CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion regarding the peer review of the pesticide risk assessment of the active substance 2,5-dichlorobenzoic acid methylester

Issued on 26 September 2008

SUMMARY

2,5-dichlorobenzoic acid methylester is one of the 84 substances of the third stage Part B of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the EU-Commission.

Germany being the designated rapporteur Member State submitted the DAR on 2,5-dichlorobenzoic acid methylester in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 19 June 2007. The peer review was initiated on 10 December 2007 by dispatching the DAR for consultation of the Member States and the sole applicant Stähler International GmBH&CoKG. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in June-July 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in August-September 2008 leading to the conclusions as laid down in this report.

This conclusion was reached on the basis of the evaluation of the representative uses as a plant growth regulator/fungicide for grafting in grapevines, indoor use only. Full details of the GAP can be found in the attached list of endpoints.

[1] 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 "Rebwachs WF", a wax formulation containing 0.035 g/kg 2,5-dichlorobenzoic acid methylester and 1g/kg 8-hydroxyquinoline; it has no CropLife International code.

No residue methods are supplied or required for this active substance because the use will not lead to residues in plants, animals or the environment.

Sufficient analytical data relating to physical, chemical and technical properties are available to ensure that at least limited quality control measurements of the plant protection product are possible. The method of analysis for the active substance in the formulation has been identified as a data gap. There are also data gaps for Henry's law constant, octanol/water partition co-efficient and for water solubility. The technical specification cannot be finalised as new batch data are required. Further information on the starting materials has also been identified as a data gap.

In the mammalian metabolism studies 2,5-dichlorobenzoic acid methylester was rapidly and completely absorbed after oral administration, it suffered extensive metabolism to the free acid[2] and the glycine conjugate[3] and was rapidly excreted almost exclusively via urine. Acute oral toxicity was moderate in rat and classification with Xn, R22 ("harmful if swallowed") was proposed. No classification was proposed for dermal or inhalation toxicity, although no study could be concluded by inhalation due to the physico-chemical properties of the active substance; it was not a skin irritant and no potential for skin sensitisation was found, however, classification with Xi, R36 ("irritating to eyes") was proposed. Only one 28-day oral study in rat gave indication of the No Observed Adverse Effect Level (NOAEL) for the substance (100 mg/kg bw/day). The waiving of further short term-, long term- and reproductive studies was considered acceptable on the basis of the low amount of the active substance present in the product (0.0035 %), the low production volume (10-20 kg/year) and the lack of consumer exposure through residues. No potential for genotoxicity or neurotoxicity was observed. No Acceptable Daily Intake (ADI) or Acute Reference Dose (ARfD) were allocated due to the lack of data, but are not required for the single use notified. The Acceptable Operator Exposure Level (AOEL) was 0.1 mg/kg bw/day based on the oral 28-day study in rat and applying a safety factor of 1000. As no study was provided, a default dermal absorption value of 100 % was assumed for the risk assessment. The level of operator exposure calculated for the representative formulation "Rebwachs WF" was below the AOEL according to the TGD[4]. Considering the very specific use of 2,5-dichlorobenzoic acid methylester, worker and bystander exposure were not considered relevant.

[2] M11.7: 2,5-dichlorobenzoic acid
[3] M7.2: 2,5-dichlorobenzoylglycine
[4] Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances, Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, Part I (Risk Assessment for Human Health), EUR 20418 EN/1

The active substance 2,5-dichlorobenzoic acid methylester is used as grafting wax for improved callus formation. This is very early in the life-cycle of a vine and it is circa four years before a harvestable crop is produced. Over this period of time the residue will be completely broken down and therefore there will be no significant residues in grapes.

No reliable studies on the fate and behaviour in the environment or calculations of predicted environmental concentrations (PEC) in soil, surface water, ground water or air of 2,5-dichlorobenzoic acid methylester were available. Due to the representative use of the active substance and the handling of the treated grafts thereafter, the contamination of the environment with 2,5-dichlorobenzoic acid methylester or its possible metabolites is regarded as negligible. A data gap was identified for a ready biodegrability test, but only for classification and labelling purposes.

A risk assessment to non-target species was not conducted. Due to the representative use of 2,5-dichlorobenzoic acid methylester, the exposure of non-target species was considered to be negligible. As for the classification and labelling of the active substance, a data gap was identified to provide acute aquatic toxicity studies.

Key words: 2,5-dichlorobenzoic acid methylester, peer review, risk assessment, pesticide, plant growth regulator

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000 as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. 2,5-dichlorobenzoic acid methylester is one of the 84 substances of the third stage, part B, covered by the Regulation (EC) No 1490/2002 designating Germany as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Germany submitted the report of its initial evaluation of the dossier on 2,5-dichlorobenzoic acid methylester, hereafter referred to as the draft assessment report, received by EFSA on 19 June 2007. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1095/2007 on 10 December 2007 to the Member States and the main applicant Stähler International GmBH&CoKG 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, EFSA identified and agreed on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in expert meetings in June-July 2008. 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 during a written procedure with the Member States in August-September 2008 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 Protection Products and their Residues (PPR).

In accordance with Article 11c(1) of the amended 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 endpoints for the active substance as well as the formulation is provided in appendix 1.

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

- the comments received,
- the resulting reporting table (revision 1-1 of 15 April 2008)

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 (revision 2-1 of 23 September 2008).

Given the importance of the draft assessment report including its addendum (compiled version of August 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

2,5-dichlorobenzoic acid methylester is the used common name for methyl-2,5-dichlorobenzoate (IUPAC); there is no ISO common name.

2,5-dichlorobenzoic acid methylester is presented as a plant growth regulator/fungicide; it's mode of action is unknown.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

At the moment no minimum purity of 2,5-dichlorobenzoic acid methylester as manufactured can be given, because further clarification is needed. In the original DAR only two batches were analysed; further data were supplied, however, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review. However, it was pointed out that these new data consisted of three batches; two of them were the same batches already submitted with a re-analysis which resulted in a different impurity profile. The meeting of experts felt that the whole data-set was poor and a new batch analysis with fully validated methods of analysis has been identified as a data gap. Therefore there is no specification for this active substance.

It was also noted that full details of all starting materials were not available. No FAO specification exists for this active substance.

