European Commission

Draft Renewal Assessment Report prepared according to Regulation (EC) N° 1107/2009

Heptamaloxyloglucan

Volume 1

Rapporteur Member State: France
Co-Rapporteur Member State: Spain

Version History

When	What
2020-09	Initial RAR

The RMS is the author of the Assessment Report. The Assessment Report is based on the validation by the RMS, and the verification during the EFSA peer-review process, of the information submitted by the Applicant in the dossier, including the Applicant's assessments provided in the summary dossier. As a consequence, data and information including assessments and conclusions, validated and verified by the RMS experts, may be taken from the applicant's (summary) dossier and included as such or adapted/modified by the RMS in the Assessment Report. For reasons of efficiency, the Assessment Report should include the information validated/verified by the RMS, without detailing which elements have been taken or modified from the Applicant's assessment. As the Applicant's summary dossier is published, the experts, interested parties, and the public may compare both documents for getting details on which elements of the Applicant's dossier have been validated/verified and which ones have been modified by the RMS. Nevertheless, the views and conclusions of the RMS should always be clearly and transparently reported; the conclusions from the applicant should be included as an Applicant's statement for every single study reported at study level; and the RMS should justify the final assessment for each endpoint in all cases, indicating in a clear way the Applicant's assessment and the RMS reasons for supporting or not the view of the Applicant.

Table of contents

Level 1

Heptamaloxyloglucan

1 STATEMENT OF SUBJECT MATTER AND PURPOSE FOR WHICH THIS REPORT HAS BEEN PREPARED AND BACKGROUND INFORMATION ON THE APPLICATION

1.1 CONTEXT IN WHICH THIS DRAFT ASSESSMENT REPORT WAS PREPARED

1.1.1 Purpose for which the draft assessment report was prepared

This renewal assessment report (RAR) has been prepared in accordance with Commission Regulation (EC) No 844/2012 and Guidance Document SANCO/2012/11251 rev. 5 in order to evaluate the supplementary dossier submitted by Elicityl, and to allow a decision on the renewal of the approval of the active substance heptamaloxyloglucan under Commission Regulation (EC) No 1107/2009.

Heptamaloxyloglucan has no current entry in Annex VI of CLP Regulation (EU) 1272/2008. The combined template RAR/CLH report is used in accordance with Guidance Document SANCO/12592/2012 rev. 2. However, as no classification is proposed for Heptamaloxyloglucan at this stage of the renewal procedure, the corresponding sections were not fulfilled in Volume 1 and a proposal for harmonised classification is not intended to be submitted to ECHA.

1.1.2 Arrangements between rapporteur Member State and co-rapporteur Member State

According to Commission Implementing Regulation (EU) No 2016/183 France was designated Rapporteur Member State (RMS) and Spain assigned as Co-Rapporteur Member State (Co-RMS).

France, as RMS, evaluated the dossier submitted by the applicants and draft the Renewal Assessment Report for all the sections whereas, Spain, as Co-RMS, conducted a pre-peer review of this report. Any deviating views on critical issues between the RMS and the Co-RMS have been reported in Volume 1 Level 3 section 3.1.9.

1.1.3 EU Regulatory history for use in Plant Protection Products

In May 2006, Elicityl SA, submitted an application for the inclusion of the active substance heptamaloxyloglucan in Annex I of the Directive 91/414/EEC. France was designated RMS to carry out the detailed examination of the dossier and report the conclusions to the Commission.

France submitted on 26 July 2007 to the EFSA the report of their examination, hereafter referred to as the draft assessment report, including, as required, a recommendation concerning the possible inclusion of heptamaloxyloglucan in Annex I to the Directive.

The assessment reports have been peer reviewed by the Member States and the EFSA and presented to the Commission on 17 July 2009.

The review was finalised on 27 November 2009 in the format of the Commission review report (Review report for the active substance heptamaloxyloglucan - SANCO/10502/09 - final, 27 October 2009). Heptamaloxyloglucan was listed in Annex I of Directive 91/414/EEC on 1st June 2010 (Commission Directive 2010/14/UE) with the following specific provisions:

- PART A

Only uses as plant growth regulator may be authorised.

- PART B

For the implementation of the uniform principles of Annex VI, the conclusions of the review report on heptamaloxyloglucan, and in particular Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health on 27 November 2009 shall be taken into account.

Heptmaloxyloglucan has been included in Annex IV of Regulation (EC) No 396/2005 (Commission Regulation (EU) No 500/2013 of 30 May 2013).

1.1.4 Evaluations carried out under other regulatory contexts

The RMS is not aware of any evaluation carried out under other regulatory contexts for heptamaloxyloglucan.

1.2 APPLICANT INFORMATION

1.2.1 Name and address of applicant(s) for approval of the active substance

ELICITYL SA
746 avenue Ambroise Croizat
F-38920 Crolles, France
Tel : +33 4 76 40 71 61
Fax: +33 4 76 45 59 50
contact@elicityl.fr
www.elicityl-oligotech.com
Contact person: **********

1.2.2 Producer or producers of the active substance

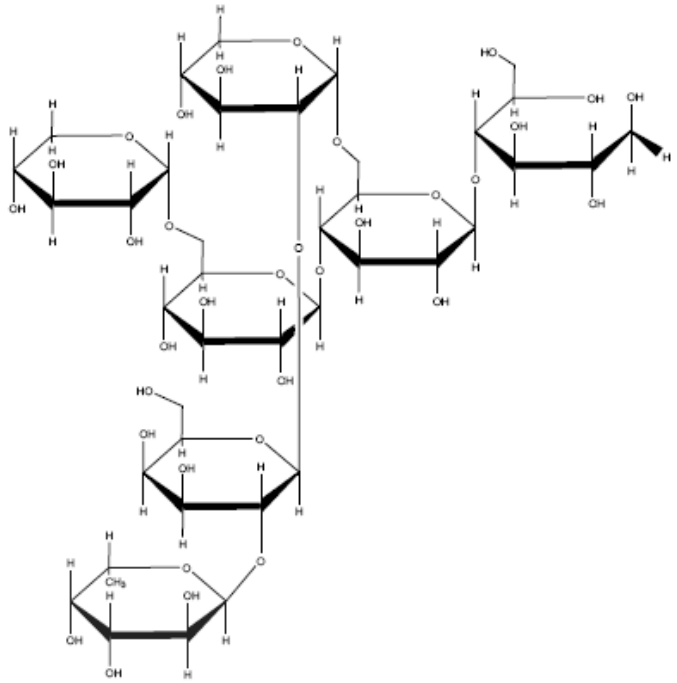
ELICITYL SA
746 avenue Ambroise Croizat
F-38920 Crolles, France
Tel : +33 4 76 40 71 61
Fax: +33 4 76 45 59 50
contact@elicityl.fr
www.elicityl-oligotech.com
Contact person: **********

1.2.3 Information relating to the collective provision of dossiers

No task force has been formed.

