CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance bromuconazole[1]

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SUMMARY

Bromuconazole is one of the 79 substances of the third stage Part A of the review programme covered by Commission Regulation (EC) No 1490/2002[3]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission 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.

Belgium being the designated rapporteur Member State submitted the DAR on bromuconazole in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 14 November 2005. Following a quality check on the DAR, the peer review was initiated on 5 May 2006 by dispatching the DAR for consultation of the Member States and the sole applicant Bayer CropScience (later Sumitomo Chemical Agro Europe SAS). Subsequently, the comments received on the DAR were examined by the rapporteur Member State and remaining issues were agreed during a written procedure in February – March 2007. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in July and October 2007.

A discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in February-March 2008 leading to the conclusions as set out in the EFSA Conclusion finalised on 26 March 2008 (EFSA Scientific Report (2008) 136).

Following the Commission Decision of 3 November 2008 (2008/832/EC)[4] concerning the non-inclusion of bromuconazole in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Sumitomo Chemical Agro Europe S.A. made a resubmission application for the inclusion of bromuconazole in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[5]. The resubmission dossier included further data in response to the areas of concern identified in the review report (SANCO/120/08) as follows:

• the potential for contamination of surface water and groundwater;

• the high toxicity to aquatic organisms.

1 On request from the European Commission, Question No EFSA-Q-2010-00032, issued on 29 July 2010.
2 Correspondence: praper@efsa.europa.eu
3 OJ No L 224, 21.08.2002, p. 25 as last amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)
4 OJ No L 295, 04.11.2008, p.53
5 OJ L 15, 18.01.2008, p.5
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In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, Belgium, being the designated rapporteur Member State, submitted an evaluation of the additional data on bromuconazole in the format of an Additional Report. The Additional Report was received by the EFSA on 8 October 2009.

In accordance with Article 19, the EFSA distributed the Additional Report to the Member States and the applicant for comments on 20 October 2009. The EFSA collated and forwarded all comments received to the Commission on 7 December 2009.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission requested the EFSA to conduct a focused peer review in the area of ecotoxicology and to deliver its conclusions on bromuconazole.

The conclusion from the original review was reached on the basis of the evaluation of the representative use as a fungicide on wheat. The conclusion of the peer review of the resubmission was reached on the basis of the same representative use. Full details of the representative use can be found in Appendix A to this report.

The representative formulated product for the evaluation was „Granit 200 SC", a suspension concentrate formulation (SC).

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (the German S19 method has been validated). For the other matrices only single methods are available to determine residues of bromuconazole. Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

In mammals, bromuconazole oral LD_{50} is 328 mg/kg bw (classification as „harmful if swallowed" (Xn; R22), proposed). The acute toxicity by the dermal and inhalation routes is low (LD_{50} > 2000 mg/kg bw and LC_{50} > 5 mg/L). Bromuconazole is neither a skin nor an eye irritant. It is not a skin sensitiser.

In repeated dose toxicity studies, the liver is the target organ. In subchronic tests, the dog is the most sensitive species, with an overall relevant NOAEL of 2.5 mg/kg bw/day, whereas in rat the NOAEL is 13.8 mg/kg bw/day. In genotoxicity testing there was some indication of weak clastogenicity *in vitro*, however there was no indication of positive results *in vivo*, neither in the micronucleus assay nor in the UDS assay. Overall, bromuconazole was considered devoid of genotoxic potential.

The relevant NOAEL for long-term toxicity and carcinogenicity in rat is 0.88 mg/kg bw/day: treatment-related neoplastic lesions in rodents occurred at high doses: hepatocellular and cholangiocellular carcinomas in rats and hepatocellular carcinoma in mice. In both rats and mice, the tumours were likely caused by liver toxicity and subsequent cell renewal. Overall, it was agreed that bromuconazole does not have carcinogenic potential relevant to humans. Bromuconazole did not show any reproductive toxicity potential: parental and foetal toxicity NOAELs were established at 1.3 mg/kg bw/day, while the reproductive NOAEL was established at 141 mg/kg bw/day. As for developmental toxicity, in the rat the relevant maternal NOAEL is 70 mg/kg bw/day, whereas the developmental NOAEL is 10 mg/kg bw/day, based on a dose-dependent increase of placental weight and ossification delays or supernumerary bones in a number of skeletal structures. It was agreed to propose classification Cat 3, Xn; R63, „May cause harm to unborn child". The ADI of 0.01 mg/kg bw/day was set based on the relevant long-term toxicity/carcinogenicity NOAEL of 0.88 mg/kg bw/day from the 2-year rat study, applying a safety factor (SF) of 100. For the ARfD, the value is based on the developmental NOAEL of 10 mg/kg bw/day from the rat study, with a SF of 100, leading to an ARfD of 0.1 mg/kg bw. The AOEL of 0.025 mg/kg bw/day was set on basis of the NOAEL of 2.5 mg/kg bw/day from the 90-day dog study (applying a standard SF of 100). The operator exposure assessment showed exposure levels below the AOEL (15.6%) according to the German model with the use of gloves during mixing/loading and application, and coveralls and sturdy footwear during

application. The estimated exposure for re-entry activities (scouting) is 4.5% of the AOEL. The bystander exposure is estimated to be 1.6% of the AOEL.

The metabolism of bromuconazole was investigated in wheat. Additional metabolism data were submitted for the category of fruit crops. A metabolic pathway could be established in cereals. At harvest, bromuconazole was still a major part of the terminal residue in cereal matrices, and identified metabolites were individually below 10% of the total residue. However, there was an indication of preferential metabolism of one bromuconazole diastereomer (LS 850647), as a significant shift in the ratio of diastereomers was found in the residues determined in the mature cereal crop when compared to the ratio in the initially applied bromuconazole. Whether the ratio of enantiomers in each diastereomer was subject to any shift was not investigated. In rotational crops studies there was uptake of residues from soil into succeeding cereal, oilseed, root and leafy crops. Upon analysis of the residues the two bromuconazole diastereomers were identified as major residue, and similar to the primary cereal metabolism their ratio had been shifted compared to the one in the bromuconazole applied to the soil. No information is available on the ratio of enantiomers in each diastereomer.

The submitted livestock metabolism data in ruminants and poultry allows to establish a metabolic pathway, and suggests that no residues in food of animal origin above the limit of quantification are expected when cereals treated according to the cGAP are used in livestock diet. The data imply that there might be preferential metabolism of one diastereomer also in livestock animals. The ratio of enantiomers in each diastereomer was not investigated. As plant and livestock residue data indicate that from the representative use no significant consumer exposure to bromuconazole residues is expected, the observed shift of the isomer ratio in the terminal residue is currently not a concern with regard to consumer safety. This may have to be reconsidered when authorisation of uses is sought that lead to consumer exposure to bromuconazole residues above the limit of quantification. The meeting of experts noted that all studies were performed using phenyl-labelled bromuconazole only, and thus the fate of the triazole moiety of the molecule was not investigated. The experts agreed that, based on the available data and information, cleavage of the molecule cannot be excluded and further investigation of the triazole moiety of the molecule is required to address consumer exposure to potential metabolites originating from molecule breakdown, as e.g. triazole derivative metabolites. Until then, the plant and animal residue definition is provisional. Triazole derivative metabolites are considered of concern due to their toxicological profile. In the absence of data investigating the fate of the triazole moiety of the bromuconzole molecule and the magnitude of potentially occurring metabolites originating from the triazole moiety, the consumer exposure cannot be assessed and consequently the consumer risk assessment is not finalised. As a breakdown of the bromuconazole molecule leading to the occurrence of metabolites relevant to consumer safety cannot be excluded, the issue is regarded as a critical area of concern.

In soil under aerobic conditions bromuconazole exhibits moderate to very high persistence forming several minor (< 10% AR) metabolites. Mineralisation was limited accounting for only 1-4.4% AR after 100-120 days. The formation of unextractable residues was a sink, accounting for 5-17.6 % AR after 100-120 days. A laboratory soil photolysis study indicated that photolysis may contribute to the degradation of bromuconazole at the soil surface. As a consequence, the experts agreed that the available field dissipation rates did not represent biodegradation that can be used as input to FOCUS modelling. However, following the resubmission application, field degradation rates normalised to FOCUS reference conditions that excluded photolysis losses were estimated. These estimates are considered appropriate for use as input to FOCUS modelling. Bromuconazole exhibits medium to low mobility in soil. Bromuconazole is essentially stable to hydrolysis, and photolysis is not expected to be a significant process in the breakdown of bromuconazole in natural aquatic systems. In dark natural sediment water systems bromuconazole partitioned from the water column to sediment where it exhibited very high persistence. The terminal metabolite, CO_2, accounted for a maximum of 0.9 % AR at 100 days (study end). Unextracted sediment residues were a sink but represented maximum 15% AR at study end. Satisfactory FOCUS surface water exposure estimates were available for use in the EU level aquatic risk assessment, with spray drift and run-off mitigation being accounted for in step 4 calculations. The potential for groundwater contamination resulting from the representative use

assessed, was concluded to be low in geoclimatic conditions represented by all 9 pertinent FOCUS groundwater scenarios.

Bromuconazole belongs to the group of triazole fungicides that are suspected to have potential endocrine disrupting properties. No information was provided to address this point with regard to the potential effects on birds and fish, and a data gap was identified. No new information on this point was provided in the Additional Report and the data gap remains.

The TER values for herbivorous birds were all above the Annex VI triggers, indicating a low risk for herbivorous birds. Also for insectivorous birds the TER values for acute and short-term exposure were well above the trigger, however the long-term TER was below the trigger of 5, indicating a potential high long-term risk. In the Additional Report higher tier studies (mainly from open literature) were presented to select the focal species and to determine the proportion of different food types (PD) of the focal species. Two different approaches were used to refine the risk assessment. The first approach included the selection of representative focal species, and estimations of PD for these species. The second approach was to include the decline of residues in insects (f_{twa} = 0.53) in the first-tier long-term risk assessment. The TERlt values based on the PD refinements, and those based on the use of f_{twa} of decline of residues in insects, were all above the Annex VI trigger values. Therefore the long-term risk to insectivorous birds was assessed as low. The risk to earthworm- and fish-eating birds was assessed as low.

The acute TERs for herbivorous and insectivorous mammals were above the Annex VI trigger of 10 (including refinement of residues in plant material), however the long-term TERs were below the Annex VI trigger, indicating a high risk. The choice of the long-term end point was discussed again in the experts‟ meeting (PRAPeR 75), and it was agreed that the NOAEL for mammals of 13.8 mg as/kg bw/d is the relevant ecotoxicological end point. TER calculations for insectivorous mammals based on this NOAEL are provided in the DAR and in the Additional Report and were above the Annex VI trigger value, indicating a low long-term risk for insectivorous mammals. In the resubmission, a higher tier risk assessment for herbivorous mammals was based on the rabbit as focal species in late cereal growth stages. The higher tier risk assessment for herbivorous mammals was discussed in the experts‟ meeting (PRAPeR 75), and it was concluded that the available information is not sufficient to address the potential high long-term risk for herbivorous mammals. The risk to earthworm- and fish-eating mammals was assessed as low.

Bromuconazole is very toxic to aquatic organisms. The applicant provided a bridging study with the new formulation SCAE0307 and *Daphnia magna*. The formulation SCAE0307 is less toxic than the previously assessed formulation EXP 10064-B, and has a toxicity comparable to that of the active substance. Member States experts at PRAPeR 75 agreed that the end points for the active substance should be used in the risk assessment. A low long-term risk was identified from the FOCUS step3 PECsw values in the D3 ditch, D4 pond, D4 stream, D5 pond, D5 stream, D6 pond, R1 pond and R1 stream scenarios. However, a potential high long-term risk was indicated for aquatic invertebrates from the FOCUS step3 PECsw values for the D1 ditch, D1 stream, D2 ditch, D2 stream, R3 stream and R4 stream scenarios, and further refinement was needed. The TERs were re-calculated with a 10m no-spray buffer zone for the drainage scenarios and a 10m no-spray buffer zone including a vegetated filter strip to mitigate the run-off. The long-term TER values were above 10 in 2 full FOCUS run-off scenarios (R3 stream and R4 stream). However, the TER values estimated with the drainage scenarios D1 ditch, D1 stream, D2 ditch, D2 stream were below the Annex VI trigger values even with a 10m no-spray buffer zone. Overall, taking into account the FOCUS step 3 and 4 scenarios, it can be concluded that the risk of bromuconazole to aquatic organisms was assessed as low for more than the half of the scenarios.

The risk assessment for non-target arthropods was not in accordance with the ESCORT II scheme. The standard glass plate tests suggest that there will be some adverse effects on sensitive non-target arthropods. Extended laboratory studies gave an indication that the risk to non-target arthropods is low. Concerns were raised with regard to the comparability of the different formulations used in the

studies with non-target arthropods. EFSA agrees to the assessment of the RMS that the formulations are sufficiently similar to conclude on the risk to non-target arthropods for the representative use. The applicant informed that a different formulation than Granit will be marketed. It is suggested that a risk assessment for this formulation is conducted at Member State level after the decision on Annex I inclusion.

The formulation Granit had no significant effect on organic matter decomposition over a six months period in a litter bag test at an application rate of 180 g a.s./ha and 500 g a.s./ha. The soil concentration was calculated in the DAR as 0.67 mg a.s./ha. This concentration covers the plateau maximum PEC_{soil} of 0.232 mg a.s./kg soil (2 x 0.200 kg a.s./ha). In conclusion, the risk of bromuconazole to non-target macro-organisms was assessed as low.

Effects of > 25% on nitrogen transformation were observed at an application rate of 400 g a.s./ha (0.53 mg a.s./kg soil). This concentration covers the plateau maximum PEC_{soil} of 0.232 mg a.s./kg soil (2 x 0.200 kg a.s./ha). The risk of bromuconazole to soil non-target micro-organisms was assessed as low.

The risk to bees, earthworms, non-target plants, and biological methods of sewage treatment was assessed as low.

KEY WORDS

Bromuconazole, peer review, risk assessment, pesticide, fungicide

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BACKGROUND

Commission Regulation (EC) No 1490/2002[6], as amended by Commission Regulation (EC) No 1095/2007[7] lays down the detailed rules for the implementation of the third stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure for organising, upon request of the Commission of the European Communities (hereafter referred to as „the Commission"), a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the designated rapporteur Member State. Bromuconazole is one of the 79 substances of the third stage, part A of the review programme covered by the Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007 designating Belgium as rapporteur Member State (RMS).

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Belgium submitted the report of its initial evaluation of the dossier on bromuconazole, hereafter referred to as the DAR (Belgium, 2005), to the EFSA on 14 November 2005. Following an administrative evaluation, the revised version of the DAR was distributed for consultation on 5 May 2006 to the Member States and the main applicant Bayer CropScience as identified by the RMS. The original notification had been filed by Aventis Crop Science.

The comments received on the DAR were evaluated and addressed by the RMS. Based on this evaluation, EFSA and Member States identified and agreed during a written procedure in February – March 2007 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 experts" meetings in July and October 2007. The reports of these meetings have been made available to the Member States electronically.

A discussion of the outcome of the consultation of experts took place during a written procedure with Member States in February - March 2008 leading to the conclusions as set out in the EFSA Conclusion finalised on 26 March 2008 (EFSA Scientific Report (2008) 136) (EFSA, 2008).

Following the Commission Decision of 3 November 2008 (2008/832/EC)[8] concerning the non-inclusion of bromuconazole in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Sumitomo Chemical Agro Europe S.A. made a resubmission application for the inclusion of bromuconazole in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[9]. The resubmission dossier included further data in response to the areas of concern identified in the review report (SANCO/120/08) (European Commission, 2008) as follows:

• the potential for contamination of surface water and groundwater;

• the high toxicity to aquatic organisms.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, Belgium, being the designated RMS, submitted an evaluation of the additional data on bromuconazole in the format of an Additional Report (Belgium, 2009). The Additional Report was received by the EFSA on 8 October 2009.

[6] OJ L224, 21.08.2002, p.25
[7] OJ L246, 21.9.2007, p.19
[8] OJ No L 295, 04.11.2008, p.53
[9] OJ L 15, 18.01.2008, p.5

In accordance with Article 19, the EFSA distributed the Additional Report to the Member States and the applicant for comments on 20 October 2009. The EFSA collated and forwarded all comments received to the Commission on 7 December 2009. At the same time the collated comments were forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant‟s response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 7 January 2010, the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on bromuconazole within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 18 January 2010; the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant‟s response to the comments, and the RMS‟ subsequent evaluation thereof, it was concluded that the EFSA should organise a consultation with Member State experts in the area of ecotoxicology, and that further information should be requested from the applicant in the area of fate and behaviour in the environment.

The outcome of the telephone conference, together with EFSA‟s further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in consultation with Member State experts, and the additional information to be submitted by the applicant, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in June 2010.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative use as a fungicide on wheat as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion (EFSA, 2010). The Peer Review Report comprises the following documents:

the comments received on the Additional Report,

the Reporting Table (rev. 1-1 of 18 January 2010)

the Evaluation Table (15 July 2010)

the report of the scientific consultation with Member State experts

Given the importance of the Additional Report including its addendum (compiled version of May 2010 containing all individually submitted addenda) (Belgium, 2010) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

The documents of the Peer Review Report and the final addendum developed and prepared during the course of the initial review process are made publicly available as part of the background documentation to the original conclusion finalised on 26 March 2008 (EFSA, 2008).

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Bromuconazole is the ISO common name for 1-[(2RS,4RS:2RS,4SR)-4-bromo-2-(2,4-dichlorophenyl)tetrahydrofurfuryl]-1H-1,2,4-triazole (IUPAC).

Bromuconazole is a conazole fungicide; other examples of members of this class are fenbuconazole and myclobutanil. It causes inhibition of C-14-demethylase in sterol biosynthesis. It is used as a broad-spectrum fungicide, with preventative and curative action, for control of diseases caused by ascomycetes, basidiomycetes, and deuteromycetes.

The representative formulated product for the evaluation was „Granit 200 SC", a suspension concentrate formulation (SC).

The evaluated representative use is as a fungicide on wheat. Full details of the representative use can be found in Appendix A.

CONCLUSIONS OF THE EVALUATION

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

The minimum purity of bromuconazole as manufactured should not be less than 960 g/kg sum of diasteromers (LS850646 + LS850647), with LS850646 (CAS 114544-80-2) ranging between 500 to 560 g/kg and LS850647 (CAS 114544-81-9) ranging between 420 to 480 g/kg. These ranges imply ratios LS850646/LS850647 between 1.04:1 and 1.33:1. At the moment no FAO specification exists.

The only outstanding issue for the specification is that additional accuracy data are identified as a data gap for impurity LS880225. The technical material contains no relevant impurities. The content of bromuconazole in the representative formulation is 200 g/L (pure).

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of bromuconazole or the respective formulation.

The main data regarding the identity of bromuconazole and its physical and chemical properties are given in Appendix A.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of bromuconazole in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

Therefore, sufficient data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. bromuconazole in food of plant origin (cereals only) and bromuconazole in soil, water and air. It should be noted however that the residue definitions for plants and animals are provisional (refer to section 3).

Residues in products of plant origin (cereals only) can be determined with a multi-method (the German S19 method has been validated) with an LOQ of 0.05 mg/kg. Products of animal origin are analysed by GC-ECD with confirmation by GC-MS; the LOQ was 0.01 mg/kg for milk and 0.02 mg/kg for the other matrices.

Soil is analysed by GC-ECD with an LOQ of 0.02 mg/kg, confirmation is by using a column of different polarity. Water is also analysed by GC-ECD with an LOQ of 0.1 µg/L, with confirmation by

GC-MS. Air is analysed by LC-MS/MS with an LOQ of 0.4 µg/m^3. A method of analysis for body fluids and tissues is not required as bromuconazole is neither toxic nor highly toxic.

2. Mammalian toxicity

Bromuconazole was discussed in a meeting of experts in July 2007 (PRAPeR 29). Bromuconazole is a mixture of 2 diastereomeric pairs of enantiomers (LS850646 and LS850647). The key toxicological studies have been performed with an average 52:45 ratio. Triggered by a question from PRAPeR 30 (Residues), the meeting of experts noted that in the 28-day study in rat (Broadmeadow, 1989) an increased plasmatic level of isomer LS850646 was observed when compared to isomer LS850647, at ca. 132 mg/kg bw/day: this might be an indication that the toxicological studies cover, only to a certain extent, a possible shift to isomer LS850646 in residues. Based on the available information, reference values for separate isomers could not be derived. A data gap was highlighted concerning the isomerisation shift in residues of isomer LS850646 against isomer LS850647, in order to show that the toxicological profile does not differ significantly from that supported in the DAR, in case a different ratio is produced. Also the issue of impurities was discussed during the meeting. All impurities were tested for acute toxicity or genotoxicity: none of the impurities showed an LD_{50} higher than the parent compound, and none showed genotoxic potential. The experts confirmed that the batches used for the toxicological tests were equivalent to the technical specification. During the resubmission phase no new toxicological data relevant to the risk assessment were summarised in the Additional Report.

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

Bromuconazole is rapidly absorbed in the rat. Based upon the radioactivity in bile, urine, cage wash, tissues and carcass at 48h post-dose, an absorption rate of 88% was agreed. Bromuconazole is rapidly and almost completely eliminated; it is widely distributed in tissues, mainly in liver and kidney, fat, ovaries and uterus tissue. Bromuconazole is extensively metabolised, through oxidation and ring-opening of the tetrahydrofurane moiety, followed by a glucuronide-conjugation or by the formation of a sulphate ester, and hydroxylation of the phenyl ring.