The content of 2,5-dichlorobenzoic acid methylester in the representative formulation is 0.035 g/kg (pure).

Beside the specification, 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 2,5-dichlorobenzoic acid methylester or the respective formulation. However, the following data gaps were identified:

- Henry's law constant
- Water solubility at pH 7
- Log P_{ow} at pH 4 and 7
- Method of analysis for the active substance in the formulation

The requirement for Log P_{ow} at pH 4 and 7 was agreed by the meeting of experts, however, given that the meeting also agreed that it will not dissociate, it seems that the requirement is not logical. But as this data gap was agreed by the meeting of experts, it will remain.

The main data regarding the identity of 2,5-dichlorobenzoic acid methylester and its physical- and chemical properties are given in appendix 1.

However, sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that at least limited quality control measurements of the plant protection product are possible. The main issue being the data gap for the method of analysis for the active substance in the formulation.

No residue methods are supplied or required for this active substance because the use will not lead to residues in plants or the environment.

2. Mammalian toxicology

2,5-dichlorobenzoic acid methylester was discussed at the PRAPeR meeting of experts on mammalian toxicology (PRAPeR 54) in July 2008 on basis of the draft assessment report (June 2007) and the addendum of May 2008.

No analysis of the impurity profile of the batches used in the toxicological studies is available. However, the meeting agreed that, considering the notified product, this is not an issue of concern.

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

In rat, bioavailability of 2,5-dichlorobenzoic acid methylester was almost complete comparing the total renal excretion after oral and intravenous application as shown by 90 % and 99 % of the administered dose being eliminated by urine following intravenous and oral administration, respectively, within 24 hours. In faeces, less than 1 % of the dose was recovered after low dosing of 10 mg/kg bw which increased to about 10 % with a high dosing of 1000 mg/kg bw. Distribution of the radioactivity was observed according to the excretion organs; highest concentrations of the active substance were found in the gastrointestinal tract and content, blood, liver and kidneys and no particular accumulation has been detected.

The free acid[5] and the glycine conjugate[6] were identified and characterised as major metabolites of 2,5-dichlorobenzoic acid methylester representing respectively 73.4 % and 18.6% of the administered single low dose in the 24-hour urine samples. In addition, three acylglucuronide isomers[7] were detected dose-dependently each accounting for up to 2 % of the dose administered.

The meeting discussed the relevance of the metabolite 2,5-dichlorobenzoic acid. It was noted that the parent is likely to be of similar toxicity as the metabolite, for which more toxicological information is probably available. The Member State experts agreed with the rapporteur Member State to consider 2,5-dichlorobenzoic acid as a relevant metabolite.

2.2. ACUTE TOXICITY

The acute oral toxicity of 2,5-dichlorobenzoic acid methylester was moderate with an oral LD_{50} in rat of 1030 mg/kg bw; classification as **Xn ("harmful")**, and risk phrase **R22 ("harmful if swallowed")** was proposed. Low toxicity was observed upon dermal administration; the acute toxicity test by inhalation could not be concluded due to technical problems to reach the necessary concentrations in the aerosol caused by the physico-chemical properties of the active substance. 2,5-dichlorobenzoic acid methylester was not irritating to skin; in the eye-irritation study, only a 10 % dilution of the substance was used, which lead to slightly irritating effects, not triggering classification as tested, however, it could not be ruled out that the concentrate would not lead to stronger irritation to the eyes and therefore the experts agreed to propose a classification as **Xi ("irritant")**, and risk phrase **R36 ("irritating to eyes")** as a precautionary principle. In a Magnusson and Kligman test, no symptom of skin sensitisation was observed with 2,5-dichlorobenzoic acid methylester.

[5] M11.7 : 2,5-dichlorobenzoic acid
[6] M7.2 : 2,5-dichlorobenzoylglycine
[7] M5.0 : 2,5-dichlorobenzoic acid glucuronide I;
M5.8 : 2,5-dichlorobenzoic acid glucuronide II;
M6.5 : 2,5-dichlorobenzoic acid glucuronide III

2.3. SHORT TERM TOXICITY

The short term effects of 2,5-dichlorobenzoic acid methylester were investigated in a two-week study (dose range-finding and considered as supplementary) and in a 28-day study by gavage in rat, including neurological screening investigations.

In the 28-day study, clinical signs of neurotoxic effects were apparent at 300 and 900 mg/kg bw/day; additionally, the high dose of 900 mg/kg bw/day presented reduced bodyweight and haematological parameters, liver and heart toxicity as well as oligospermia in the epididymis. **The NOAEL was the dose level of 100 mg/kg bw/day**. Although some weaknesses were highlighted by the experts in the reporting of the original study, it was considered as acceptable in this case, provided that a clear statement is made that this is only justifiable taking into account the restricted use of the plant protection product.

No short term toxicity study was submitted with a second (non-rodent) species. The argumentation presented for the waiving of these studies was based on the low amount of active substance present in the product (0.0035 %) and the low production volume (10-20 kg/year), and the fact that there is no consumer exposure, and a maximum application time of two months is foreseen for operator exposure. The experts agreed that, for the representative use of the active substance, the non-submission of further short term studies is acceptable.

2.4. GENOTOXICITY

2,5-dichlorobenzoic acid methylester was tested in three *in vitro* and one *in vivo* assay measuring several endpoints of potential genotoxicity such as gene mutation using bacteria and mammalian cells and chromosomal aberrations.

Results from the mutagenicity studies indicated that 2,5-dichlorobenzoic acid methylester does not induce reverse mutation in any of the bacterial strains tested of *Salmonella typhimurium* and *Escherichia coli*. No clastogenic effect was seen using Chinese hamster ovary (CHO) cells; no mutagenic effect was induced in either the CHO/hypoxanthine-guanine phosphoribosyl transferase (HPRT) forward mutation assay *in vitro*, or in the mouse micronucleus test *in vivo*.

Overall, no genotoxic potential was attributed to 2,5-dichlorobenzoic acid methylester.

2.5. LONG TERM TOXICITY

No long term toxicity- or carcinogenicity studies have been submitted. Negative genotoxicity tests were provided. Considering the reasoning provided in 2.3 for waiving short term studies, and in view of the lack of consumer exposure, no ADI is required, therefore the non-submission of these studies was considered acceptable by the experts.

