European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

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

(Question No EFSA-Q-2009-322)

Issued on 17 July 2009

SUMMARY

Heptamaloxyloglucan is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[2] France received an application from Elicityl SA for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision of 2007/560/EC[3].

Following the agreement between the European Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State France submitted the report of its initial evaluation of the dossier on heptamaloxyloglucan, hereafter referred to as the Draft Assessment Report (DAR), which was received by EFSA on 26 July 2007.

The peer review was initiated on 21 January 2008 by distributing the DAR for consultation of the Member States and the applicant. Subsequently, the comments received on the DAR were examined 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 data made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in April – May 2009.

A final consultation on the outcome of the experts' discussions took place during a written procedure with the Member States in June 2009 leading to the conclusions as laid down in this report.

This conclusion was reached on the basis of the evaluation of the representative use as a plant elicitor on grapevines to make them frost hardy. Full details of the GAP can be found in the list of end points attached at Appendix A. The representative formulated product for the evaluation was 'PEL101GV'; it is a lyophilisate (freeze-dried cake). It appears as a white solid block that can break into shiny crumbs of different sizes and shapes after shaking. 'PEL101GV' cannot be assigned to any of the formulation codes. The codes which are the

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[2] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19

[3] OJ No L 213, 15.8.2007, p. 29

closest to the preparation are 'SP' (water soluble powder) and 'SG' (water soluble granule), as 'PEL101GV' is a solid to be used for dissolution in water, however the preparation is neither a powder nor a granule. Therefore, it is labelled as 'XX'.

Due to the nature of this compound being an extract from apple pomace, there is no need for methods of analysis for monitoring in food and feed. Risk managers should consider if methods for monitoring are necessary in relation to environmental matrices. Methods for the environmental matrices were not submitted but are likely to be available in published literature. 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.

Heptamaloxyloglucan is generally regarded as safe for human exposure, since it is an oligosaccharide, which is a component of the vegetative cell walls and thus naturally present in food from plant origin, such as drinks (it is extracted from apples). Toxicological studies showed that heptamaloxyloglucan has low acute oral and dermal toxicity. It is not a skin or eye irritant, nor a skin sensitizer. Heptamaloxyloglucan has also low short-term oral toxicity, since the NOAEL from a 28-day rat study was the highest dose level tested (1000 mg/kg bw/day). The weight of evidence indicates that heptamaloxyloglucan is not a genotoxic agent. Thus, since heptamaloxyloglucan is an oligosaccharide which is a component of the vegetative cell walls and thus naturally present in food from plant origin, and considering its low acute and short-term toxicity and lack of genotoxic potential, long-term toxicity-, carcinogenicity- and reproductive toxicity studies were not performed, and were not required. Likewise, it was agreed not to propose an acceptable daily intake (ADI), or an acceptable operator exposure level (AOEL) or an acute reference dose (ARfD), and therefore operator, bystander and worker exposure estimates were considered not necessary.

A full residue assessment and consumer risk assessment is not necessary for this compound given its nature and the fact that no toxicological reference values are set for this substance.

The information provided by the applicant from published scientific literature was assessed as sufficient to identify the likely route of microbially mediated degradation of heptamaloxyloglucan in soil. These data indicated that the formation of the monomeric sugars D-glucopyranose, D-glucitol, D-xylopyranose, D-galactopyranose and L-fucopyranose as breakdown products would be expected. In a guideline ready biodegradability study that utilised a sewage sludge inoculum, the measurements resulted in heptamaloxyloglucan being classified as readily biodegradable. Information to quantitatively assess the rate of degradation of heptamaloxyloglucan in soil and natural waters or adsorption to soil was not available. Based on water solubility data heptamaloxyloglucan would be expected to be mobile in soil. However, valid worst-case environmental exposure assessments for heptamaloxyloglucan in soil and surface water were performed using conservative assumptions that enabled a satisfactory risk assessment to be completed. The potential for heptamaloxyloglucan to contaminate groundwater at concentrations above the parametric drinking water limit of 0.1µg/L, when used according to the applied for intended use assessed, was concluded to be low.

The risk to non-target organisms was expected to be low for the representative use evaluated.

Key words: heptamaloxyloglucan, peer review, risk assessment, pesticide, elicitor, frost hardy

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC France received an application from Elicityl SA for inclusion of the active substance heptamaloxyloglucan in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision of 2007/560/EC.

Following the agreement between the European Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State France submitted the report of its initial evaluation of the dossier on heptamaloxyloglucan, hereafter referred to as the Draft Assessment Report (DAR) (France, 2007), which was received by EFSA on 26 July 2007. The DAR was distributed for consultation to the Member States and the applicant on 21 January 2008.

The comments received on the DAR were evaluated 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 data made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in April – May 2009. The reports of these meetings have been made available to the Member States electronically.

A final consultation on the outcome of the experts' discussions took place during a written procedure with the Member States in June 2009 leading to the conclusions as laid down in this report.

During the peer review of the DAR and the consultation of technical experts no critical issues were identified for consultation of the Panel on Plant Protection Products and their Residues (PPR).

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

The documentation developed during the peer review was compiled as a peer review report (EFSA, 2009) comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's DAR:

- the comments received,
- the resulting reporting table (revision 1-1; 11 February 2009),

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; 15 July 2009).

Given the importance of the DAR including its addendum (compiled version of June 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.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Heptamaloxyloglucan is the given common name for this substance; it has no ISO common name. This is because it is an oligosaccharide, which, according to ISO rules, will not be allocated to an ISO common name. Full details of its IUPAC name and structure are given in Appendix A.

The representative formulated product for the evaluation was 'PEL101GV'; it is a lyophilisate (freeze-dried cake). It appears as a white solid block that can break into shiny crumbs of different sizes and shapes after shaking. 'PEL101GV' cannot be assigned to any of the formulation codes. The codes which are the closest to the preparation are 'SP' (water soluble powder) and 'SG'(water soluble granule), as 'PEL101GV' is a solid to be used for dissolution in water, however the preparation is neither a powder nor a granule. Therefore, it is labelled as 'XX'.

The evaluated representative use is as a plant elicitor on grapevines to make them frost hardy. Full details of the GAP can be found in Appendix A.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of heptamaloxyloglucan as manufactured should not be less than 780 g/kg. At the moment no FAO specification exists.

