CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance myclobutanil[1]

(Question No EFSA-Q-2009-00606)

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SUMMARY

Myclobutanil is one of the 79 substances of the third stage Part A of the review programme covered by Commission Regulation (EC) No 1490/2002.[2] This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Belgium being the designated rapporteur Member State submitted the DAR on myclobutanil in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 4 July 2005. The peer review was initiated on 29 March 2006 by dispatching the DAR for consultation of the Member States and the sole applicant Dow AgroSciences. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed on during a written procedure in October – November 2006. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in March 2007.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 14 November 2007 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide as proposed by the applicant which comprises air assisted broadcast spraying to table and wine grapes and apples in the fruit development stage, against powdery mildew, black rot and scab, in Northern and Southern Europe, up to a maximum 4 applications at a maximum individual application rate per spray of 48 g a.s./ha on grapes, and 90 g a.s./ha on apples, with an interval of 10 days between applications.

[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance myclobutanil. *EFSA Scientific Report* (2009) 298, 1-97

[2] OJ No L 224, 21.08.2002, p. 25, as amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

The representative formulated product for the evaluation was 'Systhane 20 EW', an emulsion, oil in water (EW) containing 200 g/L myclobutanil.

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. Adequate methods are available to monitor all compounds given in the respective residue definitions for monitoring. Residues in food of plant origin can be determined with a multi-method.

In mammals, myclobutanil LD_{50} is 1600 mg/kg bw (classification as **R22** "Harmful if swallowed" is proposed). It is not toxic via dermal and inhalation routes (LD_{50} >2000 mg/kg bw and LC_{50}>5.1 mg/L). Myclobutanil is not a skin irritant or a skin sensitiser. The European Chemicals Bureau (ECB) classified myclobutanil with **R36** ("Irritating to eyes"). The primary target organ following exposure to myclobutanil is the liver. Myclobutanil induces liver enlargement accompanied by slight induction of biotransformation enzymes (in rats and mice). An overall subchronic NOAEL of 100 ppm was proposed (3.09 mg/kg bw/day). Myclobutanil does not show any genotoxic potential. In long-term studies in rat, the target organ appeared to be the testes (bilateral testicular atrophy and aspermatogenesis). The relevant NOAEL for long-term toxicity is 2.5 mg/kg bw/day from the rat study. Myclobutanil did not show any carcinogenic potential. In a two-generation rat study, myclobutanil, at a dietary concentration of 1000 ppm (80 mg/kg bw/day) produced reduced parental body weight and liver effects and decreased weight gain in pups during lactation; at slight parental toxic doses the number of females delivering litters was reduced and the incidence of still-born pups increased. The relevant parental, offspring and reproductive NOAEL is 16 mg/kg bw/day. Myclobutanil is already classified as **Repr. Cat 3, R63** ("Possible risk of harm to the unborn child"). The relevant parental NOAEL is 94 mg/kg bw/day, while the relevant developmental NOAEL is 31 mg/kg bw/day. No indication of any other neurological effects was found in the toxicological studies. The proposed **Acceptable Daily Intake** (ADI) is based on the relevant NOAEL from the long-term rat study, applying a safety factor of 100, giving an **ADI of 0.025 mg/kg bw/day**. The **Acceptable Operator Exposure Level (AOEL) of 0.03 mg/kg bw/day** was agreed to be based on the overall NOAEL (90-day and 1-year in dog) of 3.09 mg/kg bw/day, with a safety factor of 100. The rat developmental toxicity study was considered as the most appropriate to use for setting the **Acute Reference Dose (ARfD)**. An NOAEL of 31.3 mg/kg bw/day was established due to embryotoxic effects (altered viability index). Based on this NOAEL and an assessment factor of 100 the proposed **ARfD is 0.31 mg/kg bw**. There is a 300-fold margin between the proposed ARfD and the LOAEL for developmental effects in the rat developmental toxicity study. The operator, worker and bystander exposure estimates showed levels below the AOEL even when no PPE is worn (German model).

The metabolism of myclobutanil was investigated in grapes, apples (representative uses) and additionally in wheat. In grapes and apples at harvest, the major components of the residue

were myclobutanil and its metabolite RH-9090[3] in free and conjugated form. A metabolic cleavage of the myclobutanil molecule which would generate triazole derivative metabolites was - in contrast to the wheat study - not observed in apples and grapes. Based on the available plant metabolism data for the categories fruit and cereals it was concluded that the metabolism is not comparable amongst different crop groups. As for the representative uses, however, it was agreed that the relevant residue for the category fruit crops should be defined as myclobutanil and its metabolite RH-9090 (free and conjugated). A sufficient number of residue trials in apples and grapes are available; however, there is still evidence required that the submitted trials cover the proposed residue definition. In processing studies it was investigated how the residue levels of myclobutanil and metabolite RH-9090 change when apples and grapes are processed to juice, wine, puree etc. However, a study investigating the effects of processing on the nature of the residues was identified as necessary since under processing conditions significant amounts of one or more degradation products, initially not present in the raw commodities, could be generated.

The investigation of residues in rotational and succeeding crops was considered not relevant since both apples and grapes are perennial crops that are usually not grown in rotation with other crops. However it was highlighted that in the long term the issue of potential uptake of triazole derivative metabolites could become relevant and should be followed up separately as this concern is not specific to the active substance myclobutanil alone but common to a number of triazole pesticides.

Since significant exposure of livestock to residues in feed may occur, a metabolism study in ruminants was triggered. The majority of the experts agreed that the level of identification was insufficient in the available study and thus a robust residue definition for food of animal origin could not be concluded on. Consequently, the relevance of the available feeding study for the assessment and likely necessary MRL proposals for food of animal origin can only be decided on when a residue definition has been concluded.

As a consequence of the identified data gaps, the consumer risk assessment with regard to the notified representative uses on apples and grapes cannot be finalised. Moreover, the risk assessment with regard to the two isomers of myclobutanil was not addressed.

It is noted that in addition to exposure from residues in food, the consumer could be exposed to residues of myclobutanil butyric acid,[4] a potential metabolite from ground water used as drinking water, but currently an assessment of the relevance of the metabolite and consequently of consumer risk is not available. An additional exposure to myclobutanil residues from groundwater used as drinking water can also not be excluded.

In soil under aerobic conditions myclobutanil exhibits high to very high persistence, forming the minor soil metabolite myclobutanil butyric acid (accounting for a maximum of 6% of

[3] RH-9090: (2*RS*,5*RS*) 2-(4-chlorophenyl)-5-hydroxy-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile
[4] myclobutanil butyric acid: (3*RS*) 3-(4-chlorophenyl)-3-cyano-4-(1*H*-1,2,4-triazol-1-yl)butanoic acid

applied radioactivity (AR)) which exhibits low to moderate persistence. Mineralisation of both the chlorophenyl and triazole rings to carbon dioxide was limited and accounted for only 0.2 to 1.7% AR after 120 days. The formation of unextractable residues was a sink, accounting for 4 to 16% AR after 120 days. Myclobutanil exhibits medium to low mobility in soil, myclobutanil butyric acid exhibits very high mobility in soil. There was no indication that adsorption of either myclobutanil or myclobutanil butyric acid was affected significantly by differing soil pH. Data on degradation in soil under anaerobic conditions are not available and it was considered they will be necessary to support the applied for use on apples in some territories of the EU.

In dark natural sediment water systems myclobutanil partitioned from the water column to sediment where it exhibited very high persistence. The terminal metabolite, CO_2, accounted for a maximum of 0.3% AR at 105 days (study end). Unextracted sediment residues were a sink but represented only 4.3 to 9.8% AR at study end. The necessary surface water and sediment exposure assessments were appropriately carried out using the agreed FOCUS scenarios approach for myclobutanil at steps 3 and 4, with spray drift mitigation being applied at step 4. These values are the basis for the risk assessment discussed in this conclusion.

On the basis of the available reliable information, it cannot be excluded that for the applied for intended uses, groundwater exposure by myclobutanil above the parametric drinking water limit of 0.1 µg/L, will not occur over a wide range of European geoclimatic conditions. In addition for the metabolite myclobutanil butyric acid, groundwater exposure above the parametric drinking water limit might be expected and it cannot be excluded that concentrations > 0.75µg/L (a key assessment trigger from the groundwater metabolite relevance guidance document) may occur. A groundwater metabolite non relevance assessment is therefore necessary for myclobutanil butyric acid but this assessment is not available.

The risk to birds and mammals was assessed as low except the long-term risk to herbivorous mammals from the use in apple orchards. A refined risk assessment applying interception factors of 65% and 70% resulted in a TER of 5.18 which is above the Annex VI trigger of 5. The risk of secondary poisoning from uptake of contaminated earthworms was assessed as low. A data gap was identified in the experts' meeting for the submission of a risk assessment for fish-eating birds and mammals since it was not possible to exclude that the $logP_{ow}$ of myclobunatil is >3. Myclobutanil is very toxic to aquatic invertebrates. The TERs based on FOCUS step 3 PEC_{sw} were above the Annex VI triggers for the representative use on grapes. For the use in apple orchards risk mitigation measures such as a no-spray buffer zone of 14 metres is required to achieve TERs above the Annex VI triggers. The assessment of the $logP_{ow}$ value was inconclusive. In the expert meeting a data gap for a bioconcentration study with fish was identified since four applications are foreseen and chronic and repeated exposure of fish is expected. The risk to bees, non-target arthropods, earthworms, other soil non-target macro-organisms, soil non-target micro-organisms, non-target plants and

biological methods of sewage treatment was assessed as low. It was identified that the risk assessment did not address the potential for different myclobutanil isomer ratios to be present in the environment.

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

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BACKGROUND

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

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 myclobutanil, hereafter referred to as the draft assessment report, to the EFSA on 4 July 2005. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the revised version of the draft assessment report was distributed for consultation on 29 March 2006 to the Member States and the main applicant Dow AgroSciences as identified by the rapporteur Member State.

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

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings in March 2007. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 14 November 2007 leading to the conclusions as laid down in this report.

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

In accordance with Article 11(4) of the Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the

same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix A.

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

- the comments received;
- the resulting reporting table (rev. 1-1 of 20 December 2006)

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

- the reports of the scientific expert consultation;
- the evaluation table (rev. 2-1 of 15 November 2007).

Given the importance of the draft assessment report including its addendum (compiled version of January 2009 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can be found in the original draft assessment report together with the peer review report, both of which are publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Myclobutanil is the ISO common name for (*RS*)-2-(4-chlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile (IUPAC).

Myclobutanil belongs to the class of conazole fungicides. Myclobutanil is a systemic fungicide with preventive, curative and eradicant properties. It is a sterol biosynthesis inhibitor, inhibiting primarily the C-14-demethylation step in the fungal sterol biosysnthesis pathway. The active substance is absorbed by the leaves and stems and is transported upward in the plant into areas of new growth via the xylem. Myclobutanil is used against powdery mildew, black rot and scab in horticulture and viticulture.

The representative formulated product for the evaluation was 'Systhane 20 EW', an emulsion, oil in water (EW) containing 200 g/L myclobutanil, registered under different trade names in Europe.

The representative uses evaluated comprise foliar spraying against powdery mildew (*Uncinula necator),* and black rot *(Guignardia bidwelli)* in table and wine grapes and against

scab (*Venturia inaequalis*) and powdery mildew (*Podosphaera leucotricha*) in apples at the fruit development stage, in all EU countries, up to a maximum four applications at a maximum individual application rate per spray of 48 g a.s./ha on grapes, respective 90 g a.s./ha on apples, with an interval of 10 days between applications.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of myclobutanil is 925 g/kg. The technical material is a racemic mixture (1:1). No FAO specifications exist.

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 myclobutanil or the respective formulation. The main data regarding the identity of myclobutanil and its physical and chemical properties are given in appendix A.

Adequate analytical methods are available for the determination of myclobutanil in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material. However the rapporteur Member State identified 1-methyl-2-pyrrolidinone as relevant impurity in the technical active substance, the experts of the PRAPeR 16 meeting concluded that the determination of the relevant impurity in the formulation was not required as the justification that it would not form during the manufacture of the formulation or during storage was accepted. However, the method may be a requirement at Member State level.

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

The German modular multi-method DFG S19 is suitable as an enforcement method for the determination of residues of myclobutanil in matrices of plant origin (apples, grapes) with a LOQ of 0.05 mg/kg.

Currently it is not deemed necessary to define a residue or propose MRLs for food of animal origin, however the German multi-residue method DFG S19 (extended revision) using GC-ECD allows the determination of metabolite RH-9090[5] in matrices of animal origin (milk, eggs, meat, liver and kidney) with a LOQ of 0.01 mg/kg.

Residues of myclobutanil in soil can be determined with the German multi-residue enforcement method DFG S19 using GC-ECD with a LOQ of 0.05 mg/kg.

[5] RH-9090: (2*RS*,5*RS*) 2-(4-chlorophenyl)-5-hydroxy-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile

HPLC-MS-MS methods are available for the determination of residues of myclobutanil in water (drinking water, groundwater, surface water) with a LOQ of 0.05 µg/L and in air with a LOQ of 0.7 µg/m³.

Analytical methods for residues for body fluids and tissues are not required since myclobutanil is not classified as toxic or very toxic.

Adequate methods are available to monitor all compounds given in the respective residue definitions where these have been finalised, i.e. myclobutanil in food of plant origin (apples, grapes), in soil, water and in air.

2. Mammalian toxicology

Myclobutanil was discussed in a meeting of experts in March 2007. Myclobutanil tested in toxicological studies was a racemic mixture. A general data gap was identified during the meeting: the information on the comparability of the toxicological studies performed with technical material of different purities was missing, as well as toxicological information on impurities. The point on the issue was still open after the meeting.

The applicant was requested to provide a case and/or data to show that the increased levels of two impurities (3 and 8) will not have a significant adverse effect on the toxicity of technical myclobutanil. Both impurities are present in the 'old' batches, as well as in the 'new' batches. Their amounts are increased. The rapporteur Member State considered that their increase is not of toxicological concern.

From the confidential part of the DAR it is evident that the increase of the impurities was reported for the technical specification of a purity of 92.5% compared to the batches with a lower purity. So far the meeting only considered the "old" batches with a lower purity, which varies from 79 to 93%.

The purity of the batches used in the new acute toxicity studies is 95.7%. No information is available on the impact of the impurities with regard to the toxicological parameters. The point could not be closed.

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

In rats and mice, myclobutanil is rapidly absorbed; comparing urinary excretion after oral and intravenous administration of a single low dose suggests that bioavailability is important in rats, reaching 100%. Therefore, no correction for oral absorption is required. Myclobutanil is widely distributed with high levels detected in liver, kidney, and intestine. No significant accumulation was seen after 96 hours from administration.

Metabolism is extensive; low levels of unchanged parent compound are detected in urine and faeces. There is no cleavage of the molecule and the major metabolic pathway involves oxidation of the butyl side chain. Most of an oral dose is eliminated in urine and faeces within 24 to 48 hours.

2.2. ACUTE TOXICITY

Myclobutanil LD_{50} is 1600 mg/kg bw. Classification as R22 "Harmful if swallowed" was proposed. It is not toxic via dermal and inhalation routes (LD_{50} > 2000 mg/kg bw and LC_{50} > 5.1 mg/L 4 h, nose only, highest obtainable concentration).

Myclobutanil is not a skin irritant or a skin sensitiser. The need of classification R36 "Irritating to eyes" was discussed in the experts' meeting. Based on the information available classification would not be necessary. However, it was noted that the European Chemicals Bureau (ECB) had already classified the substance with R36.

The applicant submitted a new acute toxicity package, available in the experts' meeting. Compared with the previous source the new source has a different level of purity. It was unclear whether the manufacturing process was changed. The results of the acute studies show lower toxicity. It was not clear whether the effects are related to the substance itself or the impurities. The previous source was proposed to be classified with Xn; R22, which does not apply any longer to the new source.

The meeting decided to consider only the 'old' source with the lower purity. Evidence of comparability between the old and the new sources has to be proven to have the new submitted studies considered. Therefore a data gap was proposed: information on the comparability of the toxicological studies performed with technical material of different purity is required, as well as toxicological information on impurities.

2.3. SHORT-TERM TOXICITY

The primary target organ following exposure to myclobutanil is the liver. Myclobutanil induces liver weight increase associated with hepatocellular hypertrophy, in rats, mice and dogs. Liver enlargement is accompanied by slight induction of biotransformation enzymes (in rats and mice only). Rats and mice appeared to be of comparable sensitivity towards myclobutanil. In the 90-day rat study, hepatocellular necrosis was evident at high doses. The relevance of liver effects in dogs (90-day and 1-year study) was discussed during the meeting. The two studies have been performed with different batches with different levels of purity. The liver weight increases between 9 and 52%. In the 90-day dog study the liver enzymes are not affected up to 1600 ppm although the liver weight increased. In both studies reduced body weight gain and decrease of food intake were observed at the highest dose levels (1600 ppm).

Taking into account the increased organ weight together with histological alterations (hepatocyte hypertrophy) at the level of 200 ppm in the 90-day dog study, the meeting

proposed to set the NOAEL at 10 ppm for the 90-day dog study and a NOAEL of 100 ppm for the 1-year dog study. An overall subchronic NOAEL of 100 ppm was proposed (corresponding to 3.09 mg/kg bw/day).

Skin irritation and/or gross and microscopic changes of the treated skin were observed after application of myclobutanil formulations at 100 mg/kg bw/day. The NOAEL for local effects is 10 mg/kg bw/day, whereas no systemic toxic effects were reported (NOAEL systemic toxicity 100 mg/kg bw/day).

2.4. GENOTOXICITY

Myclobutanil did not show any genotoxic potential in both *in vitro* and *in vivo* genotoxicity tests.