2.6. REPRODUCTIVE TOXICITY

No reproductive toxicity study was provided. Considering the reasoning provided in 2.3 for waiving short term studies, mainly based on the low amount of the active substance in the plant protection

product and the low production volume, the experts agreed that the non-submission of reproduction toxicity studies is acceptable. It was noted that even considering the worst classification regarding reproductive or developmental toxicity, the plant protection product would not be labelled in view of the low concentration of the active substance.

2.7. NEUROTOXICITY

No neurotoxicity study was submitted. A 28-day study in rat including a neurological screening was available; no signs of neurotoxicity were seen in the acute toxicity studies. It is not a substance that would trigger delayed neurotoxicity or specific neurotoxicity investigations, therefore no study is required.

2.8. FURTHER STUDIES

No study was submitted, none is required.

2.9. MEDICAL DATA

No adverse health effects which could be related to 2,5-dichlorobenzoic acid methylester have been observed in employees at the production plant since 20 years. Further data on the diagnosis of poisoning and proposed treatment were provided in the addendum.

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

ADI

Based on the submitted database, it was not possible to derive an ADI. However, considering the way of application of 2,5-dichlorobenzoic acid methylester in "Rebwachs WF", no exposure of consumers is foreseen, as no residues are expected to occur. Therefore, **no ADI for 2,5-dichlorobenzoic acid methylester was allocated.**

AOEL

The rapporteur Member State proposed to base the AOEL on the oral 28-day study in rat with a NOAEL of 100 mg/kg bw/day and applying a safety factor of 1000 due to the limited number of studies submitted (only one species was tested for short term exposure, no oral 90-day study and no reproductive toxicity study were provided). Since oral absorption was quite complete, no correction factor was required relative to oral absorption. **The resulting AOEL was 0.1 mg/kg bw/day.** The meeting agreed with this proposal.

ARfD

Initially in the draft assessment report, the rapporteur Member State proposed to set the ARfD at 1 mg/kg bw based on the oral 28-day study in rat with a NOAEL of 100 mg/kg bw/day and applying

a safety factor of 100. On the basis of the notified use the meeting of experts concluded that no ARfD was necessary. It was highlighted once more that this is a specific exception, in line with the waiving of many toxicological studies. **No ARfD was allocated.**

2.11. DERMAL ABSORPTION

No study was performed on the dermal absorption of 2,5-dichlorobenzoic acid methylester, therefore a **default value of 100 %** was agreed on the basis of the physico-chemical properties of the active substance.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product "Rebwachs WF" consists of grafting wax containing nominal 0.035g/kg of 2,5-dichlorobenzoic acid methylester and 1g/kg of 8-hydroxyquinoline. The assessment below has only considered the 2,5-dichlorobenzoic acid methylester component of the formulation. Since there is no agreed procedure for performing combined assessments for more than one active substance, combined exposure to 2,5-dichlorobenzoic acid methylester and 8-hydroxyquinoline has to be taken into account at Member State level. Consequently, the risk assessment for the formulation cannot be concluded for the operators.

"Rebwachs WF" is used to provide physical protection and aid callus formation on grafted grapevines. The grafting of the grapevines is mostly done in greenhouses. They are dipped into the melted undiluted product/wax and put into a forcing box. Later on the young grape vines are placed into the soil.

Operator exposure

According to the notifier an operator uses in general 12-15 kg "Rebwachs WF"/day (8 hours/day). The total duration of the procedure is two months at maximum (about 40 working days). The concentration of 2,5-dichlorobenzoic acid methylester in the product is 0.035 g/kg. Therefore, one person (using 15 kg "Rebwachs WF"/day) uses 0.525g 2,5-dichlorobenzoic acid methylester/day.
Due to the lack of an appropriate exposure model, the operator exposure estimates were based on default values from the TGD[8]. Based on worst-case assumptions (for inhalation exposure it was assumed that the whole amount of active substance goes into the air) estimated systemic exposure to 2,5-dichlorobenzoic acid methylester accounted for **51.5 % of the proposed systemic AOEL** of 0.1 mg/kg bw/day. By using appropriate personal protective equipment (PPE) as gloves, exposure will be reduced further. In addition, greenhouses are normally well aerated.

[8] Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances, Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, Part I (Risk Assessment for Human Health), EUR 20418 EN/1

The risk assessment of the inhalation of the wax melted at 65–75 °C was also discussed by the experts; it was concluded that the relevant approved workplace-exposure limits should apply in the case of paraffin wax fumes.

Worker exposure

Worker exposure was not considered relevant as no exposure is expected. The grapevines are planted in nurseries after some weeks of storage in forcing boxes; by this time, most of the active substance will have dissipated by chemical or physical means.

Bystander exposure

According to the specific use of 2,5-dichlorobenzoic acid methylester in greenhouses where the presence of bystanders is not expected during treatments, bystander exposure was not considered relevant.

3. Residues

The active substance 2,5-dichlorobenzoic acid methylester is used as a grafting wax for improved callus formation. This is very early in the life-cycle of a vine and it is circa four years before a harvestable crop is produced. Over this period of time the residue will be completely broken down and therefore there will be no significant residues in grapes.

4. Environmental fate and behaviour

2,5-dichlorobenzoic acid methylester was discussed at the PRAPeR experts' meeting for environmental fate and behaviour (PRAPeR 52) in July 2008 on the basis of the draft assessment report (June 2007) and the addendum (May 2008).

Reliable studies, experiments on the environmental fate and behaviour or PEC calculations of 2,5-dichlorobenzoic acid methylester were not available. Due to the representative use of the active substance and the handling of the treated grafts thereafter, contamination of the environment with 2,5-dichlorobenzoic acid methylester or its possible metabolites was regarded as negligible. Therefore, with the exception of ready biodegradability, no data gap was proposed by the peer review.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

Information on route of degradation of 2,5-dichlorobenzoic acid methylester in soil was not available. For comparison, some information on route of degradation of chloramben, 2,3,6-trichlorobenzoic acid and dicamba in soil was included in the draft assessment report, although the dossier of

2,5-dichlorobenzoic acid methylester did not contain this information. Therefore, the conclusion from the DAR that 2,5-dichlorobenzoic acid methylester would have a similar degradation pathway as these compounds, was not accepted by the meeting of experts. This information regarding chloramben, 2,3,6-trichlorobenzoic acid and dicamba is not essential and the risk assessment can be finalised without these data.
It was agreed that due to the representative use in the greenhouse as wax formulation, soil exposure to 2,5-dichlorobenzoic acid methylester is expected to be negligible.