The technical material may contain the mycotoxin patulin, which is present in the starting material (apple pomace). The maximum level for this compound set by the PRAPeR 69 meeting of experts on mammalian toxicology is 50 µg/kg; this level is to be confirmed by the requirement for additional batch data.

The content of heptamaloxyloglucan in the representative formulation is 874 g/L (pure). The minimum purity of the active substance is 780 g/kg, therefore the batches will have to be blended to achieve the required content in the formulation.

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 heptamaloxyloglucan or the respective formulation. However, the following data requirement was identified:

- 3-batch data with analysis of patulin

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

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

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

Due to the nature of this compound being an extract from apple pomace, there is no need for methods of analysis for monitoring in food and feed. Risk managers should consider if methods for monitoring are necessary in relation to environmental matrices. Methods for the environmental matrices were not submitted but are likely to be available in published literature. A method for body fluids and tissues is also not required, as the active substance is classified as neither toxic nor very toxic.

2. Mammalian toxicity

Heptamaloxyloglucan was discussed during the PRAPeR 69 meeting of expert on mammalian toxicology in May 2009 on the basis of the DAR (France, 2007).

During the meeting it was agreed that the batches tested in the mammalian toxicity package cover the technical specification.

2.1. Absorption, distribution, excretion and metabolism (toxicokinetics)

No studies on toxicokinetics were performed and are not required. Nevertheless, since the active substance is a xyloglucan-derived oligosaccharide, and xyloglucan is the principal hemicellulosis component of primary cell walls of dicotyledonous and non-graminaceous monocotyledonous plants, the expected behaviour of heptamaloxyloglucan in mammals is the same as that of cellulose and hemicellulose. Thus, heptamaloxyloglucan as parent substance is presumed not to be absorbed in the gastrointestinal tract, and a fraction of ingested active substance can undergo hydrolysis and fermentation in the gastrointestinal tract releasing glucidic monomer units and short-chain fatty acids, which are naturally occurring in food.

2.2. Acute toxicity

Heptamaloxyloglucan is not acutely toxic to rats via the oral or dermal routes (LD_{50} higher that 5000 mg/kg bw and 2000 mg/kg bw, respectively). It is not a skin or eye irritant, nor a skin sensitizer in the Local Lymph Node Assay (LLNA). The acute inhalation toxicity was not investigated, nor required.

2.3. Short-term toxicity

Oral short-term toxicity was studied in a dietary 28-day rat study, where no systemic toxicity was observed up to a dose level of 1000 mg/kg bw/day (highest dose level tested).

2.4. Genotoxicity

Two *in vitro* genotoxicity studies were performed in order to evaluate the genotoxicity of heptamaloxyloglucan. Negative results were found in the bacterial gene mutation assay and in the gene mutation assay in L5178Y mouse lymphoma cells.

2.5. Long-term toxicity and carcinogenicity

Long-term toxicity and carcinogenicity studies were not performed, nor required based on the fact that heptamaloxyloglucan is a naturally occurring substance including in drinks (it is extracted from apples), and also on the proven low toxicity from the available toxicity studies.

2.6. Reproductive and developmental toxicity

Reproductive toxicity studies were not performed, nor required based on the fact that heptamaloxyloglucan is a naturally occurring substance including in drinks (it is extracted from apples), and also on the proven low toxicity from the available toxicity studies.

2.7. Neurotoxicity

The chemical structure of heptamaloxyloglucan is not structurally related to neurotoxicants, and therefore no studies were performed to assess neurotoxicity.

2.8. Further studies

No further studies were performed. They are not required.

2.9. Medical data

This product has not been marketed. No adverse effects have been reported during any phase of the development or production of the active substance.

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

ADI and ARfD:

In the DAR, the rapporteur Member State proposed not to set an ADI and ARfD based on the proven low toxicity of the compound from the available toxicity studies. In addition, heptamaloxyloglucan is an oligosaccharide, which is a component of the vegetative cell walls and thus naturally present in food from plant origin such as drinks (it is extracted from apples). The PRAPeR 69 meeting of experts agreed that setting of an ADI and ARfD is not required.

AOEL:

In the DAR, the rapporteur Member State proposed to use the NOAEL of 1000 mg/kg bw/day (highest dose level tested) from the available oral 28-day rat study, and to apply a safety factor of 1000 (10x factor for interspecies variability, 10x factor as only one species was tested, and 10x factor for the use of a 28-day study), resulting in 1 mg/kg bw/day. Nevertheless, based on the same reasons considered for the ARfD and ADI, the PRAPeR 69 meeting of experts agreed that the setting of an AOEL is not required.

2.11. Dermal absorption

Experimental data are not available, however, based on the physico-chemical properties of heptamaloxyloglucan, the dermal absorption can be expected to be 10% or lower. Nevertheless, the PRAPeR 69 meeting of experts agreed that as operator, worker and bystander exposure estimates are not required (see point 2.12), dermal absorption values are not required.

2.12. Exposure to operators, workers and bystanders

'PEL101GV' is formulated as a lyophilisate inside a flask. 'PEL101GV' is intended to be used as an agricultural frost-protecting agent through a trailed broadcast air-assisted sprayer or a hand-held sprayer on grapevines. The maximum application rate is 0.437 g a.s/hectare.

In the DAR operator exposure estimates were performed. Nevertheless, the PRAPeR 69 meeting of experts considered that as no reference values have been set (see point 2.10), operator, worker and bystander exposure estimates are not required. Moreover, as the compound is of low toxicity and is a normal part of the diet, no adverse effects are anticipated.

3. Residues

In practice, heptamaloxyloglucan is prepared from dry apple pomace by enzymatic hydrolysis and deacetylation/reduction after fractioning and purification. The samples are then purified and conditioned by lyophilisation.

Dry pomace used for the purification comes from apples that are suitable for human consumption. These apples are washed, ground and squeezed, then the pomace is dehydrated and stored under conditions preventing development of the fungi responsible for the production of mycotoxins (patulin). The product is used on grapevine plants for protection against freezing temperatures during the spring season. Heptamaloxyloglucan is a molecule signal that can naturally stimulate the metabolism of the grapevine to increase its tolerance to cold. It acts as an elicitor exhibiting chemical structure and conformation of xyloglucan heptamer when it protects grapevine plants against frost. As the result of its binding to receptors at the cell surface, second messengers including changes in redox ratio, membrane potential and production of active oxygen species are generated and diffused to specific targets within the cell to bring about physiological responses, which occurs in the time scale of minutes. The early responses, e.g. the increase of glutathione reductase activity and a shift in the partitioning of photosynthates toward soluble sugar synthesis, are the mechanisms underlying acclimation to cold temperatures. Heptamaloxyloglucan is applied at nanomolar range concentration on plants, at growth stages BBCH 7 to 16; it improves the frost hardiness of the grapevines since it limits tissue necrosis, mediates osmotic adjustment for protecting organelles and can reduce the inhibition of photosynthesis. Heptamaloxyloglucan, if consumed, will be broken down to simple sugars and will be utilised as an energy source and will exhibit no toxic effects. No mammalian toxicological reference vales have been set for this compound.