1.3 IDENTITY OF THE ACTIVE SUBSTANCE

1.3.1 Common name proposed or ISO-accepted and synonyms	Heptamaloxyloglucan
1.3.2 Chemical name (IUPAC and CA nomenclature)	
IUPAC	*{[α-D-Xyl p-*(1→6)]*-β-D-Glc p-*(1→4)}{[*α-L- Fuc p-*(1→2)*-β-D-Gal p-*(1→2)*-α-D-Xyl p-*(1→6)]*-β-D-Glc p-*(1→4)}*-D-Glc-ol* with: Xyl p: xylopyranosyl Glc p: glucopyranosyl Fuc p: fucopyranosyl Gal p: galactopyranosyl Glc-ol: glucitol
CA	/
1.3.3 Producer's development code number	EL101GV EL101GV xyloglucan
1.3.4 CAS, EEC and CIPAC numbers	
CAS	870721-81-6

EEC	Not available
CIPAC	Not available
1.3.5 Molecular and structural formula, molecular mass	
Molecular formula	$C_{40}H_{70}O_{33}$
Structural formula	
Molecular mass	1078.96 g/mol
1.3.6 Method of manufacture (synthesis pathway) of the active substance	Considered as confidential information please refer to Vol. 4
1.3.7 Specification of purity of the active substance in g/kg	780 g/kg
1.3.8 Identity and content of additives (such as stabilisers) and impurities	
1.3.8.1 Additives	Considered as confidential information please refer to Vol. 4
1.3.8.2 Significant impurities	Considered as confidential information please refer to Vol. 4
1.3.8.3 Relevant impurities	Patulin (max 50 µg/kg)
1.3.9 Analytical profile of batches	Considered as confidential information please refer to Vol. 4

1.4 INFORMATION ON THE PLANT PROTECTION PRODUCT

1.4.1 Applicant	ELICITYL SA 746 avenue Ambroise Croizat F-38920 Crolles, France
1.4.2 Producer of the plant protection product	ELICITYL SA 746 avenue Ambroise Croizat F-38920 Crolles, France

1.4.3 Trade name or proposed trade name and producer's development code number of the plant protection product	PEL101GV
1.4.4 Detailed quantitative and qualitative information on the composition of the plant protection product	
1.4.4.1 Composition of the plant protection product	Technical Heptamaloxyloglucan, 100 %w/w
1.4.4.2 Information on the active substances	Heptamaloxyloglucan, min. 780 g/kg
1.4.4.3 Information on safeners, synergists and co-formulants	None
1.4.5 Type and code of the plant protection product	The formulation code which are the closest to the preparation are SP, SG or ST, however the applicant claims that PEL101GV is neither a powder nor a granule nor a tablet. It is a solid to be used after dissolution in water. Considering the properties of the product, RMS considers it should be considered as a water soluble powder (SP).
1.4.6 Function	Protection against frost damage
1.4.7 Field of use envisaged	Grape
1.4.8 Effects on harmful organisms	No claimed effect on harmful organisms

1.5 DETAILED USES OF THE PLANT PROTECTION PRODUCT

1.5.1 Details of representative uses

Crop and/or situation (a)	Member State	Product Name	F G I (b)	Pests or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc of a.i. g/kg (i)	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Interval between applications (min)	mg a.i./hl min max (l)	Water l/ha min max	mg a.i./ha min max (l)		
Vine	FR	PEL101GV	F	Frost damage	XX	780 g/kg	Foliar spraying using an air pressured system	BBCH 07-16 (budding to 6 leaves) Early spring	4	4 days	109.25 mg mg ai/hL	100-400	0.54 – 437 mg ai/ha	F	1-4 applications 12 to 48 h before freezing temperatures

(a) For crops, the EU and Codex classification (both) should be taken into account ; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) *e.g.* biting and sucking insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes – GIFAP Technical Monograph N° 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant – type of equipment used must be indicated
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI - minimum pre-harvest interval

RMS comment: This GAP table format is different from the one provided by the applicant. RMS has updated the table format following EFSA request. EFSA has requested to "update the GAP table using the template on the EC website (for chemical active substances)". The applicant is kindly asked to check if this update is in accordance with its initial GAP table.

1.5.2 Further information on representative uses

- Details on method of application for specialised applications e.g. soil fumigants:
Application of PEL101GV must be done by spraying method using a pressurized system.

- Details on number and timing of applications and duration of protection, in case the GAP table gives ranges:
The maximum number of applications to grapevines is 4 per growing season and the minimum interval between applications is 4 days.

- Necessary waiting period or other precautions to avoid phytotoxic effects on succeeding crops:
Not relevant for the representative use (Grapevines).

- Proposed instructions for use.
See Volume 3 CP B.3.8

1.5.3 Details of other uses applied for to support the setting of MRLs for uses beyond the representative uses

Not applicable.

1.5.4 Overview on authorisations in EU Member States

PEL101GV has already been registered in France.

Level 2

Heptamaloxyloglucan

2 SUMMARY OF ACTIVE SUBSTANCE HAZARD AND OF PRODUCT RISK ASSESSMENT

Summary of methodology proposed by the applicant for literature review and for all sections

A literature review was carried out by the applicant for heptamaloxyloglucan and its glucidic monomer units according to Article 8(5) of Regulation (EC) No 1107/2009. The review itself is in accordance with the EFSA Guidance document as published in "EFSA Journal 2011; 9(2):2092". The review was made in order to identify scientific peer-reviewed open literature on heptamaloxyloglucan and its glucidic monomer units dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of the dossier. The reliability assessment for relevant studies was done according to Klimisch et al (1997). The detailed process, key words used, analysis of relevance and reliability, and results were presented in Volume 3 CA B6, 3 CA B7, 3 CA B8 and 3 CA B9. The overall results are shown below (results from all sections combined - toxicology, dietary safety, environmental fate or ecotoxicology fields):

	HEPTAMALOXYLOGLUCAN			
Study selection process	Toxicology	Residues	Fate	Ecotoxicology
Total number of publications retrieved (with duplicates) (global search results)	17 611			
Total number of publications retrieved removing too old literature (before 2008)	14 941			
Total number of publications retrieved after removing of duplicates	5 964			
Number of publications excluded after rapid assessment for relevance according to title (irrelevant literature)	5 731			
Number of publications further assessed in detail (possible relevant literature)	233			
Number of publications excluded according to irrelevance of title for respective section (excluded literature for this section)	151	163	198	129
Number of publications further assessed according to abstract for respective section (possible relevant literature for this section)	82	70	35	104
Number of publications excluded according to irrelevance of abstract for respective section (excluded literature for this section)	82	64	22	61
Number of publications further assessed according to full-text for respective section (possible relevant literature for this section)	0	6	13	43
Number of publications excluded according to irrelevance of full-text for respective section (excluded literature for this section)	0	2	10	31
Number of publications not excluded for relevance after detailed assessment (i.e. relevant publications) (included literature)	0	4	3	12

The outcomes of the review of scientific open literature are discussed by the RMS in Volumes 3 of the RAR for each section.

2.1 IDENTITY

2.1.1 Summary or identity

The minimum purity of heptamaloxyloglucan as manufactured should not be less than 780 g/kg. At the moment no FAO specification exists. It is proposed not to modify the specification of minimum purity of the active substance.

The technical material may contain the mycotoxin patulin, which may be 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.

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. Analysis of patulin content has been performed in recent starting material batches; an analytical

method is also available to determine patulin content in the technical substance. The analytical results obtained for the starting material (apple pomace) of heptamaloxyloglucan and for the technical active substance demonstrate that the patulin is not present at a level ≥ 50 µg/kg.

The main data regarding the identity of heptamaloxyloglucan are given in Vol. 4.

2.2 PHYSICAL AND CHEMICAL PROPERTIES [EQUIVALENT TO SECTION 7 OF THE CLH REPORT TEMPLATE]

2.2.1 Summary of physical and chemical properties of the active substance

Pure and technical heptamaloxyloglucan is a clear beige powder with no odour. The chemical structure of the impurities is closed to the structure of the active substance (other xyloglucans with a higher molecular weight).
Heptamaloxyloglucan has a melting point of 172°C. A decomposition is observed at 281,4 -305°C, and no boiling point was observed up to 525°C.
Its relative density is between 1.39 and 1.55 at 20°C. The physical state of active substance: "freeze dried cake" explains the variability of the measure. Its vapour pressure has not been measured but is estimated from QSAR program (1.1 x 10^{-11} Pa). It is highly soluble in water (>500 g/L) and not very soluble in organic solvents (from 1 mg/L in n-heptane to 10 g/L in methanol), with a partition coefficient log Kow < 0.
It is hydrolytically stable at pH 4, 7 and 9 and does not dissociate. In the UV/Vis wavelengths, it has no peak absorption with molecular absorption coefficient higher than 10 L/mol/cm, therefore it is considered photochemically stable.
Based on literature, structural formula and oxygen balance, it is concluded that the substance is not explosive, has no oxidizing properties, is not flammable nor auto-flammable. However, as a potential risk of dust explosion cannot be excluded due to the physical form of heptamaloxyloglucan (combustible fine particles), the precautionary statement P271 is proposed by the applicant. In water (1 g/L) it is not surface active.