2.5. LONG-TERM TOXICITY

In male rats an increased incidence of testicular atrophy occurred bilaterally. These effects appeared clearly at the 12-month sacrifice. There was no increased incidence of neoplastic findings in any of the organs of treated animals. Liver changes consisted of minimal to moderate centrilobular to midzonal hepatocellular enlargement and vacuolisation. Bilateral aspermatogenesis occurred and was accompanied by hypospermia and cellular debris in the epididymides. In mice, liver effects consisted in hepatocellular necrosis, foci of altered hepatocytes and hepatocellular vacuolation.

The relevant NOAEL for long-term toxicity is 2.5 mg/kg bw/day from the rat study. Myclobutanil did not show any carcinogenic potential.

2.6. REPRODUCTIVE TOXICITY

In a two-generation rat study, myclobutanil produced reduced parental body weight and liver effects and decreased weight gain in pups during lactation; at slight parental toxic doses the number of females delivering litters was reduced and the incidence of still-born pups increased. In the meeting it was discussed whether the results, observed at high dose levels, justify classification with R62. Findings in the testes at the highest dose tested may be linked to aromatase inhibition. A decreased number of females delivering litters was also observed at the highest dose level tested. Systemic toxicity was observed at 200 ppm. The meeting agreed that these findings do not warrant the classification with R62. The relevant parental, offspring and reproductive NOAEL is 16 mg/kg bw/day.

A developmental rat study was conducted at doses ranging from 31 to 469 mg/kg bw/day. Fertility of females was not affected. Clinical signs of toxicity were observed in dams at 312 and 469 mg/kg bw/day. Viability index of foetuses was reduced at 93 mg/kg bw/day onwards with a concomitant increase in resorptions per litter and litters with more than 2 resorptions. It was noted that myclobutanil is already classified as Repr. Cat 3., R63 (“Possible risk of harm to the unborn child”). The relevant parental NOAEL is 94 mg/kg bw/day, while the relevant developmental NOAEL is 31 mg/kg bw/day.

2.7. NEUROTOXICITY

Myclobutanil does not have any potential to cause delayed neurotoxicity. Hence, no test of delayed neurotoxicity was required and none have been conducted. No indication of any other neurological effects was found in the toxicological studies.

2.8. FURTHER STUDIES

An oral acute toxicity study was carried out on two main metabolites of myclobutanil in plants (RH-9090 and RH-9089[6]) and on two impurities in myclobutanil. The most important metabolic route in plants is via production of RH-9090[7], which can further be transformed to RH-9089[8]. Both metabolites were major metabolites in the rat.

The relevance of metabolites RH-9090 and RH-9089 was discussed in the meeting. The metabolites RH-9090 and RH-9089 are major rat metabolites (>10%). The meeting agreed on the relevance, because of the parent toxicological properties. Their equivalent toxicity is not proven but it can be presumed they are in the same range of toxicity.

It was discussed whether the toxicity observed is more related to the metabolites or related to myclobutanil. Information on the amounts of metabolites occurring in the residues is needed and therefore confirmation from the PRAPeR experts' meeting on residues was required. The meeting on residues presented information about the residue levels. The rapporteur Member State considered that toxicological studies performed with the parent compound cover the toxicity of both metabolites. Taking into account the estimated consumer exposure via the residues in relation to their amount in the rat metabolism it was agreed that they do not pose any concern.

Acute oral toxicity of myclobutanil metabolites in plants and impurity RH-8812 was comparable to that of myclobutanil. RH-8813 was not classified for acute oral toxicity.

Myclobutanil butyric acid[9] would be expected to exceed 0.1µg/L (and concentrations might exceed 0.75µg/L) in vulnerable groundwater aquifers (see data gap discussed in section 4.2.2). In the DAR, no toxicological information or assessment is available.

2.9. MEDICAL DATA

The available medical surveillance data on manufacturing plant personnel working with myclobutanil, show no abnormalities to suggest adverse effects on health.

[6] RH-9089: (2*RS*) 2-(4-chlorophenyl)-5-oxo-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile
[7] Referenced also in the DAR as alcohol or M4
[8] Referenced also in the DAR as ketone or M3
[9] myclobutanil butyric acid: (3*RS*) 3-(4-chlorophenyl)-3-cyano-4-(1*H*-1,2,4-triazol-1-yl)butanoic acid.

Clinical cases and poisoning incidents have shown a range of symptoms common to chemical poisoning events, which include irritation of skin, eyes, nose or throat, nasal congestion, headaches, nausea and vomiting.

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

Acceptable daily intake (ADI)

The proposed ADI is based on the relevant NOAEL derived from the long-term rat study (NOAEL 2.5 mg/kg bw/day). An assessment factor of 100 was applied, giving an ADI of **0.025 mg/kg bw/day**.

Acceptable operator exposure level (AOEL)

In the experts' meeting the AOEL was discussed. It was agreed to base it on the overall NOAEL (90-day and 1-year dog) of 3.09 mg/kg bw/day, resulting in an AOEL of **0.03 mg/kg bw/day** with a safety factor of 100.

Acute reference dose (ARfD)

The rat developmental toxicity study was considered as the most appropriate to use for setting the ARfD. A NOAEL of 31.3 mg/kg bw/day was established in this study due to embryotoxic effects (altered viability index). Based on this NOAEL and an assessment factor of 100 the proposed ARfD is **0.31 mg/kg bw**. There is a 300-fold margin between the proposed ARfD and the LOAEL for developmental effects in the rat developmental toxicity study. The experts agreed on the value.

2.11. DERMAL ABSORPTION

The dermal absorption values proposed in the DAR for 'Systhane 20 EW' were 18% for the concentrate and 30% for the dilution. A new *in vitro* study with rat and human skin was submitted and the results were presented in an addendum to the DAR. A correction factor was not necessary for the concentrate, but for the dilution a correction factor of 2.7 was established. A recalculation of the values has been done during the meeting because the faecal excretion has not been considered in the first calculation. The revised values are 25% for the concentrate and 15% for the dilution.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The potential operator exposure was estimated for the intended use of 'Systhane 20 EW', an emulsion (oil in water) formulation containing 200 g/L myclobutanil. It is used as a fungicide, one or more applications per crop, per season during the fruit/grain growth/ripening of grapes and apples.

It was highlighted by the meeting on physical-chemical properties that the racemic mixture consists of two possible optic isomers in the ratio 50:50. This was not specifically considered by the mammalian toxicology meeting. The experts agreed that provided the racemic mixture

is stable then this concern is covered by the toxicological tests performed. To this aim a data gap was set after the PRAPeR experts meeting to address the impact of different isomer ratios on the exposure assessment of myclobutanil for operators, workers and bystanders.

Operator exposure

Applying a dermal absorption factor of 25% for the concentrate and 15% for the diluted formulation, and considering the AOEL established during the experts' meeting, the rapporteur Member State was asked to perform new calculations for operator, worker and bystander exposure (submitted in the addendum March 2007 and reported below).

Operator exposure estimates

	% of AOEL	
	No PPE	**PPE**
UK POEM model		
Grapes, orchard	34%	6.6%
Apples, orchard	39%	10%
German model		
Grapes, orchard	42%	30%
Apples, orchard	80%	56%

The operator exposure estimates showed levels below the AOEL of 0.03 mg/kg bw/day even when no PPE is worn.

EFSA note: During the commenting phase on the EFSA draft conclusion and during the evaluation meeting held in Parma on 14 and 15 November 2007, some inaccuracies have been highlighted for operator and worker exposure estimates (e.g. the re-calculations provided by the rapporteur Member State have been performed considering, for both UK POEM and German model, a treated area of 8 ha, which is not the standard proposed by the UK POEM. This would lead to an underestimation of the operator exposure). Therefore, after the meeting it was decided to revise calculations in order to provide the correct assessment. It is noted that re-calculations presented in the EFSA addendum does not change the final conclusion on the risk assessment, with regard to the safety of intended uses. The EFSA addendum is not peer reviewed.

The correct figures are as follows

Crop/application method	% of AOEL	
	No PPE worn	**PPE**
UK POEM model		
Grapes, orchard	160%	54.8% (gloves during M/L)
Apples, orchard	286%	75.1% (gloves during M/L and application)

German model		
Grapes, orchard	42%	-
Apples, orchard	80%	-

Conclusions: the estimated exposure levels for the operator are below the AOEL, without the use of PPE for the German model and with the use of PPE for the UK POEM.

Worker exposure

According to the rapporteur Member State the exposure of workers re-entering the field treated with 'Systhane 20 EW' was estimated to be 32% of the AOEL (Poppendorf, 1992).

EFSA note: in the Evaluation meeting it was noted that the refinement has not considered new parameters properly (in particular, the maximum dislodgeable foliar residue (DFR) has not been calculated according to the relevant application rate). However, even applying the correct DFR, the estimated exposure for the highest application rate (apples) represents the 61.7% of the AOEL (see EFSA addendum). It is noted the only the exposure occurring after 1 single application has been estimated.

Bystander exposure

Bystander exposure was considered to be brief and incidental, and estimated to be less than 1% of the AOEL. In the evaluation meeting, the UK reiterated that calculating bystander exposure according to the study by Lloyd *et al*. (1987) instead of Lloyd *et al*. (1983) would have provided a more precise figure.

3. Residues

Myclobutanil was discussed in the meeting of experts in Parma in March 2007 (PRAPeR 20, Round 4). Two addenda to the DAR were submitted. Of these, only the addendum of March 2007 was peer reviewed.

It is noted that myclobutanil consists of two optical isomers (enantiomers). It should also be noted that the methods of analysis used in all the residue studies were not stereoselective. Thus the regulatory dossier provides no information on the behaviour of each individual myclobutanil enantiomer in plants and livestock. Therefore all residues reported as myclobutanil in this conclusion are for the sum of the two enantiomers. It is not known if either isomer is metabolised or degraded more quickly than the other in the matrices studied.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of myclobutanil was investigated in grapes, apples (category fruit) and wheat (cereals) with myclobutanil ^{14}C-labelled in either the phenyl or triazole ring of the molecule. The notified representative uses are on grapes and apples. Foliar application was

made at a rate equivalent to the GAP supported for grapes or exaggerated (6.7 N) in terms of the GAP supported for apples. The PHI in the grape was shorter than the minimum PHI defined in the GAP while in the apple study the PHI was equivalent to GAP conditions.

In grapes and apples at harvest, the major components of the total radioactive residues (TRR) were parent myclobutanil (66% in grapes, 49% in apple), and the non conjugated and conjugated alcohol metabolite RH-9090 (together 15% in grapes and 35% in apple). A considerable amount of myclobutanil was recovered on/in the peel of the fruits as reflected by the results for the analysed pomace (72% in grape pomace, 56% in apple pomace). In contrary, in apple and grape juice the level of metabolite RH-9090 (including sugar conjugate) was increased (47% in grape juice, 68% in apple juice) when compared to the myclobutanil levels determined (26 to 33% in grape juice, 22 to 24% in apple juice). In both apple and grape the metabolite RH-9089 was detected as a minor metabolite (up to 4% TRR). No other metabolites were identified. The rate of identification of metabolites was considered satisfactory. No significant difference between the two labels with regard to the metabolite pattern was found.

Based on the results of the metabolism studies in apples and grapes it has been proposed that the metabolic pathway of myclobutanil in fruit proceeds mainly via the non-aromatic hydroxylation of the side-chain of myclobutanil to form the alcohol RH-9090. This metabolite is either further conjugated with sugar (glucoside, malonyl glucoside) or reduced to form the ketone RH-9089. None of the metabolites formed in apples and grapes was of particular toxicological concern as they were also found in rat metabolism.

Another route of degradation of myclobutanil seems to occur in cereals (wheat); however wheat is not a representative use. In addition to myclobutanil and metabolite RH-9090, present in important amounts in wheat grain and straw were triazolyl alanine[10] and triazolyl acetic acid.[11] This indicated a metabolic cleavage of myclobutanil at the phenethyl triazole linkage which lead to generation of the metabolite triazolyl alanine with further degradation to the metabolite triazolyl acetic acid. These metabolites are not specific to myclobutanil but to all triazole pesticides.

With regard to the triazole derivative metabolites: 1,2,4-triazole,[12] triazole alanine and triazole acetic acid, the PRAPeR meeting of experts in toxicology (PRAPeR 14) in January 2007 concluded that toxicological end points and reference values should be adopted as a result of their effect on reproduction and development.

Based on the myclobutanil metabolism studies available on the fruits and cereals categories, it is concluded that the metabolism is not comparable between the two crop groups.

[10] Triazolyl alanine: (2*RS*) 2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid; also referenced in the DAR as RH-3968 or TA
[11] Triazolyl acetic acid: 1*H*-1,2,4-triazol-1-ylacetic acid; also referenced in the DAR as RH-4098 or TAA
[12] 1,2,4-triazole: 1*H*-1,2,4-triazole; also referenced in the DAR as RH-0118

Specifically, triazole derivate metabolites were found in the wheat metabolism study, while triazole derivate metabolites were not found in the apples and grapes metabolism studies.

The experts in the meeting PRAPeR 20 agreed that a general residue definition covering all crops categories can not be proposed based on the available data. It was concluded that, if in the future new uses other than fruits and cereals will be envisaged, new metabolism studies might be necessary to particularly address potential occurrence of triazole derivate metabolites in those crops.

As metabolism studies are available for grapes and apples, it is considered that the broad category of fruit crop is sufficiently covered. Therefore, the residue definition has been proposed as:

myclobutanil, metabolite RH-9090 free and conjugated expressed as myclobutanil for risk assessment and,

myclobutanil alone for monitoring purposes.

The proposed definitions should be limited to the fruit crop category. A conversion factor could not be concluded as further clarification with regard to the analysed residue in the submitted residue trials is necessary (see next paragraph).

Although the critical GAP for both apples and grapes defines four applications, the older sets of the submitted residue trials in apple and grapes from Northern and Southern Europe (seasons 1986, 1996/97) were conducted using higher numbers of applications (6 to 12).

As it is agreed that the last application prior to harvest is the most critical in terms of the residue level in the harvested crop, it is expected that additional early season application prior to formation of the fruit would not contribute significantly to the residue level present at harvest from the four last applications at the end of the season. Therefore the submitted residue trials with a higher number of applications were considered to support the critical GAP. In addition more recent residue trials (2004) including also trials with four applications were submitted to supplement the trials with a higher application rate and to compare the results of the different sets of trials.

Myclobutanil and the metabolite RH-9090 are the residues analysed in the trials. All results are supported by acceptable storage stability data. However, the applicant should provide evidence that the submitted trials cover the residue definition, in particular with regard to conjugates. It should be demonstrated that the method used would extract all the conjugates and that the hydrolysis step in the method gives an acceptable yield.

Studies simulating representative processing conditions and investigating the behaviour of the relevant residues were not submitted. A data requirement was identified in the peer review since significant residue may occur in crops to be processed (apples, grapes). After the PRAPeR 20 meeting, a study on the effects of the nature of the residues was provided in

the addendum of June 2007, however this was not peer reviewed. Also studies on the effects of processing on the residue levels are available in apples and grapes. In these studies myclobutanil and RH-9090 residues were analysed in grape juice and wine and in apple juice, purée, cooked apple and pomace. A concentration of residues was found in apple pomace.

No data was submitted on processing of grapes to raisins.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Even though myclobutanil is highly to very highly persistent in soil (refer to section 4.1), the investigation of residues in succeeding crops was considered not relevant since both apples and grapes are perennial crops that are usually not grown in rotation with other crops. Any potential residue taken up from soil by the trees should most likely be myclobutanil.

The formed soil metabolite myclobutanil butyric acid was present only at low levels in soil and is therefore not considered a residue of concern for fruit crops. In year long laboratory soil incubation studies (see section 4.1.1) no 1,2,4-triazole was formed in the soil at detectable levels, but it cannot be excluded that it will be formed long term from continuous use of this compound and there may be uptake of this compound and or other 1,2,4-triazole derivatives. This issue of triazole metabolites concerns a number of active substances and will need to be followed up separately in the future.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Significant exposure of livestock to residues in feed may occur when fruit pomace is used in livestock diet, in particular in ruminant diet. Therefore, in a study with dairy cattle a mixture of myclobutanil and the two metabolites RH-9090 and RH-9089 was administered to lactating cows in order to reflect a possible exposure of ruminants to residues from treated crops. However, the ratio of compounds in the applied testing material does not reflect that occurring in fruit pomace, but it could be accepted as to the aim of a metabolism study. Myclobutanil was labelled on the phenyl ring and the metabolites were labelled on the triazole ring. The identification rate of residues was generally low (circa 50% in milk, circa 30% in liver, circa 40% in kidney; no identification in muscle and fat due to the low level of total residues). The majority of the experts in the PRAPeR 20 meeting agreed that the level of identification was insufficient and a robust residue definition for risk assessment and monitoring could not be concluded on the basis of the available data. Therefore, a new data gap was identified with regard to a ruminant metabolism study where the compound is labelled on both rings. Other points previously identified for discussion by experts have no longer been considered in the meeting since a new ruminant metabolism study is required.

Currently a residue definition in ruminant products can not be proposed.

It is noted that after the meeting of experts the rapporteur Member State indicated in a letter to EFSA (13 June 2007) their disagreement with the identified data gap for a ruminant metabolism study.

There was also a feeding study in cows with myclobutanil submitted. In this feeding study one of the compounds tested was the diol RH-0294[13] (erroneously referred to in the DAR as carboxylic acid). The relevance of this feeding study for the residues assessment can only be decided when an animal residue definition is concluded.

Apple and grapes products are not relevant feeding stuffs in poultry diet. Even though not required to support the representative uses, a study in laying hens was submitted and evaluated in the DAR. From a qualitative point of view, the metabolism in poultry is considered sufficiently investigated. Myclobutanil and two metabolites (RH-9090 and RH-9089) are likely to be the predominant components of the residue. Any contribution from triazole metabolites in the poultry diet will need to be considered in addition, if relevant for future uses.

With regard to the notified representative uses the experts at the meeting concluded that due to the data gap for the ruminant metabolism study a restriction could be proposed that fruit pomace from treated crops must not be fed to animals.