2.2. Acute toxicity

Bromuconazole oral LD_{50} is 328 mg/kg bw (rat study), therefore it was proposed for classification as „harmful if swallowed" (Xn; R22). The acute toxicity by the dermal and inhalation routes is low (LD_{50} > 2000 mg/kg bw and LC_{50} > 5 mg/L). Bromuconazole is neither a skin nor an eye irritant. It is not a skin sensitising agent.

2.3. Short term toxicity

The short-term toxicity of bromuconazole was assessed in rat, mouse and dog. The target organ is the liver in all species. The dog is the most sensitive species, showing increased alkaline phosphatase and alanine aminotransferase activity together with altered albumin and globulin levels, and increased liver weight at high doses. Adverse effects in skin (erythema) and peripheral lymph nodes (lymphadenitis) were also observed. At Maximum Tolerated Dose (MTD), a slight effect on the blood occurred, with decreased red blood cells and haemoglobin levels, increased mean corpuscular volume and platelet counts, and increased circulation of the white blood cells. It was considered that 2.5 mg/kg bw/day is the overall relevant NOAEL in dog. During the meeting of experts the NOAEL in the 90-day rat study was discussed. The RMS set the NOAEL at 40 ppm (2.7 mg/kg bw/day), based on fatty vacuolation at the next higher dose of 200 ppm. This value was considered to be in line with the relevant NOAEL in dogs. However, the fatty vacuolation at 200 ppm represented a very borderline case, since it occurred in only 2 females out of 10, without any other effects. The experts finally agreed to set the NOAEL in rat at 200 ppm (=13.8 mg/kg bw/day), taking into account the (mild) nature of the findings at 200 ppm.

2.4. Genotoxicity

Bromuconazole was tested in 6 *in vitro* and 2 *in vivo* tests. There was some indication of weak clastogenicity *in vitro*, in the presence of exogenous rat metabolisation. The compound could also be

considered weakly positive at cytotoxic doses, in one out of two mammalian gene-mutation assays, but was negative in the bacterial genotoxicity battery. There was no indication that the compound elicited UDS in rat liver cells *in vitro*. No positive results were generated *in vivo*, neither in the micronucleus assay nor in the UDS assay. Overall, bromuconazole was considered devoid of genotoxic potential.

2.5. Long term toxicity

As in subchronic toxicity studies, also for long-term exposure liver was the target organ (hepatocyte fatty vacuolation, liver enlargement at necropsy, nodular hyperplasia) in both rats and mice. The relevant NOAEL of 20 ppm (0.88 mg/kg bw/day) was selected from the rat study, mainly based upon the increased hepatocyte vacuolation in females. The carcinogenic potential of bromuconazole was discussed in the meeting of experts. Treatment-related neoplastic lesions (exceeding historical control data) in rats occurred at the top-dose in females, where two animals showed hepatocellular carcinoma and one a cholangiocellular carcinoma. Mice showed hepatocellular carcinoma at high doses (the incidence was just outside the historical control range). In both rats and mice, the tumours occurred at the top-doses, likely caused by liver toxicity and subsequent cell renewal. The tumours could also be considered as incidental, since the mechanism of action was not clearly elucidated. In both cases, they would not trigger classification. The experts agreed to keep the NOAELs as set by the RMS (20 ppm in rat and mouse) that would cover the occurrence of tumours at high doses. It was agreed that bromuconazole does not have carcinogenic potential relevant to humans.

2.6. Reproductive toxicity

In a two-generation study, bromuconazole caused maternal toxicity at 200 ppm (13.8 mg/kg bw/day) and above (decreased body weights). In addition, a slight increase of pre-coital interval and gestation length occurred in the F0-generation, and adult F0/F1 animals also showed increased liver weights, associated with hepatocyte fatty vacuolation at the top-dose. The F2 generation showed slightly decreased body weight gain at 200 ppm. Both parental and foetal toxicity NOAEL were established at 20 ppm, corresponding to 1.3 mg/kg bw/day. It was concluded that bromuconazole is not a reproductive toxicant to the rat, and the reproductive NOAEL was established at the highest dose of 141 mg/kg bw/day. As for developmental toxicity, in the rat the relevant maternal NOAEL is 70 mg/kg bw/day; at the same dose onwards a dose-dependent increase of placental weight was considered a sign of foetal toxicity, together with ossification delays or supernumerary bones in a number of skeletal structures. Therefore, it was concluded that 10 mg/kg bw/day is the developmental NOAEL. The higher prevalence of supernumerary cervical ribs was considered possibly relevant for humans. Increased placental weight was not observed in the rabbit, but in the absence of a valid mechanism of action, it was considered potentially adverse. In the meeting of experts, the classification as developmental toxicant Class 3 (Xn; R63, „May cause harm to unborn child") proposed by the RMS was discussed. It was noted that usually supernumerary ribs are considered as variations rather than as malformations. But, indeed they appeared at doses where no maternal toxicity was observed. It was considered that the "domed head" (a hydrocephalus-like malformation) was a typical observation upon exposure to triazoles. The findings were confirmed in a study with dermal application and supported by the occurrence of typical triazole induced malformations at high doses. The experts agreed to propose classification as R63.

2.7. Neurotoxicity

Bromuconazole does not have a structural relationship with organophosphate compounds or compounds known for neurotoxicity/delayed neurotoxicity potential. No studies are available and they are not required.

2.8. Further studies

The metabolite LS860364 was considered an intermediate in the rat metabolism study (debromylated intermediate before 5-hydroxylation of the tetrahydrofurannic cycle of bromuconazole). It was recovered as a fish, plant and soil metabolite. In the rat, LS860364 was not more toxic than bromuconazole (LD_{50} 1347 mg/kg bw); it is negative for genotoxicity *in vitro*. The impurities

LS880225, LS880226, RPA 405516, RPA 405517 were of the same toxicity as bromuconazole, whereas RPA 400063 and RPA 400064 showed lower toxicity. Therefore, no further assessment of their toxicological profile was triggered.

2.9. Medical data

Annual health surveillance data submitted by the applicant, including examination of lung function, haematology and biochemistry and skin condition, did not reveal abnormal results. No epidemiological studies involving exposure to bromuconazole are available. No data from the open medical literature are published.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

Acceptable daily intake (ADI)

The ADI of 0.01 mg/kg bw/day was set based on the relevant long-term toxicity/carcinogenicity NOAEL of 0.88-1.09 mg/kg bw/day from the 2-year rat study, applying a SF of 100. For the developmental effects in rats there is margin of safety of 7000.

Acute reference dose (ARfD)

For the ARfD, the experts agreed to base the value on the developmental NOAEL of 10 mg/kg bw/day from the rat study, with a SF of 100, leading to an ARfD of 0.1 mg/kg bw. This ensures a margin of safety of more than 2000 in respect to the major findings of the study (malformations at the top dose) and 700 for the supernumerary cervical ribs occurring at 70 mg/kg bw/day.

Acceptable operator exposure level (AOEL)

The dog appeared to be the most sensitive species. The AOEL was set on basis of the NOAEL of 2.5 mg/kg bw/day from the 90-day dog study (applying a SF of 100). The AOEL was set at 0.025 mg/kg bw/day.

EFSA note: during the commenting phase of the draft conclusion, SE commented that the NOAEL from the 2-generation study is lower than the 90-day dog study NOAEL and relevant for the setting of an AOEL of 0.014 mg/kg bw/day (SF 100), based on decreased body weight changes on pups and maternal. The data package included in the DAR would show that the pups and pregnant rats are more sensitive to the treatment of bromuconazole than adult animals. SE also noted that the outcome from the operator exposure would not change using the proposed AOEL. However, it could be important at national level for the registration of other products containing bromuconazole.

2.11. Dermal absorption

During the meeting of experts, the submitted *in vitro* studies (Walters 1990, 1991) were analysed, showing several shortcomings (mass balance absent, application site radioactivity disregarded), making the studies hardly acceptable. The experts agreed to dismiss the *in vitro* studies and to use the values from the *in vivo* study. It was decided to consider for the representative formulation „Granit 200 SC" dermal absorption values of 5% and 45% for the concentrate and the dilution, respectively.

2.12. Exposure to operators, workers and bystanders

The formulation of bromuconazole, a suspension concentrate (SC) containing 200 g/L bromuconazole, is proposed to be used as a fungicide in foliar application on cereals.

Operator exposure

	Application method (crop)	Treated area (ha/day)	Systemic exposure (mg/kg bw/day)	% of systemic AOEL
German model	Tractor, field crops	20	0,05941 mg /kg bw/day 0.003858 mg /kg bw/day	240 15.6*
UK POEM	Tractor, hydraulic boom and nozzles	50	0.3293 mg/kg bw/day 0.05021 mg/kg bw/day	1317.2 200°

*Gloves during M/L and application and coveralls and boots during application
°Gloves during M/L and application

The operator exposure is estimated to be below the AOEL only for the calculations with the German model and considering the use of PPE (gloves during M/L and application and coveralls and boots during application).

EFSA notes that the correct calculations are presented in the revised DAR (June 2007), but not in the toxicology Addendum to the DAR submitted in June 2007.

Worker exposure

The worker exposure was estimated according to the following equation:

$D = DFR \times TF \times AR \times P$,

where:

- DFR is the dislodgeable foliar residue

- TF is the transfer factor

- WR is the working rate

- AR is the application rate, which is maximally 0.2 kg a.s./ha

- P is the penetration factor

Assuming a DFR=0.003 mg a.s./cm², a transfer factor TF=5000 cm²/person/h (field-crop estimation), a working rate of 1h/d (scouting task), and a default penetration factor (PPE used)=5%, and a skin absorption of 45%,

$D = 0.003$ mg /cm² $\times$ 5000 cm²/person/h $\times$ 1/60 kg$\times$ 1h/day $\times$ 0.2 kg/ha $\times$ 0.05 $\times$ 0.45 = 0.00114 mg/kg bw/day.

The estimated exposure for re-entry activities (scouting) is 4.5% of the AOEL.

EFSA notes that the correct calculations are presented in the revised DAR (June 2007), but not in the toxicology Addendum to the DAR submitted in June 2007.

Bystander exposure

During the meeting of experts, the RMS was asked to re-calculate bystander exposure considering that bystanders‟ clothing does not provide a 100% protection to the spray drift. The RMS recalculated the dermal exposure, taking into account the greatest possible exposed skin area, 2 m² instead of 0.4225m². In this case, the dermal exposure would be 0.00039 mg/kg bw; together with the inhalation exposure, equivalent to 0.044% of the AOEL, the total exposure would be 1.6% of the AOEL.

3. Residues

Bromuconazole was discussed in the meeting of experts in residues (PRAPeR 30) in July 2007. Bromuconazole is a mixture of two diastereomeric pairs of enantiomers (4 bromuconazole isomers). The ratio of the diastereomers LS850646 and LS850647 is not defined, but the substance used in the submitted tests and studies had a ratio of diasteromers ranging between 1.04 : 1 and 1.33 : 1. The ratio of the enantiomers in each diastereomer was not reported but is assumed to be approximately 1 : 1.

All metabolism studies (plant and livestock) were performed using phenyl-labelled bromuconazole only, and thus the fate of the triazole moiety of the molecule was not investigated. Initially, the RMS considered that studies with a radiolabel on other moieties than the phenyl-ring are not required, because cleavage of the compound does not seem to occur. However, in studies with wheat a considerable part of the total radioactive residues (TRR) was not identified. It is not known whether these residues still contain the triazole moiety. Therefore, in the PRAPeR 30 meeting the RMS and the experts agreed that cleavage of the molecule cannot be excluded and further investigation of the triazole moiety is required. Triazole derivative metabolites are expected to be of toxicological concern, and to prove their presence or absence is considered essential for a reliable risk assessment.

Therefore the meeting of experts proposed a general data gap for the exposure of the consumer to triazole derivative metabolites to be addressed for all areas i.e. primary crops, rotational crops, and animal matrices. As no new studies conducted with triazole-labelling were made available in the resubmission dossier, the data gaps concerning triazole-labelled studies in primary cereal crops, in rotational crops, and in livestock were confirmed.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

Plant metabolism was investigated in wheat, representative for cereal crops, and in apples and bananas, representative for the category of fruit crops.

In a study on wheat, following foliar applications according to the representative GAP (*ca* 1N rate) and soil treatment (corresponding to *ca* 0.75 N rate of a foliar treatment) respectively, the amount of volatile residues was very low. After soil treatment less than 1% and after foliar treatment less than 0.1% of the applied radioactivity was recovered as volatile residues. After foliar application most of the radioactivity was located in the leaves and stems (24.3 mg/kg), while residues in grain were low (0.04 mg/kg). Large portions of the residue were unavailable for solvent extraction, in particular in the grains (44% TRR). Bromuconazole represented a significant portion of the extractable residues in all plant parts. In the leaves and stems extracts, about 51-64% of the radioactivity was identified as bromuconazole (corresponding to *ca* 38-48% TRR in leaves and stems), and in grain 49% of the extractable radioactivity co-eluted with the bromuconazole isomers (corresponding to *ca* 27% TRR in grain). Upon acid hydrolysis a decrease in polar compounds and an increase of less polar metabolites including bromuconazole was observed, indicating the presence of conjugates of bromuconazole and its metabolites. After soil treatment, a constant uptake and translocation of radioactivity to aerial plant parts was observed, so that at harvest a considerable part of the radioactivity was located in the leaves and stems (5.7 mg/kg). Total residues in grain were low (0.15 mg/kg), but were found to be an order of magnitude higher than following a foliar treatment. Bromuconazole represented ca 6 - 15% of the

radioactivity in leaves and stems extracts (corresponding to *ca* 4-10 % TRR) while most of the extracted radioactivity remained unresolved (68-93%). Residues in grains were not further investigated.

In a second study, wheat plants were treated by foliar application according to the representative GAP (1N rate). At harvest, the main constituent of the total residue in all investigated wheat matrices i.e. grain, chaff and straw was bromuconazole (mixture of diastereomers, free and conjugated), corresponding to 16-35% TRR. In wheat grains, metabolite C was also found at significant levels (12% TRR). It was not identified, but could be characterised as a multi-component fraction. A significant amount of the residue in the tested wheat matrices remained unknown (21-45% TRR). In straw and chaff, this unknown fraction consisted of several metabolites present at low levels, none of which represented more than 2.5 % of the TRR. In grains however, the unknown fraction consisted mainly of multiple small fractions which were not further analysed. The largest un-analysed individual fraction represented approximately 20 % TRR. However, this unknown radioactivity was found to be polar in nature, even more than the unidentified metabolites in straw and chaff. This might indicate an extensive metabolism. The study analysed residues of bromuconazole for its diastereomers LS850646 and LS850647, but not for the enantiomers in each diastereomer. Results of the composition of the final bromuconazole residue indicated a shift towards the LS850646 isomer (ratio about 70: 30 in straw and grain and 92: 8 in wheat chaff).

Although no uses in fruit have been supported in the EU peer review, metabolism studies with bromuconazole in apples and bananas following brushing and spraying of individual fruits were submitted and evaluated. In the study on bananas migration of the residue to the pulp was very low and residues were mainly found on the peel. Bromuconazole was not extensively metabolised by the banana plant within 30 days after treatment, and hence represented the major part of the residue (78% TRR in peel, 98% in pulp). The data suggest that there was only little change in the diastereomer ratio (from initially 1.22 : 1 to 1.78 : 1 in banana pulp; however based on very low residue levels and therefore not conclusive). Minor metabolites (0.5- 2% TRR) could be identified as debrominated metabolite (LS860364), 3-hydroxy metabolite (LS 860550/860551), 2-ketone metabolite (LS870353) and 5-H-2-ketone metabolite (RPA 401527). The level of conjugated metabolites in banana peel and pulp was low (1% TRR). The study in apples demonstrates a small translocation of the residues into the pulp of the fruits after application to the apple surface, but the residues remain principally in the peel. Most of the radioactivity present at harvest (78 days after application) was extractable with methanol (79-95% TRR), however the identification rate of extracted radioactivity from peel and pulp was low (7-15% TRR). Mainly identified was bromuconazole (12% TRR in peel, 3% TRR in pulp). The ratio of isomers of bromuconazole was not investigated. Formation of hydroxylated metabolites (LS850920 and RPA 406117) (together < 5% TRR) and conjugates was found to a minor extent. The majority of radioactivity was characterised as fractions consisting of several metabolites (individually < 10% TRR) that were not further analysed. A shortcoming of the apple study with regard to storage stability data was identified, however this is not relevant for the assessment of the representative use in cereals, but may need to be assessed for future uses.

Based on the studies on wheat, banana and apple, the metabolic pathway shows the elimination of bromine followed by hydroxylation and oxidation of the furan ring with an eventual conjugation of the metabolites. A major part of the residue remains as bromuconazole, however, given the predominance of the diastereomer LS850646 in the terminal residue, a stereoselective metabolism is assumed in cereals. The available data do not permit a conclusive statement on whether or not stereoselective metabolism may also occur in fruits. It is noted that none of the plant metabolism studies investigated the ratio of enantiomers in each diastereomer. The meeting of experts agreed that from the available plant metabolism data it was not possible to conclude on the residue definition, because there were no triazole-ring labelled studies. The experts concluded that a triazole-ring labelled study is required for cereals. The provisional residue definition for risk assessment and monitoring purposes was agreed as bromuconazole isomers. The proposed definition is currently limited to the representative use in cereals. After the peer review of the resubmission application the residue definition is still provisional since the fate of the triazole moiety of bromuconazole in crops has not been clarified. A triazole-ring

labelled study is still required for cereals to adequately characterise the nature of the residue. It is noted that triazole derivative metabolites are of toxicological concern and to prove their presence or absence is considered essential for a reliable risk assessment.

Supervised residue trials were carried out according to the representative use on wheat in Northern and Southern Europe. The two diastereomers of bromuconazole were analysed separately in all samples. No data were submitted on the ratio of enantiomers in each diastereomer of bromuconazole. Residues in grains were consistently below the LOQ (0.005 mg/kg or 0.01 mg/kg respectively) for either diastereomer. In straw residues of LS850646 and LS850647 were with few exceptions consistently above the LOQ (0.025 mg/kg for each diastereomer). The straw results confirmed the observation in the radiolabel studies of a shifted isomer ratio of LS850646 and LS850647 (in average 70: 30, exceptionally around 80: 20). Based on the trial results HRs (Highest Residues) and STMRs (Supervised Trials Median Residues) could be derived for each relevant data set on grains and straw, and an MRL could be proposed for wheat grain (refer to 3.4). Valid storage stability data for the individual diastereomers of bromuconazole support the residue values found in supervised residue trials. No investigation of the behaviour and the level of residues under processing conditions has been necessary due to the insignificant level of residues in wheat grain. Straw is usually not processed.

3.1.2. Succeeding and rotational crops

The DT_{90} for bromuconazole ranges between 170 and 709 days. Investigation of residues in rotational crops was therefore necessary.

A confined rotational crop study with ^{14}C-bromuconazole (phenyl-labelled) was conducted using radish, lettuce, mustard and wheat planted after aging of the treated soil (1.5N rate) for 1 month, 3 months and 1 year. The results indicate an up-take of residues by crops from soil. Significant residue levels were found in wheat, especially in the straw (up to 0.62 mg/kg) and in the forage (up to 0.13 mg/kg). The levels of radioactivity found in radish, wheat grain, lettuce and mustard ranged between 0.01 and 0.04 mg/kg, depending on the pre-plant interval. Samples of lettuce, mustard and wheat grain were not further analysed. Upon analysis of the extracted radioactivity from wheat and radish samples bromuconazole was the main constituent (13 - 56%) of the total residue. Bromuconazole levels up to 0.08 mg/kg were found in straw, 0.05 mg/kg in forage and 0.02 mg/kg in radish roots. As observed in primary metabolism crop studies, residues of the bromuconazole diastereomer LS850646 were higher than that of LS850647, suggesting stereo-specific processes also in rotational crops, however no data are available on the ratio of isomers in soil to draw any firm conclusion. The ratio of enantiomers in each bromuconazole diastereomer was not investigated. Metabolites were identified that had also been found in the primary crop studies, but none of them was present at levels above 0.01 mg/kg. In addition, a number of unidentified metabolites could be characterised, and showed an intact phenyl-triazole bond. The metabolic pattern in rotational crops and directly treated crops was found to be similar. However, as only phenyl-labelled bromuconazole was used and a large portion of radioactivity was not identified, no information is available on whether or not triazole derivative metabolites might have been present in the crops. Therefore, the meeting of experts identified a data gap for a rotational crop metabolism study with triazole-labelled compound.

In rotational crop residue trials the level of bromuconazole residues was investigated in cereals. Wheat was sown between 30 and 300 days after an application of bromuconazole to the preceding wheat plants. However, it is noted that the application rate in the trials was only half the critical rate (0.5 N) of the representative use. At harvest of the rotational wheat, bromuconazole levels in grain and straw were all below the LOQ of 0.02 mg/kg for grain and 0.05 mg/kg for straw, respectively. In wheat forage residues up to 0.02 mg/kg were found at the shortest pre-plant interval of 30 days. A further study on the level of residues in rotational leafy crops and turnips was considered not acceptable by the RMS as important data are missing in the report.

Taking the information from the confined study and the rotational wheat residue trials together, the experts concluded that residues of bromuconazole *per se* are not expected to occur in rotational crops above 0.05 mg/kg when bromuconazole is used according to the representative cGAP in cereals.

Though the LOQ of the monitoring method (multi method) is at 0.05 mg/kg, method validation data are only available for cereals. The LOQ for plant commodities other than cereals is currently unknown. It could be possible that residues in plants grown as rotational crops exceed the value of 0.01 mg/kg that is usually set as a default MRL if no different MRL is proposed for these crops. With regard to whether triazole metabolites may reach quantifiable levels in rotational crops, no conclusion is currently possible. Therefore, the meeting of experts proposed a data gap for a rotational crop metabolism study with a triazole-label. The data gap is still open after the peer review of the resubmission application.