2.2.1.1 Evaluation of physical hazards [equivalent to section 8 of the CLH report template]

2.2.1.1.1 Explosives *[equivalent to section 8.1 of the CLH report template]*

Table 1: Summary table of studies on explosive properties

Method	Results	Remarks	Reference
Statement	Not explosive	-	Burosse, V., Ambrosi, D., 2006 ASC 05/23

2.2.1.1.1.1 Short summary and overall relevance of the provided information on explosive properties

Considering the overall chemical structure of the substance and its impurities, as well as their functionalities (carbohydrates) and the oxygen balance, no explosive property is expected.

2.2.1.1.1.2 Comparison with the CLP criteria

Experimental test can be waived as the substance does not bear any functionalities that are known to potentially bring explosive properties.

2.2.1.1.1.3 Conclusion on classification and labelling for explosive properties

Not classified for explosive properties.

2.2.1.1.2 Flammable gases (including chemically unstable gases) *[equivalent to section 8.2 of the CLH report template]*

Table 2: Summary table of studies on flammable gases (including chemically unstable gases)

Method	Results	Remarks	Reference

2.2.1.1.2.1 Short summary and overall relevance of the provided information on flammable gases (including chemically unstable gases)

Not applicable, the substance is not a gas

2.2.1.1.2.2 Comparison with the CLP criteria

Not applicable

2.2.1.1.2.3 Conclusion on classification and labelling for flammable gases

Not classified as flammable gas.

2.2.1.1.3 Oxidising gases *[equivalent to section 8.3 of the CLH report template]*

Table 3: Summary table of studies on oxidising gases

Method	Results	Remarks	Reference

2.2.1.1.3.1 Short summary and overall relevance of the provided information on oxidising gases

Not applicable, the substance is not a gas

2.2.1.1.3.2 Comparison with the CLP criteria

Not applicable

2.2.1.1.3.3 Conclusion on classification and labelling for oxidising gases

Not classified as oxidising gas.

2.2.1.1.4 Gases under pressure *[equivalent to section 8.4 of the CLH report template]*

Table 4: Summary table of studies on gases under pressure

Method	Results	Remarks	Reference

2.2.1.1.4.1 Short summary and overall relevance of the provided information on gases under pressure

Not applicable, the substance is not a gas under pressure

2.2.1.1.4.2 Comparison with the CLP criteria

Not applicable

2.2.1.1.4.3 Conclusion on classification and labelling for gases under pressure

Not classified as gas under pressure.

2.2.1.1.5 Flammable liquids *[equivalent to section 8.5 of the CLH report template]*

Table 5: Summary table of studies on flammable liquids

Method	Results	Remarks	Reference

2.2.1.1.5.1 Short summary and overall relevance of the provided information on flammable liquids

Not applicable, the substance is not a liquid

2.2.1.1.5.2 Comparison with the CLP criteria

Not applicable

2.2.1.1.5.3 Conclusion on classification and labelling for flammable liquids

Not classified as flammable liquid.

2.2.1.1.6 Flammable solids *[equivalent to section 8.6 of the CLH report template]*

Table 6: Summary table of studies on flammable solids

Method	Results	Remarks	Reference
Statement	Not flammable solid		Burosse, V., Ambrosi, D., 2006 ASC 05/23

2.2.1.1.6.1 Short summary and overall relevance of the provided information on flammable solids

Although carbohydrates are known combustible materials, they are considered as non flammable solids.

2.2.1.1.6.2 Comparison with the CLP criteria

Experimental test was waived considering the chemical structure of the substance, and the fact that such carbohydrate oligomers are known not to be flammable.

2.2.1.1.6.3 Conclusion on classification and labelling for flammable solids

Not classified as flammable solid.

2.2.1.1.7 Self-reactive substances *[equivalent to section 8.7 of the CLH report template]*

Table 7: Summary table of studies on self-reactivity

Method	Results	Remarks	Reference
Statement	Not self-reactive		Burosse, V., Ambrosi, D., 2006 ASC 05/23

2.2.1.1.7.1 Short summary and overall relevance of the provided information on self-reactive substances

Based on its chemical structure, the substance is not self-reactive.

2.2.1.1.7.2 Comparison with the CLP criteria

The substance does not bear any chemical functionalities that could bring self-reactive properties.

2.2.1.1.7.3 Conclusion on classification and labelling for self-reactive substances

Not classified as self-reactive.

2.2.1.1.8 Pyrophoric liquids *[equivalent to section 8.8 of the CLH report template]*

Table 8: Summary table of studies on pyrophoric liquids

Method	Results	Remarks	Reference

2.2.1.1.8.1 Short summary and overall relevance of the provided information on pyrophoric liquids

Not applicable, the substance is not a liquid.

2.2.1.1.8.2 Comparison with the CLP criteria

Not applicable

2.2.1.1.8.3 Conclusion on classification and labelling for pyrophoric liquids

Not classified as pyrophoric liquid.

2.2.1.1.9 Pyrophoric solids *[equivalent to section 8.9 of the CLH report template]*

Table 9: Summary table of studies on pyrophoric solids

Method	Results	Remarks	Reference

2.2.1.1.9.1 Short summary and overall relevance of the provided information on pyrophoric solids

The substance is very soluble in water, it is intended to be used after dilution in water and the experience shows that it is not pyrophoric.

2.2.1.1.9.2 Comparison with the CLP criteria

No pyrophoric properties were observed experimentally.

2.2.1.1.9.3 Conclusion on classification and labelling for pyrophoric solids

Not classified as pyrophoric solid.

2.2.1.1.10 Self-heating substances *[equivalent to section 8.10 of the CLH report template]*

Table 10: Summary table of studies on self-heating substances

Method	Results	Remarks	Reference
Statement	Not self-heating		Burosse, V., Ambrosi, D., 2006 ASC 05/23

2.2.1.1.10.1 Short summary and overall relevance of the provided information on self-heating substances

Based on its structure, the substance is not self-heating.

2.2.1.1.10.2 Comparison with the CLP criteria

Carbohydrate oligomers such as heptamaloxyloglucan are known not to have self-heating properties.

2.2.1.1.10.3 Conclusion on classification and labelling for self-heating substances

Not classified as self-heating substance.

2.2.1.1.11 Substances which in contact with water emit flammable gases *[equivalent to section 8.11 of the CLH report template]*

Table 11: Summary table of studies on substances which in contact with water emit flammable gases

Method	Results	Remarks	Reference

Method	Results	Remarks	Reference
EEC A.6	No gas evolved upon dilution of the substance in water		Ricau, H., 2006a 05-905012-002

2.2.1.1.11.1 Short summary and overall relevance of the provided information on substances which in contact with water emit flammable gases

The substance is used in solution in water and no flammable gas evolves upon dilution in water.

2.2.1.1.11.2 Comparison with the CLP criteria

No flammable gas evolves upon dilution

2.2.1.1.11.3 Conclusion on classification and labelling for substances which in contact with water emit flammable gases

Not classified as a substance that emits flammable gas in contact with water.

2.2.1.1.12 Oxidising liquids *[equivalent to section 8.12 of the CLH report template]*

Table 12: Summary table of studies on oxidising liquids

Method	Results	Remarks	Reference

2.2.1.1.12.1 Short summary and overall relevance of the provided information on oxidising liquids

Not applicable as the substance is not a liquid.

2.2.1.1.12.2 Comparison with the CLP criteria

Not applicable

2.2.1.1.12.3 Conclusion on classification and labelling for oxidising liquids

Not classified as oxidising liquid

2.2.1.1.13 Oxidising solids *[equivalent to section 8.13 of the CLH report template]*

Table 13: Summary table of studies on oxidising solids

Method	Results	Remarks	Reference
Statement	The substance has no oxidising properties		Burosse, V., Ambrosi, D., 2006 ASC 05/23

2.2.1.1.13.1 Short summary and overall relevance of the provided information on oxidising solids

Based on its chemical structure, its functionalities and the oxygen balance, the substance has no oxidising properties.