3.3. CONSUMER RISK ASSESSMENT

Currently the consumer risk assessment with regard to the notified representative uses is not finalised.

- It is not confirmed whether the available residue data include all compounds of the residue definition for risk assessment i.e. also the conjugated form of metabolite RH-9090.
- Consumer exposure from food of animal origin could not be considered due to lack of sufficient data.
- Data on the nature of residues in processed commodities was not submitted, but should be available. Significant amounts of one or more degradation products, initially not present in the raw commodities, may be generated under processing.
- Moreover, the nature of the final residue in plant and animal commodities was not studied with regard to the two isomers of myclobutanil. Thus it is not known if either isomer is metabolised or degraded more quickly and to which ratio of isomers consumers and livestock may be exposed. The experts in PRAPeR 20 agreed the applicant should address the consumer risk assessment with regard to the two the isomers of myclobutanil. It is noted that the rapporteur Member State disagrees with this data gap.

[13] RH-0294: (2*RS*,5*RS*) 2-(4-chlorophenyl)-5,6-dihydroxy-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile.

- Finally, the exposure and risk assessment does currently not consider the issue of triazole derivative metabolites. These metabolites may be present in animal products upon exposure to myclobutanil. It was also highlighted that in the long term, the issue of potential uptake of triazole derivative metabolites in crops in the orchard or vineyard could become relevant. The issue of triazole derivative metabolites should be followed up separately as this concern is not specific to the active substance myclobutanil alone but to a number of triazole pesticides.

A preliminary consumer risk assessment by the rapporteur Member State without consideration of the above listed issues indicated that the intake of residues from the use of myclobutanil in apples and grapes might be below the reference values (ADI, ARfD) both for the chronic and acute exposure. It is however stressed once more that a robust and peer reviewed assessment of the dietary risk for consumers linked to the use of myclobutanil is currently not available.

It is also noted that the myclobutanil butyric acid metabolite may leach to ground water at significant levels (refer to section 4.2.2: EFSA would expect the 0.1µg/L trigger to be exceeded in a majority of FOCUS scenarios and it could not be excluded that a concentration of >0.75µg/L would occur in some scenarios). Therefore, an additional exposure of consumers can be expected when ground water is used as drinking water. Moreover there are indications that also the active substance myclobutanil has the potential to contaminate groundwater (see 4.2.2). Currently no exposure assessment and risk assessment with regard to the residues in ground water is available.

3.4. PROPOSED MRLS

The proposed EU MRLs for apples and table/wine grapes are 0.5 mg/kg and 1 mg/kg respectively.

MRLs for products of animal origin are likely to be necessary but could not be concluded.

4. Environmental fate and behaviour

Myclobutanil was discussed at the PRAPeR experts' meeting for environmental fate and behaviour in March 2007 (PRAPeR 17). The fate and behaviour characteristics of the potential very minor soil metabolite 1,2,4-triazole (not identified in the available studies; a metabolite with the potential to be formed by several triazole moiety containing active substances) was discussed at the PRAPeR experts' meeting for environmental fate and behaviour in January 2007 (PRAPeR 12). It should also 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 myclobutanil enantiomer in the environment. Therefore all residues reported as myclobutanil in this conclusion are for the sum of the two enantiomers. It is not known if either isomer is degraded more quickly than the other in the environmental matrices studied.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Soil experiments (three different soils) were carried out under aerobic conditions in the laboratory (20°C, 40% maximum water holding capacity (MWHC)) in the dark with myclobutanil applied as test substance. The formation of residues not extracted by acidified acetonitrile:water were a sink for the applied chlorophenyl (one soil tested) and triazole ring-^{14}C-radiolabels (all three soils tested) which accounted for 4 to 16% of the applied radiolabel (AR) after 120 days. Mineralisation to carbon dioxide of the triazole ring-^{14}C-radiolabel accounted for only 0.2 to 1.6% AR, whilst for the chlorophenyl ring-^{14}C-radiolabel this value was 1.7% AR (both after 120 days). The most significant but minor (<10% AR) extractable breakdown product present was myclobutanil butyric acid (maximum 6% AR at 76 days). At 120 days (study end) myclobutanil still accounted for 80 to 92% of the applied radioactivity.

Data on anaerobic degradation in soil were not available. However these data are not necessary to complete an assessment for the applied for representative use on vines as the experts agreed that vines are unlikely to be cultivated under geoclimatic conditions where soils will become saturated and consequently anaerobic. However the experts considered this could not be excluded for the representative use on apples. The experts therefore identified a data gap for an anaerobic soil metabolism study to support the applied for use on apples.

Though a laboratory soil photolysis study was available there was agreement by the experts that the study was not reliable with respect to the amount of metabolites formed (identified metabolite accounted for a maximum of 4% AR) and the photolysis rate of degradation due to the low light energy and narrow wavelength range provided by the lamp in the experiment. They however felt that there was no reason to challenge the identification of the metabolite (RH-9089) characterised as being formed under the experimental conditions of the study. They also considered the fact that the myclobutanil molecule does not absorb light energy above 290nm to indicate direct soil photolysis will not occur, so the limited degradation observed in the available study would result from indirect photolytic processes which may not be a very reproducible phenomenon. In line with a PPR panel opinion[14] the experts agreed that due to the low light absorbance of the myclobutanil molecule, soil photolysis would not be expected to be a significant process contributing to the degradation of myclobutanil and consequently a new soil photolysis study was considered unnecessary.

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

The rate of degradation of myclobutanil was estimated from the results of the studies described in 4.1.1 above. DT_{50} were: 192 to 574 days (single first-order non-linear

[14] See page 9 of Opinion of the Scientific Panel on Plant protection products and their Residues on a request from the Commission related to the revision of Annexes II and III to Council Directive 91/414/EEC concerning the placing of plant protection products on the market - Fate and Behaviour in the Environment: The EFSA Journal (2007) 448, 1-17.

regression, 20°C 40% MWHC, three different soils). Laboratory rate of degradation experiments dosed with myclobutanil were available on a further three different soils. DT_{50} were: 191 to 354 days (single first-order non-linear regression, 22°C, percent MWHC not reported). After normalisation to FOCUS reference conditions[15] (20°C and -10kPa soil moisture content when the experimental soil moisture was reported), this range of single first-order DT_{50} becomes 164 to 515 days (geometric mean that is appropriate for use in FOCUS modelling 306 days). Clearly as the duration of these experiments was 120 to 161 days there is greater than usual uncertainty in these DT_{50} values since they are all extrapolated beyond the durations of these laboratory studies.

The minor (maximum 6% AR) soil degradation product of myclobutanil, myclobutanil butyric acid was applied as test substance to four soils and incubated in the laboratory (aerobic dark 25°C and 1/3 bar soil water holding capacity WHC for two soils and slightly below 1/3 bar WHC for the other two soils, note the fact that two of the soils had a lower moisture content was not reported in the DAR). Single first-order DT_{50} values from these studies were calculated to be 5 to 42 days (5, 7, 22 and 42 days). After normalisation to FOCUS reference conditions (20°C and -10kPa soil moisture content) these values were 7.3 to 36.7 days (7.3, 8.2, 23.6 and 36.7 days; geometric mean that is appropriate for use in FOCUS modelling 15.1 days). The experts at the meeting noted that in the experiment (LUFA 3A loam soil) dosed with myclobutanil (myclobutanil first-order DT_{50} 191 days) which had the maximum observed formation of myclobutanil butyric acid (6% AR), that the kinetic formation fraction of myclobutanil butyric acid from myclobutanil was ca. 60%.

From discussions at the PRAPeR 12 meeting in January 2007 it was identified that the potential (but very minor as not detected in the available appropriately radiolabelled studies) soil metabolite 1,2,4-triazole degrades in laboratory soil experiments with single first-order DT_{50} of 6 to 12 days (20°C 40% MWHC, three different soils, normalised to FOCUS reference conditions (20°C and -10kPa soil moisture content single first-order DT_{50} 5 to 10 days)). Because of this relatively rapid transformation rate compared to the breakdown rate of myclobutanil, soil residues of this metabolite would be expected to present at only very low levels.

Field soil dissipation studies (bare soil) were provided from four sites in Germany where applications were made at the end of May and the beginning of June. Using the residue levels of parent myclobutanil determined over the whole core sampled (0 to 20cm soil layer), DT_{50} were estimated to be 9 to 58 days with DT_{90} being greater than a year. Only at one study site had the residue declined to <10% of the initial measured concentration at the last sampling time (368 to 387 days after application). The pattern of degradation was clearly biphasic but calculated DT_{90} values were not presented in the DAR (only noted as being >1 year). In the addenda the results of normalising the field DT_{50} from these field trials to reference conditions of 20°C (but not soil moisture content) using the modified day length approach

[15] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

assuming first-order kinetics[16] and non-linear regression was reported. However the experts were not able to assess the goodness of fit resulting from this exercise, as plots of the decline curves were not provided in the addendum available to the experts attending the meeting. It was not clear to the experts if the normalisation procedure that resulted in the biphasic degradation pattern observed in the not normalised kinetic fitting subsequently became adequately described by first-order kinetics, as was assumed by the fitting procedure used. Only r^2 values were reported by the rapporteur Member State in the addendum to indicate how representative the estimated normalised first-order DT_{50} were and this not particularly robust measure of reliability of the estimated DT_{50} values, indicates that the fits may not be acceptable (low r^2 values 0.322, 0.696, 0.736 and 0.776). The experts agreed that it was not possible to use these normalised first-order field DT_{50} values as the basis of the environmental exposure estimate in the absence of a visual inspection of the fitted curves, to refute the indication given by the low r^2 values that these estimated DT_{50} were too unreliable. EFSA was subsequently able to confirm that the pattern of decline following normalisation (as graphically presented in the original study report[17]) was not well described by first-order kinetics and still showed a biphasic pattern of decline, as was suspected by the experts at the meeting.

In field accumulation studies carried out at one site in Germany (bare soil application) and one site in California (air assisted broadcast spray applications to grapevines) concentrations increased following the first 2 and 3 years of applications respectively. Further applications in subsequent years did not result in any further accumulation.

The longest available laboratory myclobutanil single first-order soil DT_{50} of 574 days (highly extrapolated value) was agreed by the peer review for use in PEC_{soil} calculations, that included a calculation of accumulation as required for this persistent substance (as the pattern of biphasic decline observed in the field studies was not adequately characterised in the DAR).

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

The adsorption / desorption of myclobutanil was investigated in five soils in satisfactory batch adsorption experiments. Calculated adsorption K_{Foc} values varied from 226 to 920 mL/g, (mean 517 mL/g) (1/n 0.85 to 0.91, mean 0.88). There was no evidence of a correlation of adsorption with pH.

The adsorption / desorption of myclobutanil butyric acid was investigated in four soils in satisfactory batch adsorptions experiments. Calculated adsorption K_{doc} values were 18 to 46

[16] as described in FOCUS (2006) "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration" Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference SANCO/10058/2005 version 2.0, 434 pp.

[17] Page 40, Reeves G., (2006) Modelling the leaching of myclobutanil and a potentially relevant metabolite (ß-4-chlorophenyl-ß-cyano-γ-(1*H*1,2,4-triazole)butyric acid) to groundwater in the EU using PEARL and the FOCUS scenarios. Report No: GHE-P-11416.

mL/g (mean 36 mL/g). There was no clear evidence of a correlation of adsorption with pH, though the only alkaline soil investigated (pH 7.8) had the lowest adsorption value. The experts accepted in this case to use the mean value (36 mL/g) in leaching modelling as adsorption values in all the soils is relatively low.

From discussions at the PRAPeR 12 meeting in January 2007 it was identified that the potential (but very minor, not detected in the available appropriately radiolabelled studies) soil metabolite 1,2,4-triazole has K_{Foc} values estimated from satisfactory batch adsorption experiments in four soils of 43 to 120 mL/g, (mean 89 mL/g) (1/n 0.83 to 1.02, mean 0.92). There was no evidence of a correlation of adsorption with pH.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Myclobutanil was essentially stable under sterile hydrolysis conditions at 50°C at pH 4, 7 and 9. Myclobutanil will not undergo direct aqueous photolysis as there is no significant absorption by the molecule at wavelengths ≥ 290 nm.

A ready biodegradability test (OECD 301D) indicated that myclobutanil is 'not readily biodegradable' using the criteria defined by the test.

In water-sediment studies (two systems studied at 20°C in the laboratory) myclobutanil dissipated by partitioning to sediment (observed water decline single first-order DT_{50} 4 days where sediment organic carbon content (OC) was 3.18% and 20 days where sediment OC content was 0.62%). Subsequent degradation in sediment was slow (whole system single first-order DT_{50} was 415 days for the lower OC system and 838 days in the higher OC system, both estimates are uncertain as they are extrapolated significantly beyond the study duration of 105 days, mean value 626 days). No single metabolite (five resolved by chromatography) accounted for >4.7% AR in either the water or sediment compartment of the experiment. None were identified. The terminal metabolite, CO_2, accounted for only 0.3% AR of the triazole ring radiolabel by 105 days. Residues not extracted from sediment by acidified acetonitrile and Soxhlet extraction were a sink representing 4.3 to 9.8% AR at study end (105 days), though of course the major sink for the applied radioactivity was parent myclobutanil extracted from the sediment. The experts agreed that for sediment a myclobutanil single first-order DT_{50} of 626 days (mean whole system values) and for water a default value of 999 days were acceptable for use as FOCUSsw scenario calculation input. They also agreed the calculation for accumulated concentrations in sediment as set out in the addendum that also used a sediment DT_{50} of 626 days.

PEC surface water to static water bodies from just spray drift were presented in the DAR. These were not appropriate for use in the EU level assessment that requires FOCUS surface water approaches to be used.

For myclobutanil, FOCUS surface water modelling was evaluated up to step 3 for the use on grape vines (late growth stages highest potential for spray drift) and steps 3 (pond scenarios) and 4 (stream and ditch scenarios) for the use on apples (early growth stages highest potential for spray drift). The peer review noted that the soil DT_{50} used in calculations (282 days) was shorter than the available reliable lab data indicate is appropriate (306 days) but concluded that this would not effect the PEC values as the pesticide application timer (PAT) algorithm ensures drainage and runoff events occur shortly after application and the exposure is driven by spray drift and not myclobutanil moving from soil. The peer review therefore agreed these PEC surface water as presented in the updated DAR for multiple applications and in the addendum for single applications (where this was the highest calculated value) were appropriate for use in risk assessment (in line with FOCUS guidance). At step 4 (apple use) the only mitigation considered was no spray drift buffer zones of 12 and 14 m that were implemented following the methods prescribed by FOCUSsw guidance. For sediment PEC the accumulated concentrations from the defined number of applications per year and use in successive years were calculated in the addendum using FOCUS step 3 default buffer distances for both vines and apples for the FOCUS scenarios that gave the highest PEC_{sed} (apples D4 pond and vines D6 ditch, see updated DAR). The peer review agreed these PEC_{sed} were appropriate for use in risk assessment and would encompass the expected sediment concentrations at all the other FOCUS scenarios.

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

The substance input parameters for groundwater modelling appropriate for use in FOCUS scenario groundwater modelling identified by the peer review from the available acceptable data are a myclobutanil single first-order DT_{50} 306 days (laboratory experiment derived value), K_{Foc} 517 mL/g, 1/n=0.88; myclobutanil butyric acid single first-order DT_{50} 15.1 days, kinetic formation fraction from myclobutanil of 0.6 (60%) and K_{doc} of 36 mL/g, 1/n=1. The meeting of experts maintained the data requirement for further FOCUS scenario groundwater exposure modelling to be provided as none of the available simulations used substance parameters considered comparable to these. In any new modelling it might be possible to utilise appropriate myclobutanil DT_{50} derived from field dissipation studies normalised to reference conditions, if the approach used was reported in a transparent way and strictly adhered to all pertinent FOCUS kinetics guidance recommendations (particularly those relating to handling the results from field experiments that indicate a biphasic pattern of disappearance). The experts' concerns regarding the currently available exercise to normalise field dissipation study DT_{50} values and reasons why the results of this exercise cannot be used for the assessment at the moment are already described in detail in section 4.1.2.

On the basis of the available groundwater simulations as described in the DAR and addendum that utilise more favourable substance property parameters than are appropriate[18]

[18] The more favourable values were a myclobutanil single first-order DT_{50} 282 or 250 days (laboratory), adsorption values as agreed by the peer review; myclobutanil butyric acid single first-order DT_{50} 14.5 days, kinetic formation fraction from myclobutanil of 0.06 (6%) and K_{doc} as agreed by the peer review, 1/n=0.9.

(most significantly myclobutanil DT_{50} that is too short and myclobutanil butyric acid kinetic formation fraction one tenth the appropriate value) the parent myclobutanil was calculated to be present in leachate leaving the top 1 m soil layer at 80th percentile annual average concentrations in the range <0.001 to 1.16 µg/L for apples with 7 out of 9 scenarios being >0.1 µg/L, and <0.001 to 0.517 µ/L for vines with 6 out of 7 scenarios being >0.1 µg/L. For myclobutanil butyric acid this range was <0.001 to 0.03 µg/L for apples and <0.001 to 0.021 µ/L for vines. Although these values for myclobutanil butyric acid are all < 0.1 µg/L, if an appropriate kinetic formation fraction had been used in simulations, EFSA would expect the 0.1 µg/L trigger to be exceeded in a majority of FOCUS scenarios and it could not be excluded that a concentration of >0.75 µg/L would occur in some scenarios.

As the potentially very minor soil metabolite 1,2,4-triazole was not detected in any of the soil route of degradation studies and it degrades relatively quickly compared to myclobutanil (see 4.1.2), it can be concluded that the potential for 1,2,4-triazole to reach groundwater from the application of myclobutanil is negligible.