For the above reasons, a specific consumer risk assessment is not necessary.

4. Environmental fate and behaviour

Heptamaloxyloglucan was discussed at the PRAPeR 67 meeting of experts on environmental fate and behaviour in April 2009.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

Literature in scientific journals provided in the applicant's dossier, the key aspects of which were summarised in the DAR, demonstrated that oligosaccharides (including heptamaloxyloglucan) can be degraded in soil by microorganisms. Based on the evidence in these papers, the proposed route of degradation in soil of heptamaloxyloglucan involves the formation of D-glucopyranose, D-glucitol, D-xylopyranose, D-galactopyranose and L-fucopyranose, which are all monomeric sugars. It is considered that the amount of heptamaloxyloglucan, that will be added to the soil environment from the requested use (annual dose 1.75 g/ha), will be trivial compared to the total loading of oligosaccharides that will result from biota (especially plant cell wall materials that are rich in xyloglucans), that will also be precursors of a range of monomeric sugars.

EFSA and the Member State experts were content that the available information was sufficient to address the regulatory requirements and demonstrated that the breakdown products from the use requested would result in a negligible difference in the nature and level of carbohydrates in soil.

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

No information was provided that would have enabled a quantitative characterisation of the rate of degradation of heptamaloxyloglucan in soil to be derived. However, it was agreed that the risk assessment for the requested use could be completed without such quantitative information. A predicted environmental concentration (PEC) soil is available for heptamaloxyloglucan that is based on a maximum annual total dose (see Appendix A).

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

No information was provided that would have enabled a quantitative characterisation of the mobility of heptamaloxyloglucan in soil to be derived. However, it was agreed that the risk assessment for the requested use could be completed without such quantitative information, assuming that soil adsorption would be expected to be very low. This expectation was based on the high measured water solubility (>500g/L at 20°C).

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Heptamaloxyloglucan was shown to be stable under sterile hydrolysis conditions and would not be expected to be subject to direct aqueous photolysis, due to its low light absorption at wavelengths >290nm. Heptamaloxyloglucan was shown to be readily biodegradable in a modified Sturm test (OECD 301B); the test utilises a sewage sludge inoculum. No experimental information on the fate and behaviour of heptamaloxyloglucan in natural sediment water systems was provided. It is considered that the amount of heptamaloxyloglucan that may reach natural water systems from the requested use (annual dose 1.75 g/ha), will be trivial compared to the total loading of oligosaccharides that will

result from biota (especially plant cell wall materials that are rich in xyloglucans). Therefore, it was accepted that the risk assessment for the requested use could be completed without further experimental evidence. A PEC surface water and sediment is available for heptamaloxyloglucan, which is based on a maximum annual total dose and used the FOCUS step 1 calculator (see corrigendum 1 to Vol3 B.8 of the DAR of January 2009 (France, 2009) and Appendix A of this conclusion).

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

The PRAPeR 67 meeting of experts discussed the case made by the applicant that for the requested use soil exposure is low due to the low application rate requested, and that 'short-chain soluble oligosaccharides such as heptamaloxyloglucan are readily accessible to enzymatic degradation on the soil and in its superficial layers. Therefore it is not expected that heptamaloxyloglucan reach groundwater at levels > 0.1µg/L.'

To support the discussions the experts carried out FOCUS groundwater simulations using both the PELMO and PEARL models for the FOCUS vine specified scenarios, assuming a soil DT_{50} of 1000 days (very conservative worst-case value), a Koc of 0 and 1/n of 1. 50% crop interception was assumed and 4 applications at 4 day intervals of 0.437 g a.s./ha were used for these simulations. The resulting PEC groundwater values were in the range 0.1 to 0.26 µg/L (80^{th} percentile year annual average concentrations leaving the top 1m soil layer as defined for the FOCUS methodology). The experts concluded that having the knowledge that heptamaloxyloglucan was shown to be readily biodegradable in a modified Sturm test, they could qualitatively judge that the soil degradation rate of heptamaloxyloglucan and its sugar breakdown products would be more rapid than the 1000 days assumed in their FOCUS simulations. The experts therefore felt confident, that for the use applied for, they were able to conclude that heptamaloxyloglucan and its degradation products would not reach deeper soil layers such that groundwater concentrations would exceed 0.1µg/L, despite the fact that heptamaloxyloglucan would be expected to have low soil adsorption.

4.3. Fate and behaviour in air

Air exposure by heptamaloxyloglucan would be expected to be low based on the quantitative structure activity relationship (QSAR) estimated vapour pressure of $1.1x10^{-11}$ Pa at 20°C.

5. Ecotoxicology

Heptamaloxyloglucan was discussed at the PRAPeR 68 meeting of experts on ecotoxicology in May 2009, on the basis of the Draft Assessment Report from May 2007 and corrigendum 1 (January 2009) of the final addendum (France, 2009).

The supported use evaluated was against frost damage in grapevines; the maximum application rate was 0.437 g a.s./ha up to 4 applications. The representative formulation was 'PEL101GV'.

5.1. Risk to terrestrial vertebrates

No data on the toxicity of heptamaloxyloglucan on birds were available since it is part of the bird diet. However, on the basis of the mammalian toxicity data, heptamaloxyloglucan can be

considered of low toxicity to other terrestrial vertebrates. No risk is expected and therefore no further data were requested.

5.2. Risk to aquatic organisms

Acute toxicity studies on fish (*Oncorhynchus mykiss*), daphnia (*Daphnia magna*) and algae (*Scenedesmus subspicatus*) were performed with the technical heptamaloxyloglucan. A low toxicity was observed. The TER values based on initial PEC_{sw} of FOCUS Step 1 were well above the Annex VI triggers, indicating a low risk to aquatic organisms.

