazole)
water	Parent (fuberidazole)
sediment	-
groundwater	-

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the environment

	RMS/peer review proposal
Preparation	Not proposed.

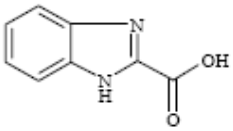
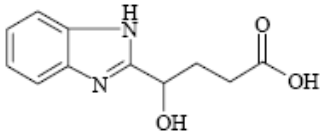
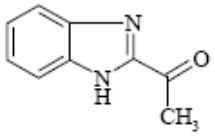
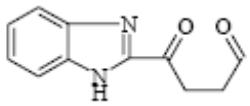
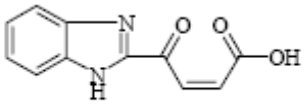
‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry

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

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
M01 2-carboxybenzimidazole	1*H*-benzimidazole-2-carboxylic acid	
M09	4-(1*H*-benzimidazol-2-yl)-4-hydroxybutanoic acid	
M11 2-acetylbenzimidazole	1-(1*H*-benzimidazole-2-yl)ethanone	
M15 oxobutanal benzimidazole	4-(1*H*-benzimidazol-2-yl)-4-oxobutanal	
M16 *cis*-oxobutenoic acid	(2*Z*)-4-(1*H*-benzimidazol-2-yl)-4-oxobut-2-enoic acid	
M17 *trans*-oxobutenoic acid	(2*E*)-4-(1*H*-benzimidazol-2-yl)-4-oxobut-2-enoic acid