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

Information on rate of degradation of 2,5-dichlorobenzoic acid methylester in soil was not available.
It was agreed that due to the representative use in the greenhouse as wax formulation, soil exposure to 2,5-dichlorobenzoic acid methylester is expected to be negligible.
PECsoil was calculated using the results of an experiment, which was not accepted by the Member State experts due to insufficient information on the methodology.

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

Information on the mobility of 2,5-dichlorobenzoic acid methylester in soil was not available.
It was agreed that due to the representative use in the greenhouse as wax formulation, soil exposure to 2,5-dichlorobenzoic acid methylester is expected to be negligible.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Neither information on hydrolytic degradation, photochemical degradation of 2,5-dichlorobenzoic acid methylester or experiments in water-sediment systems, nor a ready biodegradability test or PECsw/sed calculations were available in the original dossier. It was agreed that due to the representative use in the greenhouse as wax formulation, direct or indirect exposure of surface waters to 2,5-dichlorobenzoic acid methylester is expected to be negligible.
For classification and labelling purposes information on ready biodegradability is required (in accordance with the provisions of Council Directive 67/548/EEC), therefore a data gap was identified for a ready biodegradability test. The study had already been submitted to the rapporteur Member State, however in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review.

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

PECgw calculations or information on the potential ground water contamination of 2,5-dichlorobenzoic acid methylester or its possible metabolites were not available. It was agreed that due to the representative use in the greenhouse as wax formulation, exposure of ground water to 2,5-dichlorobenzoic acid methylester is expected to be negligible.

4.3. FATE AND BEHAVIOUR IN AIR

2,5-dichlorobenzoic acid methylester is a highly volatile compound, its vapour pressure is 0.32 kPa at 20 °C and 0.37 kPa at 25 °C. Assuming an atmospheric hydroxyl radical concentration of $5x10^5$ radicals in a cm^3 (for 24 hours a day), the estimated photo-oxidative degradation half-life in the atmosphere was 46.3 days using the method of Atkinson. The experts agreed that the potential for long range atmospheric transport is an intrinsic property of the substance; however, taking into account the particular use of the substance and the type of formulation, very little releases to the environment are expected. Member States should be aware that other formulations with the active substance applied for other uses may result in a potential for long range atmospheric transport.

5. Ecotoxicology

2,5-dichlorobenzoic acid methylester was discussed at the PRAPeR expert's meeting for ecotoxicology (PRAPeR 53, sub-group 1) in July 2008 on the basis of the draft assessment report (DAR) and the addendum from May 2008.

The relevant supported use evaluated was against *Bortytis cinerea* in grape vine grafting for improved callusing (indoor application). The name of the product is "Rebwachs WF" with a concentration of 0.035g/kg of 2,5-dichlorobenzoic acid methylester and 1g/kg of 8-hydroxyquinoline.

Due to the indented use the exposure to non-target species was considered negligible, therefore no standard risk assessment was conducted.

5.1. RISK TO TERRESTRIAL VERTEBRATES

No studies were provided. As relevant exposure was considered to be negligible, no data were required. A risk assessment was not necessary.

5.2. RISK TO AQUATIC ORGANISMS

No relevant exposure was expected for the aquatic environment (see paragraph 4.2.1). In an experiment aimed at the determination of the release of 2,5-dichlorobenzoic acid methylester and 8-hydroxyquinoline from a fortified "Rebwachs WF" formulation into water (Frauen *et al*., 2004), only 2.4% of 2,5-dichlorobenzoic acid methylester and less than 24% of 8-hydroxyquinoline could be dissolved in the water after intensive shaking. Therefore, risk assessment to aquatic organisms was

not necessary. For classification and labelling purposes, static acute toxicity studies on fish, daphnia and algae were submitted by the applicant and evaluated by the rapporteur Member State in addendum 1 (May 2008) as not valid. In view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review. Therefore, a data gap was identified by the meeting of member state experts to provide further acute aquatic toxicity studies allowing the classification and labelling of 2,5-dichlorobenzoic acid methylester.

5.3. RISK TO BEES

No studies were provided. As relevant exposure was considered to be negligible, no data were required. A risk assessment was not necessary.

5.4. RISK TO OTHER ARTHROPOD SPECIES

No studies were provided. As relevant exposure was considered to be negligible, no data were required. A risk assessment was not necessary.

5.5. RISK TO EARTHWORMS

No studies were provided. As relevant exposure was considered to be negligible, no data were required. A risk assessment was not necessary.

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

No studies were provided. As relevant exposure was considered to be negligible, no data were required. A risk assessment was not necessary.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No studies were provided. As relevant exposure was considered to be negligible, no data were required. A risk assessment was not necessary.

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

No studies were provided. As relevant exposure was considered to be negligible, no data were required. A risk assessment was not necessary.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No studies were provided. As relevant exposure was considered to be negligible, no data were required. A risk assessment was not necessary.

6. Residue definitions

Soil

Definition for risk assessment: not set or required

Definition for monitoring: not set or required

Water

Ground water

Definition for exposure assessment: not set or required

Definition for monitoring: not set or required

Surface water

Definition for risk assessment: not set or required

Definition for monitoring: not set or required

Air

Definition for risk assessment: 2,5-dichlorobenzoic acid methylester

Definitions for monitoring: not set or required

Food of plant origin

Definition for risk assessment: not set or required

Definition for monitoring: not set or required

Food of animal origin

Definition for risk assessment: not set or required

Definition for monitoring: not set or required

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
None		

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 activity
None					

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
None	

Air

Compound (name and/or code)	Toxicology
2,5-dichlorobenzoic acid methylester	The acute toxicity test by inhalation could not be concluded due to technical problems to reach the necessary concentrations in the aerosol caused by the physico-chemical properties of the active substance – this was accepted by the experts considering the low amount of active substance in the product and no risk was anticipated[9]

[9] The applicant announced the submission of an acute toxicity study by inhalation conducted with the formulation at Member State level.