5.3. Risk to bees

An acute toxicity study on *Apis mellifera* was performed with the technical heptamaloxyloglucan that investigated oral and contact exposure. A low toxicity was observed. Literature data were also submitted as additional information on acute toxicity of carbohydrates to bees. Carbohydrates usually represent a source of energy for honeybees. However, some sugars could be poisonous for bees, as for example the galactose monomer of heptamaloxyloglucan. The rapporteur Member State proposed a risk assessment based on the assumption that heptamaloxyloglucan was degraded completely to galactose. The calculated HQ was far below the Annex VI trigger, indicating a low risk to honeybees.

5.4. Risk to other arthropod species

No studies on the toxicity of heptamaloxyloglucan to non-target arthropods were performed. Since heptamaloxyloglucan is part of the usual food of arthropods, additional exposure was considered negligible and no risk was expected.

5.5. Risk to earthworms

No studies on the toxicity of heptamaloxyloglucan to earthworms were performed, however, further testing was considered not necessary. Using evidence from the literature, it was demonstrated that heptamaloxyloglucan is degraded by micro-organism species into monomeric sugars. In addition, low amount of residues is expected to reach the soil. Therefore, the risk to earthworms was considered low.

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

No data were provided. Since low soil exposure was expected, the risk to other soil non-target macro-organisms was considered low.

5.7. Risk to soil non-target micro-organisms

No data were provided. Since low soil exposure was expected, the risk to soil non-target micro-organisms was considered low.

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

A study with the technical heptamaloxyloglucan on the vegetative growth of 3 terrestrial plants (wheat, mustard and red cover) was provided. No adverse effects were observed at concentration up to 20 g a.s./ha (45-fold greater than the application rate of heptamaloxyloglucan). The risk was considered low.

5.9. Risk to biological methods of sewage treatment

No data were provided. The risk to biological methods of sewage treatment was considered low.

6. Residue definitions

6.1. Soil

Definition for risk assessment:	heptamaloxyloglucan
Definition for monitoring:	heptamaloxyloglucan (no methods available, risk managers to consider if methods are needed)

6.2. Water

6.2.1. Ground water

Definition for exposure assessment:	heptamaloxyloglucan
Definition for monitoring:	heptamaloxyloglucan (no methods available, risk managers to consider if methods are needed)

6.2.2. Surface water

Definition for risk assessment	
in surface water:	heptamaloxyloglucan
in sediment:	heptamaloxyloglucan
Definition for monitoring:	heptamaloxyloglucan (no methods available, risk managers to consider if methods are needed)

6.3. Air

Definition for risk assessment:	heptamaloxyloglucan
Definition for monitoring:	heptamaloxyloglucan (no methods available, risk managers to consider if methods are needed)

6.4. Food of plant origin

Definition for risk assessment:	not necessary
Definition for monitoring:	not necessary

6.5. Food of animal origin

Definition for risk assessment:	not necessary
Definition for monitoring:	not necessary

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

6.6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
heptamaloxyloglucan	No quantitative data available but accumulation not expected.	No data available to conduct a quantitative risk assessment. However, a low risk is expected, due to the low exposure.

6.6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
heptamaloxyloglucan	No quantitative data available but high mobility expected.	No, see section 4.2.2	Elicitor of a physiological response in plants (plant growth regulator)[4].	Not relevant	No effects to the limit tests

[4] Therefore may be considered a pesticide according to the definition in Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption (OJ L 330, 5.12.1998, p. 32)

6.6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
heptamaloxyloglucan	TER values based on initial PEC_{sw} of FOCUS Step 1 were well above the Annex VI triggers, indicating a low acute risk to aquatic organisms.

6.6.4. Air

Compound (name and/or code)	Toxicology
heptamaloxyloglucan	No data available, not required.

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

- Batch data on 3 batches of material used in manufacturing, analysing for patulin (relevant for the representative uses evaluated, data requirement identified by EFSA in June 2009, proposed submission date unknown, refer to chapter 1).

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

This conclusion was reached on the basis of the evaluation of the representative use as a plant elicitor on grapevines to make them frost hardy. Full details of the GAP can be found in the list of end points attached at Appendix A. The representative formulated product for the evaluation was 'PEL101GV'; it is a lyophilisate (freeze-dried cake). It appears as a white solid block that can break into shiny crumbs of different sizes and shapes after shaking. 'PEL101GV' cannot be assigned to any of the formulation codes. The codes which are the closest to the preparation are 'SP' and 'SG', as 'PEL101GV' is a solid to be used for dissolution in water, however, the preparation is neither a powder nor a granule. Therefore, it is labelled as 'XX'.

Due to the nature of this compound being an extract from apple pomace, there is no need for methods of analysis for monitoring in food and feed. Risk managers should consider if methods for monitoring are necessary in relation to environmental matrices. Methods for the environmental matrices were not submitted but are likely to be available in published literature. 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.

Heptamaloxyloglucan is generally regarded as safe for human exposure, since it is an oligosaccharide which is a component of the vegetative cell walls, and thus naturally present in food from plant origin such as drinks (it is extracted from apples). Toxicological studies showed that heptamaloxyloglucan has low acute oral and dermal toxicity. It is not a skin or eye irritant, nor a skin sensitizer. Heptamaloxyloglucan has also low short-term oral toxicity, since the NOAEL from a 28-day rat study was the highest dose level tested (1000 mg/kg bw/day). The weight of evidence indicates that heptamaloxyloglucan is not a genotoxic agent. Thus, since heptamaloxyloglucan is an oligosaccharide which is a component of the vegetative cell walls and thus naturally present in food from plant origin, and considering its low acute and short-term toxicity and lack of genotoxic potential, long-term toxicity-, carcinogenicity- and reproductive toxicity studies were not performed, and were not required. Likewise, it was agreed not to propose an ADI, AOEL or ARfD, and therefore operator, bystander and worker exposure estimates were considered not necessary.

A full residue assessment and consumer risk assessment is not necessary for this compound given its nature and the fact that no toxicological reference values are set for this substance.

The information available on the environmental fate and behaviour of heptamaloxyloglucan in the environment was considered sufficient to carry out an environmental exposure assessment at EU level for the applied for intended use. The potential for heptamaloxyloglucan to contaminate groundwater at concentrations above the parametric drinking water limit of 0.1µg/L, when used according to the applied for intended use assessed, is considered low.

The risk to non-target organisms was expected to be low for the representative use evaluated.

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

None.

ISSUES THAT COULD NOT BE FINALIZED

None.

CRITICAL AREAS OF CONCERN

None.