The experts concluded that for other uses than the representative GAP in cereals the residue situation in rotated crops should be reconsidered.

3.2. Nature and magnitude of residues in livestock

Related to the representative use in wheat, significant levels of bromuconazole are mainly expected in straw. The theoretical intake of bromuconazole exceeds the trigger value of 0.1 mg/kg total diet for cattle. Moreover, based on its $\log_{Pow}$ bromuconazole is classified as fat soluble, which indicates a risk for accumulation of residues in animal tissues. Hence, metabolism and excretion of residues were studied in lactating cows and goats following repeated oral administration of ^{14}C phenyl-labelled bromuconazole.

In the study with cows (0.04 and 0.4 mg/kg bw/d), identification and characterisation of metabolites was limited to urine and faeces. However, it could be concluded that the major route of elimination of radioactivity after oral absorption is via the urine (66-82% of administered dose), most probably by conjugation of bromuconazole (*ca* 5-14% TRR) and its metabolites. The residue in the faeces (15% of administered dose) is composed of bromuconazole (*ca* 10-40% TRR) and of conjugated compounds. None of the metabolites in urine and faeces were properly quantified, but a metabolic pathway was postulated based on the qualitative findings by retention time comparison. This metabolic pathway proposes the elimination of bromine followed by hydroxylations, oxidations and finally conjugation.

Elimination through the milk was very low and a plateau was reached after two days. At sacrifice, significant levels of radioactivity were found in low-dose-group liver (0.08 mg/kg), kidney (0.04 mg/kg) and subcutaneous fat (0.03 mg/kg). Residues in fat were not further investigated. In liver and kidneys, attempts for identification were not successful, but it was demonstrated that the extracted residue is composed of a whole range of minor components. Only minor levels of bromuconazole were identified in the liver.

In a second study with lactating goats (1 and 20 mg/kg feed DM) the majority of the administered radioactivity was recovered in urine (66-70%) and faeces (21%). Elimination through the milk was very low (< 0.1%), and a plateau was reached after 24 hours. 0.3-0.4% of the administered radioactivity were recovered in tissues and organs. Upon characterisation of residues in excreta, tissue and organs, bromuconazole was recovered in faeces (*ca* 10% TRR), liver (2-3% TRR) and kidney (1% TRR), while no bromuconazole was found in urine and milk samples. Of the two diastereomers, LS850646 appeared to be the predominant one in the liver while in faeces the diastereomer ratio of the unabsorbed bromuconazole was about 1:1, suggesting a preferential metabolism of one diastereomer in the goat upon absorption of the compound. The ratio of enantiomers in each bromuconazole diastereomer was not investigated.

Identification of metabolites in the goat study was not successful and the metabolic pathway postulated based on the study with cows could not be confirmed. The distribution of radioactivity, however, is similar to the one observed in the cow study and, considering the exposure levels in practice, significant residues are only expected in liver and kidney. In these two tissues, bromuconazole was found at very minor levels. The remaining residue was not identified, but the major part of this residue was released after enzymatic hydrolysis, and significant parts of it were water soluble. This might indicate the presence of polar multi-component fractions, which is consistent with the large range of metabolites observed in rat metabolism studies.

Taking all provided information together it can be concluded that administered bromuconazole is largely excreted via the urine upon a rapid metabolisation in the animal body. Significant residues were only found in metabolising organs. Identification of individual metabolites in organs and tissues was not successful. A metabolic pathway in ruminants was postulated based on identification of metabolites extracted from urine and on tentatively identified metabolites from faeces.

Although intakes of bromuconazole by poultry are not expected to be significant, hen metabolism data with radiolabelled bromuconazole were submitted and evaluated in the DAR. The administered radioactivity was mainly recovered in the excreta (89-92%). Residues in eggs and tissues were low (together 0.5% of the administered dose). In egg whites, steady state conditions were not clearly observed, as levels of radioactivity were very variable within time, while in egg yolks, radioactivity levels were more consistent and reached steady state conditions after 4-5 days upon first dosing. Upon characterisation of residues bromuconazole (both isomers) was identified as a major component in the egg yolk (14-22% TRR) and egg white (30-38% TRR), in the abdominal fat (39% TRR) and in skin with attached fat (37% TRR). There were only occasional finding of low levels (ca 1% TRR or less) of bromuconazole in hen excreta samples, livers and muscle samples. A significant shift of the ratio of bromuconazole diastereomers was found in egg white residues, that seemed to increase with duration of dosing (from 16 : 1 at day 5 up to 29 : 1 at day 14 of dosing), and some isomer shift was also observed in egg yolk (1.6 : 1 to 2.1 : 1). The ratio of enantiomers in each bromuconazole diastereomer was not investigated. Identification of metabolites was mainly carried out from hen excreta samples, and based on the qualitative findings a metabolic pathway was postulated. This pathway shows elimination of bromine followed by hydroxylation and oxidation. Eventually, metabolites are all conjugated, resulting in sulphate esters and glucuronides.

The livestock studies indicated that bromuconazole is extensively absorbed, metabolised, and rapidly eliminated via the excreta. Elimination through milk or eggs is a minor route, and significant residues are not expected in these tissues when assuming a realistic intake. After sacrifice, significant levels of radioactive residues were only encountered in the liver and kidney. Identification of metabolites in tissue and organs was very poor, and metabolites were only identified in the excreta. The nature of the residue in edible tissues remains unknown, especially in liver and kidneys. Nevertheless, most of the unidentified metabolites were characterised as polar and were only released after enzymatic digestion. This indicates an extensive degradation and is consistent with rat metabolism studies.

Livestock metabolism studies were only performed using phenyl-labelled bromuconazole, and the fate of the triazole moiety was therefore not properly investigated in these studies. As concluded for crops, the exposure of the consumer to triazole metabolites needs to be addressed for all areas, including animal matrices. It should be noted that it is likely that this will require a ruminant metabolism study with a radiolabel in the triazole moiety, as there were considerable amounts of unidentified radioactivity in the studies already provided.

Therefore, it was proposed by the experts to preliminarily define the residue in edible animal matrices as bromuconazole (sum of isomers) for monitoring and risk assessment purposes. Whether in relation to the use of bromuconazole the triazole metabolites will have to be defined as a relevant residue in food of animal origin remains open at this stage. Upon peer review of the resubmission application in 2010 this conclusion has not changed. No new data have become available.

On the basis of the available ruminant metabolism data and the estimated livestock dietary burden from the representative cereal use, no total residues above the LOQ are expected to occur in food of animal origin. Therefore, at this stage, livestock feeding studies are not required and MRLs for the residue definition bromuconazole can be proposed at LOQ level of the analytical method for monitoring purposes.

The meeting of experts highlighted that for the future further consideration of the livestock data may be required when other uses are intended.

3.3. Consumer risk assessment

Considering the residues of bromuconazole alone there are no acute or chronic intake concerns for all categories of consumers, as bromuconazole is not present above the limit of quantification in food of animal and plant origin (LOQ of 0.05 mg/kg in cereals assumed for all plant) when applied according to the representative cGAP in wheat. Theoretical maximum daily intake (TMDI) estimates, based on the limit of quantification and WHO European and national consumption data (UK, Germany) range between 4 and 14% of the ADI. The estimated short-term intakes (IESTI), considering the primary crop, food of animal origin and succeeding crops are all well below 10% of the ARfD.

However, the metabolism of bromuconazole may lead to residues of triazole derivative metabolites that are considered of concern due to their toxicological profile, or to any further up-to-date unknown metabolites containing the triazole ring and originating from the breakdown of the bromuconazole molecule. In the absence of residue data investigating the fate of the triazole moiety of the bromuconazole molecule the nature of the residue cannot be adequately characterised and the consumer risk assessment cannot be finalised. This conclusion, drawn in a previous peer review, has not changed upon reviewing the Additional Report of October 2009 drawn up following the resubmission application. Assumptions used by the RMS in a theoretical risk assessment on triazole derivative metabolites were rebutted by the peer review. Studies on other triazole pesticide compounds clearly demonstrate that data with a labelling in the counter moiety of the molecule (i.e. phenyl-label) are unsuitable to estimate the magnitude of triazole derivative metabolites, and that such extrapolation leads very likely to a significant underestimate of the actual amount of triazole derivative metabolites present. Moreover, the potential for occurrence of additional, currently unknown metabolites originating from breakdown of the bromuconazole molecule could not be addressed by this theoretical estimate. A revised risk assessment on triazole derivative metabolites using data on other triazole pesticide compounds could not be considered by EFSA, since only those studies that were included in the dossier at the time of the resubmission application could be taken into consideration in the peer review. As a breakdown of the bromuconazole molecule leading to the occurrence of metabolites relevant to consumer safety cannot be excluded, the issue is regarded as a critical area of concern.

It should also be noted that currently insufficient toxicological data are available to address other ratios of isomers than those tested with the bromuconazole batches used in the toxicological studies (refer to section 2 of this document). A shift of the diastereomer ratio LS850646 / LS850647 beyond that margin was observed in plant and livestock metabolism studies.

However, in terms of the representative use on cereals, the consumer exposure to either bromuconazole diastereomeric pair of enantiomers is expected to be insignificant, and thus no particular consumer risk with regard to the ratio of isomers has been identified. For uses other than the representative use the issue should be carefully reconsidered.

3.4. Proposed MRLs

MRLs were proposed for bromuconazole isomers on the basis of the available residue data for wheat and the findings in the ruminant metabolism studies.

Wheat grain	0.05* mg/kg
Milk	0.01* mg/kg
Ruminant meat	0.02* mg/kg
Ruminant fat	0.02* mg/kg
Ruminant liver	0.02* mg/kg
Ruminant kidney	0.02* mg/kg

The LOQ for plant commodities other than cereals is currently unknown as method validation data have only been submitted for cereals. It could be possible that residues in plants grown as rotational crops will exceed the value of 0.01 mg/kg that is usually set as a default MRL if no different MRL is proposed for these crops.

It is also noted that, as for other triazole pesticides, the monitoring residue definition is provisional, since at the moment no conclusion is possible whether triazole derivative metabolites might need to be included in the residue to be monitored.

4. Environmental fate and behaviour

Bromuconazole was discussed at the PRAPeR experts‟ meeting for fate and behaviour in the environment (PRAPeR 27) in July 2007, on the basis of the DAR and the revised DAR dated June 2007. As a consequence of a resubmission application an Additional Report was provided by the RMS and in reply to the comments received on this report two addenda were prepared, one dated December 2009, the second March 2010 (Belgium, 2010). It should be noted that the methods of analysis used in all the fate and behaviour studies were not stereoselective. Therefore, the regulatory dossier provides no information on the behaviour of each individual bromuconazole isomer in the environment, except for the adsorption/desorption properties. As a result, all residues reported as bromuconazole in this conclusion are for the sum of the two diastereomeric pairs of enantiomers. It is not known if any isomer is degraded more quickly than the others in the environmental matrices studied.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

In a laboratory (dark, aerobic, 22 ºC, 80% moisture capacity at 0.33 bar) study on 2 loamy sand soils dosed with [phenyl-^{14}C]-bromuconazole, mineralization to CO_2 was low, accounting to 1.3-4.4% AR after 120 days. At this incubation time, the non-extractable radioactivity reached 10.2-17.6% of the applied radioactivity. Several minor metabolites were detected, none accounted for more than 1.5% AR at any sampling time. In a supplemental study performed with an exaggerated dose, some of these degradation products were identified. Under dark anaerobic conditions in the laboratory, the major metabolite M4 (LS871387) was formed at a maximum level of 10.1% AR at day 181 and no other resolved unidentified components in extracts accounted for > 1.5% AR. No mineralisation occurred in the study. At the meeting of experts it was agreed that no further assessment with respect to anaerobic conditions is required for bromuconazole. In a laboratory soil photolysis study the degradation rate of bromuconazole was faster in the irradiated samples (non-linear single first-order DT_{50} = 78 days, summer sunlight at 50ºN latitude) than in dark controls (DT_{50} = 296 days). Therefore, photolysis may contribute to the degradation of bromuconazole at the soil surface. No novel extractable breakdown products were identified in addition to those found in the dark experiment and never exceeded 2.6% AR at any sampling point.

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

Additionally to the study presented under the route section, rate of degradation of bromuconazole in soil was also investigated in another soil at 20ºC at 60% field capacity and different incubation conditions (sterile, reduced dose and reduced moisture). According to Annex II data requirements, a further laboratory aerobic rate of degradation study should be provided on an additional soil. However, there was agreement by the experts that the available data with 3 soils already indicate that field studies are triggered, and it was concluded that no further degradation rate studies in soil are needed. The degradation rates were re-calculated using single first-order non-linear regression and indicated that bromuconazole can be classified as high to very high persistent (DT_{50} = 329-1028 day at 20-22ºC).

Field dissipation of bromuconazole was investigated in 7 locations in Germany (bare soil study design). In the original reports[10] the essential information on the field phase (sites description and

[10] (I) Fischer (1993). Bromuconazole. Determination of its residue in soil samples of the Rhône-Poulenc Agro study no.90-197. A&M, Cologne, Germany. Report n° A & M 025/92, BCS n° C016643. (II) Lenz (1994). Analytical determination of residues of the active ingredient bromuconazole from the outdoor study RPA10064F. Biochem GmbH, Karlsruhe, Germany. Report n° Biochem 91 50 10 140. BCS n° C016419

history at the trial sites, characterisation of the soils profile, applied formulations and doses, sampling details, climatic data) were not reported. Concerns were raised also on the kinetics and the correlation coefficient for the estimated DT_{50} values. In the updated DAR (June 2007), the RMS indicated that the GLP trials were conducted at sites where the soil and weather conditions are typical of those found at locations where bromuconazole could be used, but no additional information to support the argumentation was provided by the RMS. Re-calculated field dissipation DT_{50} values using non-linear regression together with the goodness of fit were also provided in the revised DAR. The experts on fate and behaviour agreed that the field dissipation studies should not be considered valid, because too much crucial information on the experimental design were not available, and therefore a data gap was identified for adequate field dissipation studies. During the meeting it was also highlighted that there is a need for a good estimate of microbial degradation from these field studies for modelling purposes, that is to say that the kinetic assessment of the study design of any new studies would need to exclude the photolytic degradation that is expected to occur at the soil surface. Further information on the field trials (soil classification, soil pH and organic carbon content, application rate and type of growing crop) were provided in a revised version of the DAR dated January 2008, which was not peer reviewed. Following the resubmission application the RMS Additional Report was peer reviewed by the Member States and EFSA. The conclusion of this review was that these 7 field dissipation trials could be relied on now more information of the field phase of the experiments had been provided. Reliable non-linear regression, single first-order dissipation DT_{50} were available for 6 of these trial sites giving a range of values of 45-201 days. At the 7th trial site (Lübek) a clear biphasic decline was apparent that might be expected to result from photolysis causing rapid initial decline. After this rapid initial decline a reliable first-order second phase dissipation DT_{50} of 657 days was estimated (see addendum to the Additional Report dated March 2010; Belgium, 2010). As the representative uses assessed are for growth stages where crop canopy shading at the soil surface is expected, the soil exposure assessment (predicted environmental concentration) PEC soil including accumulation potential from applications in successive years (see Appendix A) was calculated using this first-order dissipation DT_{50} of 657 days, that excludes photolysis contributing significantly to the decline.

The potential for soil accumulation of bromuconazole was investigated in one study with annual application to continuous spring cereals (1 trial in Germany and 1 trial in UK). The studies indicated that accumulation may occur (2.56 times the single application rate); however, the plateau concentration was not reached in the German site after four years. Re-calculation of normalized field dissipation rate for bromuconazole from soil accumulation data was provided in the updated DAR (June 2007). The experts agreed with the RMS assessment that accumulation studies were adequately documented but did not contain enough data points to derive reliable dissipation and/or degradation rates for bromuconazole.

In the resubmission application dossier a new kinetic assessment was completed on the available 7 reliable field dissipation studies to provide true degradation rates that excluded photolysis that would have occurred at the soil surface in the trials, and normalised the trials to FOCUS reference conditions (20ºC and field capacity (PF2) soil moisture). This normalisation followed FOCUS kinetics guidance (FOCUS, 2006), used a Q10 of 2.2, Walker equation coefficient of 0.7 and the time step normalisation procedure. The purpose of this normalisation was to obtain a geometric mean field degradation rate (single first-order DT_{50}) that excluded all surface processes (including photolysis) that would be appropriate to use in FOCUS scenario modelling approaches for groundwater and surface water exposure estimations. The influence of soil surface processes was eliminated by excluding the time zero sample concentrations from the fitting. This normalisation utilised daily weather data from the closest available weather stations to the field trial sites. As some of these weather stations were not that close (5 to 79 km), the applicant was asked to provide information that would enable it to be concluded that, particularly for the precipitation, the weather station data would have been representative of the conditions that occurred at the experimental sites. Evaluations of these assessments can be found in the RMS Additional Report, and in relation to the topography between the experimental sites and weather stations, in the addendum dated March 2010. The final conclusion of this assessment was that for 5 of the trial sites, the daily temperature and precipitation data from the weather stations could be used for normalising the DT_{50} to reference conditions, but for 2 of the trial

sites (Karlsruhe and Kraichtal) only a temperature normalisation could be justified, as the topography would indicate that there could have been significant differences in precipitation between the site of the experiment and the weather station. As the normalisation for soil moisture can only make the normalised single first-order DT_{50} shorter, the consequence is that a more conservative leaching assessment resulted than would have been presented if it had been possible to normalise all of the trials to reference soil moisture conditions. Therefore, the final conclusion of this exercise was that the geomean single first-order degradation DT_{50} from the 7 trial sites that would be appropriate for use in FOCUS scenario modelling where both temperature and moisture correction routines are enabled (and a Q10 of 2.2 and Walker equation coefficient of 0.7 are implemented) would be 228 days (with the range of normalised values in the data set being 83 to 747 days).

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

The soil adsorption/desorption characteristics of the two diastereoisomers (LS850646 and LS850647) contained in bromuconazole were determined separately in one batch adsorption/desorption study available for bromuconazole with 4 soils (pH 5.7-8.0; organic carbon content: 0.46-2.44%). The results showed that the adsorption pattern fits the Freundlich equation, with K_{foc} values ranging from 474 to 1086 mL/g for isomer LS850646 (1/n = 0.78-0.85) and from 627 to 1539 mL/g for isomer LS850647 (1/n = 0.76-0.86). There was no indication of adsorption being pH dependent. It was agreed in PRAPeR 27 that the mean K_{foc} value of 757 mL/g and 1/n = 0.82 were the appropriate values for bromuconazole as input parameters for FOCUS modelling. Laboratory soil column leaching studies were performed with either freshly-applied or after aerobic incubation for 30 days in four soils. The results showed a low mobility for bromuconazole with maximum 0.6% AR and 2% AR recovered in the leachate of the fresh residue and aged residue experiment respectively. The nature of the radioactivity (62.4-97.6% AR) indicated that bromuconazole and very minor metabolites (not further identified) were retained in the top 6 cm soil layer. In another study the leaching of bromuconazole was investigated in two soils, following an aging period of 210 days. Analysis of the leachates and soil segments showed that movement was limited and that metabolites (each less than 2.5% AR) and unextracted residues remained primarily in the top 5 or 10 cm of the soil leaching columns.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Bromuconazole was essentially stable under sterile hydrolysis conditions at 25ºC at pH 4, 5, 7 and 9.

A study with the UV-adsorption properties of bromuconazole in water at pH 4 and pH 9 was submitted. Results indicated that bromuconazole will not undergo direct aqueous photolysis at pH and that photolysis in aqueous solution is pH dependent (with an estimated DT_{50} of 18 days at pH 4). However, some deficiencies in the recovery of the applied radioactivity in the study conducted at pH 4 were observed. In addition, during the peer review, concerns were raised by the experts of the physical/chemical properties section on the pH 4 buffer constituents: it was not clear if they were contaminated or contained some impurity that acted as a photosensitizer. The issue could not be transferred to the fate and behaviour section as bromuconazole was discussed in the section on physical-chemical properties after the PRAPeR 27 meeting. However, as the molar adsorption coefficient (ε) at a wavelength ≥ 290 nm is < 10L mol^{-1} cm^{-1}, it can be concluded that photolysis is not expected to be a significant process in the breakdown of bromuconazole in natural aquatic systems.

A ready biodegradability test (OECD 301B) indicated that bromuconazole is "not readily biodegradable" using the criteria defined by the test.

The water-sediment study (2 systems studied at 20ºC in the laboratory) demonstrated that bromuconazole dissipated quite rapidly from water by partitioning to sediment (first-order multi-compartment $DT_{50\ water}$ of 1.3-2 days; $DT_{90\ water}$ of 53.8-235 days) where it subsequently degraded slowly. In the total system, single first-order DT_{50} values were 272-277 days. No metabolites were

identified and none accounted for > 1% AR. Mineralisation was negligible (0.6-0.9% AR after 100 days) and bound residues reached maximum level of 15% AR at day 100.