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

- The purity of all raw materials used in the manufacturing process was identified as a data gap (relevant for all uses evaluated, data gap identified by PRAPeR meeting of experts July 2008, proposed submission date unknown, refer to chapter 1).
- 5-batch data with supporting analytical data were identified as a data gap (relevant for all uses evaluated, data gap identified by PRAPeR meeting of experts July 2008, proposed submission date unknown, refer to chapter 1).
- Henry's law constant was identified as a data gap (relevant for all uses evaluated, data gap identified by PRAPeR meeting of experts July 2008, proposed submission date unknown, refer to chapter 1).
- Solubility in water at pH 7 was identified as a data gap (relevant for all uses evaluated, data gap identified by PRAPeR meeting of experts July 2008, proposed submission date unknown, refer to chapter 1).
- Octanol/water partition co-efficient at pH 4 and 7 has been identified as a data gap (relevant for all uses evaluated, data gap identified by PRAPeR meeting of experts July 2008, proposed submission date unknown, refer to chapter 1).
- Analytical method for the plant protection product has been identified as a data gap (relevant for all uses evaluated, data gap identified by PRAPeR meeting of experts July 2008, proposed submission date unknown, refer to chapter 1).
- Ready biodegrability test of 2,5-dichlorobenzoic acid methylester for classification and labelling purpose was identified as a data gap (relevant for all uses evaluated, data gap identified by PRAPeR meeting of experts July 2008, study has been submitted to the RMS, not evaluated nor peer reviewed, refer to chapter 4.2.1).
- Acute toxicity studies on aquatic organisms for classification and labelling purpose was identified as a data gap (relevant for all uses evaluated, data gap identified by PRAPeR 53 meeting of experts July 2008, proposed submission date unknown, refer to section 5.2).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

This conclusion was reached on the basis of the evaluation of the representative uses as a plant growth regulator/fungicide for grafting in grapevines, indoor use only. Full details of the GAP can be found in the attached list of endpoints.

The representative formulated product for the evaluation was "Rebwachs WF" a wax formulation containing 0.035 g/kg 2,5-dichlorobenzoic acid methylester and 1g/kg 8-hydroxyquinoline; it has no CropLife International code.

No residue methods are supplied or required for this active substance because the use will not lead to residues in plants, animals or the environment.

Sufficient analytical data relating to physical, chemical and technical properties are available to ensure that at least limited quality control measurements of the plant protection product are possible. The method of analysis for the active substance in the formulation has been identified as a data gap. There are also data gaps for Henry's law constant, octanol/water partition co-efficient and for water solubility. The technical specification cannot be finalised as new batch data are required. Further information on the starting materials has also been identified as a data gap.

In the mammalian metabolism studies, 2,5-dichlorobenzoic acid methylester was rapidly and completely absorbed after oral administration, it suffered extensive metabolism to the free acid and the glycine conjugate and was rapidly excreted almost exclusively via urine. Acute oral toxicity was moderate in rat and classification with Xn, R22 ("harmful if swallowed") was proposed. No classification was proposed for dermal or inhalation toxicity, although no study could be concluded by inhalation due to the physico-chemical properties of the active substance; it was not a skin irritant and no potential for skin sensitisation was found, however, classification with Xi, R36 ("irritating to eyes") was proposed. Only one 28-day oral study in rat gave indication of the NOAEL for the substance (100 mg/kg bw/day). The waiving of further short term-, long term- and reproductive studies was considered acceptable on the basis of the low amount of the active substance present in the product (0.0035 %), the low production volume (10-20 kg/year) and the lack of consumer exposure through residues. No potential for genotoxicity or neurotoxicity was observed. No ADI or ARfD were allocated due to the lack of data, but are not required for the single use notified. The AOEL was 0.1 mg/kg bw/day based on the oral 28-day study in rat and applying a safety factor of 1000. As no study was provided, a default dermal absorption value of 100 % was assumed for the risk assessment. The level of operator exposure calculated for the representative formulation "Rebwachs WF" was below the AOEL according to the TGD. Considering the very specific use of 2,5-dichlorobenzoic acid methylester, worker and bystander exposure were not considered relevant.

The active substance 2,5-dichlorobenzoic acid methylester is used as grafting wax for improved callus formation. This is very early in the life-cycle of a vine and it is circa four years before a harvestable crop is produced. Over this period of time the residue will be completely broken down and therefore there will be no significant residues in grapes.

Due to the representative use of the active substance and the handling of the treated grafts thereafter, the contamination of any environmental compartment with 2,5-dichlorobenzoic acid methylester or its possible metabolites is regarded as negligible. A ready biodegrability test is needed, but only for classification and labelling purposes.

A risk assessment to non-target species was not conducted. Due to the representative use of 2,5-dichlorobenzoic acid methylester, the exposure of non-target species was considered to be negligible. As for the classification and labelling of the active substance, a data gap was identified to provide acute aquatic toxicity studies.

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

- The use is restricted to the "Rebwachs WF" formulation containing 0.035g/kg 2,5-dichlorobenzoic acid methylester for the treatment of grapevine cuttings (refer to point 2.3, 2.5, 2.6).

Critical areas of concern

- There is no specification for this active substance.
- The operator exposure assessment for 8-hydroxyquinoline and combined risk assessment for the formulation (2,5-dichlorobenzoic acid methylester + 8-hydroxyquinoline) could not be concluded and are to be considered at Member State level.
- The limited data package only supports the one representative use and one plant protection product, only indoor use has been considered.
- The consumer risk assessment is only based on the premise of a 'no dietary exposure situation' for humans and livestock animals from the notified representative use. No data were submitted to study and assess the residue behaviour of 2,5-dichlorobenzoic acid methylester in plants and livestock animals in order to define the relevant residues for dietary consumer risk assessment.