REFERENCES

EFSA (European Food Safety Authority), 2009. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance heptamaloxyloglucan, EFSA Scientific Report (2009) 334.

France, 2007. Draft Assessment Report (DAR) on the active substance heptamaloxyloglucan prepared by the rapporteur Member State France in the framework of Directive 91/414/EEC, May 2007.

France, 2009. Final Addendum to the Draft Assessment Report on heptamaloxyloglucan, compiled by EFSA, June 2009.

APPENDICES

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

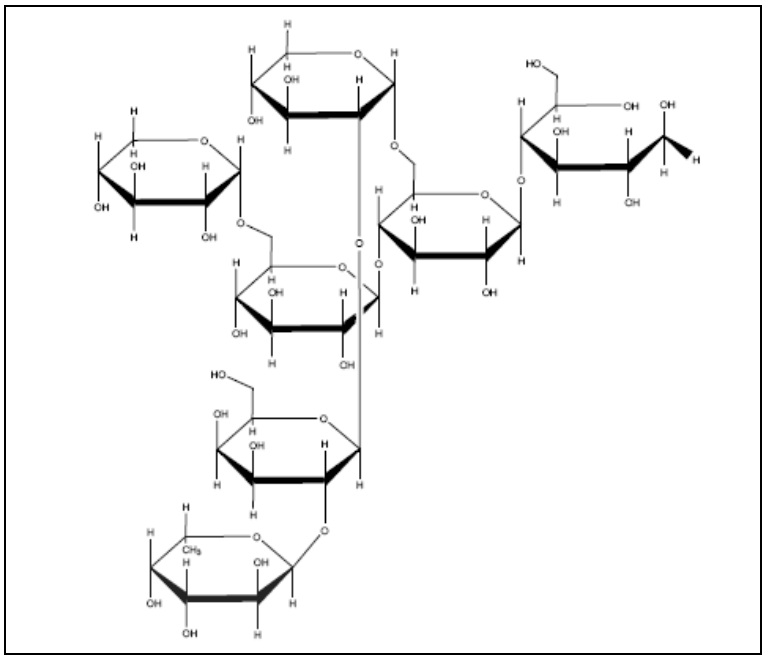
Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Heptamaloxyloglucan is the name used to describe this compound; it does not have an ISO name.
Function (e.g. fungicide)	Elicitor (plant growth regulator)
Rapporteur Member State	France
Co-rapporteur Member State	

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	$\{[\alpha\text{-D-Xyl}p\text{-}(1\to6)]\text{-}\beta\text{-D-Glc}p\text{-}(1\to4)\}\{[\alpha\text{-L-Fuc}p\text{-}(1\to2)\text{-}\beta\text{-D-Gal}p\text{-}(1\to2)\text{-}\alpha\text{-D-Xyl}p\text{-}(1\to6)]\text{-}\beta\text{-D-Glc}p\text{-}(1\to4)\}\text{-D-Glc-ol}$ Xyl p : xylopyranosyl Glc p : glucopyranosyl Fuc p : fucopyranosyl Gal p : galactopyranosyl Glc-ol : glucitol
Chemical name (CA)	/
CIPAC No	Not available
CAS No	870721-81-6
EEC No (EINECS or ELINCS)	Not available
FAO Specification (including year of publication)	No FAO specification
Minimum purity of the active substance as manufactured (g/kg)	780 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	Patulin max level 50 µg/kg
Molecular formula	C40H70O33
Molecular mass	1078 g/mol

Structural formula



Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	-172°C (purity: 99%)
Boiling point (state purity) ‡	none
Temperature of decomposition (state purity)	The sample starts to decompose à 281.4°C(purity :> 99%)
Appearance (state purity) ‡	Pure active substance: Clear beige powder (>87%) Technical grade active substance : Clear beige powder
Vapour pressure (state temperature, state purity) ‡	1.1 10-11 Pa at 20°C (Calculation with QSAR)
Henry's law constant ‡	0.24 10-13 Pa.m3.mol-1 at 20°C
Solubility in water (state temperature, state purity and pH) ‡	> 500 g/l at 20°C (purity: 87%)
Solubility in organic solvents ‡ (state temperature, state purity)	At 20°C (>87%): Methanol: 10 g/l (RSD 6%) acetone : 3 mg/l (RSD 43%) n-octanol : 19 mg/l (RSD 22%) p-xylene: 1 mg/l ethyl acetate: 1 mg/l (RSD 79%) 1,2-dichloroethane:15 mg/l (RSD 47%) n-heptane: 1 mg/l (RSD 72%)
Surface tension ‡ (state concentration and temperature, state purity)	72 ±0.2 mN/m. at 20°C at 1 g/L (purity : > 87%)
Partition co-efficient ‡ (state temperature, pH and purity)	pH not relevant – Log Kow = -15.96 (calculation with KOWWIN program)
Dissociation constant (state purity) ‡	No pka was found of 1.0 to 12.0

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Molar extinction rates were determined to be : <table><tr><td></td><td>pH 5</td><td>pH 7</td><td>pH 9</td></tr><tr><td>Wavelength (nmp</td><td>285</td><td>288</td><td>292</td></tr><tr><td>Absorbance (µA)</td><td>0.0444</td><td>0.038</td><td>0.025</td></tr><tr><td>e (L.mol^{-1}.cm^{-1})</td><td>4.4</td><td>3.8</td><td>2.5</td></tr></table> (purity : 99.9%)
Flammability ‡ (state purity)	Not flammable (theoretical evaluation)
Explosive properties ‡ (state purity)	Not explosive (theoretical evaluation)
Oxidising properties ‡ (state purity)	Not oxidizing (theoretical evaluation)

Summary of representative uses evaluated ("Heptamaloxyloglucan")*

Crop and/or situation (a)	Member State or Country	F, G or I (b)	Pests or group of pests controlled (c)	Product name	Formulation		Application				Application per treatment			PHI (days)	Remarks (m)
					type (d-f)	Conc of as (i)	method kind (f-h)	growth stage & season (j)	number min-max (k)	interval between applications	mg as/hL; min-max	water L/ha; min-max	mg as/ha; min-max		
Grapevine	EU – North	F	*Frost damage*	PEL 101GV	XX	874g/L	Foliar spray	BBCH 7 to BBCH 16 (budding to 6 leaves)	1 –4 12 to 48h before freezing temperatures	4 days at least	0.54 to 108 mg/hl	100-400	0.54-437 mg as/ha	F	

a. For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
b. Outdoor or field use (F), glasshouse application (G) or indoor application (I)
c. E.g. biting and sucking insects, soil born insects, foliar fungi, weeds,etc.