2.2.1.1.13.2 Comparison with the CLP criteria

Based on its chemical structure, the substance has no oxidising properties.

2.2.1.1.13.3 Conclusion on classification and labelling for oxidising solids

Not classified for oxidising properties.

2.2.1.1.14 Organic peroxides *[equivalent to section 8.14 of the CLH report template]*

Table 14: Summary table of studies on organic peroxides

Method	Results	Remarks	Reference

2.2.1.1.14.1 Short summary and overall relevance of the provided information on organic peroxides

Not applicable as the substance does not contain peroxides.

2.2.1.1.14.2 Comparison with the CLP criteria

Not applicable.

2.2.1.1.14.3 Conclusion on classification and labelling for organic peroxides

Not classified as organic peroxides.

2.2.1.1.15 Corrosive to metals *[equivalent to section 8.15 of the CLH report template]*

Table 15: Summary table of studies on the hazard class corrosive to metals

Method	Results	Remarks	Reference

2.2.1.1.15.1 Short summary and overall relevance of the provided information on the hazard class corrosive to metals

Considering its chemical structure, the substance is not corrosive to metals.

2.2.1.1.15.2 Comparison with the CLP criteria

No corrosiveness to metals is expected for this substance

2.2.1.1.15.3 Conclusion on classification and labelling for corrosive to metals

Not classified as corrosive to metals.

2.2.2 Summary of physical and chemical properties of the plant protection product

The plant protection product PEL101GV is made of 100% technical active substance EL101GV.
The preparation is a highly expanded white beige odourless freeze dried cake that is not surface active. Based on literature, structural formula and oxygen balance, it is concluded that the preparation is not flammable, not explosive and does not possess oxidizing or auto-flammability properties. However, as a potential risk of dust explosion cannot be excluded due to the physical form of EL101GV (combustible fine particles), the precautionary statement P271 is proposed.
When dispersed at 1% w/v in water, it has a pH of 7.02 and the density of the solid preparation is included between 1.39 and 1.55 g/cm^3. The preparation has an immediate wettability and during a wet sieve test, none material remains on a 75 µm sieves. At 1 g/L in water, no foam remains after 3 minutes, indicating that the preparation is not a foaming product. The dilution stability was demonstrated, the degree of dilution was 100% at 1.2% w/w in water.
The physical and chemical properties of the preparation were stable after an accelerated storage procedure (14 days at 54°C) in commercial packaging (glass bottle). The shelf life stability of 24 months at ambient temperature is also demonstrated in the commercial packaging (glass bottle).

2.3 DATA ON APPLICATION AND EFFICACY

2.3.1 Summary of effectiveness

PEL101GV is presently the only one Heptamaloxyloglucan based product registered in EU (in France only). The only one use registered is the use frost damage on vine described in B.3.3.

Considering that the substance is approved and authorization of the plant protection product containing the substance has already been evaluated according to the Uniform Principles (Regulation (EC) No 546/2011), no other efficacy documentation is deemed to be necessary at this stage.

More detailed consideration will be fully assessed in the context of subsequent applications for products authorization.

2.3.2 Summary of information on the development of resistance

Not relevant. Heptamaloxyloglucan is not intended for the control of harmful organisms.

2.3.3 Summary of adverse effects on treated crops

No adverse effects on treated crops were identified in previous evaluation. However no data was provided on the potential effect on vinification.
Applicant is invited to pay attention to argue the absence of negative effects on vinification following the use of PEL101GV. Data may be based on practical field data from technical institutes.
These consideration will be fully assessed in the context of subsequent applications for products authorization.

2.3.4 Summary of observations on other undesirable or unintended side-effects

No undesirable or unintended side-effects were identified in previous evaluation.
More detailed consideration will be fully assessed in the context of subsequent applications for products authorization.

2.4 FURTHER INFORMATION

2.4.1 Summary of methods and precautions concerning handling, storage, transport or fire

Handling:
If large quantities are handled, avoid formation of dusty atmosphere (risk of explosion).
The tank must be correctly rinsed to avoid all traces of a preceding treatment. Fill the tank with water up to 50% of the given volume of pulverisation. Open the bottle of the preparation and add 15 mL of water in the bottle with the pipette.
Close the flask with the plastic stopper and mix to obtain a good solubilisation of the product, then pour the solution obtained in the tank and at least twice rinse the bottle with 15 mL of water.
It is recommended to empty in the tank flushing waters of the bottle. Finish filling the tank until given volume.

Storage:
PEL101GV is stable for two years in its original packaging when stored between + 5°C to + 35°C.

Transport:
Not concerned by UN Recommendations on the transport of dangerous goods.

Procedures for cleaning application equipment and protective clothing:
Application equipment and protective clothing:
Decontamination of equipment, packaging is achieved by washing with water plus detergent.

2.4.2 Summary of procedures for destruction or decontamination

Unwanted amounts of heptamaloxyloglucan and technical material EL101GV can be destroyed best by combustion in a licensed incinerator.
Decontamination of equipment, packaging a.s.o. is achieved by washing with water plus detergent.

2.4.3 Summary of emergency measures in case of an accident

Personal Precautions:

Traditional individual protections.

Environmental Precaution:
Heptamaloxyloglucan is a substance extracted from plant. It does not have any other effect on grapevine than enhancing its natural resistance to cold. More particularly, it does not have pesticide, fungicide or bactericide activity. Heptamaloxyloglucan respects the environment because of the dose used and its biodegradability.

Methods of Cleaning Up:
Collect mechanically (sponge)

2.5 METHODS OF ANALYSIS

2.5.1 Methods used for the generation of pre-authorisation data

Validated method for the determination of heptamaloxyloglucan and its impurities in the technical active substance are available. The analytical technique is highly specific and no confirmatory method is required.

Heptamaloxyloglucan is a branched xyloglucan molecule extracted from apples with neither additive nor chemical product. It is composed of 7 hexose residues: glucopyranosyl, fucopyranosyl, xylopyranosyl and galactopyranosyl. The terminal glucose residue is reduced as a glucitol residue. All these hexose and hexol residues are natural components of the apple and of other dicotyledonous plants, where they are major constituents of cellulose and hemicellulose molecules, which are themselves the principal components of cell walls.

It is reasonable to consider that these different natural substances are rapidly degraded by soil macro- and micro-organisms as a natural component of humus. This degradation leads to simple components, also present in the natural environment.

Therefore, analytical methods for risk assessment could not be validated properly in any case, especially for this natural substance for which a natural background would have to be taken into account.

2.5.2 Methods for post control and monitoring purposes

As heptamaloxyloglucan is a naturally occurring non-toxic active substance, and as no MRL are set in plants, no analytical methods are required in plants, soil, water and air, according to guideline SANCO 825/00 rev. 9.1.
No methods are required for residues in animal and human body fluids and tissues, as the active substance heptamaloxyloglucan is naturally present in plants, and that there is no definition of residues in these matrices.

2.6 EFFECTS ON HUMAN AND ANIMAL HEALTH

More detailed results of the studies are presented in Volume 3, section B.6.