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of myclobutanil ($1.98x10^{-4}$ Pa at 20°C) means that myclobutanil would be classified under the national scheme of The Netherlands as slightly volatile, indicating limited losses due to volatilisation might be expected. Based on the results of a laboratory wind tunnel experiment where a myclobutanil formulation were applied to a soil and dwarf runner beans, it was estimated that up to 2.6% of the myclobutanil applied was lost (assumed to the air compartment but only loss from the treated matrix was measured) from bean plants in 24 hours, losses from soil were negligible. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half life estimated at 7.6 hours (assuming an atmospheric hydroxyl radical concentration of $1.5x10^{6}$ radicals cm^{-3}) indicating the small proportion of applied myclobutanil that will volatilise would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

Myclobutanil was discussed at the PRAPeR experts' meeting for ecotoxicology in March 2007 (PRAPeR 18). Information on the composition of the batches used in the ecotox studies was missing and a data requirement was identified. Information on three batches out of ten was made available by the applicant before the expert meeting. The experts agreed to leave the data requirement open since information on the remaining seven batches was missing. Furthermore a data gap was identified for the submission of information on the ecotoxicological relevance of impurities 3, 8 and 14. In the risk assessment it was not specifically considered that myclobutanil is a racemic mixture. It should be noted that this adds some unquantified uncertainty to the outcome of the risk assessment. The impact of different isomer ratios on the environmental risk assessment of myclobutanil is to be addressed.

Concerns were raised during the peer review process with regard to potential for endocrine disrupting properties of myclobutanil since it belongs to the group of triazole fungicides. No specific concern with regard to endocrine disruption in mammals was identified in the section on toxicology. Some information should be made available by the applicant to address potential endocrine effects in birds and fish in particular.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The representative evaluated uses of myclobutanil are as fungicide on grapes with four applications of 0.048 kg/ha, and on apples with four applications of 0.090 kg/ha per season. The risk to insectivorous birds and small herbivorous mammals was assessed for the orchard/vine/hop scenario in accordance with SANCO/4145/2000. For birds all TER values were well above the relevant Annex VI trigger, thus indicating a low risk.

The first tier risk assessment for small herbivorous mammals from use on grapes resulted in acute TER of 176 and long-term TER of 5.18. Since these values meet the Annex VI triggers of 10 and 5, respectively, the risk in is considered as low. For the use on apples the acute TER was 94 and the long-term TER 2.8, hence indicating a first-tier high long-term risk.

The long-term risk assessment for mammals was refined in the DAR by applying an interception factor of 70%, which is applicable for apples at the stage of foliage development and on vine at flowering. However, the applicant has indicated that two applications are foreseen also at the stage of flowering in apples. At this stage interception is 65% according to the generic guidance for FOCUS ground water scenarios SANCO/321/2000 rev.2. The experts suggested that the long-term risk should be recalculated for four applications and interception factors of 65% and 70%. The rapporteur Member State recalculated the long-term TER for herbivorous mammals as 5.18 according to the suggestions made in the expert meeting. The resulting TER of 5.18 exceeds the trigger of 5. The acute and long-term risk to small herbivorous mammals is low for all representative uses evaluated.

Triazolyl alanine and triazolyl acetic acid were detected in plants as the two main plant metabolites of myclobutanil. The acute oral toxicity of these metabolites was less than or comparable to that of myclobutanil. The NOAEL for developmental effects of triazolyl alanine was higher than for myclobutanil. Studies on developmental and reproductive toxicity are not available for triazolyl acetic acid. However the plant metabolites were also formed in the rat metabolism studies and hence the risk from the metabolites to herbivorous mammals is considered to be covered by the risk assessment for myclobutanil.

The determination of log P_{ow} for myclobutanil was inconclusive but it cannot be excluded that it would be greater than 3. A study on bioaccumulation in earthworms is available, showing a low BCF value of 0.46 to 0.47 and the risk from secondary poisoning of earthworm-eating birds and mammals is therefore considered to be low. A bioconcentration study with fish was not available and the potential for secondary poisoning of fish-eating

birds and mammals has not been assessed in the DAR. A data gap for submission of a bioconcentration study with fish was identified in the expert meeting.

Since the application of myclobutanil is not intended for leafy crops, the rapporteur Member State did not consider a risk assessment for intake of contaminated drinking water as necessary. However it was agreed in previous expert meetings that an acute TER according to SANCO 4145/2000 should be conducted. The acute TER was calculated as 105 for birds and 618 for mammals by the rapporteur Member State in the updated version of the DAR from June 2007 (not peer reviewed).

In summary, it can be concluded that the risk to wild birds and mammals from exposure to myclobutanil under conditions of the intended representative uses is low.

5.2. RISK TO AQUATIC ORGANISMS

Myclobutanil is very toxic to aquatic invertebrates, with the lowest EC_{50} of 0.24 mg a.s./L obtained for *Mysidopsis bahia.* Available studies do not indicate that the formulation 'Systhane 20 EW' is significantly more toxic than what could be expected based on the content of myclobutanil.

The first-tier acute TER values were calculated as the ratio of the toxicity to PEC_{max} in surface water for the different FOCUS scenarios that are applicable to the proposed uses. For the assessment of chronic risk 21 d TWA PEC_{sw} was used in the DAR. A NOEC of 0.2 mg/L for rainbow trout (*Oncorhyncus mykiss*) was derived in a 21-day juvenile growth test with no effects observed in the highest concentration tested. A $NOEC_{growth}$ of 0.98 mg/L for fathead minnow (*Pimephales promales*) from an early life stage study is also available. The choice of end point for the risk assessment was discussed in the experts' meeting and the majority of the experts proposed to use the value of 0.2 mg a.s./L since rainbow trout was the most sensitive species for acute toxicity. The member state experts agreed to use the global maximum PEC_{sw} for the TER calculation since the time window on which the time weighted average PEC_{sw} should be calculated was not determined by observations on the time to onset of effects.

For the use on vine the FOCUS R4 stream scenario (PEC_{sw} = 1.536 µg a.s./L) was the worst case scenario. The TER values for all groups of aquatic organisms were above the Annex VI trigger and thus a low acute and chronic risk can be concluded for the use on vine.

For the use on apples, risk mitigation is required in eight out of ten FOCUS step 3 scenarios. For the worst case FOCUS scenario R3 stream (PEC_{sw} = 2.228 µg a.s./L) a buffer zone of 14 m is required to achieve TERs above the trigger of 100 for aquatic invertebrates. The mitigation measures will also cover the long-term risk.

Myclobutanil was detected in sediment at concentrations of 66 to 85% of applied at the end of the water/sediment study. A water spiked study with *Chironomus riparius* is available to

assess the risk to sediment dwelling organisms. The NOEC of 4.98 mg a.s./L derived from the study was recalculated to 6.07 mg a.s./kg sediment in the DAR and compared to 21 d TWA PEC values for the different FOCUS scenarios. The expert meeting agreed that the NOEC of 6.07 mg a.s./kg sediment should be compared with the worst case maximum PEC_{sed} from FOCUS modelling. The TER values were well above the Annex VI trigger of 10 based on worst case PEC_{sed} values of 8.2 µg a.s./kg (FOCUS step 3+accumulation calculation, D6 ditch) for the use on grapes and 41 µg a.s./kg (FOCUS step3+accumulation calculation, D4 pond) for the use on apples.

No major metabolites were detected in the water/sediment study, and no major metabolites that potentially could contaminate surface water via drainage or run off were detected in the soil degradation studies. However in the situation where groundwater may become surface water, a risk assessment to aquatic organisms is required for myclobutanil butyric acid.

The assessment of log P_{ow} for myclobutanil was inconclusive and the experts' meeting considered it necessary to require a bioconcentration study with fish since four applications are foreseen and chronic and repeated exposure cannot be excluded.

Overall it is concluded that the risk to aquatic organisms is low for the use on grapes. Risk mitigation measures such as no-spray buffer zones of up to 14 m are required for the use on apples.

5.3. RISK TO BEES

The oral and contact toxicity of the formulation 'Systhane 20 EW' to bees is low. The HQ values are in the range 1.2 to 2.6 for single applications. The risk to honeybees was considered as low from the intended uses.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The dose rates applied in the first-tier studies with *Typhlodromus pyri, Aphidius rhopalosiphi, Coccinella septempunctata* and *Pardosa* did not cover the maximum application rates on apples and vine if a multiple application factor is considered. Since the studies were not of a dose-response design, no LR_{50} could be derived and consequently no HQs were calculated.

A semi-field study in which hop plants were treated with four applications of 'Systhane 20 EW' (4 × 54 g a.s./ha and 4 × 300 g a.s./ha) did not show any significant effects on behaviour or reproductive capacity of *A. rhopalosiphi*. Effects of 'Systhane 20 EW' on *T. pyri* were tested in field trials in an apple orchard in southern Germany with 9 × 180 g a.s./ha. No effects on predatory mite eggs and adults were observed. The study was discussed in the experts' meeting and considered to be valid. Additionally, an extended study with *Crysoperla carnea* showed no effects of greater than 50% on mortality or reproduction at rates of 766 g a.s./ha and 1380 g a.s./ha. Therefore, the risk to non-target arthropods was considered to be sufficiently addressed and no further studies are required.

5.5. RISK TO EARTHWORMS

The acute risk to earthworms was assessed in the DAR by comparing the LC_{50} for technical myclobutanil with the maximum peak PEC_{soil} of 0.359 mg a.s./kg soil (grapes) and 0.672 mg a.s./kg soil (apples) after last application on top of the average plateau concentration calculated for repeated application during several years. The long-term risk was assessed by comparing the NOEC from a reproduction study with the formulation 'Systhane 20 EW' with the average plateau PEC_{soil} of 0.289 mg a.s./kg soil (grapes) and 0.544 mg a.s./kg soil (apples). Acute TER values were 348 and 186 for the use on vine and apples respectively, and the long-term TER values were 17.8 and 9.5. It is the EFSA view that for the first-tier assessment, also the risk for long-term/reproduction effects should be assessed by comparing the NOEC with the peak PEC_{soil} following the last application on top of the plateau concentration. This would result in long-term TER values of 14.3 and 7.7 for vine and apples respectively. Since all TER values are above the relevant Annex VI trigger the risk to earthworms can be considered as low.

Additionally an acute study with the minor soil metabolite myclobutanil butyric acid showing lower toxicity to earthworms than myclobutanil is available.

From a bioconcentration/depuration study, using myclobutanil ^{14}C-labbeled at the chlorophenyl ring, the BCF in earthworms was determined to be 0.46. This indicates that myclobutanil does not readily bioconcentrate in earthworm tissue.

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

The DT_{90} value in soil for myclobutanil in laboratory and field studies is greater than 1 year and hence studies on organisms contributing to organic matter breakdown are required. A reproduction study with *Folsomia candida* using 'Systhane 20 EW' is available. Based on the corrected NOEC of 10.25 mg a.s./kg soil TER values of 35.5 and 18.8 were derived using the plateau PEC_{soil} of 0.289 mg a.s./kg soil (grapes) and 0.544 mg a.s./kg soil (apples). If the peak PEC_{soil} following the last application on top of the accumulation plateau (0.359 mg a.s./kg soil (grapes) and 0.672 mg a.s./kg soil (apples)) would be used than the TERs would still be above the Annex VI trigger of 5. The risk to collembolan species can therefore be considered as low.

A litter bag study was triggered based on the persistence of myclobutanil in soil. The study by Galicia (2002) was evaluated as not acceptable by the rapporteur Member State. The experts agreed with this assessment since no positive control was used and the test substance concentrations were not measured. The study of Mallet (2004) was considered acceptable. No effects on organic matter breakdown was observed in the test at the measured concentrations of 0.1247 to 0.1460 mg a.s./kg soil. This concentration covers the PEC_{soil} after one year of use on grapes and in apple orchards. The tested concentration is clearly below the PEC_{max} of 0.359 and 0.672 mg a.s./kg soil. However taking into account that no effects were observed in the litter bag study and that the risk to earthworms and collembola was assessed

as low it is assumed that the risk to soil dwelling non-target macro-organisms is low and no new litter bag study is considered necessary.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

Effects on soil nitrogen transformation and soil respiration were studied using the formulation 'Systhane 24E' which is considered as comparable to the lead formulation. No deviations >25% compared to the control were observed at soil concentrations of 2.93 mg formulation/kg soil. This concentration corresponds to 0.7 mg a.s./ha and covers the maximum peak PEC_{soil}.

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

Results from vegetative vigour and seedling emergence tests with four monocotyledon and six dicotelydon species using 'Systhane 20 EW' indicate that the risk to non-target plants is low for the evaluated uses on vine and apple. The highest effect in the vegetative vigour test was 60% inhibition of shoot weight at 900 g a.s./ha for *Brassica oleracea*. In the seedling emergence test 33% inhibition of shoot weight was observed for *Lolium perenne* at a dose rate of 300 g a.s./ha.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The EC_{50} was determined to 71 mg a.s./L in an activated sludge respiration inhibition test. Since this is significantly higher than the PEC_{sw} no adverse effects on biological methods of sewage treatment are expected should myclobutanil reach sewage treatment plants.

6. Residue definitions

Soil

Definitions for risk assessment: myclobutanil
Definitions for monitoring: myclobutanil

Water

Ground water

Definitions for exposure assessment: myclobutanil and myclobutanil butyric acid
Definitions for monitoring: myclobutanil, identified data gaps have to be filled before the need for monitoring of myclobutanil butyric acid can be excluded.

Surface water

Definitions for risk assessment: water: myclobutanil
sediment: myclobutanil
Definitions for monitoring: myclobutanil

Air

Definitions for risk assessment: myclobutanil

Definitions for monitoring: myclobutanil

Food of plant origin

Definitions for risk assessment: myclobutanil, RH-9090[19] free and conjugated expressed as myclobutanil (limited to category of fruit crops only)

Definitions for monitoring: myclobutanil (limited to category of fruit crops only)

Food of animal origin

Definitions for risk assessment: no conclusion possible with the available data.

Definitions for monitoring: no conclusion possible with the available data.

[19] RH-9090: (2*RS*,5*RS*) 2-(4-chlorophenyl)-5-hydroxy-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
myclobutanil	High to very high persistence Single first-order DT_{50} 191 to 574 days (20 to 22°C, 40%MWHC or not reported soil moisture) Biphasic, DT_{50} 9 to 58 days, DT_{90} >1 year (German field studies)	The risk to soil dwelling organisms was assessed as low.

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
myclobutanil	Medium to low mobility K_{Foc} 226 to 920 mL/g	Data requirement identified but with available information at 7 out of 9 scenarios for apples and 6 out of 7 scenarios for vines, concentrations are above 0.1 µg/L.	Yes	Yes	Very toxic to aquatic organisms.
myclobutanil butyric acid	Very high mobility K_{doc} 18 to 46 mL/g	Data requirement identified but expectation is that concentrations will exceed 0.1 µg/L and concentrations might exceed 0.75 µg/L.	No information available	No information available	Approximately one order of magnitude less toxic to aquatic organisms compared to myclobutanil

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Myclobutanil (water and sediment)	Very toxic to aquatic organisms. All TERs are above the Annex VI trigger for the uses in grapes. No spray buffer zones of up to 14 metres are required for the use in apple orchards.

Air

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

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

- Information on the comparability of the toxicological studies performed with technical material of different purity is required, as well as toxicological information on impurities (relevant for all representative uses evaluated; no submission date proposed by the applicant; data gap identified by the meeting of experts; refer to section 2 Mammalian toxicology).
- A groundwater metabolite non relevance assessment[20] and aquatic risk assessment for the metabolite myclobutanil butyric acid will be required once the data requirement for additional groundwater exposure assessments is satisfied (relevant for all representative uses evaluated; no submission date proposed by the applicant; data gap identified by EFSA refer to sections 2.8, 4.2.2 and 5.2).
- Impact of different isomer ratios on the exposure assessment of myclobutanil for operator, worker and bystander to be addressed (relevant for all applied for intended uses; data gap identified by EFSA after the expert meeting; no submission date proposed; refer to section 2.12).
- The applicant should provide evidence that the submitted residues trials for apples and grapes cover the residue definition for risk assessment in particular with regard to conjugates. It should be demonstrated that the method used would extract all the conjugate and that the hydrolysis step in the method gives an acceptable yield (relevant for all representative uses evaluated; no submission date proposed by the applicant; data gap identified by the meeting of experts, refer to section 3.1.1).
- A study simulating representative processing conditions is required. This study should investigate the behaviour of the relevant residue, including relevant metabolites, on crops to be processed (relevant for all representative uses evaluated; study submitted by the applicant in June 2007 and evaluated in the addendum of June 2007 but not peer reviewed; data requirement identified in the commenting period on the DAR and confirmed by the meeting of experts in residues, refer to section 3.1.1).
- A ruminant metabolism study is required where the compound is labelled on both rings (relevant for the representative use on apples; no submission date proposed by the applicant; data gap identified by the meeting of experts, refer to section 3.2).
- The applicant should address the consumer risk assessment with regard to the two myclobutanil isomers (relevant for all representative uses evaluated; no submission date proposed by the applicant; data gap identified by the meeting of experts, refer to section 3.3).
- An anaerobic soil metabolism study (relevant for the use evaluated on apples; no submission date proposed by the applicant; data gap identified by the meeting of experts in residues, refer to section 4.1.1).
- Myclobutanil DT_{50} derived from field dissipation studies should be normalised to FOCUS reference conditions, and reported in a transparent way, strictly adhering to all

[20] Following the: Guidance document on the assessment of the relevance of metabolites in groundwater of substance regulated under council directive 91/414/EEC. SANCO/221/2000-rev.10 25 February 2003.

pertinent FOCUS kinetics guidance recommendations taking particular note of recommendations for handling biphasic patterns of disappearance in field experiments and implementing them in FOCUS leaching models. PEC groundwater for myclobutanil and myclobutanil butyric acid to be recalculated using an appropriate first-order normalised field DT_{50} for myclobutanil in accordance with FOCUS recommendations, if this is possible and an appropriate kinetic formation fraction for the metabolite myclobutanil butyric acid. Other input parameters used in any lower-tier assessment to be those identified as appropriate in section 4.2.2 of this conclusion. Two FOCUS models (PEARL and PELMO or PRZM) should be used; data requirement reconfirmed at the expert meeting on fate and behaviour (PRAPeR 17 in March 2007); (relevant for all representative uses evaluated; no submission date proposed by the applicant; refer to section 4.2.2.).