d. E.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

e. GCPF codes - GIFAP Technical monograph No2, 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 plants - type of equipment used must be indicated
i. Concentration in g ai/kg of g ai/L
j. Growth stage at last treatment (BBCH monograph, Growth stages of plants, 1997, Blackwell, ISBN 3-8263-3152-4)
k. The minimum and maximum number of applications possible under practical conditions must be provided.
l. PHI - minimum pre-harvest interval
m. Remarks may include: extent of use / economic importance / restrictions

Methods of Analysis

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

Technical as (analytical technique)	HPAEC-PAD
Impurities in technical as (analytical technique)	HPAEC-PAD Patulin ISO 8128-1
Plant protection product (analytical technique)	HPAEC-PAD

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Thus, as heptamaloxyloglucan is a naturally occurring non-toxic active substance, and that no MRLs are set in plants, no analytical methods are required in plants. The residue definition for soil, water and air is set as heptamaloxyloglucan but no methods are available; it is up to risk managers to decide if methods are necessary for this particular active substance.
Food of animal origin		
Soil		
Water	surface	
	drinking/ground	
Air		

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	none
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	none
Soil (analytical technique and LOQ)	none
Water (analytical technique and LOQ)	none
Air (analytical technique and LOQ)	none
Body fluids and tissues (analytical technique and LOQ)	none

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

	RMS/peer review proposal
Active substance	none

Mammalian toxicology

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	No data, not required.
Distribution ‡	
Potential for accumulation ‡	
Rate and extent of excretion ‡	
Metabolism in animals ‡	
Toxicologically relevant compounds ‡ (animals and plants)	
Toxicologically relevant compounds ‡ (environment)	

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw (f)	
Rat LD_{50} dermal ‡	> 2000 mg/kg bw (m/f)	
Rat LC_{50} inhalation ‡	No data, not required	
Skin irritation ‡	Non irritant	
Eye irritation ‡	Non irritant	
Skin sensitisation ‡	Non sensitiser (LLNA)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Rat 28-d oral study: no critical effect	
Relevant oral NOAEL ‡	NOAEL : 1000 mg/kg bw/d (highest dose level tested)	
Relevant dermal NOAEL ‡	No data, not required	
Relevant inhalation NOAEL ‡	No data, not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

Ames test: negative Mutation assay at the TK locus in mouse lymphoma cells: negative No genotoxic potential.	

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

Target/critical effect ‡	No data, not required	
Relevant NOAEL ‡		
Carcinogenicity ‡		

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No data, not required	
Relevant parental NOAEL ‡		
Relevant reproductive NOAEL ‡		
Relevant offspring NOAEL ‡		

Developmental toxicity

Developmental target / critical effect ‡	No data, not required	
Relevant maternal NOAEL ‡		
Relevant developmental NOAEL ‡		

Neurotoxicity (Annex IIA, point 5.7)

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

Medical data ‡ (Annex IIA, point 5.9)

This product has not been marketed. No adverse health effects have been reported during any phase of development or production of the a.s.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	Not necessary		
AOEL ‡	Not necessary		
ARfD ‡	Not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (PEL 101GV)	No data, not required

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Not necessary
Workers	Not necessary
Bystanders	Not necessary

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

	RMS/peer review proposal
Substance classified (name)	Heptamaloxyloglucan: not classified

Residues

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

Plant groups covered	No data, not required. Heptamaloxyloglucan is a signal molecule (elicitor) naturally occurring at low levels in plant tissues.
Rotational crops	No data, not required.
Metabolism in rotational crops similar to metabolism in primary crops?	No data, not required.
Processed commodities	The effects of the vinification process on the nature of heptamaloxyloglucan residue will be similar to those on the xyloglucans naturally present in the cell walls of grapes.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Not relevant
Plant residue definition for risk assessment	Not relevant
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 - Not relevant
Time needed to reach a plateau concentration in milk and eggs	-
Animal residue definition for monitoring	None - Not relevant
Animal residue definition for risk assessment	None - Not relevant
Conversion factor (monitoring to risk assessment)	None - Not relevant
Metabolism in rat and ruminant similar (yes/no)	-
Fat soluble residue: (yes/no)	Not relevant

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

No data, not required.

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

No data, not required.

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

No data, not relevant.

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)

No data, not required.

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

ADI	None - Not relevant
TMDI (% ADI) according to WHO diet	Not relevant
TMDI (% ADI) according to national (to be specified) diets	Not relevant
IEDI (WHO Diet) (% ADI)	Not relevant
NEDI (specify diet) (% ADI)	Not relevant
Factors included in IEDI and NEDI	Not relevant
ARfD	None - Not relevant
IESTI (% ARfD)	Not relevant
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not relevant
Factors included in IESTI and NESTI	Not relevant

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	
None	-	-	-	-

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6	
Grapevine	Heptamaloxyloglucan is a natural component of dicotyledone plant walls. This substance is already present in different food, among them apple juice, and dietary supplement. Therefore no toxicologically relevant residues occur after application of heptamaloxyloglucan to grapevines. The proposition is to include heptamaloxyglucan in the Annex IV of regulation 396/2005/EC (active substances for which no MRL are required).

Fate and behaviour in the environment

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

Mineralization after 100 days ‡	No study, not required. From literature, the degradation of heptamaloxyloglucan by endogenous soil microorganisms naturally occurring in soil would lead to various mono- or disaccharides. No other relevant metabolites, degradation or reaction products is expected to appear.
Non-extractable residues after 100 days ‡	No study, not required.
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	No study, not required.

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

Anaerobic degradation ‡

Mineralization after 100 days	No study, not required.
Non-extractable residues after 100 days	No study, not required.
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No study, not required.

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No study, not required.

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

Laboratory studies ‡

Parent	Aerobic conditions
	Not available. Not required.

Met 1	Aerobic conditions
	No relevant metabolite expected. Not required.

Field studies ‡

Parent	Aerobic conditions
	Not available. Not required.

Met 1	Aerobic conditions
	No relevant metabolite expected. Not required.

pH dependence ‡ (yes / no) (if yes type of dependence)	Not required.
Soil accumulation and plateau concentration ‡	Not available. Not required.

Laboratory studies ‡

Parent	Anaerobic conditions
	Not available. Not required.