2.6.1 Summary of absorption, distribution, metabolism and excretion in mammals *[equivalent to section 9 of the CLH report template]*

Table 16: Summary table of toxicokinetic studies

Method	Results	Remarks	Reference
Not relevant	Biochemistry and Molecular Biology of Plants	Public literature	KCA 5.1/01 (KCA 6.2.1/01) Buchanan B.B., Gruissen W., and Jones R.L. 2000
Not relevant	Oligosaccharides as signals and substrates in the plant cell wall.	Public literature	KCA 5.1/02 Fry S. and al. 1993
Not relevant	Xyloglucans	Public literature	KCA 5.1/03 Hayashi T. 1989
Not relevant	Basic aspects of digestion and absorption.	Public literature	KCA 5.1/04 Wahbe T.G. and Christie D.L. 2006

Not relevant	Hydrolysis of oligosaccharides by polyelectrolytes.	Public literature	KCA 5.1/05 Heyraud A., Rinaudo M. 1981
Not relevant	Hydrolysis study at pH 2.2 and 50°C during 2 days	Unpublished	KCA 5.1/06 Havet S. 2007
Not relevant	Nutrition	Public literature	KCA 5.1/07 Alvarez E.E. and Sanchez P.G. 2006
Not relevant	Polysaccharide degradation by human intestinal bacteria during growth under multi-substrate limiting conditions in a three-stage continuous culture systems	Public literature	KCA 5.1/08 Macfarlane S. et al. 1998
Not relevant	Absorption, distribution, metabolism and excretion (ADME) of eight known dietary monosaccharides required for glycoprotein synthesis and cellular recognition processes.	Public literature	KCA 5.1/09 Gardiner T. 2000a
Not relevant	Dietary fucose: Absorption, distribution, metabolism and excretion (ADME) and biological activity.	Public literature	KCA 5.1/10 Gardiner T. 2000b
Not relevant	Dietary galactose: Absorption, distribution, metabolism and excretion (ADME) and biological activity.	Public literature	KCA 5.1/11 Gardiner T. 2000c
Not relevant	Dietary glucose: Absorption, distribution, metabolism and excretion (ADME) and biological activity.	Public literature	KCA 5.1/12 Gardiner T. 2000d
Not relevant	Dietary xylose: Absorption, distribution, metabolism and excretion (ADME) and biological activity.	Public literature	KCA 5.1/13 Gardiner T. 2000e
Not relevant	Sorbitol	Public literature	KCA 5.1/14 Ramberg J. 2005
Not relevant	Short-chain fatty acids and human colonic function : roles of resistant starch and nonstarch polysaccharides	Public literature	KCA 5.1/15 Topping D.L. and Clifton P.M. 2001
Not relevant	Physiological effects of dietary complex carbohydrates and its metabolites in certain diseases	Public literature	KCA 5.1/16 Kattak M.M.A. 2002

2.6.1.1 Short summary and overall relevance of the provided toxicokinetic information on the proposed classification(s)

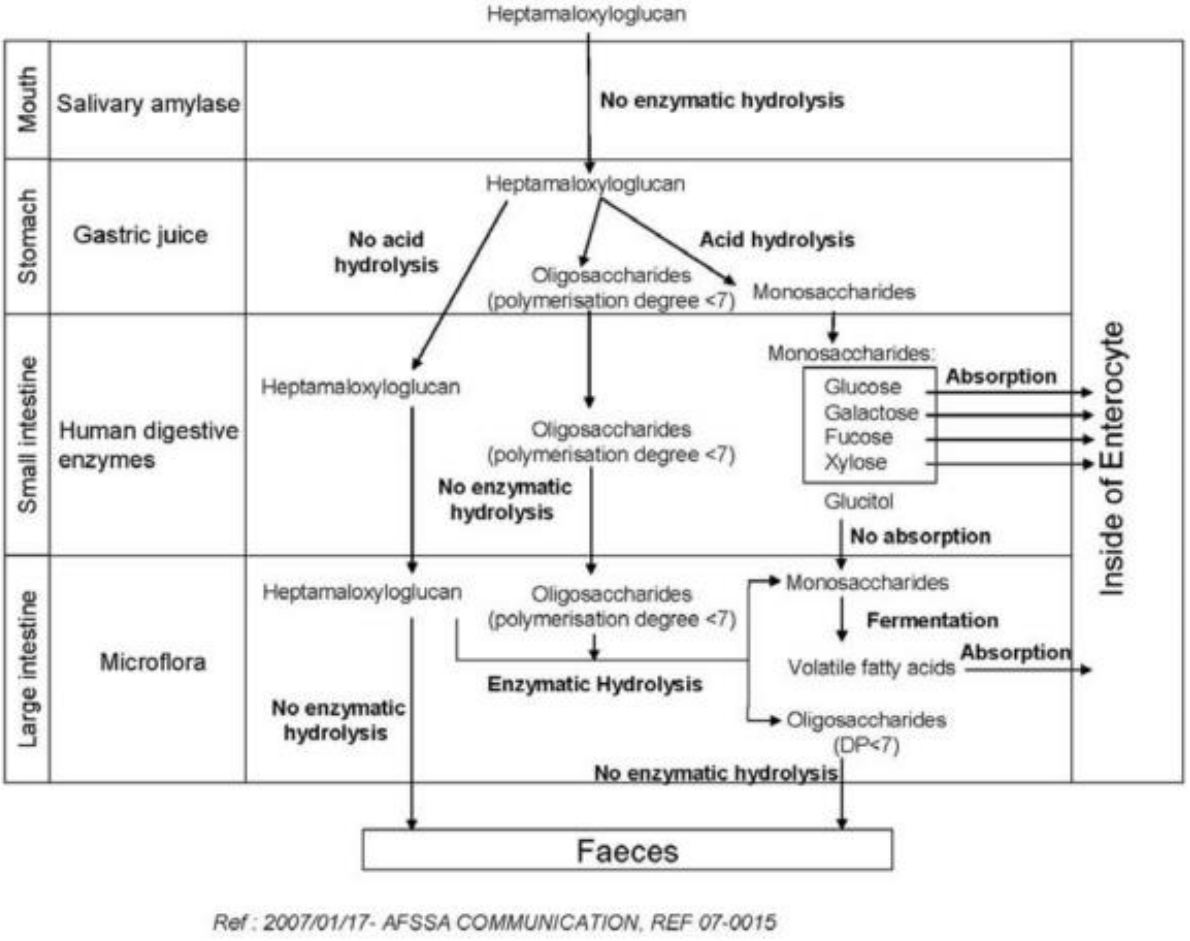
The ADME data provided by the applicant is mainly based on literature review.

Heptamaloxyloglucan is not absorbed. Via the oral route, it is expected heptamaloxyloglucan to be hydrolysed by acid hydrolysis in the stomach and by enzymatic hydrolysis (microflora) in the large intestine into several monosaccharides (absorbable glucose, fucose, xylose and galactose; unabsorbable glucitol) and oligosaccharides.

- Monosaccharides are absorbed in the small intestine by passive diffusion like any dietary saccharide (except glucitol) or metabolised in the large intestine, the bacteria of the microflora by fermentation into fatty acids.
- Hexamers are not absorbable. They pass into the large intestine where they can undergo enzymatic hydrolysis or the remaining fraction of unmetabolized or unhydrolyzed heptamaloxyloglucan be excreted in the faeces.

Via the dermal route, no study was submitted by the applicant. Due to the active substance physico-chemical properties (K_{ow} of EL101GV is low, $< 10^{-4}$) and its high molecular weight (1078 g/mol), dermal absorption is not expected. In addition, no adverse event was observed following the acute dermal toxicity test on heptamaloxyloglucan.

For inhalation absorption, no study was submitted by the applicant. The ADME argumentation has mainly been built on the active substance physico-chemical properties and its molecular weight. Please refer to the section B.6.2.3 acute toxicity by inhalation, i.e. this RMS would consider this concern addressed and that ADME inhalation study can be waived if an acute inhalation toxicity study was provided.



Ref : 2007/01/17- AFSSA COMMUNICATION, REF 07-0015

Figure 2.6.1.1-1: Probable fate of the heptamaloxyloglucan after oral intake

2.6.2 Summary of acute toxicity

2.6.2.1 Acute toxicity - oral route [equivalent to section 10.1 of the CLH report template]

Table 17: Summary table of animal studies on acute oral toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Value LD_{50}	Reference
Acute Oral toxicity OECD 423 GLP: Yes Acceptable	Rat Sprague-Dawley Females 3/group	Heptamaloxyloglucan (EL101GV) Batch n°: ALP0103 Purity: 96.2% w/w Vehicle: Sterile water	300 and 2000 mg/kg b.w. Single-dose oral gavage	> 2 000 mg/kg b.w.	KCA 5.2.1/01 ******** 2006 b Study N° 20030812ST

Table 18: Summary table of human data on acute oral toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 19: Summary table of other studies relevant for acute oral toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No relevant study				

2.6.2.1.1 Short summary and overall relevance of the provided information on acute oral toxicity

After a single oral administration of Heptamaloxyloglucan (EL101GV) to female Sprague-Dawley rats at the dose level of 300 or 2000 mg/kg b.w., no mortality or treatment-related clinical signs were recorded.