- Information on the composition of the batches used in the ecotox studies is required (relevant for all representative uses; data requirement identified during the peer review and confirmed by the PRAPeR 18 expert meeting on ecotoxicology in March 2007; the composition of three batches was submitted prior to the expert meeting but no submission date proposed by the applicant for the outstanding seven batches; refer to section 5).
- A bioconcentration study with fish is required (relevant for all representative uses; data gap identified at the PRAPeR 18 expert meeting on ecotoxicology in March 2007; no submission date proposed by the applicant; refer to section 5.2).
- A risk assessment for fish-eating birds and mammals (relevant for all representative uses; data gap identified at the PRAPeR 18 expert meeting on ecotoxicology in March 2007; no submission date proposed by the applicant; refer to section 5.1).
- Information should be made available by the applicant to address potential endocrine effects of myclobutanil in birds and fish in particular (relevant for all representative uses; data gap identified at the PRAPeR 18 expert meeting on ecotoxicology in March 2007; no submission date proposed by the applicant; refer to section 5).
- Impact of different isomer ratios on the environmental risk assessment of myclobutanil is to be addressed (relevant for all applied for intended uses; data gap identified by EFSA after the expert meeting; no submission date proposed; refer to sections 4 and 5).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as proposed by the applicant which comprise foliar spraying against powdery mildew (*Uncinula necator)*, and black rot *(Guignardia bidwelli)* in table and wine grapes and against scab (*Venturia inaequalis*) and powdery mildew (*Podosphaera leucotricha*) in apples at the fruit development stage, in all EU countries, up to a maximum four applications at a maximum individual application rate per spray of 48 g a.s./ha on grapes, and 90 g a.s./ha on apples, with an interval of 10 days between applications.

The representative formulated product for the evaluation was 'Systhane 20 EW', an oil in water emulsion (EW) containing 200 g/L myclobutanil, registered under different trade names in Europe.

Adequate analytical methods are available to monitor all compounds given in the respective residue definitions.

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

In mammalian toxicity tests, myclobutanil is harmful if swallowed, it is not toxic via dermal and inhalation routes, and it is not a skin irritant or a skin sensitiser. The ECB has classified myclobutanil with R36 ("Irritating to eyes"). The overall subchronic NOAEL is 3.09 mg/kg bw/day. Myclobutanil does not show any genotoxic or carcinogenic potential. The relevant NOAEL for long-term toxicity is 2.5 mg/kg bw/day. The relevant parental, offspring and reproductive NOAEL is 16 mg/kg bw/day. Myclobutanil is classified as Repr. Cat 3, R63 ("Possible risk of harm to the unborn child"). The relevant parental NOAEL is 94 mg/kg bw/day, while the relevant developmental NOAEL is 31 mg/kg bw/day. No indication of any other neurological effects was found in the toxicological studies. The ADI is 0.025 mg/kg bw/day, the AOEL 0.03 mg/kg bw/day and the ARfD is 0.31 mg/kg bw. The operator, worker and bystander exposure estimates showed levels below the AOEL.

The metabolism of myclobutanil was investigated in grapes, apples (representative uses) and additionally in wheat. In grapes and apples at harvest, the major components of the residue were myclobutanil and its metabolite RH-9090 in free and conjugated form. A metabolic cleavage of the myclobutanil molecule which would generate triazole derivative metabolites was, in contrast to the wheat study, not observed in apples and grapes. Based on the available plant metabolism data for the categories fruit and cereals it was concluded that the metabolism is not comparable amongst different crop groups. As for the representative uses, however, it was agreed that the relevant residue for the category fruit crops should be defined as myclobutanil and its metabolite RH-9090 (free and conjugated). A sufficient number of residue trials in apples and grapes are available; however, there is still evidence required that the submitted trials cover the proposed residue definition. Processing studies investigated how the residue levels of myclobutanil and metabolite RH-9090 change when apples and grapes are processed to juice, wine, puree etc. However, the need for a study investigating the effects of processing on the nature of the residues was identified, as under processing conditions significant amounts of one or more degradation products, initially not present in the raw commodities, could be generated.

The investigation of residues in rotational and succeeding crops was considered not relevant since both apples and grapes are perennial crops that are usually not grown in rotation with

other crops. However it was highlighted that in the long term the issue of potential uptake of triazole derivative metabolites could become relevant and should be followed up separately as this concern is not specific to the active substance myclobutanil alone but common to a number of triazole pesticides.

Since a significant exposure of livestock to residues in feed may occur, a metabolism study in ruminants was triggered. The majority of the experts agreed that the level of identification was insufficient in the available study and thus a robust residue definition for food of animal origin could not be concluded on. Consequently, the relevance of the available feeding study for the assessment and likely necessary MRL proposals for food of animal origin can only be decided on when a residue definition has been concluded. As a consequence of the identified data gaps the consumer risk assessment with regard to the notified representative uses apples and grapes cannot be finalised. Moreover, the risk assessment with regard to the two isomers of myclobutanil was not addressed.

It is noted that in addition to the exposure from residues in food, the consumer could be exposed to residues of myclobutanil butyric acid, a potential metabolite in ground water used as drinking water, but currently an assessment of the relevance of the metabolite and consequently of consumer risk is not available. An additional exposure to myclobutanil residues from groundwater used as drinking water can also not be excluded.

The information available on the fate and behaviour in the environment is generally sufficient to carry out an appropriate environmental exposure assessment at the EU level for total myclobutanil isomers, with the notable exception that further assessments (regarding soil degradation rate of the active substance, soil kinetic formation fraction of the metabolite myclobutanil butyric acid from myclobutanil and FOCUS groundwater modelling) are required to finalise the groundwater exposure assessment. In addition a laboratory anaerobic soil degradation study was identified as being necessary to support the applied for intended use on apples in territories where anaerobic soil conditions occur and coincide with apple growing areas. On the basis of the available reliable information, it cannot be excluded that for the applied for intended uses, groundwater exposure by myclobutanil above the parametric drinking water limit of 0.1 µg/L will not occur over a wide range of European geoclimatic conditions. In addition for the metabolite myclobutanil butyric acid, groundwater exposure above the parametric drinking water limit might be expected and it cannot be excluded that concentrations > 0.75 µg/L (a key assessment trigger from the groundwater metabolite relevance guidance document) may occur. A groundwater metabolite non relevance assessment is therefore necessary for myclobutanil butyric acid but this assessment is not available.

The first tier risk assessment indicated a potential high risk to herbivorous mammals from the use in apple orchards. A refined risk assessment applying interception factors of 65% and 70% resulted in a TER of 5.18 which is above the Annex VI trigger of 5. The risk of secondary poisoning from uptake of contaminated earthworms was assessed as low. A data

gap was identified in the experts meeting for the submission of a risk assessment for fish-eating birds and mammals since it was not possible to exclude that the log P_{ow} of myclobutanil is greater than 3. Myclobutanil is very toxic to aquatic invertebrates. The TERs based on FOCUS step 3 PEC_{sw} were above the Annex VI triggers for the representative use on grapes. For the use in apple orchards, risk mitigation measures such as a no-spray buffer zone of 14 metres is required to achieve TERs above the Annex VI triggers. The assessment of the log P_{ow} value was inconclusive. In the expert meeting, a data gap for a bioconcentration study with fish was identified since four applications are foreseen and chronic and repeated exposure of fish is expected. It was identified that the risk assessment did not address the potential for different myclobutanil isomer ratios to be present in the environment.

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

- Risk mitigation measures such as a no-spray buffer zone of up to 14 metres are required to achieve TERs above the trigger for aquatic organisms for the representative use on apples.

CRITICAL AREAS OF CONCERN

- The consumer risk assessment cannot be finalised. It is currently unclear whether the available residue data include all compounds of the residue definition for risk assessment, whether there might be exposure of consumers from food of animal origin and from drinking water. Additionally, data on the nature of residues in processed food is not available. Finally, the consumer exposure and risk assessment is not sufficiently addressed with regard to the triazole derivative metabolites and the two isomers of myclobutanil.
- The groundwater exposure assessment cannot be finalised. Based on the available reliable data there are indications that the active substance myclobutanil has the potential to contaminate groundwater under a wide range of geoclimatic conditions.
- It is expected that the metabolite myclobutanil butyric acid will contaminate vulnerable groundwater (though an assessment of the level and extent of contamination is not finalised) and a groundwater non relevance assessment and aquatic risk assessment are not available for this metabolite.

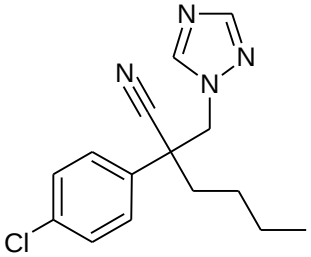
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

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

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

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(*RS*)-2-(4-chlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile
Chemical name (CA) ‡	α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile
CIPAC No ‡	442
CAS No ‡	88671-89-0
EEC No (EINECS or ELINCS) ‡	No number currently available
FAO Specification (including year of publication)‡	No FAO specification exists for myclobutanil
Minimum purity of the active substance as manufactured (g/kg) ‡	925 g/kg (industrial scale production) (racemic mixture, i.e. ratio of R/S-isomers = 1:1)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	1-methyl-2-pyrrolidinone < 1 g/kg
Molecular formula ‡	$C_{15}H_{17}ClN_4$
Molecular mass ‡	288.8 g/mol
Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

<table>
<tr><td>Melting point (state purity) ‡</td><td>70.9 °C (98.75%)</td></tr>
<tr><td>Boiling point (state purity) ‡</td><td>390.8 °C (98.75%)</td></tr>
<tr><td>Temperature of decomposition (state purity)</td><td>Not applicable (melting point and boiling point could be determined)</td></tr>
<tr><td>Appearance (state purity) ‡</td><td>white crystals, odourless (98.75%);
colourless to white crystals, faint aldehyde odour (95.4%)</td></tr>
<tr><td>Vapour pressure (state temperature, state purity) ‡</td><td>1.98 x 10^{-4} Pa at 20°C (99.9%)</td></tr>
<tr><td>Henry’s law constant (Pa m^3 mol^{-1}) ‡</td><td>4.33 x 10^{-4} Pa.m^3.mol^{-1} at 20°C (99.9%)</td></tr>
<tr><td>Solubility in water (state temperature, state purity and pH) ‡</td><td>pH 3-5, 20°C : 124 mg/L (99.9%)</td></tr>
<tr><td></td><td>pH 7, 20°C : 132 mg/L (99.9%)</td></tr>
<tr><td></td><td>pH 9-11, 20°C : 115 mg/L (99.9%)</td></tr>
<tr><td>Solubility in organic solvents (state temperature, state purity) ‡</td><td>
<table>
<tr><td></td><td>at 20°C in g/L (95.6%)</td></tr>
<tr><td>n-heptane</td><td>1.02</td></tr>
<tr><td>xylene</td><td>270</td></tr>
<tr><td>1,2-dichloroethane</td><td>> 250</td></tr>
<tr><td>methanol</td><td>> 250</td></tr>
<tr><td>n-octanol</td><td>102</td></tr>
<tr><td>acetone</td><td>> 250</td></tr>
<tr><td>ethyl acetate</td><td>> 250</td></tr>
</table>
</td></tr>
<tr><td>Surface tension
(state concentration and temperature, state purity)‡</td><td>46.8 mN/m at 24°C (90% saturated solution) (92.1%)</td></tr>
</table>

Partition co-efficient (state temperature, pH and purity) ‡	log Pow = 2.89 (calculated; pH 7, 20°C); log Pow = 3.5 (estimation); log Pow = 3.17 (experimental - shake flask method; 20°C, pH 4,7,9) (99.7%)
	Effect of pH does not need to be addressed (molecule will not be ionized at environmentally relevant pH values)
Dissociation constant (state purity) ‡	Myclobutanil is calculated to have a basic pKa of 2.30 ± 0.10 This indicates that the molecule will not be ionized at environmentally relevant pH values.
UV/VIS absorption (max.) incl. ε (state purity, pH) ‡	in unbuffered methanol (98.75%): λ_{max} 203 nm; ε = 16400 $L.mol^{-1}.cm^{-1}$ λ_{max} 219 nm; ε = 17900 $L.mol^{-1}.cm^{-1}$ λ_{max} 267 nm; ε = 500 $L.mol^{-1}.cm^{-1}$ λ_{max} 273 nm; ε = 500 $L.mol^{-1}.cm^{-1}$ at $\lambda \geq 290$ nm : ε = 0 $L.mol^{-1}.cm^{-1}$
Flammability (state purity) ‡	not highly flammable; not flammable in contact with water or damp air (92.1%) not auto-flammable (92.1%)
Explosive properties (state purity) ‡	not explosive (95.6%)
Oxidising properties (state purity) ‡	not oxidising (95.6%)

Summary of representative uses evaluated (Myclobutanil)*

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 (days) (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		
Table/wine Grapes FB0269	N & S Europe	Systhane 20 EW (GF-1317)	F	Powdery Mildew (*Uncinula necator)* and black rot *(Guignardia bidwelli)*	EW	200	Air-assisted spraying	Fruit development	4	10	0.003-0.0048	1000	0.03-0.048	14	[1]

* Uses for which the risk assessment can not be concluded are marked grey.

Apples FP0226	N & S Europe	Systhane 20 EW (GF-1317)	F	Scab (*Venturia inaequalis*) and powdery mildew (*Podosphaera leucotricha*)	EW	200	Air-assisted spraying	Fruit development	4	10	0.0048-0.006	1000-1500	0.048-0.09	14	[1]

[1] Groundwater exposure assessment not finalised; data gaps for a risk assessment of secondary poisoning of fish-eating birds and mammals and a bioconcentration study with fish; consumer risk assessment not finalised,

Remarks:

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.*
(b) fumigation of a structure)
(c) Outdoor or field use (F), glasshouse application (G) or indoor
(d) application (I)
(e) *e.g.* biting and suckling insects, soil born insects, foliar fungi,
(f) weeds
(g) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule
(h) (GR)
GCPF Codes - GIFAP Technical Monograph No 2, 1989
All abbreviations used must be explained
Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, 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
(l) under practical conditions of use must be provided
(m) PHI - minimum pre-harvest interval
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)	GC-FID conf. by MS no CIPAC method available
Impurities in technical as (analytical technique)	GC-FID conf. by MS
Plant protection product (analytical technique)	GC-FID conf. by column of different polarity no CIPAC method available

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Multi-method DFG S19 (extended revision): module E1; LOQ 0.05 mg/kg (myclobutanil)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Multi method DFG S19 (extended revision): GC-ECD, conf. by column of different polarity; metabolite RH-9090; LOQ = 0.01 mg/kg (milk, meat, kidney, liver); ILV available Single method ER 58.13: ***GC-ECD, conf. by GC-NPD; metabolite RH-9090; LOQ = 0.01 mg/kg (fat); ILV available (method ref. ER 59.6)***
Soil (analytical technique and LOQ)	Multi method DFG S19 (extended revision) : GC-ECD, conf. by column of different polarity (Myclobutanil); LOQ = 0.05 mg/kg
Water (analytical technique and LOQ)	Single method GRM 03.14 : LC-MS/MS (Myclobutanil); LOQ = 0.05 µg/L (surface water, groundwater, drinking water)
Air (analytical technique and LOQ)	Single method: HPLC-MS-MS; LOQ ≈ 0.7 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

Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	0.2-1.6 % after 120 d, [^{14}C-triazole]-label (n= 3) 1.7 % after 120 d, [^{14}C-chlorophenyl]-label (n= 1) Sterile conditions: no acceptable study, not required
Non-extractable residues after 100 days ‡	4.1-15.9 % after 120 d, [^{14}C-triazole]-label (n= 3) 8.0 % after 120 d, [^{14}C-chlorophenyl]-label (n= 1) Sterile conditions: no acceptable study, not required
Relevant metabolites - name and/or code, % of applied (range and maximum) ‡	No major metabolite Minor metabolite myclobutanil butyric acid (max 6%AR at 76 days)

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

Anaerobic degradation ‡	No acceptable study, not required for the use on grape vines. Data gap identified for the use on apples.
Soil photolysis ‡	No satisfactory study available. Not required due to the low light absorbance of the myclobutanil molecule > 290nm.