FOCUS surface water modelling was evaluated up to step 4 for cereals scenarios with one and two applications of bromuconazole. Because of the persistence of the active substance in the water-sediment study ($DT_{90\ whole\ system}$ > 900 days) the applicant was asked to provide FOCUSsw modelling that takes into account the potential for accumulation in sediment as outlined in SANCO/4802/2001 section 8.7.3 (FOCUS, 2001). Additionally, the peer review requested further clarifications on the mitigation measures employed in step 4 calculations for run-off scenarios, as in July 2007 there was no agreed standardised way of implementing this reduction in FOCUSsw at EU level. The assumption used in step 4, together with the calculations of the possible accumulation of bromuconazole in sediment for three scenarios were provided in the revised version of the DAR (June 2007) and discussed at the meeting of experts. The selected scenarios (D1, D4 and R4) were regarded as the worst-case scenarios for PEC_{sed} calculations, but results for PEC_{water} values were not provided. It was noted that when drift mitigation with vegetative buffer strips are used in the modelling, the resulting driving forces for water body contamination are run-off and drainage. Therefore, depending on when the most important run-off event occurs, the PEC_{sed} values will be more or less sensitive to the soil DT_{50} used. Unfortunately, the experts considered this value (124.9 days from field studies) not applicable (see section 4.1.2); nevertheless, they agreed that at this stage the information provided is the best available on accumulation of bromuconazole in sediment. A data gap was identified for new FOCUSsw modelling to provide PEC_{sed} taking into account accumulation in sediment, using a more reliable soil DT_{50}. It was also concluded that, as the results considering only spray drift mitigation for the water column were still missing, new FOCUSsw modelling at step 3 and step 4 with spray drift mitigation only should be provided, taking into account a more reliable soil DT_{50} value when these data become available. Provisional PECs at step 3 calculated with the unacceptable soil DT_{50} of 124.9 days were used for the risk assessment, as it is likely that a longer soil DT_{50} value will not affect significantly the results. The agreed bromuconazole input parameters, other than soil DT_{50} were: K_{foc}= 757 mL/g, 1/n=0.82, water SFO DT_{50}=277 days, sediment DT_{50}= 1000 days.

In the resubmission application (dossier evaluated in the Additional Report), new FOCUS surface water simulations up to step 4 were provided following the approach that was recommended by the first peer review as described above. These simulations utilised a geomean normalised field degradation DT_{50} (excluding the potential for soil photolysis) of 219 days. The simulations utilised a Q10 of 2.2 and Walker equation coefficient of 0.7. Accumulated concentrations in sediment were calculated at step 3 in an appropriate way. Step 4 simulations following the recommendations of the FOCUS landscape and mitigation guidance (FOCUS, 2007), were implemented using the SWAN tool and applied 10m no-spray zones for all scenarios (ca. 86% spray drift reduction) and, in addition for run-off scenarios, a combined no-spray zone and vegetative run-off buffer strip of 10m. The run-off buffer was parameterised to reduce aqueous phase inputs to TOXSWA by 60% with eroded sediment input reduced by 80%. Risk managers and others may wish to note that whilst run-off mitigation is included in the step 4 calculations available, the FOCUS landscape and mitigation guidance acknowledges that for substances with K_{Foc} < 2000 mL/g (i.e. bromuconazole), the general applicability and effectiveness of run-off mitigation measures had been less clearly demonstrated in the available scientific literature, than is the case for more strongly adsorbed compounds. Though the conclusion is that a single first-order soil DT_{50} of 228 days should ideally have been used in the simulations, it was accepted by EFSA as proposed by the RMS that the EU level aquatic risk assessment could be completed with the available simulations as the difference in soil DT_{50} of 9 days was not expected to make a significant difference to the exposure concentrations calculated. The results of these simulations can be found in Appendix A.

4.2.2. Potential for ground water contamination of the active substance their metabolites, degradation or reaction products

The leaching potential of bromuconazole to groundwater was estimated with FOCUS PEARL 3.3.3 and FOCUS scenarios for the representative use on winter cereals. The simulations utilised a Q10 of

2.2 and Walker equation coefficient of 0.7. For bromuconazole a single first-order soil DT_{50} of 219 days, K_{Foc} of 757 mL/g and 1/n of 0.82 were utilised in the simulations (both adsorption values being the most appropriate values). The results of these simulations were that 80th percentile annual average concentration in soil water leaving the top 1m soil layer were < 0.000001µg/L at 8 out of the 9 FOCUS groundwater scenarios, with the concentration at the Piacenza scenario estimated to be 0.000003 µg/L. Though the conclusion is that a single first-order soil DT_{50} of 228 days should ideally have been used in the simulations, it is clear that even without new simulations, it can be concluded that the potential for groundwater contamination above the parametric drinking water standard of 0.1µg/L is low for the representative use, in situations represented by all 9 FOCUS groundwater scenarios.

4.3. Fate and behaviour in air

Results from studies on volatilisation of bromuconazole from soil and bush beans indicated that volatilisation of the active substance is negligible 24 hours after application.

The vapour pressure of 0.4 x 10^{-5} Pa at 25ºC indicates that bromuconazole would be classified as non-volatile. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals were provided in the physical/chemical properties section of the DAR. Assuming an atmospheric concentration of 5 x 10^5 OH radical/cm^3 the estimated half-life was 16.5 hrs or 1.4 d, indicating that the small proportion of applied bromuconazole that will volatilise would be unlikely to be subject to long-range atmospheric transport.

5. Ecotoxicology

Bromuconazole was discussed at the PRAPeR Experts‟ Meeting on Ecotoxicology (PRAPeR 28) in July 2007. As a consequence of a resubmission application an Additional Report was prepared by the RMS, which was supplemented by an addendum dated December 2009 (Belgium, 2010). Bromuconazole was discussed again at the PRAPeR Experts‟ Meeting on Ecotoxicology (PRAPeR 75) in March 2010.

Bromuconazole belongs to the group of triazole fungicides that are suspected to have potential endocrine disrupting properties. No indications of endocrine disrupting effects on reproduction were found in the mammalian toxicity studies. No information was provided to address this point with regard to potential effects on birds and fish (e.g. a fish full life cycle test or a specific two generation study with birds). The experts agreed that further information should be submitted by the applicant to address the concern with regard to endocrine disruption in birds. The experts discussed at the PRAPeR 75 meeting, whether the available information is sufficient to address the potential for endocrine disruption in fish. The majority of the experts agreed that the available data are not sufficient to address the potential for endocrine disruption effects. Instead of a Full Fish Life Cycle (FFLC), an Endocrine Disruption (ED) screening study may be performed. The data gap was re-confirmed for the applicant to address the potential for endocrine disruption to birds and fish based on acknowledged guidelines.

In the resubmission, an analytical profile of 4 batches of the technical bromuconazole used in the ecotoxicology studies was provided. Bromuconazole consists of 4 isomers, however, no information was provided on the fate and behaviour of each individual bromuconazole isomer in the environment, with the exception of adsorption/desorption properties. This adds additional uncertainty to the outcome of the risk assessment and needs to be addressed further.

The experts at the PRAPeR 75 meeting agreed that data with different formulated products (i.e. EXP 10064-B and Exp10064-C) are considered to be sufficiently similar to the new formulation SCAE0307, and therefore the data available in the DAR and the Additional Report are appropriate to be used in the environmental risk assessment at EU level.

5.1. Risk to terrestrial vertebrates

The representative evaluated use of bromuconazole is as a fungicide on wheat with a first application of 0.2 kg a.s./ha at BBCH 29-31 and a second application of 0.2 kg a.s./ha two months later corresponding to BBCH 49-51 in southern Europe and BBCH 59-65 in northern Europe. The risk to birds and mammals was assessed in accordance with the Guidance Document on Risk Assessment for Birds and Mammals (SANCO/4145/2000; European Commission, 2002).

The risk to birds was assessed for large herbivorous birds for the early application and to insectivorous birds for the late application. The TER values for herbivorous birds were all above the Annex VI triggers, indicating a low risk for herbivorous birds. Also for insectivorous birds the TER values for acute and short-term were well above the trigger (199 and 113), while the long-term TER of 4.4 was below the trigger of 5 indicating a potential high long-term risk. In the Additional Report higher tier studies (mainly from open literature) were presented to select focal species and to determine the proportion of different food types (PD) of these focal species. Two different approaches were used to refine the risk assessment. The first approach included the selection of representative focal species, and estimations of PD. The following focal species and PD estimates were used:

- *Phasianus colchicus* and *Perdix perdix*, with PD values of 44 for grain weed seeds, 44 for seedling leaves, and 12 for large invertebrates.
- *Corvus corone* and *Sturnus vulgaris*, with PD values of 31 for grain weed seeds, 6 for seedling leaves, 28 for large invertebrates, and 35 for earthworms.
- *Alauda arvensis*, with PD values of 37 for grain weed seeds, 26 for seedling leaves, 31 for large invertebrates, and 6 for earthworms.
- *Emberiza calandra* with PD values of 66 for grain weed seeds, and 34 for large invertebrates.

The alternative approach was to include the decline of residues in insects (f_{twa} = 0.53), in accordance with the new Guidance of EFSA for Risk assessment of Birds and Mammals (EFSA, 2009). The TERlt values based on the PD refinements, and those based on the use of the decline of residues in insects (f_{twa}), were all above the Annex VI trigger values. Therefore, the long-term risk to insectivorous birds was assessed as low. The risk to earthworm- and fish-eating birds was assessed as low.

The risk to mammals was assessed for small herbivorous mammals for the early application, and to insectivorous mammals for the late application. The acute TERs for herbivorous and insectivorous mammals were above the Annex VI trigger of 10 (including refinement of residues in plant material), indicating a low risk. However, the long-term TERs for herbivorous and insectivorous mammals were below the Annex VI triggers, indicating a high risk. The choice of the long-term end point was discussed in the experts‟ meeting in the first review (PRAPeR 28). The experts considered the effects on bodyweight and bodyweight gain observed at the dose of 13.8 mg a.s./kg bw/day as relevant, and suggested to use the next lower dose of 1.3 mg a.s/kg bw/day as the NOAEL to be used in the risk assessment. This point was discussed again at the experts‟ meeting in the resubmission procedure (PRAPeR 75). The RMS proposed 13.8 mg as/kg bw/day as the relevant ecotoxicological end point. At this dose in the multigeneration rat study only slight effects on parental bodyweight and no effects on reproduction were observed. However, in comparison with historical controls from other long–term studies, it was noted that the effects on bodyweight were treatment related. In F2-litters the effect is -5.3% (0.05) at 200 ppm and -12% (0.001) at 2000 ppm. The statistical significance was determined by comparison with the control in the test. According to the representative GAP, the product is applied twice with a large interval. At the first application the crop is marginally palatable, however, at the second it is no longer palatable. Therefore, the exposure duration is expected to be short. The experts concluded that it was not realistic to take the bodyweight effect into account, and agreed with the RMS‟s proposal that the NOAEL in mammals of 13.8 mg as/kg bw/day is the relevant ecotoxicological end point, although it was considered that this end point is applicable only in

consideration of short exposure. TER calculations for insectivorous mammals based on this NOAEL are provided in the DAR and in the Additional Report and are above the Annex VI trigger value, indicating a low long-term risk for insectivorous mammals.

The higher tier long-term risk assessment for herbivorous mammals was based on the rabbit as focal species for late cereal growth stages, and was discussed in the experts‟ meeting (PRAPeR 75). Although most experts would accept the rabbit as the focal species for the proposed growth stages, according to the new guidance document (EFSA 2009, Annex I, Table I.2), rabbits are only relevant at early cereal growth stages (shoots, BBCH 10). In later stages, the vole (herbivorous, from BBCH 40) and the woodmouse (insectivorous/granivorous, from BBCH 10) are recommended. In conclusion, the experts considered that the available information was not sufficient to demonstrate a low long-term risk for herbivorous mammals. A data gap was identified for further information to refine the long-term risk assessment for herbivorous mammals. The risk to earthworm- and fish-eating mammals was assessed as low. No major metabolites were found in the plant metabolism studies.

A risk assessment for uptake of contaminated drinking water was considered as not required for the representative use in cereals.

5.2. Risk to aquatic organisms

Based on the available acute toxicity data, bromuconazole is proposed to be classified as very toxic to aquatic organisms. The lowest end point value for technical bromuconazole was obtained for algae, with an EC_{50} of 0.061 mg a.s./L based on an increase in biomass. Formulation studies were conducted with an SC formulation (EXP 10064-B) which was considered to be sufficiently similar to the representative formulation. The results did not indicate that the formulation would be more acutely toxic to fish and algae than expected from the content of bromocunazole. However, in the resubmission, the applicant proposed a new formulation SCAE0307 SC. The applicant provided a bridging study with the formulation SCAE0307 and *Daphnia magna*. The formulation SCAE0307 is less toxic than formulation EXP 10064-B, and has a toxicity comparable to that of the active substance. The experts during the PRAPeR 75 meeting agreed that the end point for the active substance should be used in the risk assessment.

In the Additional Report new PECsw values and a new aquatic risk assessment were provided. The Annex VI trigger values of 100 and 10 were exceeded for fish, algae, sediment-dwellers and higher aquatic plants in all FOCUS step 3 scenarios. Only one scenario (D1 ditch) gave TER values close to the trigger for *Pseudokirchneriella subcapitata*. The acute TER values for *Daphnia magna* were above the Annex VI trigger values. A low long-term risk was identified for aquatic invertebrates in the D3 ditch, D4 pond, D4 stream, D5 pond, D5 stream, D6 pond, R1 pond and R1 stream scenarios, however the long-term TER values for the scenarios D1 ditch, D1 stream, D2 ditch, D2 stream, R3 stream and R4 stream were below the trigger. Therefore, the long-term risk assessment for aquatic invertebrates needed further refinement. The TERs were calculated with a 10m no-spray buffer zone for the drainage scenarios and a 10m no-spray buffer-zone including a vegetated filter strip to mitigate the run-off. The long-term TER values were above the trigger in 2 full FOCUS run-off scenarios (R3 stream and R4 stream). However, the TER values estimated with the drainage scenarios D1 ditch, D1 stream, D2 ditch, D2 stream were below the Annex VI trigger value. Overall, taking into account the FOCUS step 3 and 4 scenarios, it can be concluded that the risk from bromuconazole to aquatic organisms was assessed as low for more than the half of the scenarios.

Bromuconazole partitions to sediment and is also persistent in the sediment. A new PEC_{sed} was provided in the Additional Report. A risk assessment for *Chironomus riparius* based on the maximum PEC_{sed} (72.8 µg bromuconazole/kg) resulted in a TER above the trigger of 10 for all relevant scenarios at FOCUS step 3, except for the D1 ditch scenario.

The bioconcentration factor was determined to be 131 for whole fish with a clearance half-life of 0.4 day. Hence the potential for bioaccumulation is considered as low.

No major metabolites were detected in the aerobic soil degradation studies or in the water/sediment studies that would pose a risk to aquatic organisms.

5.3. Risk to bees

The oral and contact toxicity of technical bromuconazole to bees is low. The hazard quotients are well below the Annex VI trigger, indicating a low risk. No first-tier studies with the formulation are available, but a semi-field study with formulated bromuconazole did not show any acute toxic effects and only short-term effects on flight intensity. Therefore the risk to bees is considered to be low.

5.4. Risk to other arthropod species

Glass plate studies with the two indicator species, *Aphidius rhopalosiphi* and *Typhlodromus pyri* were conducted with the formulation EXP10064 E which is similar to the representative formulation „Granit 200 SC" (the formulations differ only in the solvent). Mortality was 46% for *A. rhopalosiphi* and 93 % for *T. pyri* at an application rate corresponding to 260 g a.s./ha. Hence the in-field risk for *T. pyri* was considered to be high. Additional glass plate studies with *Coccinella septempunctata* (tested with EXP 10064E) and *Crysoperla carnea* (tested with the formulation EXP 100064A) using the same dose gave 60.9 % mortality for *C. septempunctata* and 23.4 % mortality for *C. carnea.* In an extended laboratory test with *C. septempunctata* no significant effects on mortality and no significant reduction in reproduction was observed at 239 g a.s./ha . No effects on mortality was observed at an application rate of 591 g a.s./ha in a standard test with *Poecilius cupreus* using the formulation EXP 10592 A. An extended laboratory study with *T. pyri* and the formulation SCAE 0307 was submitted to address the potential high risk to predatory mites. The study was assessed in the addendum of June 2007. Effects of 38% mortality were observed at an initial dose rate of 250 g a.s./ha. The RMS concluded that the risk to non-target arthropods is sufficiently addressed. However it was pointed out in the experts" meeting that the approach did not follow the ESCORT II (SETAC, 2001) scheme and that also an extended laboratory study with *A. rhopalosiphi* should be required. It was noted that no positive control was included in the test with *C. carnea* and that decreased reproduction was observed in the extended laboratory study with *C. septempunctata* at low doses which is considered a reaction induced by stress. Uncertainty remained with regard to the comparability of the different formulations used. Therefore a data gap was proposed during the experts" meeting that studies with non-target arthropods and the formulation which is intended to be used should be submitted. It was argued by the applicant and the RMS that the formulations are sufficiently similar and that the formulation intended to be marketed will be SCAE0307 which was used in the extended laboratory study with predatory mites. EFSA agrees that the formulations are sufficiently similar to allow a comparison of the test results. Taking all information together, EFSA agrees to the assessment of the RMS that the risk to non-target arthropods is likely to be low for the representative use evaluated. EFSA suggests that the data gap identified in the experts" meeting should be addressed at Member State level for the formulation that is intended to be marketed.

5.5. Risk to earthworms

The acute toxicity of bromuconazole to earthworms is low. The formulation „EXP 10064 B"/kg substrate, which was considered to be sufficiently similar to „Granit 200 SC", was more toxic than expected based on the concentration of bromocunazole. The risk assessment presented in the Additional Report was based on plateau maximum PEC_{soil} of 0.0302 mg a.s./kg (1 application) and the average plateau PEC_{soil} of 0.189 mg a.s./kg (2 applications). However, these PEC_{soil} were changed by the EFSA fate and behaviour experts to an accumulated PEC_{soil} for 2 applications of 0.232 mg as/kg soil. The resulting TER values were above the Annex VI trigger values, and therefore the risk to earthworms was assessed as low.

5.6. Risk to other soil non-target macro-organisms

The formulation Granit had no significant effect on organic matter decomposition over a six months period in a litter bag test at an application rate of 180 g a.s./ha (plateau concentration) and 500 g a.s./ha (annual cumulative application). The soil concentration was calculated in the DAR as 0.67 mg

a.s./ha. This concentration covers the plateau maximum PEC_{soil} of 0.232 mg a.s./kg soil (2 x 0.200 kg a.s./ha). In conclusion, the risk of bromuconazole to soil non-target macro-organisms was assessed as low.

5.7. Risk to soil non-target micro-organisms

Technical bromuconazole had no effects >25% after 28 days on soil respiration or nitrogen transformation at a soil concentration of 0.667 mg a.s./kg soil equivalent to an application rate of 500 g a.s./ha when compared to the control. The formulation Granit had no effects >25% on soil respiration and nitrogen transformation at a dose rate 8 times higher than the estimated maximum PEC_{soil} after 28 days in a sandy clay-loam soil. However, nitrogen transformation was observed to be affected up to 41% in a clay-loam soil at the same dose rate and up to 28% at an application rate of 400 g a.s./ha (0.53 mg a.s./kg soil). However, the effect decreased to 17% at 60 days and to 15% at 90 days and to 10% and 4.2%, respectively. This concentration covers the plateau maximum PEC_{soil} of 0.232 mg a.s./kg soil (2 x 0.200 kg a.s./ha). The risk of bromuconazole to soil non-target micro-organisms was assessed as low.

5.8. Risk to other non-target-organisms (flora and fauna)

No specific tests of effects on non-target plants were available in the DAR but a short summary of data/observations in non-cereal crops was given. No phytotoxic effects were reported but a growth regulatory response was observed in some cases. In order to confirm the absence of effects, the RMS required vegetative vigour and seedling emergence tests. The studies were summarized in the addendum of June 2007. The experts agreed to the risk assessment and concluded that the risk to non-target plants is low for the representative use evaluated.

5.9. Risk to biological methods of sewage treatment

Data from an available test with technical bromuconazole gave an EC_{50} of >1000 mg a.s./L and a NOEC of 10 mg a.s./L for inhibition of respiration rate of activated sludge micro-organisms. It is not expected that bromuconazole will reach sewage treatment plants at concentrations of >10 mg a.s./L, and hence the risk is considered to be low.

6. Residue definitions

6.1. Soil

Definitions for risk assessment: bromuconazole

Definitions for monitoring: bromuconazole isomers

6.2. Water

6.2.1. Ground water

Definitions for exposure assessment: bromuconazole

Definitions for monitoring: bromuconazole isomers

6.2.2. Surface water

Definitions for risk assessment: bromuconazole

Definitions for monitoring: bromuconazole isomers

6.3. Air

Definitions for risk assessment: bromuconazole

Definitions for monitoring: bromuconazole isomers

6.4. Food of plant origin

Definitions for risk assessment: PROVISONAL: bromuconazole [11]

Definitions for monitoring: PROVISONAL: bromuconazole isomers [12]

6.5. Food of animal origin

Definitions for risk assessment: PROVISONAL: bromuconazole

Definitions for monitoring: PROVISONAL: bromuconazole isomers

[11] For the assessed use in cereals only
[12] For the assessed use in cereals only

7. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

7.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
bromuconazole	Moderate to very high persistence Single first-order $DT_{50\,lab}$ 329-1028 days (3 soils only; 20-22°C, 80% soil moisture capacity at 0.33 bar) Field studies: single first-order DT_{50} 45-201 days (6 soils), in a 7th soil the second phase first-order DT_{50} following a more rapid initial decline was 657 days.	The risk to earthworms and organic matter breakdown was assessed as low, the studies with soil micro-organisms do not cover the preliminary maximum accumulated peak PEC soil.
M04 (anaerobic soil degradation)	No data, not required.	No data available, no data required

7.2. 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
bromuconazole	Medium to low mobility K_{Foc} 474-1539 mL/g	No	Yes	Yes	Yes

7.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
bromuconazole	Bromuconazole is very toxic to aquatic organisms.