Appendix 1 – list of endpoints

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

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

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

Active substance (ISO Common Name) ‡	2,5-dichlorobenzoic acid methylester (methyl-2,5-dichlorobenzoate) There will be no ISO common name allocated.
Function (*e.g.* fungicide)	Plant growth regulator/fungicide

Rapporteur Member State	Federal Republic of Germany
Co-rapporteur Member State	none

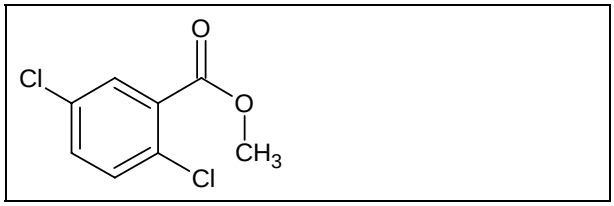
Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	methyl-2,5-dichlorobenzoate
Chemical name (CA) ‡	methyl-2,5-dichlorobenzoate
CIPAC No ‡	686
CAS No ‡	2905-69-3
EC No (EINECS or ELINCS) ‡	220-815-7
FAO Specification (including year of publication) ‡	None
Minimum purity of the active substance as manufactured ‡	open
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	open
Molecular formula ‡	$C_8H_6O_2Cl_2$
Molecular mass ‡	205.0 g/mol

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

Appendix 1 – list of endpoints

Structural formula ‡



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

Appendix 1 – list of endpoints

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	38.7 °C (> 99 %)
Boiling point (state purity) ‡	250.6 °C (> 99 %)
Temperature of decomposition (state purity)	No decomposition until 440 °C (> 99 %)
Appearance (state purity) ‡	Crystal, pale yellow, stinging aromatically odour (> 99 %)
Vapour pressure (state temperature, state purity) ‡	0.32 kPa (20 °C) 0.37 kPa (25 °C) (> 99 %)
Henry's law constant ‡	open
Solubility in water (state temperature, state purity and pH) ‡	0.087 g/L at 20°C, pH 4.5 to 4.6 (99.8 %) open for pH 7
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20°C in g/L (> 99 %) 1,2- dichloroethane > 1000 g/L ethylacetate > 1000 g/L acetone > 1000 g/L xylene > 1000 g/L methanol > 800 g/L *n*-heptane > 450 g/L
Surface tension ‡ (state concentration and temperature, state purity)	60 mN/m (20 °C) (90 % of saturated solution)
Partition co-efficient ‡ (state temperature, pH and purity)	open
Dissociation constant (state purity) ‡	no dissociation under environmental conditions

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

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UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Acetonitrile/water, 1:2 (v/v) λ_{max} (nm); ε ($L.mol^{-1}.cm^{-1}$) 203 37769 229 11852 276 7730 292 ~6000 334 ~10-15
Flammability ‡ (state purity)	Test substance could not be ignited with a flame (> 99 %)
Explosive properties ‡ (state purity)	The test substance had no explosive properties at all (> 99 %)
Oxidising properties ‡ (state purity)	The test substance had no oxidising properties (> 99 %)

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

Appendix 1 – list of endpoints

Summary of representative uses evaluated (2,5-dichlorobenzoic acid methylester)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment per 1000 grapevine graftings (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)		water L/ha			
Grape vine	Northern and Southern Europe	Rebwachs WF	I	Grape vine grafting wax for improved callussing *Botrytis cinerea*	Pastille / wax	2,5-dichloro-benzoic acid methylester 0.035 g/kg 8-Hydroxy-quinoline 1 g/kg	dipping in the undiluted product under greenhouse conditions	directly after grafting	1	-	1 kg Rebwachs WF / 1000 grape vine graftings		0.035 g Dichloro-benzoic acid methylester/ 1000 grape vine graftings 1g 8-Hydroxy-quinoline/ 1000 grape vine graftings	not relevant	In Germany the product is not authorised against *Botrytis cinerea* because there are no data which support the effect against the fungus It is only authorised as wound sealing [1]

[1] The batch data and technical specification are not acceptable

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).
(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the**

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

Appendix 1 – list of endpoints

situation should be described (e.g. fumigation of a structure) (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I) (c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds (d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989 (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	**variant (e.g. benthiavalicarb-isopropyl).** (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application (k) Indicate the minimum and maximum number of application possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

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

Appendix 1 – list of endpoints

Methods of analysis

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

Technical as (analytical technique)	open
Impurities in technical as (analytical technique)	open
Plant protection product (analytical technique)	open

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		not required
Food of animal origin		not required
Soil		not required
Water	surface	not required
	drinking/ground	not required
Air		not required

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	not required
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	not required
Soil (analytical technique and LOQ)	not required
Water (analytical technique and LOQ)	not required
Air (analytical technique and LOQ)	not required
Body fluids and tissues (analytical technique and LOQ)	not required

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

Appendix 1 – list of endpoints

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

	RMS/peer review proposal
Active substance	none

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

Appendix 1 – list of endpoints

Impact on human and animal health)

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

Rate and extent of oral absorption ‡	Rapid and extensive > 90 % (based on 24 hour renal excretion following oral and intravenous administration of 10 mg DCBME/kg bw)
Distribution ‡	Initially widely distributed; highest residues in highly perfused organs
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	Rapid and complete (>99 % renally within 7 days post-dose for single low dose)
Metabolism in animals ‡	Completely metabolised; major metabolite (60-80 %) 2,5-dichloro-benzoic acid (M11.7); conjugation products: 2,5-dichlorobenzoylglycine (M7.2) and three acylglucuronides (M5.8, M5.0, M6.5)
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and 2,5-dichloro-benzoic acid (M11.7)
Toxicologically relevant compounds ‡ (environment)	No exposure

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	1030 mg/kg bw	**Xn R22**
Rat LD_{50} dermal ‡	> 10 000 mg/kg bw	
Rat LC_{50} inhalation ‡	No data, reported to be not technically achievable	
Skin irritation ‡	Not irritating	
Eye irritation ‡	Transiently irritating at 10% dilution	**Xi R36**
Skin sensitisation ‡	Not sensitising (Maximisation Test)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Effects in neurological screening from day 1 onwards, slight anaemia, increased liver and kidney weight, fatty infiltration in the heart, oligospermia	
Relevant oral NOAEL ‡	28-day rat: 100 mg/kg bw/day	

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

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	No data on non-rodents – not required due to the very low levels used in the product	
Relevant dermal NOAEL ‡	No data – not required due to the very low levels used in the product	
Relevant inhalation NOAEL ‡	No data – not required due to the very low levels used in the product	

Genotoxicity ‡ (Annex IIA, point 5.4)