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

Method of calculation	Laboratory: first order (non-linear) kinetics Field studies: first order kinetics, biphasic degradation
Laboratory studies (range or median, with n value, with r^2 value) ‡	parent DT_{50lab} (aerobic): 20°C 40%MWHC: 192, 465 & 574 days (normalised to -10kPa or pF2: 164, 417 &515 days) 22°C unknown %MWHC: 191, 217 & 354 days (normalised to 20°C: 224, 254 & 414 days) For FOCUS gw modelling – Parent DT_{50lab} (aerobic, 1st order (non-linear) kinetics): geomean DT_{50lab} 306 d (normalised to -10kPa and 20°C with Q10 of 2.2).

parent DT_{90lab} (20°C, aerobic): 637-1906 d, mean = 1175 d (n= 6, r^2 = 0.616-0.941) (based on two studies)
myclobutanil butyric acid DT_{50lab} (25°C, aerobic 1st order kinetics): 5, 7, 22&42 days (n= 4, r^2 = 0.946-0.993, normalised to -10kPa or pF2: 7.3, 8.2, 23.6 &36.7 days) Geometric mean DT_{50lab} 15.1d (normalisation to 10kPa or pF2, 20°C).
myclobutanil butyric acid DT_{90lab} (20°C, aerobic): 23-139 d, mean = 62.5 d (n= 4, r^2 = 0.946-0.993)
DT_{50lab} (10°C, aerobic): 779 d (by calculation with Q10 of 2.2).
DT_{50lab} (20°C, anaerobic): data required for the use on apples
degradation in the saturated zone: not required

1,2,4-triazole	Aerobic conditions							
Soil type (USDA)		pH ($CaCl_2$)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/ k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		6.4	20°C / 40 % MWHC	6.32 / 21.0		5.0	0.75	SFO
Loamy sand		5.8	20°C / 40 % MWHC	9.91 / 33.0		9.9	0.81	SFO
Silt loam		6.7	20°C / 40 % MWHC	12.27 / 40.8		8.2	0.95	SFO
Geometric mean						7.4		

Agreed End-point for calculating PEC soil for EU assessments 12 days (Not normalised).
Geomean for FOCUS modelling 7.4 days

Field studies (state location, range or median with n value) ‡	DT_{50f}: Germany, bare soil, 9, 14, 58, 58 d (n= 4, r^2=0..444-0.782) 1st order. Note the pattern of degradation was biphasic but the slow phase commenced after 50% loss.
	DT_{90f}: Germany, bare soil, > 1 year (n= 4) (biphasic degradation)
Soil accumulation and plateau concentration ‡	Germany, 12 appl. of 0.045 kg a.s./ha during 3 years, bare soil highest concentration of 0.223 mg/kg in the 0-20 cm horizon reached after 2 years application California, 5 appl. of 0.134 kg a.s./ha during 3 years. highest concentration of 0.105 and 0.112 mg/kg in the 0-15 cm horizon during the 2nd and 3rd years; no increase when further applications are made.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_{Ff} /K_{oc} ‡ K_d ‡ pH dependence (yes / no) (if yes type of dependence) ‡	K_{Foc}: parent 225.7-920.0 mL/g (mean 517 mL/g, $^1/_n$= 0.851-0.912, 5 soils) K_F: parent 1.464-9.771 (mean 5.027mL/g, 5 soils) No *For FOCUS gw modelling – K_{Foc}: parent, mean 517 mL/g, $^1/_n$=0.88.
	K_{doc}: myclobutanil butyric acid 18-46 mL/g (mean 36 ml/g, 4 soils) *For FOCUS gw modelling – K_{doc}: myclobutanil butyric acid mean 36 mL/g, $^1/_n$= 1

Metabolite 1,2-4 triazole ‡							
Soil Type(USDA)	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	K_F (mL/g)	$K_F$oc (mL/g)	1/n
Silty clay	0.70	8.8			0.833	120	0.897
Clay loam	1.74	6.9			0.748	43	0.827
Sand	0.12	4.8			0.234	202	0.885[1]
Silty clay loam	0.70	7.0			0.722	104	0.922
Sandy loam	0.81	6.9			0.720	89	1.016
Arithmetic mean (of 4 values excluding the very low OC sand that was considered not representative of agricultural soils)					0.756	89	0.9155
pH dependence (yes or no)			No				

Agreed End-point for calculating FOCUS modelling arithmetic mean $K_F$oc of 89 mL/g, 1/n 0.92 excluding results of the sand soil.

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

Column leaching ‡	Not required
Aged residues leaching ‡	Not required
Lysimeter/ field leaching studies ‡	Not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	Active substance DT_{50} (d): 574 days Kinetics: 1st order worst case from lab studies.
Application rate	Crop: grapes 50% plant interception: Number of applications: 4 Interval (d): 10 Application rate(s): 48 g as/ha 5 cm soil horizon with a soil bulk density of 1.5 g/mL

Method of calculation	Active substance DT_{50} (d): 574 days Kinetics: 1st order worst case from lab studies.
Application rate	Crop: apple 50% plant interception: Number of applications: 4 Interval (d): 10 Application rate(s): 90 g as/ha 5 cm soil horizon with a soil bulk density of 1.5 g/mL

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.032	0.032	0.126 (conc just after last application)	-
Short term 24h	0.032	0.032	-	-
2d	0.032	0.032		
4d	0.032	0.032		
Long term 7d	0.032	0.032	-	-
28d	0.031	0.031		
50d	0.030	0.031		
100d	0.028	0.030		

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.060	0.060	0.236 (conc just after last application)	-
Short term 24h	0.060	0.060	-	-
2d	0.060	0.060		
4d	0.060	0.060		
Long term 7d	0.059	0.060	-	-
28d	0.058	0.059		
50d	0.056	0.057		
100d	0.053	0.057		

Accumulation PEC soil (mg a.s./kg soil)

	Initial PEC for 1 year	Concentration in soil immediately after last application = Initial PEC for 1 year x $(1-e^{-20k}) / (1-e^{-k})$	Plateau average PEC after repeated applications during several years = initial PEC for 1 year / k
Vines	0.128	0.359	0.289
Apples	0.240	0.672	0.544

k is 0.693 /DT_{50} (in year)

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) ‡	no significant hydrolysis (< 10%) after 5 d, at 50°C, pH 4, 7 and 9
Photolytic degradation of active substance and relevant metabolites ‡	Not required (Molar absorption coefficient for myclobutanil is zero for wavelengths ≥ 290 nm.)
Readily biodegradable (yes/no) ‡	No The Biological Oxygen Demand is 7.8, 13.5 and 22.4% of the Theoretical Oxygen Demand at 5, 15 and 28 days, respectively.

Degradation in water/sediment	- DT_{50} water ‡ - DT_{90} water ‡	20-4 days (dissipation from water column) 68-14 days (1st order, r^2 = 0.960-0.969, n= 2)
	- DT_{50} whole system ‡ - DT_{90} whole system ‡	415-838 days (mean 626 days selected for use in FOCUSsw modelling) 1379-2784 days (1st order, r^2 = 0.769-0.057, n= 2 (values extrapolated significantly beyond the study duration))
Mineralization		0.3 %AR (at 105 d, study end, n= 2)
Non-extractable residues		4.3-9.8% AR (at 105 d, study end, n= 2)
Distribution in water / sediment systems (active substance) ‡		Maximum level of 65.60-84.80 %AR in sediment after 105 days. DT_{50} in sediment equivalent to the DT50 whole system
Distribution in water / sediment systems (metabolites) ‡		Low levels of metabolites were detected in both sediment and water phases (unknown metabolite found at max level of 4.7% AR)

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

Parent Method of calculation	Model(s) used: SWASH, Spray drift calculator, MACRO, PRZM, TOXSWA Calculations from step 1 to 4 Scenarios: Lanna, Brimstone, Vreedepeel, Skousbo, La Jaillière, Thiva, Weiherbach, Porto, Bologna, Roujean Crop: apples and vines Mean parent $DT_{50lab(soil)}$: 282 d Mean parent $DT_{50lab(sediment)}$: 626 d (mean of 415 and 838 d) $DT_{50(water)}$: 999 d K_{foc}: parent, mean 517 mL/g, $^1/_n$= 0.88. Molecular weight : 288.8 Vapour pressure: 1.98 10^{-4} Pa Water solubility 132 mg/L
	Vines Application rate: 48 g/ha. No. of applications: 4 at 10 days interval Time of application: first appl. on 15 May Depth of water body: 30cm Apples Application rate: 90 g/ha. No. of applications: 4 at 10 days interval Time of application: first appl. on 15 April Depth of water body: 30 cm
Main routes of entry	Drift, drainage, run-off (according to standard Focus scenarios)

Summary of PEC_{SW} values for myclobutanil (Step 4 refined no-spray zones) following use of Systhane 20EW on apples (early application - worst case for spray drift)

Concentration	D3 d (12 m)	D4 p (6 m)	D4 s (14 m)	D5 p (6 m)	D5 s (14 m)	R1 p (6 m)	R1 s (14 m)	R2 s (14 m)	R3 s (14 m)	R4 s (14 m)
(µg as/L) Max. PEC_{SW}	2.135	1.588	1.874*	1.425	2.05*	1.021	2.036	2.089*	2.228*	1.909

* This value comes from calculations for a single application.

Summary of PEC_{SW} values for myclobutanil (Step 3 minimum default no-spray zones) following use of Systhane 20EW on vines (late application - worst case for spray drift)

Concentration	D6 d (3.5 m)	R1 p (6 m)	R1 s (4 m)	R2 s (4 m)	R3 s (4 m)	R4 s (4 m)
(µg as/L) Max. PEC_{SW}	0.873	0.092	1.135	0.806*	0.842*	1.536

Accumulation PEC sediment values agreed by the expert meeting to encompass the concentrations from all FOCUS scenarios

	Predicted maximum plateau concentration in sediment in µg a.s./kg soil (on the basis of DT_{50}(sediment) of 626 days)
Vines (D6 ditch, default step 3 buffer distance, 3.5m)	8.2
Apples (D4 pond, default step 3 buffer distance, 6m)	41

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

No acceptable data available, data required.

Data requirement for further modelling maintained by the meeting of experts.

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 ‡	DT_{50} : 7.6 hours, assuming global OH-concentration of 1.5 x 10^6 OH radicals/cm^3 and 12 hour day
Volatilization ‡	from plant surfaces: not significant (up to *ca* 2.6% AR) under the conditions of a wind tunnel study (24 hours in an air-flow at *ca* 1 m/s).
	from soil: minimal under the conditions of a wind tunnel study (24 hours in an air-flow at 1-1.5 m/s). (2 studies)

PEC (air)

Method of calculation	Not required

PEC$_{(a)}$

Maximum concentration	Not required

Definition of the Residue (Annex IIA, point 7.3)

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Residue definition for risk assessment Soil: myclobutanil Surface Water : myclobutanil Sediment: myclobutanil Ground water: myclobutanil, myclobutanil butyric acid. Air : myclobutanil

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) Ground water (indicate location and type of study)	The notifier submits a summary of the monitoring data available in European countries. Myclobutanil is not widely monitored in surface water and groundwater across Europe (15 EU Member States, plus Norway and Switzerland). The data provide a limited assessment of the situation.
Air (indicate location and type of study)	Not available

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R53

Ecotoxicology

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 ‡				
Colinus virginianus	myclobutanil	Acute	**LD_{50} = 510**	-
Colinus virginianus	myclobutanil	Short-term	**LC_{50} > 567**	> 5000
Anas platyrhynchos	myclobutanil	Short-term	LC_{50} > 1544	> 5000
Anas platyrhynchos	myclobutanil	Long-term	NOEC = 31.6	260
Colinus virginianus	myclobutanil	Long-term	**NOEC = 24.2**	260
Mammals ‡				
Male rat	myclobutanil	Acute	**LD_{50} = 1600**	-
Rat	myclobutanil	Long-term	**NOEL = 16**	-
Additional higher tier studies ‡				
Not required.				

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

Crop and application rate : grapes, 4 x 0.048 kg a.s./ha

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Insectivorous bird	Acute	2.60	197	10
Insectivorous bird	Short-term	1.45	> 392	10
Insectivorous bird	Long-term	1.45	16.7	5
Vermivorous bird	Long-term	0.29	83	5
Higher tier refinement (Birds)				
Not required.				

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	9.07	176	10
Small herbivorous mammal	Long-term	3.09	5.18	5
Vermivorous mammal	Long-term	0.36	44	5
Higher tier refinement (Mammals)				
Small herbivorous mammal	Long-term	1.53	10.4 (residues)	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.

Crop and application rate : apples, 4 x 0.090 kg a.s./ha

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Insectivorous bird	Acute	4.87	105	10
Insectivorous bird	Short-term	2.71	> 209	10
Insectivorous bird	Long-term	2.71	8.9	5
Vermivorous bird	Long-term	0.29	83	5
Higher tier refinement (Birds)				
Not required.				
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	17.0	94	10
Small herbivorous mammal	Long-term	5.79	2.76	5
Vermivorous mammal	Long-term	0.36	44	5

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Higher tier refinement (Mammals)				
Small herbivorous mammal	Long-term, 2 x 0.090 kg a.s./ha during flowering, 2 x 0.090 kg a.s./ha during foliage development	2.87 – 3.35	5.18 (residues)	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	myclobutanil	96 h (static)	Mortality, LC_{50}	**2.0 mg a.s./L** (initial)
Lepomis macrochirus	myclobutanil	96 h (static)	Mortality, LC_{50}	4.1 mg a.s./L (mm)
Cyprinodon variegatus	myclobutanil	96 h (flow-through)	Mortality, LC_{50}	4.7 mg a.s./L (mm)
Oncorhynchus mykiss	myclobutanil	21 d (flow-through)	Growth NOEC	**0.2 mg a.s./L** (nom)
Pimephales promelas	myclobutanil	35 d (flow-through)	Growth NOEC	0.98 mg a.s./L (mm)
Oncorhynchus mykiss	Systhane 20 EW	96 h (static)	Mortality, LC_{50}	10.3 mg form/L (**2.04 mg a.s./L**) (mm)
Oncorhynchus mykiss	myclobutanil butyric acid	96 h (static)	Mortality, LC_{50}	> 100 mg/L (nom)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Aquatic invertebrate				
Daphnia magna	myclobutanil	48 h (static)	Mortality, EC_{50}	17 mg a.s./L (mm)
Mysidopsis bahia	myclobutanil	96 h (flow-through)	Mortality, EC_{50}	**0.24 mg a.s./L** (mm)
Crassostrea virginica	myclobutanil	96 h (flow-through)	Mortality, EC_{50}	0.72 mg a.s./L (mm)
Daphnia magna	myclobutanil	21 d (semi-static)	Reproduction, NOEC	**1.0 mg a.s./L** (nom)
Daphnia magna	Systhane 20 EW	48 h (static)	Mortality, EC_{50}	7.1 mg form/L (**1.41 mg a.s./L**) (mm)
Daphnia magna	GF-1317	21 d (semi-static)	Reproduction, NOEC	1.3 mg form/L (**0.27 mg a.s./L**) (nom)
Daphnia magna	myclobutanil butyric acid	48 h (static)	Mortality, EC_{50}	> 100 mg/L (nom)
Sediment dwelling organisms				
Chironomus riparius	myclobutanil	30 d (static) s/w system	NOEC	**4.98 mg a.s./L** (mm)
Algae				
Desmodesmus subspicatus	myclobutanil	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	2.655 mg a.s./L 6.7 mg a.s./L (nom)
Pseudokirchneriella subcapitata	myclobutanil	120 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**1.1 mg a.s./L** 1.2 mg a.s/L (mm)
Pseudokirchneriella subcapitata	Systhane 20 EW	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	8.6 mg form/L (1.70 mg a.s./L) > 5.0 mg form/L (> **0.99 mg a.s./L**) (mm)
Pseudokirchneriella subcapitata	myclobutanil butyric acid	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	56.2 mg/L (mm) 69.2 mg/L (mm)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Higher plant				
Lemna gibba	myclobutanil butyric acid	7 d (static)	Fronds, EC_{50}	> 105 mg/L (mm)
Microcosm or mesocosm tests				
Not required. A microcosm or mesocosm study is not required since TER_a > 100 and TER_{lt} > 10 with appropriate buffer zones between the sprayed area and water bodies.				

[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.

Systhane 20 EW : formulation containing 19.8 % myclobutanil (batch n°: DK-2102-A)
GF-1317 : formulation containing 20.6 % myclobutanil (batch n°: E1743-16)

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

FOCUS Step 1

FOCUS Step 2

No acceptable aquatic risk assessment based on FOCUS step 1 and step 2 calculations.

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Only the worst case scenario's are presented in the Listing of End points.

State crop and application rate : grapes, late application, 4 x 0.048 kg a.s./ha

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{sw}[4] (µg a.s./L)	TER	Annex VI trigger[5]
myclo-butanil	R 4	stream	*Oncorhyn-chus mykiss*	96 h static	2.0	4 m	1.536	1302	100
myclo-butanil	R 4	stream	*Oncorhyn-chus mykiss*	21 d flow-through	0.2	4 m	1.536	130	10
Systhane 20 EW	R 4	stream	*Oncorhyn chus mykiss*	96 h static	2.04	4 m	1.536	1328	100

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{SW}[4] (µg a.s./L)	TER	Annex VI trigger[5]
myclo-butanil	R 4	stream	*Mysidopsis bahia*	96 h flow-through	0.24	4 m	1.536	156	100
myclo-butanil	R 4	stream	*Daphnia magna*	21 d semi-static	1.0	4 m	1.536	651	10
Systhane 20 EW	R 4	stream	*Daphnia magna*	48 h static	1.41	4 m	1.536	918	100
GF-1317	R 4	stream	*Daphnia magna*	21 d semi-static	0.27	4 m	1.536	176	10
myclo-burtanil	R 4	stream	*Pseudokirchneriella subcapitata*	120 h static	1.1	4 m	1.536	716	10
Systhane 20 EW	R 4	stream	*Pseudokirchneriella subcapitata*	96 h static	> 0.99	4 m	1.536	> 645	10
myclo-buranil	R 4	stream	*Chironomus riparius*	30 d static	4.98	4 m	1.536	3242	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

Systhane 20 EW : formulation containing 19.8 % myclobutanil (batch n°: DK-2102-A)

GF-1317 : formulation containing 20.6 % myclobutanil (batch n°: E1743-16)

State crop and application rate : grapes, late application, 4 x 0.048 kg a.s./ha

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./kg)	Buffer zone distance	Max. PEC_{SED} [4] (µg a.s./kg)	TER	Annex VI trigger [5]
myclo-butanil	D 6	ditch	*Chironomus riparius*	30 d static	6.07 (day 0)	3.5 m	8.2	740	10
					13.97 (day 31)	3.5 m	8.2	1704	10

FOCUS Step 4

Only the worst case scenarios are presented in the Listing of End points.