2.6.2.1.2 Comparison with the CLP criteria regarding acute oral toxicity

The oral LD_{50} of Heptamaloxyloglucan (EL101GV) in rat is greater than 2000 mg/kg b.w., and thus above the cut-off value of 2000 mg/kg b.w. for classification for acute toxicity by oral route according to CLP.

2.6.2.1.3 Conclusion on classification and labelling for acute oral toxicity

According to CLP criteria, no classification for acute oral toxicity is warranted.

2.6.2.2 Acute toxicity - dermal route [equivalent to section 10.2 of the CLH report template]

Table 20: Summary table of animal studies on acute dermal toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Value LD_{50}	Reference
Acute Dermal toxicity OECD 402 GLP: Yes Acceptable	Rat Sprague-Dawley Females and males 5/sex	Heptamaloxyloglucan (EL101GV) Batch n°: ALD0204 Purity: 86.1% w/w Moistened with water	2000 mg/kg b.w. 24-hour application	> 2 000 mg/kg b.w.	KCA 5.2.2/01 *******, 2006 a Study N° 20050508STC

Table 21: Summary table of human data on acute dermal toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 22: Summary table of other studies relevant for acute dermal toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No relevant study				

2.6.2.2.1 Short summary and overall relevance of the provided information on acute dermal toxicity

After a single dermal application of Heptamaloxyloglucan (EL101GV) to male and female Sprague-Dawley rats at the dose level of 2000 mg/kg b.w., no mortality or treatment-related clinical signs were recorded.

2.6.2.2.2 Comparison with the CLP criteria regarding acute dermal toxicity

The dermal LD_{50} of Heptamaloxyloglucan (EL101GV) in rat is greater than 2000 mg/kg bw, and thus above the cut-off value of 2000 mg/kg bw for classification for acute toxicity by dermal route according to CLP.

2.6.2.2.3 Conclusion on classification and labelling for acute dermal toxicity

According to CLP criteria, no classification for acute dermal toxicity is warranted.

2.6.2.3 Acute toxicity - inhalation route

Table 23: Summary table of animal studies on acute inhalation toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, form and particle size (MMAD)	Dose levels, duration of exposure	Value LC_{50}	Reference
No study provided					

Table 24: Summary table of human data on acute inhalation toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 25: Summary table of other studies relevant for acute inhalation toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No relevant study				

2.6.2.3.1 Short summary and overall relevance of the provided information on acute inhalation toxicity

There is no evidence submitted by the applicant that the heptamaloxyloglucan is unlikely to trigger inhalation toxicity.

In light of the above remark and lack of ADME data on the inhalation route, RMS considers that the provided elements do not bring sufficient evidence in the applicant's conclusion for inhalation endpoint and this should be substantiated by at least a read across evaluation with a suitable analogue that would have reliable acute inhalation data. If no suitable analogue is found, inhalation route testing is then required. In the absence of read across evaluation or test, a data gap will be considered for this endpoint.

2.6.2.3.2 Comparison with the CLP criteria regarding acute inhalation toxicity

No comparison with the CLP criteria regarding acute inhalation toxicity is possible.

2.6.2.3.3 Conclusion on classification and labelling for acute inhalation toxicity

No conclusion on classification and labelling for acute inhalation toxicity is possible.

2.6.2.4 Skin corrosion/irritation [equivalent to section 10.4 of the CLH report template]

Table 26: Summary table of animal studies on skin corrosion/irritation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results - Observations and time point of onset[2] - Mean scores/animal - Reversibility	Reference
Acute Skin irritation OECD 404 GLP: Yes Acceptable	Rabbit New Zealand White Females 3/group	Heptamaloxyloglucan (EL101GV) Batch n°: ALP0103 Purity: 96.2% w/w Moistened with water	0.5 g 4-hour application	No test substance-related body weight effects or clinical signs. Erythema (score of 1) in 3 animal at 1h, resolved by 24-h. Mean scores per animal at 24, 48 and 72 hours:	KCA 5.2.4/01 *******, 2006 c Study N° 20040148STC

				Erythema: 0, 0, 0 Oedema: 0, 0, 0 Non–irritating to skin.	

Table 27: Summary table of human data on skin corrosion/irritation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 28: Summary table of other studies relevant for skin corrosion/irritation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No relevant study				

2.6.2.4.1 Short summary and overall relevance of the provided information on skin corrosion/irritation

After topical application of Heptamaloxyloglucan (EL101GV) on the skin of female rabbits for 4 hours under occlusion, only minimal and transient erythema was observed.

2.6.2.4.2 Comparison with the CLP criteria regarding skin corrosion/irritation

In the skin irritation study in rabbit, as no destruction of skin tissue and no sign of irritation at 24 hours were observed, CLP criteria regarding skin corrosion/irritation are not met.

2.6.2.4.3 Conclusion on classification and labelling for skin corrosion/irritation

According to CLP criteria, no classification for skin corrosion/irritation is warranted.

2.6.2.5 Serious eye damage/eye irritation [equivalent to section 10.5 of the CLH report template]

Table 29: Summary table of animal studies on serious eye damage/eye irritation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels duration of exposure	Results - Observations and time point of onset[2] - Mean scores/animal - Reversibility	Reference
Acute Eye irritation OECD 405 GLP: Yes Acceptable	Rabbit New Zealand White Females 3/group	Heptamaloxyloglucan (EL101GV) Batch n°: ALP0103 Purity: 96.2% w/w	0.1 g Single exposure	No test substance-related body weight effects or clinical signs. After 1h post treatment, minimal and transient conjunctival redness was observed in the treated eye of the three rabbits. Mean scores per animal at 24, 48 and 72 hours: Cornea: 0, 0, 0 Iris: 0, 0, 0	KCA 5.2.5/01 *******, 2006 d Study N° 20040147STC

				Conjunctivae (redness): 0, 0, 0 Conjunctivae (chemosis): 0, 0, 0 Non–irritating to eye.	

Table 30: Summary table of human data on serious eye damage/eye irritation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 31: Summary table of other studies relevant for serious eye damage/eye irritation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No relevant study				

2.6.2.5.1 Short summary and overall relevance of the provided information on serious eye damage/eye irritation

After eye-instillation of heptamaloxyloglucan (EL101GV) to female rabbits, minimal and transient conjunctival redness was observed at 1 hour post-treatment as an only reaction.

2.6.2.5.2 Comparison with the CLP criteria regarding serious eye damage/eye irritation

In the eye irritation study in rabbit, as no sign of irritation was present at 24 hours, CLP criteria regarding eye corrosion/irritation are not met.

2.6.2.5.3 Conclusion on classification and labelling for serious eye damage/eye irritation

According to CLP criteria, no classification for eye corrosion/irritation is warranted.

2.6.2.6 Respiratory sensitisation [equivalent to section 10.6 of the CLH report template]

Table 32: Summary table of animal studies on respiratory sensitisation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
No study					

Table 33: Summary table of human data on respiratory sensitisation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 34: Summary table of other studies relevant for respiratory sensitisation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No relevant study				

2.6.2.6.1 Short summary and overall relevance of the provided information on respiratory sensitisation

No formally recognized and validated animal tests currently exist for respiratory sensitisation.

2.6.2.6.2 Comparison with the CLP criteria regarding respiratory sensitisation

Comparison with the CLP criteria regarding respiratory sensitisation is not possible.

2.6.2.6.3 Conclusion on classification and labelling for respiratory sensitisation

No classification for respiratory sensitisation is warranted.