Met 1	Anaerobic conditions
	No relevant metabolite expected. Not required.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡
Not available. Not required.

Metabolite 1 ‡
No relevant metabolite expected. Not required.

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

Column leaching ‡	No study, not required.
Aged residues leaching ‡	No study, not required.
Lysimeter/ field leaching studies ‡	No study, not required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent	DT_{50} (d): no dissipation considered
Method of calculation	Kinetics: - Field or Lab: -
Application data	Crop: vine Depth of soil layer: 5cm Soil bulk density: 1.5g/cm^3 % plant interception: no crop interception considered Number of applications: 4 Interval (d): 4 Application rate(s): 0.44 g as/ha

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.000587		0.00235	
Short term 24h	Not available. Not required.			
2d				
4d				
Long term 7d	Not available. Not required.			
28d				
50d				
100d				
Plateau concentration	Not available. Not required.			

Metabolite I	Molecular weight relative to the parent:
Method of calculation	DT_{50} (d): -
	Kinetics: -
	Field or Lab: -
Application data	-
PEC$_{(s)}$ (mg/kg)	No relevant metabolite expected. Not required.

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: not significant Met: No relevant metabolite expected.
	pH 7: not significant Met: No relevant metabolite expected.
	pH 9: not significant Met: No relevant metabolite expected.
Photolytic degradation of active substance and metabolites above 10 % ‡	No data submitted, Not required.
Quantum yield of direct phototransformation in water at Σ > 290 nm	no peak absorption with molecular absorption coefficient higher than 10 l/mol/cm.

Readily biodegradable ‡ (yes/no)	Yes.

Degradation in water / sediment

Parent	Distribution (e.g. max in water *x* after *n* d. Max. sed x % after *n* d)
	Not available, not required.

Metabolite 1	Distribution (e.g. max in water *x* after *n* d. Max. sed x % after *n* d)
	No relevant metabolite expected. Not required.

Mineralization and non extractable residues
Not available, not required.

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

Parent	Version control no. 1.1
Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 1078 Water solubility (mg/L): > 5000 (at 20°C) K_{OC}/K_{OM} (L/kg): 0mL/g for PECsw, 10000mL/g for PECsed (defaults) DT_{50} soil (d): 1000 days (default) DT_{50} water/sediment system (d): 1000 days (default) DT_{50} water (d): - DT_{50} sediment (d): - Crop interception (%): -
Parameters used in FOCUSsw step 3 (if performed)	Not necessary
Application rate	Crop: vine Crop interception: none Number of applications: 4 Interval (d): 4 Application rate(s): 0.44 g as/ha Application window: BBCH 7 to 16

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	0.6025		4.093	

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	Not required				
Southern EU					

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
Not required.						

Metabolite X	No relevant metabolite.
Parameters used in FOCUSsw step 1 and 2	Not required
Parameters used in FOCUSsw step 3 (if performed)	No relevant metabolite. Not required
Application rate	No relevant metabolite. Not required
Main routes of entry	No relevant metabolite. Not required

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	
Application rate	

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

Not required.

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

Parent	1st year	2nd year	3rd year
Annual average (µg/L)	Not available. Not required. Expert judgement that for the low annual application rate requested (*ca.* 1.75g/ha), with the knowledge that heptamaloxylglucan will be classified as 'readily biodegradable', concentrations in groundwater > 0.1µg/L are not expected.		

Metabolite X	1st year	2nd year	3rd year
Annual average (µg/L)	No relevant metabolite. Not required.		

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	Not studied - no data requested
Photochemical oxidative degradation in air ‡	Not studied - no data requested
Volatilisation ‡	from plant surfaces (BBA guideline): Not studied - no data requested
	from soil surfaces (BBA guideline): Not studied - no data requested
Metabolites	None

PEC (air)

Method of calculation	Heptamaloxyloglucan is not expected to volatilize from plant and soil surface in the air compartment (calculated vapour pressure = $1.1*10^{-11}$ Pa).

$PEC_{(a)}$

Maximum concentration	negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology) or for which a groundwater exposure assessment is triggered.	Soil: heptamaloxyloglucan Surface Water: heptamaloxyloglucan Sediment: heptamaloxyloglucan Ground water: heptamaloxyloglucan Air: heptamaloxyloglucan

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

Soil (indicate location and type of study)	-
Surface water (indicate location and type of study)	-
Ground water (indicate location and type of study)	-
Air (indicate location and type of study)	-

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

Not classified, as it is 'readily biodegradable'.

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 ‡				
	a.s.	Acute	No data available.	
	Preparation	Acute		
	Metabolite 1	Acute		
	a.s.	Short-term		
	a.s.	Long-term		
Mammals ‡				
Rat	a.s.	Acute	LD_{50} > 5000	-
	Preparation	Acute	-	-
	Metabolite 1	Acute	-	-
Rat	a.s.	Long-term	-	-
Additional higher tier studies ‡				

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

Crop and application rate

Indicator species/Category	Time scale	ETE	TER[1]	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird / small insects	Acute	0.024	> 208333 *	10
	Short-term	0.013	> 76923 *	10
	Long-term	Not relevant as log Kow of –15.96		5
Higher tier refinement (Birds)				
Insectivorous bird / small insects	Long-term	-	-	5
Tier 1 (Mammals)				
Small herbivorous mammal / short grass	Acute	# 0.11	45455	10
	Long-term	Not relevant as log Kow of –15.96		5

* TER for birds according to the guidance given in the 4145/SANCO document for an application on early stage of vine is based on comparison between the mammalian endpoints and exposure of and insectivorous birds exposed to heptamaloxyloglucan residues.