State crop and application rate : apples, early application, 4 x 0.090 kg a.s./ha

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	Buffer zone distance	Max. PEC_{SW} [4] (µg/L)	TER	Annex VI trigger [5]
myclo-butanil	R3	stream	*Oncorhyn-chus mykiss*	96 h static	2.0	14m	2.228	898	100
myclo-butanil	R3	stream	*Oncorhyn-chus mykiss*	21 d flow-through	0.2	14m	2.228	91	10
Systhane 20 EW	R3	stream	*Oncorhyn-chus mykiss*	96 h static	2.04	14m	2.228	916	100
myclo-butanil	R3	stream	*Mysidopsis bahia*	96 h flow-through	0.24	14m	2.228	107	100
myclo-butanil	R3	stream	*Daphnia magna*	21 d semi-static	1.0	14m	2.228	448	10
Systhane 20 EW	R3	stream	*Daphnia magna*	48 h static	1.41	14m	2.228	632	100
GF-1317	R3	stream	*Daphnia magna*	21 d semi-static	0.27	14m	2.228	121	10

myclo-butanil	R3	stream	*Pseudokirchneriella subcapitata*	120 h static	1.1	14m	2.228	493	10
Systhane 20 EW	R3	stream	*Pseudokirchneriella subcapitata*	96 h static	> 0.99	14m	2.228	> 445	10
myclo-butanil	R3	stream	*Chironomus riparius*	30 d static	4.98	14m	2.228	2236	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

Systhane 20 EW : formulation containing 19.8 % myclobutanil (batch n°: DK-2102-A)

GF-1317 : formulation containing 20.6 % myclobutanil (batch n°: E1743-16)

State crop and application rate : apples, early application, 4 x 0.090 kg a.s./ha

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./kg)	Buffer zone distance	Max. PEC_{SED} [4] (µg a.s./kg)	TER	Annex VI trigger [5]
myclo-butanil	D 4	pond	*Chironomus riparius*	30 d static	6.07 (day 0)	6 m	41	148	10
					13.97 (day 31)	6 m	41	341	10

Bioconcentration				
	Active substance	Metabolite 1	Metabolite 2	Metabolite 3
$logP_{O/W}$	2.89 – 3.5			

Bioconcentration				
Bioconcentration factor (BCF)[1] ‡	Since the log P_{OW} of myclobutanil is around 3, the MS agreed during Peer Review that a bioaccumulation study in fish is required.			
Annex VI Trigger for the bioconcentration factor	-	-	-	-
Clearance time (days) (CT_{50})	-	-	-	-
(CT_{90})	-	-	-	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	-	-	-	-

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

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
Systhane 20 EW[1]	> **171 µg form/bee** (33.9 µg a.s./bee)	> **200 µg form/bee** (39.6 µg a.s./bee)
Field or semi-field tests		
Not required. The hazard quotients for oral and contact toxicity are below 50, so no higher tier testing is necessary.		

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

Systhane 20 EW : formulation containing 19.8 % myclobutanil (batch n°: DK-2102-A)

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

Crop and application rate : grapes, 4 x 0.048 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
Systhane 20 EW	oral	< 1.4	50
	contact	< 1.2	50

Crop and application rate : apples, 4 x 0.090 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
Systhane 20 EW	oral	< 2.6	50
	contact	< 2.3	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]	End point	effect[3]	Trigger value
Laboratory tests						
Typhlodromus pyri	proto-nymphs	Systhane 20 EW, glass plates, 14 d	36 g a.s./ha, initial	Corrected mortality Reproduction	50.5 % - 67.3 %	50 % 50 %
Coccinella septempunctata	larvae	Systhane 20 EW, glass plates, 2 + 5 weeks	36 g a.s./ha, initial	Corrected mortality Reproduction	11.9 % -51.8 %	50 % 50 %
Pardosa sp.	-	Systhane 20 EW, sand, 14 d	45 g a.s./ha, initial	Corrected mortality Food consumption	5.6 % - 33.3 %	50 % 50 %
Extended laboratory tests						
Aphidius rhopalosiphi	adult females	Systhane 20 EW, barley plants, 2 + 12 d	36 g a.s./ha, initial	Corrected mortality Reproduction	0.00 % - 43.0 %	50 % 50 %
Aphidius rhopalosiphi	adult females	Systhane 20 EW, barley plants, 2 d + 10 d	90 g a.s./ha, initial	Corrected mortality Reproduction	41.4 % - 52.8 %	50 % 50 %
Aged residue tests						
Aphidius rhopalosiphi	adult females	Systhane 20 EW, barley plants, 2 d + 11 d	288 g a.s./ha, 0DAA	Corrected mortality Reproduction	0.00 % + 10.3 %	50 % 50 %
			780 g a.s./ha, 0DAA	Corrected mortality Reproduction	0.00 % – 10.6 %	50 % 50 %
			1200 g a.s./ha, 0DAA	Corrected mortality Reproduction	6.67 % + 2.2 %	50 % 50 %

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ha)[1,2]	End point	effect[3]	Trigger value
Chrysoperla carnea	larvae	Systhane 20 EW, bean leaves	307 g a.s./ha, 0DAA	Corrected mortality Reproduction	11.43 % + 18.7 %	50 % 50 %
			766 g a.s./ha, 0DAA	Corrected mortality Reproduction	28.57 % + 26.3 %	50 % 50 %
			1380 g a.s./ha, 0DAA	Corrected mortality Reproduction	40.0 % + 3.9 %	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
(for Reproduction parameter : negative % = adverse effect; positive % = no adverse effect)

Systhane 20 EW : formulation containing 19.8 % myclobutanil (batch n°: DK-2102-A)
formulation containing 211 g/L myclobutanil (batch n°: QC2388R301)

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

Field or semi-field tests
In the semi-field test with *Aphidius rhopalosiphi*, hop plants were sprayed at 54 g a.s./ha and at 300 g a.s./ha, both applied 4 times at 10 ± 2 days interval. Untreated barley plants, infested with aphids were placed next to the treated hop plants. The first bioassay was performed after the 1st treatment and the second bioassay was performed after the 4th treatment. The reduction in reproductive ability at the application rate of 54 g a.s./ha was 36 % (bioassay 1) and – 1.6 % (bioassay 2). The reduction in reproductive ability at the application rate of 300 g a.s./ha was 1 % (bioassay 1) and 16.7 % (bioassay 2). Systhane 20 EW has no effects on *Aphidius rhopalosiphi* up to 4 x 300 g a.s./ha. In the field test with *Typhlodromus pyri*, an apple orchard in southern Germany was treated with 0.45 L Systhane 20 EW/ha (89 mL a.s./ha) and with 0.9 L Systhane 20 EW/ha (178 mL a.s./ha), both applied 9 times between the beginning of June and the beginning of September. No effects were observed for the predatory mites (eggs and adults) and for the spider mites (eggs and adults) up to 9 x 0.9 L Systhane 20 EW/ha (equivalent to 9 x 180 g a.s./ha).

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			
Lumbricus terrestris	myclobutanil ‡	acute	LC_{50} = 250 mg a.s./kg soil d.w. $LC_{50\ corr}$ = **125 mg a.s./kg soil d.w.**
Eisenia fetida	Systhane 24 E	acute	LC_{50} = 384 mg form/kg soil d.w. (99 mg a.s./kg soil d.w.) $LC_{50\ corr}$ = **49.5 mg a.s./kg soil d.w.**
Eisenia fetida	Systhane 20 EW	long-term	NOEC = 10.3 mg a.s./kg soil d.w. $NOEC_{corr}$ = **5.15 mg a.s./kg soil d.w.**
Eisenia fetida	myclobutanil butyric acid	acute	LC_{50} > 1000 mg/kg soil d.w. $LC_{50\ corr}$ > 500 mg/kg soil d.w.
Other soil macro-organisms			
Not required.			
Collembola			
Folsomia candida	Systhane 20 EW	long-term	NOEC = 100 mg form/kg soil d.w. (20.5 mg a.s./kg soil d.w.) $NOEC_{corr}$ = **10.25 mg a.s./kg soil d.w.**
Soil micro-organisms			
Nitrogen mineralisation	Systhane 24 E	28 d	- 3 % effect at day 28 at 2.93 mg form/kg soil d.w. (0.76 mg a.s./kg soil d.w.)
Carbon mineralisation	Systhane 24 E	28 d	- 4 % effect at day 28 at 2.93 mg form/kg soil d.w. (0.76 mg a.s./kg soil d.w.)
Field studies[2]			
An earthworm bioconcentration study with myclobutanil (Hoberg J.R., 1993) was conducted. Earthworms were exposed for 14 days to soil treated with myclobutanil. The bioconcentration factor was 0.46 – 0.47 with an uptake rate constant k_u of 1.19 $days^{-1}$ and a depuration rate constant k_d of 2.52 $days^{-1}$. These results demonstrated that the ^{14}C-myclobutanil does not readily bioconcentrate in tissue of *Eisenia fetida* over a 14-day period. The small amount of ^{14}C-residues that accumulated during the exposure were completely eliminated three days after transfer to untreated artificial soil. A litter bag test (Mallet M. J., 2004) was conducted on the edge of a field sown with winter barley. Treatment with a first application of 226 g a.s./ha and a second application of 117 g a.s./ha. A good earthworm population existed at the trial site. Myclobutanil had no adverse effect on the rate of breakdown of straw litter in soil at mean concentrations of 0.1247 – 0.1460 mg a.s./kg soil. This concentration covers the worst case PEC_{soil} of 0.168 mg a.s./kg soil ($PEC_{initial}$ after last application at 20 cm soil depth in apples).			

[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

Systhane 24 E : formulation containing 25.8 % myclobutanil (batch n° : DK-2195-A)
Systhane 20 EW : formulation containing 19.9 % myclobutanil (batch n° : ES-96018)

Toxicity/exposure ratios for soil organisms

Crop and application rate : grapes, 4 x 0.048 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC[2] (mg a.s./kg soil)	TER	Trigger
Earthworms					
Lumbricus terrestris	myclobutanil ‡	acute	PEC_{max} = 0.359 mg a.s./kg soil d.w.	348	10
Eisenia fetida	Systhane 24 E	acute	PEC_{max} = 0.359 mg a.s./kg soil d.w.	138	10
Eisenia fetida	Systhane 20 EW	long-term	$PEC_{plateau}$ = 0.289 mg a.s./kg soil d.w.	17.8	5
Other soil macro-organisms					
Folsomia candida	Systhane 20 EW	long-term	$PEC_{plateau}$ = 0.289 mg a.s./kg soil d.w.	35.5	5

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

Crop and application rate : apples, 4 x 0.090 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC[2] (mg a.s./kg soil)	TER	Trigger
Earthworms					
Lumbricus terrestris	myclobutanil ‡	acute	PEC_{max} = 0.672 mg a.s./kg soil d.w.	186	10
Eisenia fetida	Systhane 24 E	acute	PEC_{max} = 0.672 mg a.s./kg soil d.w.	73.7	10
Eisenia fetida	Systhane 20 EW	long-term	$PEC_{plateau}$ = 0.544 mg a.s./kg soil d.w.	9.47	5
Other soil macro-organisms					
Folsomia candida	Systhane 20 EW	long-term	$PEC_{plateau}$ = 0.544 mg a.s./kg soil d.w.	18.8	5

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

Systhane 24 E : formulation containing 25.8 % myclobutanil (batch n° : DK-2195-A)
Systhane 20 EW : formulation containing 19.9 % myclobutanil (batch n° : ES-96018)

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

In the vegatative vigour test, no test species exhibited morphological abnormalities, except for cabbage. In addition, > 25 % shoot inhibition was noted in onion shoot weight at 300 g a.s./ha, perennial ryegrass shoot weight at 900 g a.s./ha, cabbage shoot weight at 900 g a.s./ha, cucumber shoot weight at 300 and 900 g a.s./ha and soybean shoot length and shoot weight at 900 g a.s./ha.

In the seedling emergence test, shoot weight, but not shoot length or emergence, was affected at greater than 25 % inhibition in perennial ryegrass at the maximum application rate (300 g a.s./ha) and three times the maximum application rate (900 g a.s./ha). No other adverse effects at greater than 25 % inhibition were observed for any of the nine other test species.

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

Test type/organism	End point
Activated sludge	EC_{50} (myclobutanil, 3 h) = 71 mg a.s./L
Pseudomonas sp	-

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

Compartment	
soil	myclobutanil
water	myclobutanil
sediment	myclobutanil
groundwater	myclobutanil

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, R51 for Systhane 20 EW

Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapid and extensive (100% within 96 h) after low dose application
Distribution ‡	Widely distributed; highest levels in liver, kidneys, intestine and adrenals
Potential for accumulation‡	No evidence of accumulation
Rate and extent of excretion ‡	>80% within 96 h evenly divided between urine (35-48%) and faeces (31-44%)
Metabolism in animals ‡	Extensive metabolism in rats (low level of parent compound in urine and faeces) by oxidation of the butyl side chain; no cleavage of the molecule.
Toxicologically significant compounds (animals, plants) ‡	Myclobutanil and metabolites (RH-9089, RH-9090)
Toxicologically significant compounds (environment) ‡	Myclobutanil

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	Male = 1600 mg/kg bw Xn, R22 Female = 2290 mg/kg bw
Rat LD_{50} dermal ‡	> 2000 mg/kg bw
Rat LC_{50} inhalation ‡	>5.1 mg/L 4 h, nose only, highest obtainable concentration
Skin irritation ‡	Non-irritant
Eye irritation ‡	Not irritating (according to available information), but already classified at ECB R36
Skin sensitization (test method used and result) ‡	Non-sensitizer (Maximisation test)

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver
Lowest relevant oral NOAEL / NOEL ‡	3.09 mg/kg bw/day. (90 d and 1 y dog)
Lowest relevant dermal NOAEL / NOEL ‡	100 mg/kg bw/d (4 wk rat)
Lowest relevant inhalation NOAEL / NOEL ‡	No data- not required

Genotoxicity (Annex IIA, point 5.4) ‡	No genotoxic potential

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

Target/critical effect ‡	Testes (atrophy, oligospermatogenesis) (rats); liver (mice)
Lowest relevant NOAEL / NOEL ‡	2.5 mg/kg bw/d (rat)
Carcinogenicity ‡	No carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Parental: slight body weight reduction and liver effects
	Offspring: decreased weight gain of pups during lactation
	Reproduction: Reduced number females delivering litters; increased incidence of still-born pups; at slight parental toxic dose
Lowest relevant NOAEL / NOEL ‡	Parental: 16 mg/kg bw/d
	Offspring: 16 mg/kg bw/d
	Reproductive: 16 mg/kg bw/d
Developmental target / critical effect ‡	Altered viability index without maternal toxicity; Repro.Cat 3, R63
‡ Lowest relevant developmental NOAEL / NOEL	31 mg/kg bw/d (rat study)
Lowest relevant maternal NOAEL / NOEL	94 mg/kg bw/day, (rat study) Clinical signs

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

.....	No data, not required

Other toxicological studies (Annex IIA, point 5.8) ‡

.....	Parent compound: Slight inducer of xenobiotic metabolising enzymes. Not an inducer of peroxisomal proliferation Metabolites and impurities: RH-9090 and RH9089 (plant metabolites): 300 mg/kg bw <LD50oral<1000mg/kg bw Impurities: RH-8812: 300 mg/kg bw <LD50oral<1000mg/kg bw RH-8813: LD50 oral > 3000 mg/kg bw

Medical data (Annex IIA, point 5.9) ‡

.....	No detrimental effects on health in manufacturing personnel

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.025 mg/kg bw/day	Rat, 2 y study	100
AOEL ‡	0.03 mg/kg bw/day	90 d & 1y, dog study	100
ARfD (acute reference dose) ‡	0.31 mg/kg bw	Developmental rat study	100

Dermal absorption (Annex IIIA, point 7.3) ‡

Systhane 20 EW	25% for concentrate and 15% for diluted from an in vivo rat study & comparative human/rat skin study

Acceptable exposure scenarios (including method of calculation)

Operator	RMS assessment POEM: tractor high crop, apple w/o PPE: 39% of AOEL; wine grape: 34% of AOEL w/o PPE German Model: wine grape: 42% and apple 80% of AOEL w/o PPE. EFSA assessment (with revised calculations, not peer reviewed) UK POEM (no PPE worn) Grapes, orchard 160% Apples, orchard 286% UK POEM (PPE worn) Grapes, orchard 54.8% (gloves during M/L) Apples, orchard 75.1% (gloves during M/L and appl.) German model (no PPE worn) Grapes, orchard 42% Apples, orchard 80%

Workers	RMS assessment 32% of AOEL w/o PPEs EFSA assessment (with revised calculations, not peer reviewed) 61.7% of the AOEL with gloves
Bystanders	0.15% of AOEL

Classification and proposed labelling (Annex IIA, point 10)

With regard to toxicological data	R22, R36, R63, Repr. Cat 3

Residues

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

Plant groups covered	Fruit (apples and grapes - representative uses). A metabolism study in wheat (not supported use) was also provided and evaluated.
Rotational crops	Studies not required for perennial crops.
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable
Processed commodities	Study required (data gap)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Unable to conclude
Plant residue definition for monitoring	Myclobutanil (for fruit, only)
Plant residue definition for risk assessment	Myclobutanil + RH-9090 and its conjugates expressed as myclobutanil equivalents (for fruit, only)
Conversion factor (monitoring to risk assessment)	Unable to conclude

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

Animals covered	A new ruminant metabolism study is required (data gap). A metabolism study in laying hens is available but not required.
Time needed to reach a plateau concentration in milk and eggs	Unable to conclude
Animal residue definition for monitoring	Ruminants : Unable to conclude Poultry : Not required.
Animal residue definition for risk assessment	Ruminants : Unable to conclude Poultry : Not required.
Conversion factor (monitoring to risk assessment)	Unable to conclude
Metabolism in rat and ruminant similar (yes/no)	Unable to conclude

Fat soluble residue: (yes/no)	Yes (log P*o/w* myclobutanil 3.17 at room temperature)

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

.....	Not required. Both apples and grapes are long-lived crops that are not grown in rotation with other succeeding crops. Use is only acceptable for permanent crops as rotational crops are not addressed by data. No metabolites including 1,2,4-triazole were formed at detectable levels in a year long laboratory soil incubation study, but it cannot be excluded that they will be formed long term from continuous use of this compound. [21]

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

.....	For all the studies submitted, the recovery values were generally acceptable for myclobutanil and its metabolites (RH-9090 and RH-0294) except for almond hulls and meat at 24 months. -Residues of myclobutanil can be considered as stable in apples and grapes for a minimum of 24 months under frozen storage conditions (–15°C) as no significant residue degradation occurred during storage. -Residues of myclobutanil and its metabolite RH-9090 are considered as stable in muscle and liver for up to 80 days under frozen storage conditions at –10°C. -Residues of the metabolite RH-0294 are considered as stable in milk for up to 15 months under frozen storage conditions at –10°C. -Residues of myclobutanil and its metabolite RH-9090 in almond meat and hulls are stable for 18 months at –10°C. -Residues of myclobutanil and its metabolite RH-9090 in cucumbers are stable for up to 36 months at –10°C. -Residues of myclobutanil and its metabolite RH-9090 in tomatoes are stable for up to 36

[21] Whether data on residue levels in following crops are necessary with regard to triazole derivative metabolites will need to be followed up separately in the future, as this issue concerns a number of other active substances containing the triazole moiety.

	months at –10°C.