7.4. Air

Compound (name and/or code)	Toxicology
bromuconazole	Not acutely toxic via inhalation

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

- Additional accuracy data for impurity LS880225 (relevant for all uses evaluated, data gap identified by the rapporteur Member State, date of submission unknown, refer to section 1).
- A metabolism study in cereals with the triazole-label (relevant for all uses evaluated, data gap identified by PRAPeR 30 meeting of experts, date of submission unknown, refer to section 3).
- A rotational crop metabolism study with the triazole-label (relevant for all uses evaluated, data gap identified by PRAPeR 30 meeting of experts, date of submission unknown, refer to section 3).
- The exposure of the consumer to triazole derivative metabolites needs to be addressed for all areas relevant in consumer risk assessment (relevant for all uses evaluated, data gap identified by PRAPeR 30 meeting of experts, date of submission unknown, refer to section 3).
- Bromuconazole consists of 4 isomers. This needs to be taken into account in the environmental risk assessment. Information on the toxicity and/or on the degradation of the 4 isomers in the environment is needed (relevant for all representative uses evaluated; open point identified after the expert meeting; date of submission unknown; refer to section 5).
- The potential risk of endocrine disrupting effects should be addressed for birds and fish (relevant for all representative uses evaluated; data gap identified in the meeting of experts at PRAPeR 28 in July 2007 and re-confirmed in PRAPeR 75; no submission date proposed by the applicant; refer to section 5).
- Further refinement of the long-term risk assessment for herbivorous mammals is necessary (relevant for all representative uses evaluated; data gap identified by the RMS and confirmed by EFSA after the experts‟ meeting; no submission date proposed by the applicant; refer to section 5).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative use as a fungicide on wheat. Full details of the representative use can be found in Appendix A. The representative formulated product for the evaluation was „Granit 200 SC‟, a suspension concentrate formulation (SC).

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (the German S19 method has been validated). For the other matrices only single methods are available to determine residues of bromuconazole. Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

In mammals, bromuconazole oral LD_{50} is 328 mg/kg bw (classification as „harmful if swallowed‟ (Xn; R22), proposed). The acute toxicity by the dermal and inhalation routes is low (LD_{50} > 2000 mg/kg bw and LC_{50} > 5 mg/L). Bromuconazole is neither a skin nor an eye irritant. It is not a skin sensitiser. In repeated dose toxicity studies, the liver is the target organ. In subchronic tests, the dog is the most sensitive species, with an overall relevant NOAEL of 2.5 mg/kg bw/day, whereas in rat the NOAEL is 13.8 mg/kg bw/day. In genotoxicity testing there was some indication of weak clastogenicity *in vitro*, however there was no indication of positive results *in vivo*, neither in the micronucleus assay nor in the

UDS assay. Overall, bromuconazole was considered devoid of genotoxic potential. The relevant NOAEL for long-term toxicity and carcinogenicity in rat is 0.88 mg/kg bw/day: treatment-related neoplastic lesions in rodents occurred at high doses: hepatocellular and cholangiocellular carcinomas in rats and hepatocellular carcinoma in mice. In both rats and mice, the tumours were likely caused by liver toxicity and subsequent cell renewal. Overall, it was agreed that bromuconazole does not have carcinogenic potential relevant to humans. Bromuconazole did not show any reproductive toxicity potential: parental and foetal toxicity NOAELs were established at 1.3 mg/kg bw/day, while the reproductive NOAEL was established at 141 mg/kg bw/day. As for developmental toxicity, in the rat the relevant maternal NOAEL is 70 mg/kg bw/day, whereas the developmental NOAEL is 10 mg/kg bw/day, based on a dose-dependent increase of placental weight and ossification delays or supernumerary bones in a number of skeletal structures. It was agreed to propose classification Cat 3, Xn; R63, „May cause harm to unborn child". The ADI of 0.01 mg/kg bw/day was set based on the relevant long-term toxicity/carcinogenicity NOAEL of 0.88 mg/kg bw/day from the 2 year rat study, applying a SF of 100. For the ARfD, the value is based on the developmental NOAEL of 10 mg/kg bw/day from the rat study, with a SF of 100, leading to an ARfD of 0.1 mg/kg bw. The AOEL of 0.025 mg/kg bw/day was set on basis of the NOAEL of 2.5 mg/kg bw/day from the 90-day dog study (applying a standard SF of 100). The operator exposure assessment showed exposure levels below the AOEL (15.6%) according to the German model with the use of gloves during mixing/loading and application and coveralls and sturdy footwear during application. The estimated exposure for re-entry activities (scouting) is 4.5% of the AOEL. The bystander exposure is estimated to be 1.6% of the AOEL.

The metabolism of bromuconazole was investigated in wheat. Additional metabolism data were submitted for the category of fruit crops. A metabolic pathway could be established in cereals. At harvest, bromuconazole was still a major part of the terminal residue in cereal matrices, and identified metabolites were individually below 10 % of the total residue. However, there was indication of preferential metabolism of one bromuconazole diastereomer (LS 850647), as a significant shift in the ratio of diastereomers was found in the residues determined in the mature cereal crop when compared to the ratio in the initially applied bromuconazole. Whether the ratio of enantiomers in each diastereomer was subject to any shift was not investigated. In rotational crops studies there was uptake of residues from soil into succeeding cereal, oilseed, root and leafy crops. Upon analysis of the residues the two bromuconazole diastereomers were identified as major residue, and similar to the primary cereal metabolism their ratio had been shifted compared to the one in the bromuconazole applied to the soil. No information is available on the ratio of enantiomers in each diastereomer. The submitted livestock metabolism data in ruminants and poultry allows to establish a metabolic pathway, and suggests that no residues in food of animal origin above the limit of quantification are expected when cereals treated according to the cGAP are used in livestock diet. The data imply that there might be preferential metabolism of one diastereomer also in livestock animals. The ratio of enantiomers in each diastereomer was not investigated. As plant and livestock residue data indicate that from the representative use no significant consumer exposure to bromuconazole residues is expected, the observed shift of the isomer ratio in the terminal residue is currently not a concern with regard to consumer safety. This may have to be reconsidered when authorisation of uses is sought that lead to consumer exposure to bromuconazole residues above the limit of quantification. The meeting of experts noted that all studies were performed using phenyl-labelled bromuconazole only, and thus the fate of the triazole moiety of the molecule was not investigated. The experts agreed that, based on the available data and information, cleavage of the molecule cannot be excluded and further investigation of the triazole moiety of the molecule is required to address consumer exposure to potential metabolites originating from molecule breakdown, as e.g. triazole derivative metabolites. Until then, the plant and animal residue definition is provisional. Triazole derivative metabolites are considered of concern due to their toxicological profile. In the absence of data investigating the fate of the triazole moiety of the bromuconzole molecule and the magnitude of potentially occurring metabolites originating from the triazole moiety the consumer exposure cannot be assessed and consequently the consumer risk assessment is not finalised. As a breakdown of the bromuconazole molecule leading to

the occurrence of metabolites relevant to consumer safety cannot be excluded, the issue is regarded as a critical area of concern.

The information available on the fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at EU level. The potential for groundwater contamination resulting from the representative use assessed is concluded to be low in geoclimatic conditions represented by all 9 pertinent FOCUS groundwater scenarios.

Bromuconazole belongs to the group of triazole fungicides that are suspected to have potential endocrine disrupting properties. No information was provided to address this point with regard to the potential effects on birds and fish, and a data gap was identified. No new information on this point was provided in the Additional Report and the data gap remains.

The TER values for herbivorous birds were all above the Annex VI triggers, indicating a low risk for herbivorous birds. Also for insectivorous birds the TER values for acute and short-term were well above the trigger, however the long-term TER was below the trigger of 5, indicating a potential high long-term risk. In the Additional Report higher tier studies (mainly from open literature) were presented to select the focal species and to determine the proportion of different food types (PD) of the focal species. Two different approaches were used to refine the risk assessment. The first approach included the selection of representative focal species, and estimations of PD for these species. The second approach was to include the decline of residues in insects (f_{twa} = 0.53) in the first tier long-term risk assessment. The TERlt values based on the PD refinements, and those based on the use of f_{twa} of decline of residues in insects, were all above the Annex VI trigger values. Therefore the long-term risk to insectivorous birds was assessed as low. The risk to earthworm- and fish-eating birds was assessed as low.

The acute TERs for herbivorous and insectivorous mammals were above the Annex VI trigger of 10 (including refinement of residues in plant material), however the long-term TERs were below the Annex VI trigger, indicating a high risk. The choice of the long-term end point was discussed again in the experts‟ meeting (PRAPeR 75), and it was agreed that the NOAEL for mammals of 13.8 mg as/kg bw/day is the relevant ecotoxicological end point. TER calculations for insectivorous mammals based on this NOAEL are provided in the DAR and in the Additional Report and were above the Annex VI trigger value, indicating a low long-term risk for insectivorous mammals. In the resubmission, a higher tier risk assessment for herbivorous mammals was based on the rabbit as focal species in late cereal growth stages. The higher tier risk assessment for herbivorous mammals was discussed in the experts‟ meeting (PRAPeR 75), and it was concluded that the available information is not sufficient to address the potential high long-term risk for herbivorous mammals. The risk to earthworm- and fish-eating mammals was assessed as low.

Bromuconazole is very toxic to aquatic organisms. The applicant provided a bridging study with the new formulation SCAE0307 and *Daphnia magna*. The formulation SCAE0307 is less toxic than the previously assessed formulation EXP 10064-B, and has a toxicity comparable to that of the active substance. Member States experts at PRAPeR 75 agreed that the end points for the active substance should be used in the risk assessment. A low long-term risk was identified from the FOCUS step3 PECsw values in the D3 ditch, D4 pond, D4 stream, D5 pond, D5 stream, D6 pond, R1 pond and R1 stream scenarios. However, a potential high long-term risk was indicated for aquatic invertebrates from the FOCUS step3 PECsw values for the D1 ditch, D1 stream, D2 ditch, D2 stream, R3 stream and R4 stream scenarios, and further refinement was needed. The TERs were re-calculated with a 10m no-spray buffer zone for the drainage scenarios and a 10m no-spray buffer zone including a vegetated filter strip to mitigate the run-off. The long-term TER values were above 10 in 2 full FOCUS run-off scenarios (R3 stream and R4 stream). However, the TER values estimated with the drainage scenarios D1 ditch, D1 stream, D2 ditch, D2 stream were below the Annex VI trigger values even with a 10m no-spray buffer zone. Overall, taking into account the FOCUS step 3 and 4 scenarios, it can be concluded that the risk from bromuconazole to aquatic organisms was assessed as low for more than the half of the scenarios.

The risk assessment for non-target arthropods was not in accordance with the ESCORT II scheme. The standard glass plate tests suggest that there will be some adverse effects on sensitive non-target arthropods. Extended laboratory studies gave an indication that the risk to non-target arthropods is low. Concerns were raised with regard to the comparability of the different formulations used in the studies with non-target arthropods. EFSA agrees to the assessment of the RMS that the formulations are sufficiently similar to conclude on the risk to non-target arthropods for the representative use. The applicant informed that a different formulation than Granit will be marketed. It is suggested that a risk assessment for this formulation is conducted at Member State level after the decision on Annex I inclusion.

The formulation Granit had no significant effect on organic matter decomposition over a six months period in a litter bag test at an application rate of 180 g a.s./ha and 500 g a.s./ha. The soil concentration was calculated in the DAR as 0.67 mg a.s./ha. This concentration covers the plateau maximum PEC_{soil} of 0.232 mg a.s./kg soil (2 x 0.200 kg a.s./ha). In conclusion, the risk of bromuconazole to non-target macro-organisms was assessed as low.

Effects of > 25% on nitrogen transformation were observed at an application rate of 400 g a.s./ha (0.53 mg a.s./kg soil). This concentration covers the plateau maximum PEC_{soil} of 0.232 mg a.s./kg soil (2 x 0.200 kg a.s./ha). The risk of bromuconazole to soil non-target micro-organisms was assessed as low.

The risk to bees, earthworms, non-target plants, and biological methods of sewage treatment was assessed as low.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Use of PPE is required to reduce estimated exposure levels below the AOEL (refer to point 2.12).

- Risk mitigation measures comparable to 10m no-spray buffer zones are required to identify a safe use in the relevant FOCUS scenarios R3 stream and R4 stream. However, no safe use was identified with 10m no-spray buffer zones for the D1 ditch, D1 stream, D2 ditch, D2 stream scenarios.

ISSUES THAT COULD NOT BE FINALISED

- The assessment of the potential for endocrine disruption in fish and birds could not be finalised.

- The consumer risk assessment is not finalised.

CRITICAL AREAS OF CONCERN

- A potential risk for the consumer cannot be excluded, in particular with regard to bromuconazole metabolites. The nature of the residue is not adequately characterised, since no data with triazole labelled bromuconazole are available. A breakdown of the molecule leading to the occurrence of metabolites relevant to consumer safety cannot be excluded.

- A high long-term risk was identified for herbivorous mammals.

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APPENDICES

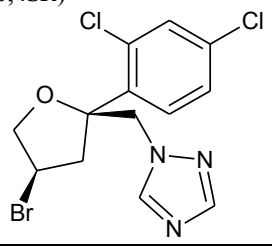
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

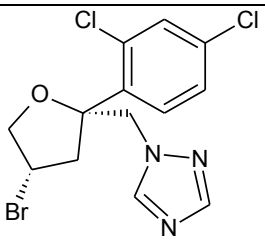
Added in October 2009:
The following list of end points is an amended version of the peer-reviewed list of end points (version dated January 2008, including changes made by EFSA in February 2008) that was included in the EFSA conclusion dated 26 March 2008 (EFSA Scientific Report (2008) No 136). Changes made as a result of the assessment of new data provided in the resubmission dossier (2009) are highlighted in yellow.

Identity, Physical and Chemical Properties, Details of Uses, Further Information

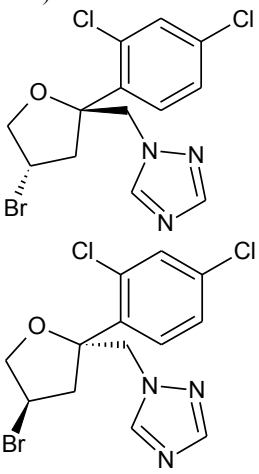
Active substance (ISO Common Name) ‡	Bromuconazole
Function (*e.g.* fungicide)	Fungicide
Rapporteur Member State	Belgium

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	1-[(2*RS*,4*RS*:2*RS*,4*SR*)-4-bromo-2-(2,4-dichlorophenyl)tetrahydrofurfuryl]-1*H*-1,2,4-triazole
Chemical name (CA) ‡	1-[[4-bromo-2-(2,4-dichlorophenyl)tetrahydro-2-furanyl]methyl]-1H-1,2,4-triazole
CIPAC No ‡	680
CAS No ‡	116255-48-2
EC No (EINECS or ELINCS) ‡	408-060-3
FAO Specification (including year of publication)‡	No FAO specification available.
Minimum purity of the active substance as manufactured (g/kg) ‡	Min. 960 g/kg Bromuconazole (LS850646 + LS850647), with LS850646 ranging between 500 to 560 g/kg and LS850647 ranging between 420 to 480 g/kg. These ranges imply ratios LS850646/LS850647 between 1.04:1 and 1.33:1
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	$C_{13}H_{12}BrCl_2N_3O$
Molecular mass ‡	377.1 g/mol
Structural formula ‡	LS 850646 (2*RS*,4*SR*) 



LS 850647(2*RS*,4*RS*)



Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	84°C (98.9%, DSC) (LS 850646 + LS 850647) 92 ± 1 °C (98.8%, capillary tube in liquid bath) (LS 850646 + LS 850647) 91°C (99.5%, DSC) (LS850646) 101°C (99.9%, DSC) (LS850647)
Boiling point (state purity) ‡	Not applicable (decomposition)
Temperature of decomposition (state purity)	194°C (98.9%)
Appearance (state purity) ‡	white to beige powder, slightly alcoholic odour (96.8%) beige powder, no characteristic odour (98.2%)
Vapour pressure (state temperature, state purity) ‡	0.4 x 10^{-5} Pa at 25°C (98.3%) (LS 850646 + LS 850647) 0.3 x 10^{-5} Pa (LS 850646) at 25°C 0.1 x 10^{-5} Pa (LS 850647) at 25°C
Henry's law constant (Pa m^3 mol^{-1}) ‡	1.05 x 10^{-5} Pa.m³.mol^{-1} at 20°C (LS850646) 1.57 x 10^{-5} Pa.m³.mol^{-1} at 20°C (LS850647)
Solubility in water (state temperature, state purity and pH) ‡	distilled water, 20°C : 49 mg/L LS850646 + 24 mg/L LS850647 (100%) distilled water, 20°C : 72 mg/L (LS850646, 100%) distilled water, 20°C : 24 mg/L (LS850647, 99.7%) No effect of pH (97.4%)
Solubility in organic solvents (state temperature, state purity) ‡	

	at 20°C in g/L (97.4%)	
	LS850646	LS850647
n-hexane	1.65	1.92
toluene	217.2	156.8
dichloromethane	499.7	353.7
methanol	295.4	188.5
1-octanol	61.4	38.5
2-propanol	57.4	39.8
acetone	318.6	219.7
ethylacetate	231.9	173.0

Surface tension (state concentration and temperature, state purity) ‡	59.8 mN/m at 21°C (90% saturated solution) (98.8%) Concentrations of diastereoisomers in test solution: LS850646: 5.74 x 10^{-2} g/L; LS850647: 1.83 x 10^{-2} g/L
Partition co-efficient (log P_{OW}) (state pH and temperature) ‡	distilled water, 20°C, 98.9% pure log P_{ow} = 3.24 (LS 850646 + LS 850647) log P_{ow} = 3.12 (LS 850646) log P_{ow} = 3.48 (LS 850647)
	Effect of pH does not need to be addressed (molecule will not be ionized at environmentally relevant pH values)
Dissociation constant (state purity) ‡	Bromuconazole does not dissociate (or appear in an ionized form) in the range of pH 2 to 7. (98.02%, OECD 112 test)
UV/VIS absorption (max.) incl. ε (state purity, pH) ‡	*LS850646 (99.9%):*

	λ_{max} (nm)	ε (L.mol^{-1}.cm^{-1})
Aqueous solutions (with 1% methanol)		
acidic	204.0 220.0*	38527 11157

neutral	202.5 220.0*	43936 10762
basic	221.5	9915
Methanol solutions		
	205.0 220.0*	21534 6790
	at λ 295 nm	0.49

LS850647 (99.3%) :

	λ_{max} (nm)	ε (L.mol^{-1}.cm^{-1})
Aqueous solutions (with 1% methanol)		
acidic	204.0 221.0*	36614 10611
neutral	203.0 220.0*	42091 10329
basic	220.5	9560
Methanol solutions		
	206.0 220.0*	22705 8205
	at λ 295 nm	2.27

* shoulder

The photolysis study, which provided different UV/VIS spectra, is in question.

Flammability (state purity) ‡	not highly flammable (98.8%) not auto-flammable (98.8%)
Explosive properties (state purity) ‡	not explosive (98.8%)
Oxidising properties (state purity) ‡	not oxidising (98.8%)

Summary of representative uses evaluated (bromuconazole)

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (day) (l)	Remarks (m)
					Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Wheat	Europe	Granit 200 SC	F	*Tapesia* spp. *Mycosphaerella graminicola* *Stagonospora nodorum* *Puccinia recondita* *Puccinia striiformis* *Blumeria graminis* f.sp. *tritici* *Fusarium* spp	SC	200 g/l	spraying	BBCH 29-31 BBCH 49-51 (S.E) 59-65 (N.E.)	1 1	c.a. 2 months	0.050-0.100 0.050-0.100	200-400 200-400	0.200 0.200		I II

I A potential risk for the consumer cannot be excluded, in particular with regard to bromuconazole metabolites. The nature of the residue is not adequately characterised, since no data with triazole-labelled bromuconazole are available. A breakdown of the molecule leading to the occurrence of metabolites relevant to consumer safety cannot be excluded.

II A high long-term risk is identified for herbivorous mammals.

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

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV (method B-488-06-91(E)) no CIPAC method available
Impurities in technical as (analytical technique)	HPLC-UV (method B-590-07-91(E)); GC-FID (method B-591-04-91(E)); Karl Fischer
Plant protection product (analytical technique)	HPLC-UV (method B-706-01-93(E)) or GC-FID (method AM004404MF1) no CIPAC method available

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Bromuconazole (isomers) Provisional
Food of animal origin		Bromuconazole (isomers) Provisional
Soil		Bromuconazole (isomers)
Water	surface	Bromuconazole (isomers)
	drinking/ground	Bromuconazole (isomers)
Air		Bromuconazole (isomers)

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Multi method DFG S19 (modified) : GC-ECD, conf. by column of different polarity or GC/MSD (Bromuconazole); LOQ = 0.05 mg/kg (cereals)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Single method AR 120-96 : GC-ECD, conf. by GC-MSD (Bromuconazole); LOQ = 0.01 mg/kg (milk), 0.02 mg/kg (beef meat, egg, bovine liver, bovine kidney, bovine fat)
Soil (analytical technique and LOQ)	Single method AR 71-89 (E) : GC-ECD, conf. by column of different polarity (Bromuconazole); LOQ = 0.02 mg/kg
Water (analytical technique and LOQ)	Single method AR 74-89 (E) : GC-ECD, conf. by GC-MSD (Bromuconazole); LOQ = 0.1 µg/L (surface water, drinking water)
Air (analytical technique and LOQ)	Single method : LC/MS/MS (Bromuconazole); LOQ = 0.4 µg/m³
Body fluids and tissues (analytical technique and LOQ)	Not required (active substance is not classified as toxic or highly toxic)

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	none

Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapid (<48h) and almost complete (88%) based on urinary and bile excretion.
Distribution ‡	Widely distributed; slight preference for liver, kidney, adrenales and blood
Potential for accumulation‡	None
Rate and extent of excretion ‡	Rapid, within 48h: 88-97%.
Metabolism in animals ‡	Extensive phase I metabolisation (hydroxylation) of the tetrahydrofurane and dichlorobenzene ring, followed by glucuronide or sulphate conjugation. Glucuronide or amino acid conjugation of triazole ring. No evidence of phenyl-, THF- or triazole ring degradates (only THF ring opening).
Toxicologically significant compounds (animals, plants and environment) ‡	Bromuconazole , TA , TAA and 1,2, 4- triazole.