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 (mg/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	a.s.	96 hr (static)	Mortality, EC_{50}	> 150 (nominal)
	a.s.	28 d (static)	Growth NOEC	No data available. Not required.
	Preparation	96 hr (flow-through)	Mortality, EC_{50}	
	Preparation	28 d(flow-through)	Growth NOEC	
	Metabolite 1	96 hr (flow-through)	Mortality, EC_{50}	
Aquatic invertebrate				
Daphnia magna	a.s.	48 h (static)	Mortality, EC_{50}	> 150 (nominal)
	a.s.	21 d (static)	Reproduction, NOEC	No data available. Not required.
	Preparation	48 h (static)	Mortality, EC_{50}	
	Preparation	21 d (static)	Reproduction, NOEC	
	Metabolite 1	48 h (static)	Mortality, EC_{50}	
Sediment dwelling organisms				
	a.s.	28 d (static)	NOEC	No data available. Not required.
	Metabolite 2	28 d (static)	NOEC	
Algae				
Scenedesmus subcapitata	a.s.	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	> 150 (nominal) > 150 (nominal)
	Preparation	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	No data available. Not required.
	Metabolite 1	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	
Higher plant				
	a.s.	14 d (static)	Fronds, EC_{50}	No data available. Not required.
	Preparation	14 d (static)	Fronds, EC_{50}	
	Metabolite 1	14 d (static)	Fronds, EC_{50}	

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg/L)
Microcosm or mesocosm tests				
not required				

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

FOCUS Step1*

Crop and application rate

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigge
a.s.	Fish	> 150	Acute	0.6025	-	$> 20*10^4$	100
a.s.	Fish		Chronic	-	-		10
a.s.	Aquatic invertebrates	> 150	Acute	0.6025	-	$> 20*10^4$	100
a.s.	Aquatic invertebrates		Chronic	-	-		10
a.s.	Algae	> 150	Chronic	0.6025	-	$> 20*10^4$	10
a.s.	Higher plants		Chronic	-	-		10
a.s.	Sediment-dwelling organisms		Chronic	-	-		10
Metabolites	Relevant organisms		-	-	-	-	-
Product	Relevant organisms		-	-	-	-	-

* PECi was not based on FOCUS as no data was available for DT_{50} and Koc. The estimated initial PEC after 4 applications considering no dissipation and no crop interception of 0.0143 µg/L was used.

FOCUS Step 2

State crop, application rate and growth stage, Northern Europe or Southern Europe

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC	TER	Annex VI Trigger
Not necessary, see above.							

Refined aquatic risk assessment using higher tier FOCUS modelling

FOCUS Step 3

State crop and application rate

Test substance	Scenario	Water body type[2]	Test organism	Time scale	Toxicity end point (mg/L)	PEC	TER	Annex VI trigger
Not necessary, see above.								

FOCUS Step 4

Crop and application rate

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point	Buffer zone distance	PEC[4]	TER	Annex VI trigger[5]
Not necessary, see above.								

Bioconcentration				
	Active substance	Metabolite 1	Metabolite 2	Metabolite 3
$logP_{O/W}$	-15.96	-	-	-
Bioconcentration factor (BCF)[1] ‡	-	-	-	-
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)
a.s. ‡	> 100	> 100
Preparation[1]	-	-
Metabolite 1	-	-
Field or semi-field tests		
not required		

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

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

Crop and application rate

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	0.0044	50
a.s.	oral	0.0044	50
Preparation	Contact	-	50
Preparation	oral	-	50

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	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡	Not deemed necessary.		
Aphidius rhopalosiphi ‡			

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

Crop and application rate

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
	Typhlodromus pyri	-	-	-	2
	Aphidius rhopalosiphi	-	-	-	2

[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/ha)[1,2]	End point	% effect[3]	Trigger value
Not required.						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

Field or semi-field tests
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	End point[1]
Earthworms			
	a.s. ‡	Acute 14 days	No study available. Not required. From literature, it was shown that earthworms ingested microflora together with soil in order to degrade oligosaccharides (heptamaloxyloglucan) into monomeric sugars.
	a.s. ‡	Chronic 8 weeks	
	Preparation	Acute	
	Preparation	Chronic	
	Metabolite 1	Acute	
	Metabolite 1	Chronic	
Other soil macro-organisms			
Soil mite	a.s. ‡		No data available. Not required.
	Preparation		
	Metabolite 1		
Collembola			
	a.s. ‡	Chronic	No data available. Not required.
	Preparation		
	Metabolite 1		
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡		No data available. Not required.
	Metabolite 1		
Carbon mineralisation	a.s. ‡		No data available. Not required.
	Metabolite 1		
Field studies[2]			
Not required			

[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

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Earthworms					
	a.s. ‡	Acute	-	-	10
	a.s. ‡	Chronic	-	-	5
	Preparation	Acute	-	-	10
	Preparation	Chronic	-	-	5
	Metabolite 1	Acute	-	-	10
	Metabolite 1	Chronic	-	-	5
Other soil macro-organisms					
Soil mite	a.s. ‡	-	-	-	-
	Preparation	-	-	-	-
	Metabolite 1	-	-	-	-
Collembola	a.s. ‡	-	-	-	-
	Preparation	-	-	-	-
	Metabolite 1	-	-	-	-

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

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

Preliminary screening data

No observed adverse effects.

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha) emergence	Exposure (g/ha)[2]	TER	Trigger
red cover, wheat, mustard	Heptamaloxyloglucan	> 20	-	Not calculated as heptamoloxyloglucan applied at very low doses (0.44 g/ha)		

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

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

Test type/organism	end point
Activated sludge	Not required.
Pseudomonas sp	

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

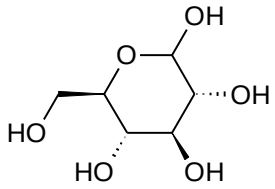
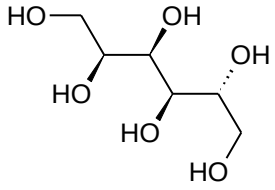
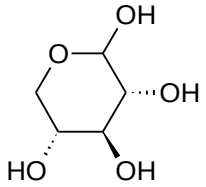
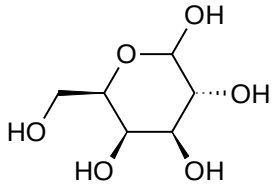
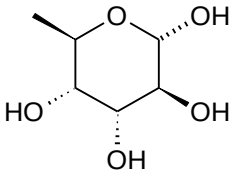
Compartment	
soil	heptamaloxyloglucan
water	heptamaloxyloglucan
sediment	heptamaloxyloglucan
groundwater	heptamaloxyloglucan

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	Not classified.

	RMS/peer review proposal
Preparation	Not classified.

APPENDIX B – USED COMPOUNDS CODE(S)

Code/Trivial name*	Chemical name	Structural formula
D-glucopyranose	D-glucopyranose	
D-glucitol	D-glucitol	
D-xylopyranose	D-xylopyranose	
D-galactopyranose	D-galactopyranose	
L-fucopyranose	L-fucopyranose	

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)

EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LLNA	Local Lymph Node Assay
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin

MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SG	water soluble granule
SP	water soluble powder
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio

TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year