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

	Ruminant: yes	Poultry: no	Pig: no
	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: 0.494mg/kgdiet. -Beef cattle: 1.5 mg/kg diet.	Not relevant	Not relevant
Potential for accumulation (yes/no):	Yes – Log P_{ow} : 3.17.	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Unable to conclude.	No calculation of the dietary burden needed.	No metabolism study required.
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels of Myclobutanil in matrices : Mean (max) mg/kg		
Feeding rate in cattle and poultry studies	-1.6 mg/kg in total diet (low treatment level) -16 mg/kg (high treatment level)	No feeding study required.	No feeding study required.
Muscle	open	N/A	N/A
Liver	open	N/A	N/A
Kidney	open	N/A	N/A
Fat	open	N/A	N/A
Milk	open	-	-
Eggs	-	N/A	-

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	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL estimated from trials according to the representative use	STMR (b)
Grapes	North Europe	The residue trials were carried out at a dosing rate ranging between 0.012 and 0.060 kg a.s./ha, 8 applications, BBCH 81-85 (fruit ripening), PHI : 0-28 days. The results are : ** Whole fruit : -*Myclobutanil* : 0.38-0.34-0.295-0.245-0.16-0.51 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : 0.02-0.015-0.01-0.02-0.02-0.03 mg/kg. Additional residue trials can be regarded as acceptable at a later PHI than 14 days (PHI : 28 days) – Summary sheets included in the addendum June 2007: -Whole fruit : -*Myclobutanil* : 0.33-0.29-0.20-0.05-0.10 mg/kg -*RH-9090 expressed as myclobutanil equiv.* : 0.02-0.01-0.02-<0.01-0.02 mg/kg	Samples of whole fruit at day 0 and at different PHIs up to normal harvest time were analysed for parent compound and its alcohol metabolite RH-9090. The residues were expressed as mg myclobutanil equivalent/kg. Decay curves are given with last sampling 28 days after last application. **Note:** **Data gap identified:** The applicant to provide evidence that the residue trials cover	1 mg/kg	0.14 mg/kg

		** Juice : -*Myclobutanil* : 0.09-0.07-0.08 mg/kg -*RH-9090 expressed as myclobutanil equivalent* :<0.01-<0.01-0.01 mg/kg. ** Young wine : -*Myclobutanil* : 0.06-0.04-0.04 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-<0.01-0.01 mg/kg. ** Mature wine : -*Myclobutanil* : 0.07-0.04-0.05 mg/kg -RH-9090 expressed as myclobutanil equivalent : <0.01-<0.01-0.02 mg/kg. ***2004 Myclobutanil residue trials.*** 4 wine grapes trials conducted at an application rate of 0.048 kg a.s./ha, BBCH 81-85 with a spray mixture concentration of 0.0048 kg a.s./hL and a spray volume of 1000 L/ha with a 10 day interval between applications and a 14 day PHI. **Grape bunches -4 applications : -*Myclobutanil* : 0.04-0.07-0.06-0.10 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-0.01-<0.01-<0.01 mg/kg -8 applications : -*Myclobutanil* : 0.07-0.08-0.14-0.08 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-0.01-0.02-0.01 mg/kg	the residue definition for risk assessment with regard to conjugates. It should be demonstrated the method used would extract all conjugates and that the hydrolysis step gives an acceptable yield.		

	South Europe	The residue trials were carried out at a dosing rate ranging between 0.037-0.057 kg a.s./ha, 6 applications, BBCH 85 –89 (fruit ripening – ripe fruit), PHI : 0-14 days. ** Whole fruit : -*Myclobutanil* : 0.063-0.043-0.09-0.04-0.10-0.13 mg/kg -RH-9090 expressed as myclobutanil equivalent : <0.01-<0.01-0.01-<0.01-0.01-0.01 mg/kg. Additional residue trials can be regarded as acceptable at a later PHI than 14 days (PHI : 28 days) – Summary sheets included in the addendum June 2007: -Whole fruit : -*Myclobutanil* : 0.08 mg/kg -*RH-9090 expressed as myclobutanil equiv.* : 0.03 mg/kg ***2004 Myclobutanil residue trials.*** 4 table grapes trials conducted at an application rate of 0.048 kg a.s./ha, BBCH 79-85 with a spray mixture concentration of 0.0048 kg a.s./hL and a spray volume of 1000 L/ha with a 10 day interval between applications and a 14 day PHI. **Grape bunches -4 applications : -*Myclobutanil* : 0.02- 0.03-0.09-0.03 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-<0.01-0.02-<0.01 mg/kg -6 applications : -*Myclobutanil* : 0.06- 0.02-0.10-0.02 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-<0.01-0.02-<0.01 mg/kg 2 further residue trials performed with a spray concentration of 0.00375 kg a.s./hL are acceptable : -*Myclobutanil* : 0.03-0.03 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-<0.01 mg/kg			0.06 mg/kg

Apples	North Europe	The residue trials were performed at a dosing rate ranging between 0.036-0.095 kg a.s./ha, 6 to 12 applications, BBCH 77 –87 (beginning ripening – ripe fruit), PHI : 0-28 days. ** Whole fruit : -*Myclobutanil* : 0.13-0.19-0.12-0.38-0.15-0.14-0.12-0.09-0.089-0.145-0.113-0.348 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-0.02-0.02-0.02-0.02-0.01-0.03-0.01-<0.01-<0.01-<0.01-<0.01 mg/kg. Additional residue trials can be regarded as acceptable at a later PHI than 14 days (PHI : 21, 28 days) – Summary sheets included in the addendum June 2007:: -Whole fruit : -*Myclobutanil* : 0.16-0.16-0.15 mg/kg -*RH-9090 expressed as myclobutanil equiv.* : <0.01-<0.01-0.03 mg/kg ** Wet pomace : -*Myclobutanil* : 0.080-0.225 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-<0.01 mg/kg. ** Juice : -*Myclobutanil* : 0.024-0.037 mg/kg -RH-9090 expressed as myclobutanil equivalent : <0.01-<0.01 mg/kg. ***2004 Myclobutanil residue trials.*** 4 trials conducted at an application rate of 0.090 kg a.s./ha, BBCH 78-85 with a spray mixture concentration of 0.006 kg a.s./hL and a spray volume of 1500 L/ha with a 10 day interval between applications and a 14 day PHI.		0.5 mg/kg	0.15 mg/kg

		**Whole fruit -4 applications : -*Myclobutanil* : 0.21-0.03-0.11-0.15 mg/kg -*RH-9090 expressed as myclobutanil equivalent* :<0.01-<0.01-<0.01-<0.01 mg/kg -12 applications : -*Myclobutanil* : 0.16-0.06-0.18-0.16 mg/kg -*RH-9090 expressed as myclobutanil equivalent* :0.02-0.01-0.03-0.02 mg/kg **Washed fruit -4 applications : -*Myclobutanil* : 0.08 mg/kg -*RH-9090 expressed as myclobutanil equivalent* :<0.01 mg/kg **Raw juice -4 applications : -*Myclobutanil* : 0.01mg/kg -*RH-9090 expressed as myclobutanil equivalent* :<0.01 mg/kg **Wet pomace -4 applications : -*Myclobutanil* : 0.23mg/kg -*RH-9090 expressed as myclobutanil equivalent* :0.01 mg/kg **Dry pomace -4 applications : -*Myclobutanil* : 0.99mg/kg -*RH-9090 expressed as myclobutanil equivalent* :0.06 mg/kg **Juice -4 applications : -*Myclobutanil* : <0.01 mg/kg			

		-*RH-9090 expressed as myclobutanil equivalent* :<0.01 mg/kg **Cooked apple -4 applications : -*Myclobutanil* : 0.04mg/kg -*RH-9090 expressed as myclobutanil equivalent* :<0.01 mg/kg **Puree -4 applications : -*Myclobutanil* : 0.02mg/kg -*RH-9090 expressed as myclobutanil equivalent* :<0.01 mg/kg			

	South Europe	The residue trials were performed at a dosing rate ranging between 0.066-0.125 kg a.s./ha, 4 to 6 applications, BBCH 81 –87 (beginning ripening – ripe fruit), PHI : 14-21 days. ** Whole fruit : -*Myclobutanil* : 0.155-0.10-0.07-0.03-0.129-0.14-0.09-0.13-0.10 mg/kg -RH-9090 expressed as myclobutanil equivalent: 0.012-0.01-0.01-<0.01-0.024-0.01-0.01-<0.01-<0.01mg/kg. Additional residue trials can be regarded as acceptable at a later PHI than 14 days (PHI : 21 days) – Summary sheets included in the addendum June 2007:: -Whole fruit : -*Myclobutanil* : 0.196 mg/kg -*RH-9090 expressed as myclobutanil equiv.* : 0.027 mg/kg ***2004 Myclobutanil residue trials.*** 4 trials conducted at an application rate of 0.090 kg a.s./ha, BBCH 78-81 with a spray mixture concentration of 0.006 kg a.s./hL and a spray volume of 1500 L/ha with a 10 day interval between applications and a 14 day PHI. **Whole fruit -4 applications : -*Myclobutanil* : 0.10-0.04-0.05-0.04 mg/kg -*RH-9090 expressed as myclobutanil equivalent* :<0.01-<0.01-<0.01-<0.01 mg/kg -6 applications : -*Myclobutanil* : 0.07-0.06-0.05-0.07 mg/kg -*RH-9090 expressed as myclobutanil equivalent* :<0.01-<0.01-<0.01-<0.01 mg/kg. 2 further residue trials performed with a spray concentration of 0.0045 kg a.s./hL are acceptable: -*Myclobutanil* : 0.043-0.07 mg/kg -*RH-9090 expressed as myclobutanil equivalent* : <0.01-<0.01 mg/kg			0.08 mg/kg

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

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

a) For myclobutanil and RH-9090:

ADI	0.025 mg/kg b.w./day
TMDI (% ADI) according to WHO European diet	**Not finalised** due to data gaps identified (conjugates, food of animal origin, isomers). Indicative, not peer reviewed assessment by RMS without considering the data gaps identified: 9%
TMDI (% ADI) according to national (to be specified) diets	**Not finalised** due to data gaps identified. Indicative, not peer reviewed assessment by RMS without considering the data gaps identified: 31.6% German model, <5% for all the categories of consumers according to the UK PSD ten Consumer model
IEDI (WHO European Diet) (% ADI)	Not calculated.
NEDI (specify diet) (% ADI)	Not calculated.
Factors included in IEDI and NEDI	n/a
ARfD	0.31 mg/kg b.w/day
IESTI (% ARfD)	Not calculated.
NESTI (% ARfD) according to national (to be specified) large portion consumption data	**Not finalised**. Indicative, not peer reviewed assessment by the RMS, pending confirmation (data gaps on conjugates, isomers) Most sensitive consumers/commodity: infants /apples : 12.6 % of ARfD according to the UK PSD ten Consumer model.
Factors included in IESTI and NESTI	-

b) For triazole derivative metabolites:

Not finalised. Risk assessment for triazole derivative metabolites should be followed up separately in the future. For details refer to EFSA conclusion chapter 3.

c) Drinking water risk assessment

Note: There might be additional consumer exposure through drinking water due to the myclobutanil butyric acid metabolite leaching to ground water at significant levels. There are indication that also myclobutanil has the potential t contaminate groundwater. For details refer to EFSA conclusion chapter 4.

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

Residue trial references	RAC/Processed commodities	Myclobutanil/RH-9090 residues in whole fruit	Myclobutanil /RH-9090 residues in processed fractions	Transfer factors (RAC/processed fraction) for myclobutanil	% of transference
		Apples			
Trial N°DEU86F21221	**Unwashed whole fruit**	0.145/<0.01	na		
	Puree	na	0.080/<0.01	*0.55*	-
	Juice	na	0.024/<0.01	*0.165*	-
Trial N°DEU86F21241	**Unwashed whole fruit**	0.348/<0.01	na		
	Puree	na	0.225/<0.01	*0.646*	-
	Juice	na	0.037/<0.01	*0.106*	-
Trial AF/8164/DE/4 GHE-P-10967 (Treatment at the critical GAP rate)	**Unwashed whole fruit**	0.08/<0.01			
	Washed fruit		0.08/<0.01	*1.0*	*100.33*
	Raw juice		0.01/<0.01	*0.125*	*7.9*
	Wet pomace		0.23/0.01	*2.87*	*100.1*
	Dried pomace		0.99/0.06	*12.37*	*71.96*
	Juice		<0.01/<0.01	*0.125*	*7.9*
	Cooked apple		0.04/<0.01	*0.5*	*50.0*
	Puree		0.02/<0.01	*0.25*	*12.0*
Trial AF/8164/DE/4 GHE-P-10967 (Treatment rate is 5 fold the critical GAP rate)	**Unwashed whole fruit**	0.51/0.05			
	Washed fruit		0.52/0.03	*1.019*	*102.18*
	Raw juice		0.06/0.02	*0.117*	*6.5*
	Wet pomace		1.57/0.05	*3.07*	*97.49*
	Dried pomace		6.0/0.25	*11.76*	*57.9*
	Juice		0.06/0.02	*0.117*	*6.5*
	Cooked apple		0.28/0.03	*0.54*	*53.91*
	Puree		0.13/0.02	*0.25*	*12.14*
		Grapes			
Trial N°RH/203/2/G	**Unwashed whole white grapes**	0.41/0.02	na		
	Juice	na	0.09/<0.01	*0.219*	*15.33*
	Young wine	na	0.06/<0.01	*0.146*	*2.90*
	Mature wine	na	0.07/<0.01	*0.170*	
Trial N°RH/203/3/G	**Unwashed whole red grapes**	0.34/0.015	na		
	Juice	na	0.07/<0.01	*0.205*	
	Young wine	na	0.04/<0.01	*0.117*	
	Mature wine	na	0.04/<0.01	*0.117*	
Trial N°RAS/18/4/F	**Unwashed whole red grapes**	0.51/0.03	na		
	Juice	na	0.08/0.01	*0.156*	*10.16*
		na	0.04/0.01	*0.078*	*3.08*

Residue trial references	RAC/Processed commodities	Myclobutanil/RH-9090 residues in whole fruit	Myclobutanil /RH-9090 residues in processed fractions	Transfer factors (RAC/processed fraction) for myclobutanil	% of transference
Apples					
	Young wine **Mature wine**	na	0.05/0.02	*0.098*	

Na : not applicable
- : Material balance not available.
RAC : Raw agricultural commodity.
Limit of Quantification for all the processed commodities : 0.01 mg/kg.
Remark :
Grapes : no data were provided on raisins.

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

Apples.....	0.5 mg/kg
Grapes.....	1 mg/kg
Ruminants milk, muscle, fat, liver and kidney	likely to be necessary, but unable to conclude

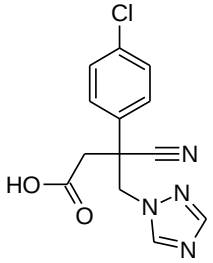
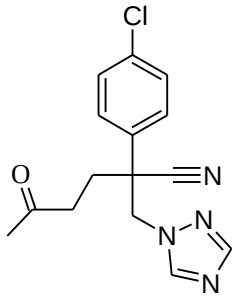
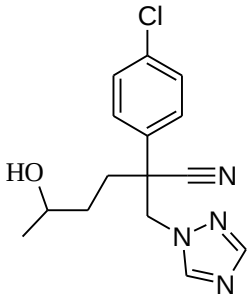
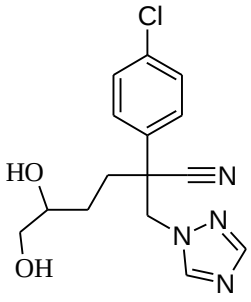
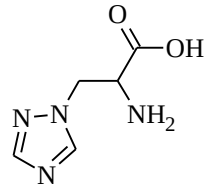
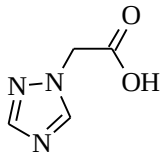
When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

APPENDIX B – ABBREVIATIONS USED IN THE LIST OF END POINTS

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

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

APPENDIX C – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
myclobutanil butyric acid	(3*RS*) 3-(4-chlorophenyl)-3-cyano-4-(1*H*-1,2,4-triazol-1-yl)butanoic acid	
RH-9089	(2*RS*) 2-(4-chlorophenyl)-5-oxo-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile	
RH-9090	(2*RS*,5*RS*) 2-(4-chlorophenyl)-5-hydroxy-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile	
RH-0294	(2*RS*,5*RS*) 2-(4-chlorophenyl)-5,6-dihydroxy-2-(1*H*-1,2,4-triazol-1-ylmethyl)hexanenitrile	
triazolyl alanine	(2*RS*) 2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid	
triazolyl acetic acid	1*H*-1,2,4-triazol-1-ylacetic acid	

1,2,4-triazole	1*H*-1,2,4-triazole