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	328 (♀) mg/kg bw ***(Xn; R22)***
Rat LD_{50} dermal ‡	>2000 mg/kg bw
Rat LC_{50} inhalation ‡	>5 mg/L air (micronised dust, 4h- nose only)
Skin irritation ‡	Not irritant
Eye irritation ‡	Not irritant
Skin sensitization (test method , result) ‡	Maximisation test, no sensitisation

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	90d/1yr dog: liver weight increase, increased alkaline phosphatase and transaminase activity, adrenal cortical vacuolation
Lowest relevant oral NOAEL / NOEL ‡	2.5 mg/kg bw/day (90-day and 1-year dog) 13.8 mg/kg bw/day (90-day, rat)
Lowest relevant dermal NOAEL / NOEL ‡	500 mg/kg bw/day (21-day, rat)
Lowest relevant inhalation NOAEL / NOEL ‡	Not available, not required

Genotoxicity (Annex IIA, point 5.4) ‡	*In-vitro:* negative bacterial, equivocal mammalian genotoxicity; weak clastogenicity (CA in CHO cells and human lymphocytes) *In-vivo:* negative in UDS and BM micronucleus Overall, no genotoxic potential.

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

Target/critical effect ‡	Liver (rat, mouse)
Lowest relevant NOAEL / NOEL ‡	0.88-1.09 mg/kg bw/day (2 yr- rat) 2.27 mg/kg bw/day (80 weeks mouse)
Carcinogenicity ‡	Hepatocellular carcinoma (rat, mouse) and cholangiocarcinoma (rat) at high dose level producing marked hepatoxicity (87.2 mg/kg bw/day in rat, 370 mg/kg bw/day in mouse).

	Overall, no carcinogenic potential relevant at human exposure levels.

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	•parents: decreased body weight gain, increased liver weight, hepatocyte fatty vacuolation •pups: decreased body weight gain (F2) No adverse reproductive effects.
Lowest relevant reproductive NOAEL / NOEL ‡	•NOAEL parental: 1.3 mg/kg bw/day •NOAEL offspring: 1.3 mg/kg bw/day •NOAEL reprotox: 141 mg/kg bw/day (highest dose)
Developmental target / critical effect ‡	Rat (maternal): decreased bodyweight gain, increased water consumption, increased liver weight Rat :increased placental weight Rat (developmental): increased 7th cervical ribs, domed head and anophthalmia at high dose ***(Xn, R63)***
	Rabbit maternal: Decreased bodyweight gain, clinical signs Rabbit developmental: Increased of visceral and skeletal variant.
Lowest relevant developmental NOAEL/NOEL ‡	•Rat NOAEL maternal: 70 mg/kg bw/day •Rat NOAEL developmental: 10 mg/kg bw/day
	Rabbit NOAEL maternal: 12.5 mg/kg bw/day Rabbit NOAEL developmental: 12.5 mg/kg bw/day

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

(i) Delayed neurotoxicity: (ii) Acute and subchronic neurotoxicity	No data, not required No data, not required

Other toxicological studies (Annex IIA, point 5.8) ‡

(i) Potential effect of bromuconazole on porphyria (dog, 29d capsule feeding) (ii) Acute toxicity, bacterial genotoxicity and/or chromosome aberration studies on metabolite LS860364 and impurities (RPA 400063, RPA 400064, LS880225, LS880226, RPA405516, RPA405517)	(i) erythema or gum reddening observed in subchronic dog studies not replicated in mechanistic study, hence no porphyria detected. (ii) Metabolite or impurities not more acutely toxic than bromuconazole, devoid of genotoxic potential.

Medical data (Annex IIA, point 5.9) ‡

	Based on the reports of the medical surveillance on manufacturing plant personnel, no effects were related to the exposure to the active substance.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/day	2-year rat	100
AOEL ‡	0.025 mg/kg bw/day	90-day and 1-year dog	100
ARfD (acute reference dose) ‡	0.10 mg/kg bw	developmental rat	100

Dermal absorption (Annex IIIA, point 7.3) ‡

In-vivo penetration study (rat) Granit EXP 10064 (=200 SC)	Low dose: 5%; High dose: 45%

Acceptable exposure scenarios (including method of calculation)

Operator	Application to cereals : UK POEM (% of AOEL) (tractor, 200 g a.s./ha, without PPE): 1317% (tractor, 60 g.a.s./ha, PPE = gloves during mixing/loading plus application): 201% BBA (% of AOEL) (tractor, 200 g a.s./ha, without PPE): 238% (tractor, 200 g a.s./ha, PPE = gloves during mixing/loading and application, and coveralls and boots during application): 15%
Workers	According to Hoernicke et al. 1998: < 4.5% of AOEL (with PPE)
Bystanders	According to Ganzelmeier 1995: < 1.6% of AOEL

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	Xn; R22 („Harmful by oral uptake“) Xn; R63 („May cause harm to unborn child“)

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)[1]
Rotational crops	Cereals (spring/winter wheat), Root and tuber vegetables (radish), Leafy vegetables (lettuce) [2]
Metabolism in rotational crops similar to metabolism in primary crops?	Pending the outcome of the metabolism study on cereals with the triazole labelling moiety.
Processed commodities	No data available – currently none required
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Provisional: [#]Bromuconazole (sum of isomers)
Plant residue definition for risk assessment	Provisional: [#] Bromuconazole (sum of isomers)
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	Lactating cows and goats Laying hens
Time needed to reach a plateau concentration in milk and eggs	Milk 1-2 days Eggs 4-5 days
Animal residue definition for monitoring	Provisional: [#] Bromuconazole (sum of isomers)
Animal residue definition for risk assessment	Provisional: [#] Bromuconazole (sum of isomers)
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Open [3]
Fat soluble residue: (yes/no)	Yes (Log $P_{O/W}$ = 3.24)

[1] Data gap for a cereal metabolism study with triazole labelling
[2] Data gap for a rotational crop study with triazole labelling
[#] This residue definition is only applicable to cereals and will have to be reconsidered regarding the triazole derivative metabolites upon submission of data addressing the identified data gaps.
[3] Inconclusive with regard to triazole derivative metabolites.

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

Rotational crop studies performed with the phenyl labelling showed that levels of bromuconazole in succeeding crops may exceed 0.01 mg/kg but are not likely to exceed 0.05 mg/kg (LOQ of the method validated for enforcement of bromuconazole residues in cereals). This conclusion is provisional and will have to be reconsidered regarding the triazole derivative metabolites.[4]

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

Wheat (grain and straw)	Stable for 20 months at -18°C

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

Note: The estimates refer only to livestock intakes of bromuconazole. Potential intakes and residue levels of triazole derivative metabolites in animals will have to be assessed separately.

	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)	yes dairy cattle 0.49 mg/kg DM beef cattle 1.2 mg/kg DM	no	no
Potential for accumulation (yes/no):	yes	n/a	n/a
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	no	no	n/a
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices [5]: Mean (max) mg/kg		
Muscle	<0.02	n/a	n/a
Liver	<0.02	n/a	n/a
Kidney	<0.02	n/a	n/a
Fat	<0.02	n/a	n/a
Milk	<0.01		
Eggs		n/a	

[4] Data gap for a rotational crop study with triazole labelling
[5] No feeding study submitted. Estimated on the basis of the available metabolism studies, bromuconazole residues are not likely to exceed the LOQ of the proposed monitoring method.

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)
Wheat	N	Grain: 3 x <0.01; 9 x <0.02; 2 x <0.025; 1 x <0.021; 8 x <0.05 Straw: 0.06; 0.13; 0.16; 0.41; 0.51; 0.55; 0.78; 0.93; 0.93; 0.98; 1.0; 1.2; 1.2; 1.3; 1.5	Since all residues in grains are below the enforcement LOQ of 0.05 mg/kg (multi-method), it is proposed to set the MRL at 0.05*mg/kg	0.05*	0.05 1.5	0.02 0.93
Wheat	S	Grain: 3 x <0.01; 4 x <0.02; 1 x <0.025 Straw: 0.086; 2x 0.14; 0.19; 0.24; 0.46; 0.57; 1.0	Since all residues in grains are below the enforcement LOQ of 0.05 mg/kg (multi-method), it is proposed to set the MRL at 0.05*mg/kg	0.05*	0.025 1.0	0.02 0.22

(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

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

Note: This consumer risk assessment is provisional and will have to be reconsidered regarding potential intake of triazole derivative metabolites.

ADI	0.01 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	9 % (cluster diet B)
TMDI (% ADI) according to EFSA PRIMo rev. 2a	10 % (NL child) all other diets use less of the ADI
TMDI (% ADI) according to national (to be specified) diets	4 % and 14 % respectively for children and infants (UK long term exposure model).
IEDI (WHO European Diet) (% ADI)	Not required.
NEDI (specify diet) (% ADI)	Not required.
Factors included in IEDI and NEDI	Not applicable.
ARfD	0.10 mg/kg bw
IESTI (% ARfD)	Wheat: 0.3 % (General population WHO consumption data) 0.5 % (Children WHO consumption data) Milk: 0.3 % (General population WHO consumption data) 0.8 % (Children WHO consumption data) Meat: 0.2 % (General population WHO consumption data) 0.3 % (Children WHO consumption data) Liver: 0.1 % (General population WHO consumption data) 0.2 % (Children WHO consumption data) Kidney: 0.2 % (General population WHO consumption data) 0.3 % (Children WHO consumption data)
IESTI (% ARfD) according to EFSA PRIMo rev. 2a	7.7 % (potatoes/UK infant) 1.8 % (Chinese cabbage/general population)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	See IESTI according to EFSA PRIMo rev. 2a
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	n/a	n/a	n/a	n/a

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

Note:

1. Proposals are relevant to the provisional monitoring residue definition, i.e. bromuconazole (isomers) only.
2. The LOQ for plant commodities other than cereals is currently unknown, as method validation data have only been submitted for cereals. It could be possible that residues in plant grown as rotational crops will exceed the value of 0.01 mg/kg that is usually set as a default MRL if no different MRL is proposed for these crops.

Wheat grain	0.05* mg/kg
Milk	0.01* mg/kg
Ruminant meat	0.02* mg/kg
Ruminant fat	0.02* mg/kg
Ruminant liver	0.02* mg/kg
Ruminant kidney	0.02* mg/kg

*LOQ

Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	1.3-4.4 % AR after 120 d, [^{14}C-phenyl]-label (n= 2)
Non-extractable residues after 100 days ‡	10.2-17.6 % AR after 120 d, [^{14}C-phenyl]-label (n= 2)
Relevant metabolites - name and/or code, % of applied (range and maximum) ‡	None

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

Anaerobic degradation ‡	No mineralization non-extractable residues: 15% AR after 90 days 2-(2,4-dichlorophenyl-2-(1,2,4-triazol-1-yl methyl)) tetrahydrofuran (LS 871387): 10% AR after 181 days [^{14}C-phenyl]-label
Soil photolysis ‡	Mineralisation: 0.6% AR after 30 days non-extractable residues: 14.7% AR after 30 days SFO DT50 irradiated : 78 days, summer sunlight 50° N no major metabolite [^{14}C-phenyl]-label

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

Method of calculation	Laboratory: non linear single first order kinetics
Laboratory studies (range or median, with n value, with r^2 value) ‡	DT_{50lab} (20-22°C, aerobic): 329-1028 d (n=3, χ^2 error = 1.9-5.9)
	DT_{90lab} (20-22°C, aerobic): 1091-3414 d (n=3, χ^2 error = 1.9-5.9)
	DT_{50lab} (10°C, aerobic): 609-1826 d (n= 2, χ^2 error = 1.8-2.1)
	DT_{50lab} (22°C, anaerobic): 356 d (n= 1, χ^2 error = 5.4)
	degradation in the saturated zone: ‡ not required
Field studies (state location, range or median with n value) ‡	SFO DT_{50} without the normalisation to FOCUS reference conditions : 45-201 days (n=6, Lubek trial site excluded) The not normalised second phase first order DT_{50} from the Lubek site is 657 days, calculated excluding the first data point (estimate excludes the apparent rapid initial decline). This was the DT_{50} selected to calculate PEC soil, as initial potential photolytic loss needs to be excluded when the GAP assessed will have crop canopy shading the soil.

	SFO Normalised DT_{50} at 20°C and pF 2 (excepted for Kraichtal and Karlsruhe sites where no soil moisture correction was applied, due to topographical difference between the weather stations and trial sites): geomean 228 days (n = 7, range 83-747 days). Both geomean and the range exclude photolysis effects. This 228 day value is the most appropriate SFO DT_{50} value for use in FOCUS groundwater and surface water modelling. *Note:* *Normalisation to FOCUS reference conditions 20°C and pF 2* were *performed with a Q10 of 2.2 and where pertinent a Walker equation coefficient of 0.7.*
Soil accumulation and plateau concentration ‡	Accumulation factors calculated in the study UK site: 2.56 DE site: no plateau reached.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence (yes / no) (if yes type of dependence) ‡	K_{oc} isomer LS850646: 474-1086 mL / g (mean 757 mL / g , $^1/_n$= 0.78-0.85, 4 soils) K_{oc} isomer LS850647: 627-1539 mL / g (mean 987 mL / g , $^1/_n$= 0.76-0.86, 4 soils) K_f: isomer LS850646: 4.5-26.5 mL / g (mean 10.5 mL / g , 4 soils) K_f: isomer LS850647: 5.0-37.5 mL / g (mean 14.5 mL / g, 4 soils) No dependence with pH *For FOCUS gw modelling – K_{oc}: parent, mean 757 mL/g, $^1/_n$=-0.82

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

Column leaching ‡	Guideline: „not stated“ Time period (d): not given Precipitation (mm): 508 mm Leachate: 0.2-0.6% total residues/radioactivity in leachate; the leachate contains predominantly the a.s. 62.4-97.6 % total residues/radioactivity retained in top 6 cm
Aged residues leaching ‡	Guideline: „not stated“ Aged for (d): 210 d Time period (d): not given Precipitation (mm): 508 mm Leachate: 1.8-2.4 % total residues/radioactivity in leachate; the leachate contains predominantly the a.s. 69.5-101.9 % total residues/radioactivity retained in top 6 cm
	Guideline: „UK MAFF“ Aged for (d): 210 d Time period (d): not given Precipitation (mm): 508 mm

	Leachate: 2.0-3.1 % total residues/radioactivity in leachate; the leachate contains 4 unidentified polar compounds. 86.8-90.3% total residues/radioactivity retained in top 6 cm
Lysimeter/ field leaching studies ‡	Not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	Guideline : 7617/VI/96 Crop: winter cereals Number of applications: 2 or 1 late application Application rate(s): 0.200 kg a.s./ha early application : 50% plant interception 2nd or single late application: 90% plant interception Application interval: 60 days soil layer: Initial: 5 cm, soil density :1.5 kg/dm3 PECsoil accumulation: 20cm for accumulation over several years followed by 5 cm for the last years applications, soil density :1.5 kg/dm3 worst case DT50 of 657 days (SFO unnormalised field dissipation DT50)

PECsoil, initial

Calculated PEC soil for 2 applications	0.160 mg a.s. / kg soil
Calculated PEC soil for 1 application	0.027 mg a.s. / kg soil

PECsoil, accumulation

calculated accumulated PEC soil for 2 applications	0.232 mg a.s. / kg soil
calculated accumulated PEC soil for 1 application	0.041 mg a.s. / kg soil

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature) ‡	
	pH 4, 25°C : DT_{50} > 30 d (LS850646, > 98%; LS850647, > 98%)
	pH 5, 25°C : DT_{50} > 30 d (LS850646, > 98%; LS850647, > 98%)
	pH 7, 25°C : DT_{50} > 30 d (LS850646, > 98%; LS850647, > 98%)
	pH 9, 25°C : DT_{50} > 30 d (LS850646, > 98%; LS850647, > 98%)
Photolytic degradation of active substance and relevant metabolites ‡	No photodegradation of Bromuconazole at 25°C in the environmentally relevant pH 9
Readily biodegradable (yes/no) ‡	Not readily biodegradable
Degradation in water/sediment - DT_{50} water ‡	2.0-1.3 d
- DT_{90} water ‡	235-53.8 d (multicompartment 1st order, r^2= 0.97-0.99, n= 2)
- DT_{50} whole system ‡	272-277 d
- DT_{90} whole system ‡	903-921 d (1st order, r^2= 0.98-0.94, n= 2)
Mineralization	0.6-0.9 %AR (at 100 d, study end, n= 2)

Non-extractable residues	15.3-15.1 %AR (at 100 d, study end, n= 2)
Distribution in water / sediment systems (active substance) ‡	Maximum of 63.0-70.4%AR in sediment after 61 days.
Distribution in water / sediment systems (metabolites) ‡	No major metabolites

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

Parent

Method of calculation	Version control no.'s of FOCUS software: „SWASH" v2.1, FOCUS PRZM v1.5.6, FOCUS MACRO v4.4.2 and FOCUS TOXSWA v 2.2.1
Parameters used in FOCUSsw Step 3 - 4	Parameters : see below
Application rate	Crop: winter cereals Application Rate: 2 x 0.2 kg a.s./ha or 1 x 0.2 kg a.s./ha (the normal agricultural practice) Time between applications: Minimum 45 days Application timing: 1 Mar – 30 May considered appropriate for BBCH 29-65. To specifically consider the normal case of a single later dose a window of 15 May – 15 June was also simulated (Actual dates set by The Pesticide Application Timing calculator (PAT) within MACRO and PRZM. Crop Interception: Calculated internally by MACRO or PRZM (foliar application defined in SWASH)

Input data for bromuconazole

Variable	Bromuconazole
	Value
DT_{50} in water (days)	277
DT_{50} in sediment (days)	1000
$DegT_{50}$ soil (days)	219 day at 20°C and pF2*
Koc (mL/g)	757
Freundlich coefficient	0.82
Vapour pressure (Pa) at 25°C	$4\ 10^{-6}$
Water Solubility (mg/L) at 20°C	49
Molecular Weight (g/mol)	377.1
Plant Uptake Value	0.5
Q10	2.2
Walker equation coefficient	0.7

*geomean of seven field studies, each normalized to 20°C and pF 2 as reported in study **B.8.1.3.1** (Jarvis T., 2009) ideally a value of 228 days should have been used.