	No genotoxic potential	

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

Target/critical effect ‡	No data, not required due to the very low levels used in the product	
Relevant NOAEL ‡	No data, not required due to the very low levels used in the product	
Carcinogenicity ‡	No data, not required due to the very low levels used in the product	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No data – not required due to the very low levels used in the product	
Relevant parental NOAEL ‡	No data – not required due to the very low levels used in the product	
Relevant reproductive NOAEL ‡	No data – not required due to the very low levels used in the product	
Relevant offspring NOAEL ‡	No data – not required due to the very low levels used in the product	

Developmental toxicity

Developmental target / critical effect ‡	No data – not required due to the very low levels used in the product	
Relevant maternal NOAEL ‡	No data – not required due to the very low levels used in the product	

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

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Relevant developmental NOAEL ‡	No data – not required due to the very low levels used in the product	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data – not required	
Repeated neurotoxicity ‡	Evidence for neurological effects in 28-day toxicity study in rats at ≥ 300 mg/kg bw/day (NOAEL: 100 mg/kg bw/day)	
Delayed neurotoxicity ‡	No data – not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data – not required
Studies performed on metabolites or impurities ‡	No data – not required due to the very low levels used in the product

Medical data ‡ (Annex IIA, point 5.9)

No health effects in manufacturing plant personnel reported

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	Not allocated - not necessary*	-	-
AOEL ‡	0.1 mg/kg bw/day	Oral 28-day, rat	1000**
ARfD ‡	Not allocated - not necessary*		

* On the submitted data base it is not possible to derive an ADI and ARfD. Considering the intended uses (kind of application of 2,5-dichlorobenzoic acid methylester in Rebwachs WF), ADI and ARfD are not needed.

** Increased safety factor since only one species and a limited number of end points tested

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50 % EC)	No data - 100 % default value

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

Appendix 1 – list of endpoints

Exposure scenarios (Annex IIIA, point 7.2)

Operator	No health problems in relation to the active substance are expected (content of 2,5-dichlorobenzoic acid methylester in the product only 0.0035 %) Based on a worst case exposure estimation the exposure is 14 % for dermal exposure and 37.5 % for inhalation exposure giving a total of 51.5 % of the AOEL.
Workers	Not relevant for the notified use
Bystanders	Not relevant (application in greenhouses)

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

	RMS/peer review proposal
Substance classified (2,5-dichlorobenzoic acid methylester)	**Xn** "Harmful" **R22** "Harmful if swallowed" **Xi** "Irritant" **R36** "Irritating to eyes"

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

Appendix 1 – list of endpoints

Residues

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

Plant groups covered	None
Rotational crops	None
Metabolism in rotational crops similar to metabolism in primary crops?	No information available
Processed commodities	None
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No information available
Plant residue definition for monitoring	Residue definition not considered necessary. Nil residue situation based on use pattern.
Plant residue definition for risk assessment	Residue definition not considered necessary. Nil residue situation based on use pattern.
Conversion factor (monitoring to risk assessment)	none

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

Animals covered	None
Time needed to reach a plateau concentration in milk and eggs	No information available
Animal residue definition for monitoring	Residue definition not considered necessary. Nil residue situation based on use pattern.
Animal residue definition for risk assessment	Residue definition not considered necessary. Nil residue situation based on use pattern.
Conversion factor (monitoring to risk assessment)	none
Metabolism in rat and ruminant similar (yes/no)	No information available
Fat soluble residue: (yes/no)	No information available

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

No information available

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

Appendix 1 – list of endpoints

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

No information available

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

No information available

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

Appendix 1 – list of endpoints

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

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
No information available						

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

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

Appendix 1 – list of endpoints

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

Consumer risk assessment not considered necessary. Nil residue situation based on use pattern.

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
No information available				

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

No MRL proposals

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

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

Appendix 1 – list of endpoints

Fate and behaviour in the environment

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

Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil.

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

Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil.

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

Laboratory studies:
Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil.

Field studies:
Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil.

pH dependence ‡ (yes / no) (if yes type of dependence)	not relevant*
Soil accumulation and plateau concentration ‡	not relevant*

* Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil.

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

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

Column leaching ‡	not relevant*
Aged residues leaching ‡	not relevant*

* Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil.

Lysimeter/ field leaching studies ‡	no studies performed

PEC (soil) (Annex IIIA, point 9.1.3)

Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil. The contamination of soil is considered negligible.

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	not relevant*
Photolytic degradation of active substance and metabolites above 10 % ‡	not relevant*
Quantum yield of direct phototransformation in water at Σ > 290 nm	not relevant*
Readily biodegradable ‡ (yes/no)	no**

* Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil.

** Test on biodegradebility (OECD 209) is available, however can not be considered according to the provisions of Commission Regulation (EC) No. 1095/2007

Degradation in water / sediment

Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil. Therefore any contamination of surface water is regarded as negligible.

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

Appendix 1 – list of endpoints

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

Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil. Therefore any contamination of surface water is regarded as negligible.

PEC ground water (Annex IIIA, point 9.2.1)

Due to the kind of application in the greenhouse as a wax formulation no direct transfer within the first 16 month to the soil can occur. After planting of the grafted scions into the vine yards, the grafted part is also above the soil. A groundwater contamination of the parent compound or its possible metabolites is therefore not expected.

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

Direct photolysis in air ‡	not studied
Quantum yield of direct phototransformation	not studied
Photochemical oxidative degradation in air ‡	DT_{50} of 46.3 d derived by the Atkinson model (version v 1.90). OH (24 h) concentration assumed = $5 \cdot 10^5$ cm^{-3}
Volatilisation ‡	not studied
	not studied
Metabolites	not studied

PEC_{air}

Method of calculation	not relevant

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: none Surface Water: none Ground water: none Air: parent compound (default)

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

Soil (indicate location and type of study)	not available

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

Appendix 1 – list of endpoints

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

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

Test on biodegradebility (OECD 209) is available, however can not be considered according to the provisions of Commission Regulation (EC) No. 1095/2007 Proposal: R53 – ”not readily biodegradable” (for precautionary reasons)

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

Appendix 1 – list of endpoints

Effects on non-target species

Rebwachs WF is applied in the greenhouse on young vine scions. Young plants are planted into the earth in the field after 16 months. In the second year, the grafts are planted into the vine yard after final paraffination in April/May. The active substance can be released into the environment in an amount of maximum 175 mg as/ha.