2.6.2.7 Skin sensitisation [equivalent to section 10.7 of the CLH report template]

Table 35: Summary table of animal studies on skin sensitisation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels duration of exposure	Results	Reference
LLNA (Local Lymph Node Assay) OECD 429 GLP: Yes Acceptable	Mice CBA/J Female Negative control group: 4 Treated group: 4 Positive control group (α-hexylcinnamaldehyde (HCA)): 4	Heptamaloxyloglucan (EL101GV) Batch n°: ANN0304 Purity: 78.1% w/w Vehicle: Dimethylformamide (DMF)	Dose levels of the test item: 1, 2.5, 5, 10 or 25% Dose levels of the positive control HCA: 25% Duration of exposure: 3 days	No mortality and no clinical signs were observed during the study. No cutaneous reactions and no noteworthy increase in ear thickness were observed in the animals of the treated groups. No lymphoproliferation and no dose-response relationship were noted at the tested concentrations, while significant lymphoproliferation was observed with HCA at 25%. Non sensitising	KCA 5.2.6/01 *******, 2006 Study N° 31168 TSS

Table 36: Summary table of human data on skin sensitisation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 37: Summary table of other studies relevant for skin sensitisation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Not relevant study				

2.6.2.7.1 Short summary and overall relevance of the provided information on skin sensitisation

The heptamaloxyloglucan (EL101GV) did not induce delayed contact hypersensitivity in the murine Local Lymph Node Assay.

2.6.2.7.2 Comparison with the CLP criteria regarding skin sensitisation

In the LLNA assay, as no cutaneous reactions from exposure to heptamaloxyloglucan were observed, CLP criteria regarding skin sensitisation are not met.

2.6.2.7.3 Conclusion on classification and labelling for skin sensitisation

According to CLP criteria, no classification for skin sensitisation is warranted.

2.6.2.8 Phototoxicity

Table 38: Summary table of studies on phototoxicity

Method, guideline, deviations if any	Test substance	Dose levels duration of exposure	Results	Reference
Not applicable, heptamaloxyloglucan is photochemically stable as it has no peak absorption with molecular absorption coefficient higher than 10 L/mol/cm at wavelength > 290nm.				

Table 39: Summary table of human data on phototoxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Not applicable.				

Table 40: Summary table of other studies relevant for phototoxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Not applicable.				

2.6.2.9 Aspiration hazard

Table 41: Summary table of evidence for aspiration hazard

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Not applicable, heptamaloxyloglucan is a solid.				

2.6.2.9.1 Short summary and overall relevance of the provided information on aspiration hazard

Not applicable.

2.6.2.9.2 Comparison with the CLP criteria regarding aspiration hazard

Not applicable.

2.6.2.9.3 Conclusion on classification and labelling for aspiration hazard

According to CLP criteria, no classification for aspiration hazard is warranted.

2.6.2.10Specific target organ toxicity-single exposure (STOT SE)

Table 42: Summary table of animal studies on STOT SE (specific target organ toxicity-single exposure)

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, route of exposure, dose levels, duration of exposure**	**Results** **- NOAEL/LOAEL** **- target tissue/organ** **- critical effects at the LOAEL**	**Reference**
Please refer to Sections 2.6.2 and 2.6.7			

Table 43: Summary table of human data on STOT SE (specific target organ toxicity-single exposure)

Type of data/report	**Test substance**	**Route of exposure Relevant information about the study (as applicable)**	**Observations**	**Reference**
No human data				

Table 44: Summary table of other studies relevant for STOT SE (specific target organ toxicity-single exposure)

Type of study/data	**Test substance**	**Relevant information about the study (as applicable)**	**Observations**	**Reference**
No relevant study				

2.6.2.10.1 Short summary and overall relevance of the provided information on specific target organ toxicity – single exposure (STOT SE)

No specific target organ toxicity was observed after a single dose/exposure of heptamaloxyloglucan.

2.6.2.10.2 Comparison with the CLP criteria regarding STOT SE (specific target organ toxicity-single exposure)

According to CLP, classification as STOT-SE should be considered when there is clear evidence of toxicity to a specific organ, especially when it is observed in the absence of lethality. As no specific target organ toxicity was observed after a single dose/exposure of heptamaloxyloglucan, CLP criteria regarding STOT-SE are not met.

2.6.2.10.3 Conclusion on classification and labelling for STOT SE (specific target organ toxicity-single exposure)

According to CLP criteria, no classification for STOT-SE is warranted.

2.6.3 Summary of repeated dose toxicity (short-term and long-term toxicity)

2.6.3.1 Specific target organ toxicity-repeated exposure (STOT RE)

Table 45: Summary table of animal studies on repeated dose toxicity (short-term and long-term toxicity) STOT RE (specific target organ toxicity - repeated exposure)

Method, guideline, deviations[1] if any, species, strain, sex, no/group	**Test substance, route of exposure, dose levels, duration of exposure**	**Results** **- NOAEL/LOAEL** **- target tissue/organ** **- critical effects at the LOAEL**	**Reference**

28-day oral rat study OECD 407 GLP: Yes Rat Sprague-Dawley Female and male 10/sex/group	Heptamaloxyloglucan (EL101GV) Batch n°: AND0706 Purity: 88.6% w/w Vehicle: sterile water Oral (gavage) Dose levels: 0, 50, 200, 1000 mg/kg b.w. Duration of exposure: 28 days	No compound related effect on mortality, clinical signs, body weight, food consumption, haematology, clinical chemistry, urinalysis and organ weights. There were no treatment-related lesions in rats dosed with heptamaloxyloglucan until 1000 mg/kg at the histopathological examination. **NOAEL > 1000 mg/kg b.w.**	KCA 5.3.1/01 **********, 2006 Study N° 20060118TRB
Performance of additional short-term and long-term toxicity tests is not deemed necessary.			

Table 46: Summary table of human data on repeated dose toxicity STOT RE (specific target organ toxicity-repeated exposure)

Type of data/report	**Test substance**	**Route of exposure Relevant information about the study (as applicable)**	**Observations**	**Reference**
No human data				

Table 47: Summary table of other studies relevant for repeated dose toxicity STOT RE (specific target organ toxicity-repeated exposure)

Type of study/data	**Test substance**	**Relevant information about the study (as applicable)**	**Observations**	**Reference**
No relevant study				

2.6.3.1.1 Short summary and overall relevance of the provided information on specific target organ toxicity – repeated exposure (short-term and long-term toxicity)

For the short-term toxicity, a 28-day rat study with daily administration of heptamaloxyloglucan at 1000 mg/kg b.w./d is available. No mortality was observed. There was no change in body weights, food and water consumption and on organ weights. No clinical signs were noted and no macroscopic and microscopic changes were observed. There were no significant differences in haematology, blood clinical chemistry or urinalysis.

No short-term dermal study was performed because no dermal absorption is expected due to the very low K_{ow} (< 10^{-4}), to the high water solubility (> 500 g/L) and to the high molecular weight (> 1000 g/mol) of heptamaloxyloglucan.

No 90-day or long-term studies have been conducted on heptamaloxyloglucan. The active substance does not represent a concern due to the nature of the active substance and lack of any toxicity in the acute or 28 day rat studies. In addition, there is no evidence of bioaccumulation potential as the unchanged molecule is not absorbed in the digestive tract, and as all metabolites are glucids or short-chain fatty acids which are involved in a large variety of metabolic pathways present in animals.

In conclusion, no sign of toxicity was observed. Thus, the relevant short-term NOAEL in rat study was >1000 mg/kg b.w./d based on the absence of systemic effects at the highest tested dose. No specific target organ was observed after a repeated exposure of heptamaloxyloglucan.

2.6.3.1.2 Comparison with the CLP criteria regarding STOT RE (specific target organ toxicity-repeated exposure)

According to CLP, classification as STOT-RE should be considered when there is clear evidence of toxicity to a specific organ, especially when it is observed in the absence of lethality. As no specific target organ toxicity was observed after repeated dose/exposure of heptamaloxyloglucan, CLP criteria regarding STOT-RE are not met.

2.6.3.1.3 Conclusion on classification and labelling for STOT RE (specific target organ toxicity-repeated exposure)

According to CLP criteria, no classification for STOT-RE is warranted.