FOCUS Step 3 PEC values for Bromuconazole application to winter cereals - Two Applications

Scenario	Application date	PECsw (µg/l)	PECsed (µg/kg)	Dominant Entry route to surface water
D1 Ditch	7 Mar, 25 Apr	6.455	72.808	Drainage
D1 Stream	7 Mar, 25 Apr	4.041	41.666	Drainage
D2 Ditch	12 Mar, 7 May	4.909	42.619	Drainage
D2 Stream	12 Mar, 7 May	3.072	25.298	Drainage
D3 Ditch	29 Feb, 20 Apr	1.105	0.780	Drift
D4 Pond	1 Mar, 18 Apr	0.668	7.674	Drainage
D4 Stream	1Mar, 18 Apr	1.350	2.877	Drainage
D5 Pond	7 Mar, 22 Apr	0.309	4.477	Drainage
D5 Stream	7 Mar, 22 Apr	0.967	0.986	Drift
D6 Ditch	5 Mar, 23 Apr	1.664	3.041	Drainage
R1 Pond	17 Mar, 2 May	0.272	3.061	Run-off
R1 Stream	17 Mar, 2 May	1.914	1.945	Run-off
R3 Stream	1 Mar, 15 Apr	2.264	3.123	Run-off
R4 Stream	5 Mar, 4 May	2.453	3.578	Run-off

FOCUS Step 3 PEC values for Bromuconazole application to winter cereals - Respective single application (early season)

Scenario	Application date	PECsw (µg/l)	PECsed (µg/kg)	Dominant Entry route to surface water
D1 Ditch	7 Mar	3.172	37.046	Drift + drainage
D1 Stream	7 Mar	2.042	21.393	Drift + drainage
D2 Ditch	12 Mar	2.281	20.916	Drainage
D2 Stream	12 Mar	1.497	12.379	Drift + drainage
D3 Ditch	29 Feb	1.261	0.608	Drift
D4 Pond	1 Mar	0.293	3.660	Drainage
D4 Stream	1 Mar	1.032	1.364	Drift
D5 Pond	7 Mar	0.163	2.456	Drainage
D5 Stream	7 Mar	1.009	0.540	Drift
D6 Ditch	5 Mar	1.278	1.754	Drift
R1 Pond	17 Mar	0.108	1.425	Run-off
R1 Stream	17 Mar	0.994	0.787	Run-off
R3 Stream	1 Mar	1.196	0.948	Run-off
R4 Stream	5 Mar	1.058	1.197	Run-off

FOCUS Step 3 PEC values for Bromuconazole application to winter cereals - Single application (later season)

Scenario	Application date	PECsw (µg/l)	PECsed (µg/kg)	Dominant Entry route to surface water
D1 Ditch	15 May	2.236	23.625	Drift + drainage
D1 Stream	15 May	1.142	12.835	Drift + drainage
D2 Ditch	23 May	1.839	17.318	Drift + drainage
D2 Stream	23 May	1.381	9.307	Drift + drainage
D3 Ditch	15 May	1.267	0.839	Drift
D4 Pond	30 May	0.177	2.379	Drift
D4 Stream	30 May	1.078	0.854	Drift
D5 Pond	27 May	0.0722	1.204	Drift
D5 Stream	27 May	1.181	0.319	Drift
D6 Ditch	15 May	1.277	2.636	Drift
R1 Pond	13 June	0.140	1.804	Run-off
R1 Stream	13 June	0.836	2.231	Drift

R3 Stream	18 May	1.172	0.917	Drift
R4 Stream	27 May	0.837	1.909	Drift

FOCUS Step 4 PEC values (10m buffer zone) for Bromuconazole application to winter cereals - Two Applications

Scenario	**Application date**	**PECsw (µg/l)**	**PECsed (µg/kg)**	**Dominant Entry route**
D1 Ditch	7 Mar, 25 Apr	6.455	72.434	Drainage
D1 Stream	7 Mar, 25 Apr	4.041	41.661	Drainage
D2 Ditch	12 Mar, 7 May	4.909	42.211	Drainage
D2 Stream	12 Mar, 7 May	3.072	25.025	Drainage
D3 Ditch	29 Feb, 20 Apr	0.149	0.114	Drift
D4 Pond	1 Mar, 18 Apr	0.665	7.538	Drainage
D4 Stream	1 Mar, 18 Apr	1.350	2.872	Drainage
D5 Pond	7 Mar, 22 Apr	0.306	4.326	Drift
D5 Stream	7 Mar, 22 Apr	0.545	0.982	Drift
D6 Ditch	5 Mar, 23 Apr	1.664	2.348	Drainage
R1 Pond*	17 Mar, 2 May	0.116 (0.261)	1.410 (2.921)	Run-off
R1 Stream*	17 Mar, 2 May	0.870 (1.914)	0.695 (1.919)	Run-off
R3 Stream*	1 Mar, 15 Apr	1.304 (2.263)	0.973 (2.995)	Run-off
R4 Stream*	5 Mar, 4 May	1.117 (2.453)	1.424 (3.540)	Run-off

* includes spray drift and run-off mitigation. Values in parentheses are spray drift mitigation only

FOCUS Step 3 PECsed accumulation values for Bromuconazole application to winter cereals - Two Applications

Scenario	**PECsed (µg/kg) Step 3**
D1 Ditch	325
D1 Stream	186
D2 Ditch	191
D2 Stream	113
D3 Ditch	3
D4 Pond	34
D4 Stream	13
D5 Pond	20
D5 Stream	4
D6 Ditch	14
R1 Pond	14
R1 Stream	9
R3 Stream	14
R4 Stream	16

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PEARL v3.3.3 Scenarios: Chateaudun, Hamburg, Jokionen, Kremsmünter,Okehampton, Piacenza, Porto , Seville,Thiva
Application rate	Crop: winter cereals Application Rate: 2 x 0.2 kg a.s./ha Application timing: 1st application: 15th March 2nd application: 1st June Crop Interception: 50% for the 1st application and 90% for the 2nd application

Input data for bromuconazole

Variable	Bromuconazole
	Value
$DegT_{50}$ soil (days)	219 day at 20°C and pF2*
Koc (mL/g)	757
Freundlich coefficient	0.82
Vapour pressure (Pa) at 25°C	$4\ 10^{-6}$
Water Solubility (mg/L) at 20°C	49
Molecular Weight (g/mol)	377.1
Plant Uptake Value	0.5
Q10	2.2
Walker equation coefficient	0.7

*geomean of seven field studies, each normalized to 20°C and pF 2 as reported in study **B.8.1.3.1** (Jarvis T., 2009)
ideally a value of 228 days should have been used.

80th percentile PEC gw for the 9 Focus scenarios (µg/L)

Scenario	PEC (µg/L)
Chateaudun	<0.000001
Hamburg	<0.000001
Jokioinen	<0.000001
Kremsmunster	<0.000001
Okehampton	<0.000001
Piacenza	0.000003
Porto	<0.000001
Seville	<0.000001
Thiva	<0.000001

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

Direct photolysis in air ‡	Not required
Quantum yield of direct phototransformation	Not required
Photochemical oxidative degradation in air ‡	estimated half life in atmosphere = 16.5 hr or 1.4 d (Atkinson calculation using global OH-concentration of 5.0 x 10^5 OH radicals/cm^3 and 12 hours irradiation per day)
Volatilization ‡	from plant surfaces: a.s. volatilization is negligible 24 hours after application
	from soil: a.s. volatilization is negligible 24 hours after application

PEC (air)

Method of calculation	Not required

$PEC_{(a)}$

Maximum concentration	Not required

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil: bromuconazole Water (GW and SW): bromuconazole Sediment: bromuconazole Air: bromuconazole

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

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	R53

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 ‡				
Anas platyrhynchos	bromuconazole	acute	> 2150	-
Colinus virginianus	bromuconazole	acute	> 2150	-
Anas platyrhynchos	bromuconazole	short-term	> 684	**> 5000**
Colinus virginianus	bromuconazole	short-term	**> 778**	**> 5000**
Coturnix coturnix japonica	bromuconazole	long-term	26.5	**250**
Mammals ‡				
Female rat	bromuconazole	acute	328	-
Rat	bromuconazole	long-term	1.3	-
Rat	bromuconazole	long-term	13.8	-
Rabbit	bromuconazole	long-term	12.5	-
Additional higher tier studies ‡				
Not required.				

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

Crop and application rate : wheat, 2 x 0.200 kg a.s./ha

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Large herbivorous bird (early)	acute	**12.5**	**172**	10
	short-term	**6.67**	**102**	10
	long-term	**3.54**	**7.5**	5
Insectivorous bird (early/late)	acute	**10.8**	**199**	10
	short-term	**6.03**	**113**	10
	long-term	**6.03**	4.4	5
Earthworm-eating bird	long-term	**0.30**	**86.6**	5
Fish-eating bird	long-term	**0.164**	**162**	5
Higher tier refinement (Insectivorous birds)				
(1) Refined risk assessment based on 4 focal species, refinement parameters FIR, residue level, PD values				
Phasianus colchicus and *Perdix perdix*	long-term	**0.28**	**94**	5
Corvus corone corone and *Sturnus vulgaris*	long-term	**0.37**	**71**	5

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Alauda arvensis	long-term	**1.20**	**22**	5
Emberiza calandra	long-term	**0.38**	**69**	5
(2) First tier long-term risk assessment including decline of residues on insects (f_{twa} = 0.53) according to EFSA Journal 2008				
Insectivorous bird (early/late)	long-term	**3.20**	**8.3**	5
Tier 1 (Mammals) TER calculation based on worst case endpoint NOAEL = 1.3 mg a.s./kg bw/day				
Small herbivorous mammal (early)	acute	**39.5**	8.31	10
	long-term	**11.2**	0.12	5
Insectivorous mammal (late)	acute	**1.76**	**186**	10
	long-term	**0.64**	2.03	5
Earthworm-eating mammal	long-term	**0.39**	**35**	5
Fish-eating mammal	long-term	**0.101**	**13**	5
Higher tier refinement (Herbivorous mammals)				
(1) Refined risk assessment based on measured residue value on leaves after 2 x 0.200 kg a.s./ha and ecotoxicologically relevant endpoint NOAEL = 13.8 mg a.s./kg bw/day.				
Small herbivorous mammal (early)	acute-term	**4.03**	**81.4**	10
(1) Refinement long-term risk for the herbivorous mammals was not considered acceptable by the experts during the meeting.				
Higher tier refinement (Insectivorous mammals)				
(1) First tier long-term risk assessment including decline of residues on insects (f_{twa} = 0.53) according to EFSA Journal 2008 and ecotoxicologically relevant endpoint NOAEL = 13.8 mg a.s./kg bw/day				
Insectivorous mammal (late)	long-term	**0.34**	**40.5**	5

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

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/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	bromuconazole	96 h (flow-through)	Mortality, LC_{50}	1.7 mg a.s./L **(mm)**

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Lepomis macrochirus	bromuconazole	96 h (flow-through)	Mortality, LC_{50}	**3.1 mg a.s./L (mm)**
Oncorhynchus mykiss	bromuconazole	21 d (flow-through)	Growth, NOEC	**0.21 mg a.s./L (mm)**
Pimephales promelas	bromuconazole	35 d (flow-through)	Growth, NOEC	0.065 mg a.s./L **(mm)**
Oncorhynchus mykiss	EXP 10064 B	96 h (semi-static)	Mortality, EC_{50}	**14 mg form/L** (2.69 mg a.s./L) **(nom)**
Oncorhynchus mykiss	EXP 10064 B	21 d (semi-static)	Growth, NOEC	**0.56 mg form/L** (0.11 mg a.s./L) **(nom)**
Aquatic invertebrate				
Daphnia magna	bromuconazole	48 h (flow-through)	Mortality, EC_{50}	**> 8.9 mg a.s./L** (mm)
Daphnia magna	bromuconazole	21 d (semi-static)	Reproduction, NOEC	**0.020 mg a.s./L** (mm)
Daphnia magna	EXP 10064 B	48 h (static)	Mortality, EC_{50}	0.43 mg form/L (0.083 mg a.s./L) (nom)
Daphnia magna	EXP 10064 B	21 d (semi-static)	Reproduction, NOEC	0.0056 mg form/L (0.0027 mg a.s./L) (nom)
Daphnia magna	SCAE 0307	48 h (static)	Mortality, EC_{50}	59.9 mg form/L (**11.2 mg a.s./L**) (nom)
Daphnia magna	SCAE 0307	21 d (semi-static)	Reproduction, NOEC	0.977 mg form/L (**0.183 mg a.s./L**) (nom)
Sediment dwelling organisms				
Chironomus riparius	bromuconazole	28 d (static) sediment-water	NOEC	**0.250 mg a.s./L** (nom) **3.125 mg a.s./kg** (nom)
Algae				
Pseudokirchneriella subcapitata	bromuconazole	96 h (static)	Biomass: E_bC_{50} (72 h) Growth rate: E_rC_{50} (72 h)	**> 3.3 mg a.s./L (nom)** **> 3.3 mg a.s./L (nom)**
Pseudokirchneriella subcapitata	bromuconazole	120 h (static)	Biomass: E_bC_{50} (72 h) Growth rate: E_rC_{50} (72 h)	0.061 mg a.s./L **(mm)** **0.169 mg a.s./L (mm)**
Anabaena flos-aquae	bromuconazole	120 h (static)	Biomass: E_bC_{50} (72 h) Growth rate: E_rC_{50} (72 h)	**0.395 mg a.s./L (mm)** **5.99 mg a.s./L (mm)**

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Pseudokirchneriella subcapitata	EXP 10064 B	120 h (static)	Biomass: E_bC_{50} (120 h) Growth rate: E_rC_{50} (24 h)	**8.3 mg form/L** (1.59 mg a.s./L) **(nom)** **15 mg form/L (2.88 mg a.s./L) (nom)**
Higher plant				
Lemna gibba	bromuconazole	14 d (static)	Fronds, EC_{50}	0.12 mg a.s./L **(initially measured)**
Microcosm or mesocosm tests				
Not required. Acceptable representative uses are shown for the majority of the FOCUS scenarios. However, risk mitigation measures are recommended at Member State level to reduce the chronic risk to *Daphnia magna*.				

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

EXP 10064 B: SC formulation containing 197.8 g/L bromuconazole (batch n° : OP 901120)
SCAE0307: SC formulation, 18.7% w/w (169.2 g/L bromuconazole), Bromuconazole 200 g/L SC consists of 2 pairs of isomers (9.87% LS850646 and 8.83% LS850647), batch n°: B8120010 1958. The applicant confirmed that this is the formulation to be marketed.
Both EXP 10064 B and SCAE 0307 are nonyl-free formulations

FOCUS Step1

FOCUS Step 2

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Toxicity Exposure Ratio˝s (TER˝s) for aquatic organisms exposed to bromuconazole in surface water for use in wheat (2 x 0.200 kg a.s./ha) based on FOCUS step 3 calculations

Test substance	Scena-rio	Water body type	Test species	Time-scale	End-point (mg a.s./L)	Buffer-zone	Max PEC_{SW}, (µg a.s./L)	TER	Annex VI Trigger value
bromuconazole	D 1	ditch	*Oncorhynchus mykiss*	96 h	1.7	1 m	6.455	263	100
	D 1	stream				1 m	4.041	421	100
	D 2	ditch				1 m	4.909	346	100
	D 2	stream				1 m	3.072	553	100
	D 3	ditch				1 m	1.105	1538	100
	D 4	pond				1 m	0.668	2545	100
	D 4	stream				1 m	1.350	1259	100
	D 5	pond				1 m	0.309	5502	100
	D 5	stream				1 m	0.967	1758	100
	D 6	pond				1 m	1.664	1022	100
	R 1	pond				1 m	0.272	6250	100
	R 1	stream				1 m	1.914	888	100
	R 3	stream				1 m	2.264	751	100
	R 4	stream				1 m	2.453	693	100
bromuconazole	D 1	ditch	*Pimephales promelas*	35 d	0.065	1 m	6.455	10	10
	D 1	stream				1 m	4.041	16	10
	D 2	ditch				1 m	4.909	13	10
	D 2	stream				1 m	3.072	21	10
	D 3	ditch				1 m	1.105	59	10
	D 4	pond				1 m	0.668	97	10
	D 4	stream				1 m	1.350	48	10
	D 5	pond				1 m	0.309	210	10
	D 5	stream				1 m	0.967	67	10
	D 6	pond				1 m	1.664	39	10
	R 1	pond				1 m	0.272	239	10
	R 1	stream				1 m	1.914	34	10
	R 3	stream				1 m	2.264	29	10
	R 4	stream				1 m	2.453	26	10

bromuconazole	D 1	ditch	*Daphnia magna*	48 h	> 8.9	1 m	6.455	> 1379	100
	D 1	stream				1 m	4.041	> 2202	100
	D 2	ditch				1 m	4.909	> 1813	100
	D 2	stream				1 m	3.072	> 2897	100
	D 3	ditch				1 m	1.105	> 8054	100
	D 4	pond				1 m	0.668	> 13323	100
	D 4	stream				1 m	1.350	> 6593	100
	D 5	pond				1 m	0.309	> 28803	100
	D 5	stream				1 m	0.967	> 9204	100
	D 6	pond				1 m	1.664	> 5349	100
	R 1	pond				1 m	0.272	> 32721	100
	R 1	stream				1 m	1.914	> 4650	100
	R 3	stream				1 m	2.264	> 3931	100
	R 4	stream				1 m	2.453	> 3628	100
bromuconazole	D 1	ditch	*Daphnia magna*	21 d	0.020	1 m	6.455	**3.10**	10
	D 1	stream				1 m	4.041	**4.95**	10
	D 2	ditch				1 m	4.909	**4.07**	10
	D 2	stream				1 m	3.072	**6.51**	10
	D 3	ditch				1 m	1.105	18	10
	D 4	pond				1 m	0.668	30	10
	D 4	stream				1 m	1.350	15	10
	D 5	pond				1 m	0.309	65	10
	D 5	stream				1 m	0.967	21	10
	D 6	pond				1 m	1.664	12	10
	R 1	pond				1 m	0.272	74	10
	R 1	stream				1 m	1.914	10	10
	R 3	stream				1 m	2.264	**8.83**	10
	R 4	stream				1 m	2.453	**8.15**	10
bromuconazole	D 1	ditch	*Pseudokirchneriella subcapitata*	120 h	0.061	1 m	6.455	**9.45**	10
	D 1	stream				1 m	4.041	15	10
	D 2	ditch				1 m	4.909	12	10
	D 2	stream				1 m	3.072	20	10
	D 3	ditch				1 m	1.105	55	10

	D 4	pond				1 m	0.668	91	10
	D 4	stream				1 m	1.350	45	10
	D 5	pond				1 m	0.309	197	10
	D 5	stream				1 m	0.967	63	10
	D 6	pond				1 m	1.664	37	10
	R 1	pond				1 m	0.272	224	10
	R 1	stream				1 m	1.914	32	10
	R 3	stream				1 m	2.264	27	10
	R 4	stream				1 m	2.453	25	10
bromuconazole	D 1	ditch	*Chironomus riparius*	28 d	0.250	1 m	6.455	39	10
	D 1	stream				1 m	4.041	62	10
	D 2	ditch				1 m	4.909	51	10
	D 2	stream				1 m	3.072	81	10
	D 3	ditch				1 m	1.105	226	10
	D 4	pond				1 m	0.668	374	10
	D 4	stream				1 m	1.350	185	10
	D 5	pond				1 m	0.309	809	10
	D 5	stream				1 m	0.967	259	10
	D 6	pond				1 m	1.664	150	10
	R 1	pond				1 m	0.272	919	10
	R 1	stream				1 m	1.914	131	10
	R 3	stream				1 m	2.264	110	10
	R 4	stream				1 m	2.453	102	10
bromuconazole	D 1	ditch	*Lemna gibba*	14 d	0.12	1 m	6.455	19	10
	D 1	stream				1 m	4.041	30	10
	D 2	ditch				1 m	4.909	24	10
	D 2	stream				1 m	3.072	39	10
	D 3	ditch				1 m	1.105	109	10
	D 4	pond				1 m	0.668	180	10
	D 4	stream				1 m	1.350	89	10
	D 5	pond				1 m	0.309	388	10
	D 5	stream				1 m	0.967	124	10
	D 6	pond				1 m	1.664	72	10
	R 1	pond				1 m	0.272	441	10
	R 1	stream				1 m	1.914	63	10
	R 3	stream				1 m	2.264	53	10
	R 4	stream				1 m	2.453	49	10

Toxicity Exposure Ratio"s (TER"s) for aquatic organisms exposed to bromuconazole in sediment for use in wheat (2 x 0.200 kg a.s./ha) based on FOCUS step 3 calculations

Test substance	Scena-rio	Water body type	Test species	Time-scale	End-point (mg a.s./kg)	Buffer-zone	Max PEC_{SED}, (µg a.s./kg)	TER	Annex VI Trigger value
bromuconazole	D 1	ditch	*Chironomus riparius*	28 d	3.125	1 m	72.808	43	10
	D 1	stream				1 m	41.666	75	10
	D 2	ditch				1 m	42.619	73	10
	D 2	stream				1 m	25.298	124	10
	D 3	ditch				1 m	0.780	4006	10
	D 4	pond				1 m	7.674	407	10
	D 4	stream				1 m	2.877	1086	10
	D 5	pond				1 m	4.477	698	10
	D 5	stream				1 m	0.986	3169	10
	D 6	pond				1 m	3.041	1028	10
	R 1	pond				1 m	3.061	1021	10
	R 1	stream				1 m	1.945	1607	10
	R 3	stream				1 m	3.123	1001	10
	R 4	stream				1 m	3.578	873	10

Toxicity Exposure Ratio"s (TER"s) for aquatic organisms exposed to bromuconazole in sediment for use in wheat (2 x 0.200 kg a.s./ha) based on worst-case accumulation plateau PECsed following repeated use over many years

Test substance	Scena-rio	Water body type	Test species	Time-scale	End-point (mg a.s./kg)	Buffer-zone	Max PEC_{SED}, (µg a.s./kg)	TER	Annex VI Trigger value
bromuconazole	D 1	ditch	*Chironomus riparius*	28 d	3.125	1 m	325	**9.62**	10
	D 1	stream				1 m	186	17	10
	D 2	ditch				1 m	191	16	10
	D 2	stream				1 m	113	28	10
	D 3	ditch				1 m	3	1042	10
	D 4	pond				1 m	34	92	10
	D 4	stream				1 m	13	240	10
	D 5	pond				1 m	20	156	10
	D 5	stream				1 m	4	781	10
	D 6	pond				1 m	14	223	10
	R 1	pond				1 m	14	223	10
	R 1	stream				1 m	9	347	10
	R 3	stream				1 m	14	223	10
	R 4	stream				1 m	16	195	10

Toxicity Exposure Ratio"s (TER"s) for aquatic organisms exposed to formulations containing bromuconazole in surface water for use in wheat (2 x 0.200 kg a.s./ha) based on FOCUS step 3 calculations

Test substance	Scena-rio	Water body type	Test species	Time-scale	End-point (mg a.s./L)	Buffer-zone	Max PEC_{SW}, (µg a.s./L)	TER	Annex VI Trigger value
EXP 10064 B	D 1	ditch	*Oncorhynchus mykiss*	96 h	2.69	1 m	6.455	417	100
	D 1	stream				1 m	4.041	666	100
	D 2	ditch				1 m	4.909	548	100
	D 2	stream				1 m	3.072	876	100
	D 3	ditch				1 m	1.105	2434	100
	D 4	pond				1 m	0.668	4027	100
	D 4	stream				1 m	1.350	1993	100
	D 5	pond				1 m	0.309	8706	100
	D 5	stream				1 m	0.967	2782	100
	D 6	pond				1 m	1.664	1617	100
	R 1	pond				1 m	0.272	9890	100
	R 1	stream				1 m	1.914	1405	100
	R 3	stream				1 m	2.264	1188	100
	R 4	stream				1 m	2.453	1097	100
EXP 10064 B	D 1	ditch	*Oncorhynchus mykiss*	21 d	0.11	1 m	6.455	17	10
	D 1	stream				1 m	4.041	27	10
	D 2	ditch				1 m	4.909	22	10
	D 2	stream				1 m	3.072	36	10
	D 3	ditch				1 m	1.105	100	10
	D 4	pond				1 m	0.668	165	10
	D 4	stream				1 m	1.350	81	10
	D 5	pond				1 m	0.309	356	10
	D 5	stream				1 m	0.967	114	10
	D 6	pond				1 m	1.664	66	10
	R 1	pond				1 m	0.272	404	10
	R 1	stream				1 m	1.914	57	10
	R 3	stream				1 m	2.264	49	10
	R 4	stream				1 m	2.453	45	10
EXP 10064 B	D 1	ditch	*Daphnia magna*	48 h	0.43	1 m	6.455	67	100
	D 1	stream				1 m	4.041	106	100
	D 2	ditch				1 m	4.909	88	100
	D 2	stream				1 m	3.072	140	100
	D 3	ditch				1 m	1.105	389	100