It was shown that < 2.5 % of 2,5-dichlorobenzoic acid methylester can be solved from the wax formulation within 24 hours after intensive shaking (Study ASU 70190, Annex II point 2.1 and AIII point 2.11, see Dossier).

Following assumptions can be made:

1000 scions treated with 1 kg Rebwachs WF	= 0.035 g 2,5-dichlorobenzoic acid methylester
1 scion	= 35 µg 2,5-dichlorobenzoic acid methylester
1 scion release 2.4 % of applied as	= 0.84 µg 2,5-dichlorobenzoic acid methylester
1 scion needs 2 m² soil	= 0.42 µg as/m² = 175 mg/ha
	= 0.0056 µg as/kg soil

Due to the expected low exposure in the field, no ecotoxicologal studies were submitted.

The justification of the notifier is accepted.

However, basic data for acute fish, daphnia and algae concerning classification and labelling of the active substance methyl-2,5-dichloro benzoate are required.

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

Species	Test substance	Time scale	Endpoint (mg/kg bw/d)	Endpoint (mg/kg feed)
Birds ‡				
	No data submitted *Justification accepted*			
Mammals ‡				
	No data submitted *Justification accepted*			
Additional higher tier studies ‡ *No data submitted – justification accepted*				

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

Appendix 1 – list of endpoints

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

Greenhouse application on scion

Indicator species/Category[2]	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)	*not relevant*			
Higher tier refinement (Birds)	*not relevant*			
Tier 1 (Mammals)	*not relevant*			
Higher tier refinement (Mammals)	*not relevant*			

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)	Endpoint	Toxicity[1] (µg/L)
Laboratory tests ‡				
Fish				
submitted study invalid, acute fish test is required for classification and labelling				
Aquatic invertebrate				
submitted study invalid, acute daphnia test is required for classification and labelling				
Sediment dwelling organisms				
No data submitted, not relevant				
Algae				
submitted study invalid, alga growth inhibition test is required for classification and labelling				
Higher plant				
No data submitted, not relevant				
Microcosm or mesocosm tests				
Not performed, not relevant				

[1] indicate whether based on nominal ($_{nom}$ = analytically confirmed) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether endpoints are presented as units of preparation or as. No indication means effects related to compound indicated in column "Test substance".
[2] additional data, studies were submitted within the framework of national authorisation, not included in dossier.

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

Appendix 1 – list of endpoints

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

Greenhouse application on scions

Test substance	Organism	Toxicity endpoint (mg as/L)	Time scale	$PEC_{sw}i$ µg/L	PEC_{tw} [a]	TER	Annex VI Trigger[1]
	not relevant, justification accepted (no exposure)						

Bioconcentration				
	Active substance	Metabolite 1	Metabolite 2	Metabolite3
logPow	3.46	-	-	-
Bioconcentration factor (BCF)[1] ‡ (k1/k2) normalised to 6 % lipid, TAR Not normalised to lipid, TAR Related to active substance (not normalised)	*No data submitted, justification accepted*	-	-	-
Annex VI Trigger for the bioconcentration factor	100			
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 Pow >3.
* based on total ^{14}C or on specific compounds

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

Laboratory tests with standard sensitive species

Species	Test Substance	Endpoint	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡	*No data submitted, justification accepted*		
Aphidius rhopalosiphi ‡	*No data submitted, justification accepted*		

[1] for preparations indicate whether endpoint is expressed in units of as or preparation

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

Appendix 1 – list of endpoints

Greenhouse application on scions

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
preparation	*Not relevant*				

[1] indicate distance assumed to calculate the drift rate

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g as/ha)[1,2]	Endpoint	% adverse effect[3]	Trigger value
No data submitted, not relevant, justification accepted						

[1] indicate whether initial or aged residues
[2] for preparations indicate whether dose is expressed in units of as or preparation
[3] indicate when the effect is not adverse

Field or semi-field tests
Field or semi-field tests were not required

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

Test organism	Test substance	Time scale	Endpoint[1]
Earthworms Greenhouse application on scion	*No data submitted, justification accepted*		
Other soil macro-organisms	*No data submitted, justification accepted*		
Soil micro-organisms	*No data submitted, justification accepted*		
Field studies[2]	*Not required*		

[1] indicate where endpoint has been corrected due to log $P_{o/w}$ > 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

Toxicity/exposure ratios for soil organisms

Greenhouse application on vine scions

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Not relevant					

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

Appendix 1 – list of endpoints

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Other soil macro-organisms					

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

Preliminary screening data

No data submitted, justification accepted

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha)[2] emergence	Exposure[1] (g/ha)[2]	TER	Trigger
	as ‡ and Preparation	*Not relevant*	*Not relevant*			

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

Not relevant

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

Test type/organism	endpoint
Activated sludge	*No data submitted, justification accepted*
Pseudomonas sp.	*Not relevant*

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

Compartment	
soil	2,5-dichlorobenzoic acid methylester
water	2,5-dichlorobenzoic acid methylester
sediment	2,5-dichlorobenzoic acid methylester
groundwater	2,5-dichlorobenzoic acid methylester

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

Appendix 1 – list of endpoints

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	*Can not be classified, due to missing data.* *Basic data set is demanded*

	RMS/peer review proposal
Preparation	*Can not be classified, due to missing data.* *Basic data set is required*

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

Appendix 2 – abbreviations used in the list of endpoints

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

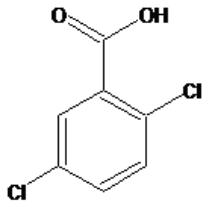
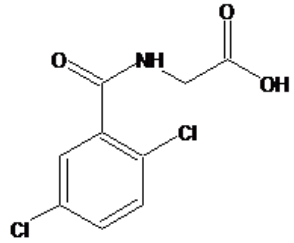
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter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

Appendix 2 – abbreviations used in the list of endpoints

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
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
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
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
yr	year

Appendix 3 – used compound code(s)

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
M11.7	2,5-dichlorobenzoic acid	
M7.2	2,5-dichlorobenzoylglycine	
M5.0 M5.8 M6.5	2,5-dichlorobenzoic acid glucuronide I 2,5-dichlorobenzoic acid glucuronide II 2,5-dichlorobenzoic acid glucuronide III