	D 4	pond				1 m	0.668	644	100
	D 4	stream				1 m	1.350	319	100
	D 5	pond				1 m	0.309	1392	100
	D 5	stream				1 m	0.967	445	100
	D 6	pond				1 m	1.664	258	100
	R 1	pond				1 m	0.272	1581	100
	R 1	stream				1 m	1.914	225	100
	R 3	stream				1 m	2.264	190	100
	R 4	stream				1 m	2.453	175	100
SCAE0307	D 1	ditch	*Daphnia magna*	48 h	11.20	1 m	6.455	1735	10
	D 1	stream				1 m	4.041	2772	10
	D 2	ditch				1 m	4.909	2282	10
	D 2	stream				1 m	3.072	3646	10
	D 3	ditch				1 m	1.105	10136	10
	D 4	pond				1 m	0.668	16766	10
	D 4	stream				1 m	1.350	8296	10
	D 5	pond				1 m	0.309	36246	10
	D 5	stream				1 m	0.967	11582	10
	D 6	pond				1 m	1.664	6731	10
	R 1	pond				1 m	0.272	41176	10
	R 1	stream				1 m	1.914	5852	10
	R 3	stream				1 m	2.264	4947	10
	R 4	stream				1 m	2.453	4566	10
SCAE0307	D 1	ditch	*Daphnia magna*	21 d	0.183	1 m	6.455	28	10
	D 1	stream				1 m	4.041	45	10
	D 2	ditch				1 m	4.909	37	10
	D 2	stream				1 m	3.072	60	10
	D 3	ditch				1 m	1.105	166	10
	D 4	pond				1 m	0.668	274	10
	D 4	stream				1 m	1.350	136	10
	D 5	pond				1 m	0.309	592	10
	D 5	stream				1 m	0.967	189	10
	D 6	pond				1 m	1.664	110	10
	R 1	pond				1 m	0.272	673	10
	R 1	stream				1 m	1.914	96	10
	R 3	stream				1 m	2.264	81	10
	R 4	stream				1 m	2.453	75	10

EXP 10064 B	D 1	ditch	*Pseudokirchneriella subcapitata*	120 h	8.3	1 m	6.455	1286	10
	D 1	stream				1 m	4.041	2054	10
	D 2	ditch				1 m	4.909	1691	10
	D 2	stream				1 m	3.072	2702	10
	D 3	ditch				1 m	1.105	7511	10
	D 4	pond				1 m	0.668	12425	10
	D 4	stream				1 m	1.350	6148	10
	D 5	pond				1 m	0.309	26861	10
	D 5	stream				1 m	0.967	8583	10
	D 6	pond				1 m	1.664	4988	10
	R 1	pond				1 m	0.272	30515	10
	R 1	stream				1 m	1.914	4336	10
	R 3	stream				1 m	2.264	3666	10
	R 4	stream				1 m	2.453	3384	10

EXP 10064 B : SC formulation containing 197.8 g/L bromuconazole (batch n° : OP 901120)
SCAE 0307 : SC formulation, 18.7% w/w (169.2 g/L bromuconazole), Bromuconazole 200 g/L SC consists of 2 pairs of isomers (9.87% LS850646 and 8.83% LS850647), batch n°: B8120010 1958

FOCUS Step 4

Toxicity Exposure Ratio¨s (TER¨s) for aquatic organisms exposed to bromuconazole in surface water for use in wheat (2 x 0.200 kg a.s./ha) based on FOCUS step 4 calculations

Test substance	**Scena-rio**	**Water body type**	**Test species**	**Time-scale**	**End-point (mg a.s./L)**	**Buffer-zone**	**Max PEC_{SW}, (µg a.s./L)**	**TER**	**Annex VI Trigger value**
bromuconazole	D 1	ditch	*Daphnia magna*	21 d	0.020	10 m	6.455	**3.10**	10
	D 1	stream				10 m	4.041	**4.95**	10
	D 2	ditch				10 m	4.909	**4.07**	10
	D 2	stream				10 m	3.072	**6.51**	10
	R 3	stream				10 m	1.304* (2.263)	15 **(8.84)**	10
	R 4	stream				10 m	1.117* (2.453)	18 **(8.15)**	10
bromuconazole	D 1	ditch	*Pseudokirchneriella subcapitata*	120 h	0.061	10 m	6.455	**9.45**	10

* includes spray drift and run-off mitigation. Values in parentheses are spray drift mitigation only

Bioconcentration				
	bromuconazole	eta-bolite 1	eta-bolite 2	eta-bolite3
$logP_{O/W}$	**3.24**	-	-	-
Bioconcentration factor (BCF)[1] ‡	*** 131 (whole fish)**	-	-	-
Annex VI Trigger for the bioconcentration factor	**100**	-	-	-
Clearance time (days) (CT_{50})	**0.401 (whole fish)**	-	-	-
(CT_{90})	**1.332 (whole fish)**	-	-	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	**3 % residues in whole fish after 21 d depuration, glucuronide conjugates of a hydroxylated derivate of bromuconazole**	-	-	-

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

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)
bromuconazole ‡	> 100 µg a.s./bee	> 500 µg a.s./bee
Field or semi-field tests		
Higher tier testing is not necessary, since the hazard quotients of bromuconazole for oral and contact toxicity are below 50. However, acceptable cage studies were conducted. Application of the test substance Granit on a crop of flowering *Phacelia* in a flight cage resulted in different effects on the honeybee in both replications. In the 1st replication only a short-term decrease of flight intensity was observed after application of the test substance. In the 2nd replication the mortality in the test substance cage after application was slightly higher than in the water treated control variant. However, no acute intoxication was noted. According to the results obtained in this study Granit can be rated as harmless to bees. Two additional cage studies were submitted by the notifier. The references are Stute (1991) and Schultz (1992). These studies are comparable with the former cage studies, although not much detail is given. In the first study (Stute, 1991) the application rate was 2.0 L Granit in 200 L water/ha for each of the two applications. The tent size was 12 m² and the crop was *Phacelia*. The application caused no perturbation of foraging behaviour. No increased mortality or adverse effects on bee-brood were seen. In the second study (Schultz, 1992) the application rate was 1.0 L Granit in 200–400 L water/ha for each of the two applications. The tent size was 12 m² and the crop was *Phacelia*. A slight increase in mortality was observed at the end of the observation period after the second application.		

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

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

Crop and application rate : wheat, 2 x 0.200 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
bromuconazole	contact	**2**	50
	oral	**0.4**	50

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

Laboratory tests with standard sensitive species
No such tests were performed.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ ha)[1,2]	Endpoint	% effect[3]	Trigger value
Laboratory tests						
Aphidius rhopalosiphi	adults	EXP 10064 E, glass plates, 48 h + 10 d	13 g a.s./ha, initial	Corrected mortality Reproduction	20.0 % + 1.2 %	50 % 50 %
			260 g a.s./ha, initial	Corrected mortality Reproduction	45.7 % + 74.4 %	50 % 50 %
Typhlodromus pyri	proto-nymphs	EXP 10064 E, glass plates, 7 d + 7 d	13 g a.s./ha, initial	Corrected mortality Reproduction	9.41 % - 6.2 %	50 % 50 %
			260 g a.s./ha, initial	Corrected mortality Reproduction	92.94 % -	50 % 50 %
Poecilus cupreus	adults	EXP 10592 A, sand, 14 d	591 g a.s./ha, initial	Corrected mortality Food consumption	0.0 % - 6.5 %	50 % 50 %
Coccinella septempunc-tata	larvae	EXP 10064 E, glass plates, 16 – 27 d	13 g a.s./ha, initial	Corrected mortality Reproduction	6.5 % - 67.7 %	50 % 50 %
			260 g a.s./ha, initial	Corrected mortality Reproduction	60.9 % + 278 %	50 % 50 %
Chrysoperla carnea	larvae	EXP 10064 A, glass plates, 2 - 3 weeks	200 g a.s./ha	Corrected mortality Reproduction	23.4 % + 2.8 %	50 % 50 %
Extended laboratory tests						
Coccinella septempunc-tata	larvae	Granit, bean leaves, 14 d	11.94 g a.s./ha, initial	Corrected mortality Reproduction	- 5.4 % - 61.7 %	50 % 50 %
			119 g a.s./ha, initial	Corrected mortality Reproduction	- 2.7 % - 93.6 %	50 % 50 %
			191 g a.s./ha, initial	Corrected mortality Reproduction	- 8.1 % - 66.0 %	50 % 50 %
			239 g a.s./ha, initial	Corrected mortality Reproduction	- 2.7 % + 19.1 %	50 % 50 %

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ ha)[1,2]	Endpoint	% effect[3]	Trigger value
Typhlodromus pyri	proto-nymphs	Bromucona-zole SC, bean leaves, 14 d	15.625 g a.s./ha, initial	Corrected mortality Reproduction	4 % - 22.5 %	50 % 50 %
			31.25 g a.s./ha, initial	Corrected mortality Reproduction	12 % + 11.3 %	50 % 50 %
			62.5 g a.s./ha, initial	Corrected mortality Reproduction	13 % - 12.3 %	50 % 50 %
			125 g a.s./ha, initial	Corrected mortality Reproduction	17 % - 38.0 %	50 % 50 %
			250 g a.s./ha, initial	Corrected mortality Reproduction	38 % - 25.4 %	50 % 50 %

[1] indicate whether initial or aged residues
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation
[3] indicate if positive percentages relate to adverse effects or not

Corrected mortality: positive values: adverse effects
Reproduction: negative values: adverse effects; positive values: no adverse effects
Food consumption: negative values: adverse effects; positive values: no adverse effects

EXP 10064 E: SC formulation containing 208 g/L bromuconazole (batch n° : OP 980605)
EXP 10592 A: EC formulation containing 197 g/L bromuconazole (batch n° : OP 940695)
EXP 10064 A: SC formulation containing 200 g/L bromuconazole (batch n° : OP 891015)
Granit (AE F125581 00 SC19 A 102): SC formulation containing 191 g/L bromuconazole (batch n°: OP 220689)

Field or semi-field tests
Not required. Laboratory and extended laboratory tests are available and no higher tier testing is required.

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			
Eisenia foetida	bromuconazole ‡	acute	**LC_{50} > 1000 mg a.s./kg soil dw** LC_{50corr} > 500 mg a.s./kg soil dw
Eisenia foetida	EXP 10064 B	acute	**LC_{50} = 1180 mg form/kg soil dw** **LC_{50corr} = 590 form/kg soil dw** LC_{50corr} = 117 mg a.s./kg soil dw
Eisenia foetida	bromuconazole ‡	chronic	**NOEC = 37.2 mg a.s./kg soil dw** $NOEC_{corr}$ = 18.6 mg a.s./kg soil dw
Other soil macro-organisms			
Not required. A litterbag test was performed.			

Test organism	Test substance	Time scale	End point[1]
Collembola			
Not required.			
Soil micro-organisms			
Nitrogen mineralisation	bromuconazole ‡	28 d	- 2.0 % effect at day 28 at 500 g a.s./ha, equivalent to 0.667 mg a.s./kg soil d.w.
	Granit	28 d (soil 1) 90 d (soil 2)	+ 20 % effect at day 28 at 2.0 kg a.s./ha, equivalent to 2.6 mg a.s./kg soil d.w. in sandy-clay loam (soil 1) - 15 % effect at day 90 at 2.0 kg a.s./ha, equivalent to 2.6 mg a.s./kg soil d.w. in clay loam (soil 2)
Carbon mineralisation	bromuconazole ‡	28 d	3.9 % effect at day 28 at 500 g a.s./ha, equivalent to 0.667 mg a.s./kg soil d.w.
	Granit	28 d (soil 1 and soil 2)	+ 2.4 % effect at day 28 at 2.0 kg a.s./ha, equivalent to 2.6 mg a.s./kg soil dw in sandy-clay loam (soil 1) - 7.5 % effect at day 28 at 2.0 kg a.s./ha, equivalent to 2.6 mg a.s./kg soil d.w. in clay loam (soil 2)
Field studies[2]			
A litterbag test was conducted. The application of 500 g bromuconazole/ha (as formulation Granit), equivalent to 0.67 mg a.s./kg soil, to straw had no significant adverse effect on organic matter decomposition under the tested field conditions over a 6 months post treatment period. This covers the plateau maximum PEC_{soil} of 0.232 mg a.s./kg soil (2 x 0.200 kg a.s./ha). Bromuconazole has no adverse effects on the nitrogen transformation and the carbon transformation in soil at an application rate of 500 g a.s./ha, equivalent to 0.667 mg a.s./kg dry soil, after 28 days. The formulation Granit has no adverse effects on the carbon transformation in a sandy-clay loam soil or in a clay-loam soil at concentrations up to 2.0 kg a.s./ha equivalent to 2.6 mg a.s./kg dry soil, after 28 days. The formulation Granit has no adverse effects on the nitrogen transformation at concentrations up to 2.0 kg a.s./ha equivalent to 2.6 mg a.s./kg dry soil in a sandy-clay loam soil after 28 days and in a clay-loam soil after 90 days. The studies cover the plateau maximum PEC_{soil} of 0.232 mg a.s./kg soil (2 x 0.200 kg a.s./ha).			

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

EXP 10064 B: SC formulation containing 197.8 g/L bromuconazole (batch n° : OP 901120)

Toxicity/exposure ratios for soil organisms

Crop and application rate : wheat, 2 x 0.200 kg a.s./ha

Test organism	Test substance	Time scale	PEC_{soil} [2] (mg a.s./kg soil dw)	TER	Trigger
Earthworms					
Eisenia foetida	**bromuconazole ‡**	**acute**	**0.232**	**>2156**	**10**
Eisenia foetida	**EXP 10064 B**	**acute**	0.232	**-504**	**10**
Eisenia foetida	**bromuconazole ‡**	**chronic**	0.232	**-80**	**5**

[1] to be completed where first Tier triggers are breached
[2] indicate which PEC soil was used (e.g. plateau PEC)

EXP 10064 B: SC formulation containing 197.8 g/L bromuconazole (batch n° : OP 901120)

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

Preliminary screening data

Effects of bromuconazole on non-target plants have never been evaluated in specific trials. However, bromuconazole has been intensively tested in non cereal crops over a number of years in a range of European countries : winter rape, sunflower, field peas, sugar beet, potato, carrot, and to a small extent top fruits and vines.

In winter rape, the crop safety was good in all trials at 200-250 g a.s./ha with 1 or 2 spring applications covering the beginning of stem elongation/pods formation growth stages. No plant growth regulator effect was found with early treatments.
In sunflower, no adverse effects were seen at 250 g a.s./ha after 2 applications in all situations with the first treatment done at capitul emergence.
In field peas, the selectivity at 200-250 g a.s./ha was always excellent with 2 applications, the first one starting early flowering.
In sugar beet, bromuconazole demonstrated a regulator effect on the development of the plants. Shortening of petioles and limbs, greener colour and more waffled aspect of the leaves were often observed after 1 application at 200 g a.s./ha. An increase of the sugar content and a better extractability rate were also generally observed but on the other hand the root yield was reduced.
In potato, greener leaves were observed after 2-3 applications at 200-400 g a.s./ha with short spray intervals of 10-12 days.
In carrot, no phytotoxicity was seen at 200-400 g a.s./ha with 2-4 sprays at 10-14 day intervals.
In top/stone fruits, bromuconazole was safe in all situations when used at 30-50 g a.s./ha. However, excessive numbers of applications and higher dose rates sometimes resulted in a plant growth response (shortened internodes) in apple trees.
In vines, bromuconazole was generally selective at 20 g a.s./ha. However, a plant growth regulator response typical to ergosterol biosynthesis inhibitor fungicides occurred occasionally. Effects were limited to a slight thickening and greening of leaves and tightening of bunches, they were variety dependant (caution should be taken with Carignan).

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (L form/ha)[2] vegetative vigour	ER_{50} (L form/ha)[2] emergence	Exposure[1] (L form/ha)[2]	TER	Trigger
All tested species	Granit Enerpar SC 200	> 1 L form/ha	-	0.025	40	5
corn, oats, oilseed rape, sunflower, soybean	Granit Enerpar SC 200	-	> 1 L form/ha	0.025	40	5
tomato	Granit Enerpar SC 200	-	0.616 L form/ha	0.025	24.6	5

[1] explanation of how exposure has been estimated should be provided (e.g. based on Ganzelmeier drift data)
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation

Ganzelmeier drift values: 90th percentile drift value for 2 applications at 1 m : 2.38 %

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

Test type/organism	End point
Activated sludge	EC_{50} (30 min) > 1000 mg a.s./L EC_{50} (3 h) > 1000 mg a.s./L
Pseudomonas sp	-

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

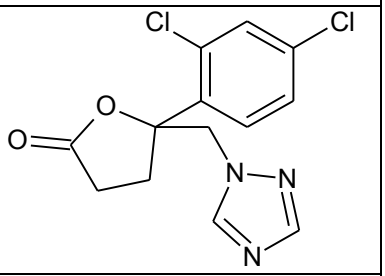
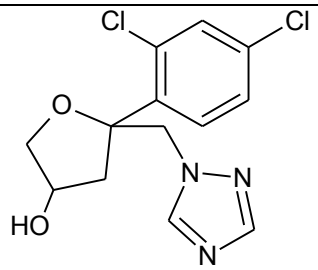
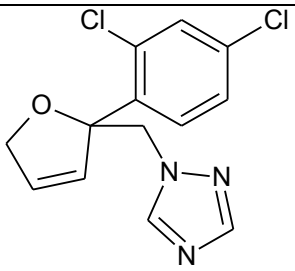
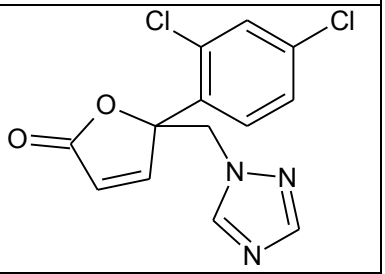
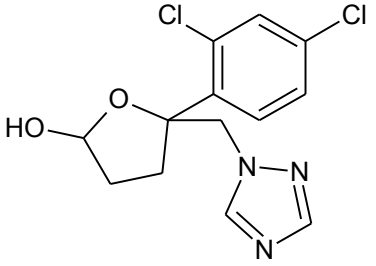
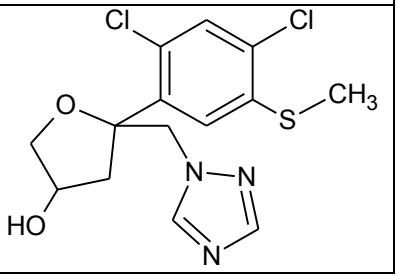
Compartment	
soil	bromuconazole
water	bromuconazole
sediment	bromuconazole
groundwater	bromuconazole

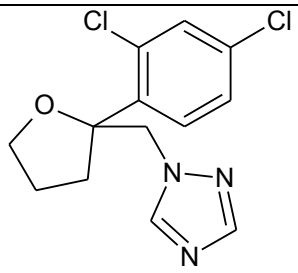
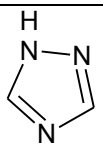
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	N, R50

	RMS/peer review proposal
Preparation	N, R50

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula*
LS 870353	(5*RS*)-5-(2,4-dichlorophenyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)dihydrofuran-2(3*H*)-one	
LS 860550/860551	1-[(2*RS*,4*RS*:2*RS*,4*SR*)-4-hydroxy-2-(2,4-dichlorophenyl)tetrahydrofurfuryl]-1*H*-1,2,4-triazole	
LS 860364	1-{[(2*RS*)-2-(2,4-dichlorophenyl)-2,5-dihydrofuran-2-yl]methyl}-1*H*-1,2,4-triazole	
RPA 401527	(5*RS*)-(2,4-dichlorophenyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)furan-2(5*H*)-one	
LS 850920	1-[(2*RS*,4*RS*:2*RS*,4*SR*)-5-hydroxy-2-(2,4-dichlorophenyl)tetrahydrofurfuryl]-1*H*-1,2,4-triazole	
RPA 406117	1-{(2*RS*,4*RS*:2*RS*,4*SR*)-4-hydroxy-2-[2,4-dichloro-5-(methylsulfanyl)phenyl]tetrahydrofurfuryl}-1*H*-1,2,4-triazole	

M4 LS871387	1-{[(2*RS*)-2-(2,4-dichlorophenyl)tetrahydrofuran-2-yl]methyl}-1*H*-1,2,4-triazole	
1,2,4-triazole	1*H*-1,2,4-triazole	

* ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DFR	dislodgeable foliar residue
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
ED	endocrine disruption
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FFLC	Full Fish Life Cycle
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use

g	gram
GAP	good agricultural practice
GC	gas chromatography
GC-ECD	gas chromatography with electron capture detector
GC-MS	gas chromatography-mass spectrometry
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MTD	Maximum Tolerated Dose
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity

NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
P	penetration factor
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TF	transfer factor
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell

WG	water dispersible granule
WHO	World Health Organisation
wk	week
WR	working rate
yr	year