2.6.4 Summary of genotoxicity / germ cell mutagenicity [equivalent to section 10.8 of the CLH report template]

Table 48: Summary table of genotoxicity/germ cell mutagenicity tests *in vitro*

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations /Results	Reference
In vitro bacterial mutagenicity (Ames) OECD 471 GLP: Yes Acceptable	Heptamaloxyloglucan (EL101GV) Batch n°: ANN0304 Purity: 78.1% w/w	*Salmonella typhimurium (TA 1535, TA1537, TA98, TA100, TA102)* 0 - 5000 µg/plate (with and without S9)	Negative (+/- S9)	KCA 5.4.1/01 Le Curieux F, 2006 Study N° FSR-IPL 030207
In vitro mammalian cell gene mutation (L5178Y Mouse lymphoma cells /TK) OECD 476 GLP: Yes Acceptable	Heptamaloxyloglucan (EL101GV) Batch n°: AND0706 Purity: 88.6% w/w	L5178Y mouse lymphoma cells 0 - 5000 µg/mL (with and without S9)	Negative (+/- S9)	KCA 5.4.1/03 Nesslany F, 2006 Study N° FSR-IPL 060230

Table 49: Summary table of genotoxicity/mutagenicity tests in mammalian somatic or germ cells *in vivo*

Method, guideline, deviations if any	Test substance	Relevant information about the study (as applicable)	Observations/Results	Reference
No study				

Table 50: Summary table of human data relevant for genotoxicity / germ cell mutagenicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

2.6.4.1 Short summary and overall relevance of the provided information on genotoxicity / germ cell mutagenicity

A battery of two *in vitro* tests was conducted to determine the genotoxic potential of heptamaloxyloglucan.

Heptamaloxyloglucan did not induce mutations in bacteria or mammalian cells *in vitro* either in the presence or in the absence of metabolic activation and is therefore considered unlikely to be mutagenic.

However, no test for clastogenicity has been provided. A read across approach with suitable analogue(s) having chromosomal aberration *in vitro* data and or micronucleus *in vitro* data would be acceptable given the nature and physico-chemical properties of the active substance.

With respect to the in vivo assessment (somatic and germ cells) no in vivo test has been performed. At least one in vivo test is required when three in vitro tests are negative. Given the nature of the active substance and the expected absence of accumulation, waiving in vivo genotoxicity tests (for both somatic and germ cells) would be acceptable if three in vitro tests had been performed. Two in vitro tests for mutagenicity have been performed and no in vivo test for somatic or germ cells have been provided. In addition, no clastogenicity test or read across have been provided.
In conclusion, if no read across or in vitro test are available, clastogenicity testing is considered as a data gap

2.6.4.2 Comparison with the CLP criteria regarding genotoxicity / germ cell mutagenicity

The mutagenicity data for heptamaloxyloglucan consists of an Ames test in bacteria and an *in vitro* test in mammalian cells. The two tests were negative outcome both with and without metabolic activation, which indicates that heptamaloxyloglucan has no mutagenesis potential. The clastogenic potential of heptamaloxyloglucan cannot be determined since no data has been submitted.

2.6.4.3 Conclusion on classification and labelling for genotoxicity / germ cell mutagenicity

According to CLP criteria, no conclusion on classification and labelling for genotoxicity / germ cell mutagenicity can be drawn.

2.6.5 Summary of long-term toxicity and carcinogenicity

Table 51: Summary table of animal studies on long-term toxicity and carcinogenicity

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, dose levels duration of exposure**	**Results - NOAEL/LOAEL - target tissue/organ - critical effects at the LOAEL**	**Reference**
No study			

Table 52: Summary table of human data on long-term toxicity and carcinogenicity

Type of data/report	**Test substance**	**Relevant information about the study (as applicable)**	**Observations**	**Reference**
No human data				

Table 53: Summary table of other studies relevant for long-term toxicity and carcinogenicity

Type of study/data	**Test substance**	**Relevant information about the study (as applicable)**	**Observations**	**Reference**
No relevant study				

2.6.5.1 Short summary and overall relevance of the provided information on long-term toxicity and carcinogenicity

For long-term toxicity and carcinogenicity, no new studies for heptamaloxyloglucan have been submitted. The literature referenced long term studies in rats and mice were considered supportive since they were conducted with similar analogue polysaccharides but with much higher molecular weights or different glucidic structure. Hence the read across to heptamaloxyloglucan could not be considered acceptable. However, given the active substance nature, physico-chemical properties and low potential for accumulation in mammals, no mutagenic effect in the two in vitro mutagenic studies and the absence of adverse effects in a 28-day rat study, the active substance is not expected to present concerns for long-term toxicity and carcinogenicity. Tests for both endpoints are considered

not necessary.

2.6.5.2 Comparison with the CLP criteria regarding carcinogenicity

Table 54: Compilation of factors to be taken into consideration in the hazard assessment

Species and strain	Tumour type and background incidence	Multi-site responses	Progression of lesions to malignancy	Reduced tumour latency	Responses in single or both sexes	Confounding effect by excessive toxicity?	Route of exposure	MoA and relevance to humans
Not applicable								

2.6.5.3 Conclusion on classification and labelling for carcinogenicity

No classification for carcinogenicity is warranted.

2.6.6 Summary of reproductive toxicity

2.6.6.1 Adverse effects on sexual function and fertility – generational studies [equivalent to section 10.10.1 of the CLH report template]

Table 55: Summary table of animal studies on adverse effects on sexual function and fertility – generational studies

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results - NOAEL/LOAEL (for sexual function and fertility, parents) - target tissue/organ - critical effects at the LOAEL	Reference
No study			

Table 56: Summary table of human data on adverse effects on sexual function and fertility

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 57: Summary table of other studies relevant for toxicity on sexual function and fertility

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No relevant study				

2.6.6.1.1 Short summary and overall relevance of the provided information on adverse effects on sexual function and fertility – generational studies

For adverse effects on sexual function and fertility, no generational studies for heptamaloxyloglucan have been reported. However, given the active substance nature, physico-chemical properties and low potential for accumulation in mammals and the absence of adverse effects in 28-day study, the active substance is not expected to present concerns for adverse effects on sexual function and fertility.

2.6.6.1.2 Comparison with the CLP criteria regarding adverse effects on sexual function and fertility

Not applicable.

2.6.6.2 Adverse effects on development [equivalent to section 10.10.4 of the CLH report template]

Table 58: Summary table of animal studies on adverse effects on development

Method, guideline, deviations[1] if any, species, strain, sex, no/group	**Test substance, dose levels duration of exposure**	**Results - NOAEL/LOAEL (for parent, offspring and for developmental effects) - target tissue/organ - critical effects at the LOAEL**	**Reference**
No study			

Table 59: Summary table of human data on adverse effects on development

Type of data/report	**Test substance**	**Relevant information about the study (as applicable)**	**Observations**	**Reference**
No human data				

Table 60: Summary table of other studies relevant for developmental toxicity

Type of study/data	**Test substance**	**Relevant information about the study (as applicable)**	**Observations**	**Reference**
No relevant study				

2.6.6.2.1 Short summary and overall relevance of the provided information on adverse effects on development

For adverse effects on development, no studies for heptamaloxyloglucan have been reported. However, given the active substance nature, physico-chemical properties and low potential for accumulation in mammals and the absence of adverse effects in 28-day study, the active substance is not expected to present concerns for adverse effects on development.

2.6.6.2.2 Comparison with the CLP criteria regarding adverse effects on development

Not applicable.

2.6.6.3 Adverse effects on or via lactation

Table 61: Summary table of animal studies on effects on or via lactation

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, dose levels duration of exposure**	**Results - NOAEL/LOAEL - target tissue/organ - critical effects at the LOAEL**	**Reference**
No study			

Table 62: Summary table of human data on effects on or via lactation

Type o data/report	**Test substance**	**Relevant information about the study (as applicable)**	**Observations**	**Reference**
No human data				

Table 63: Summary table of other studies relevant for effects on or via lactation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No relevant study				

2.6.6.3.1 Short summary and overall relevance of the provided information on effects on or via lactation

For adverse effects on or via lactation, no studies for heptamaloxyloglucan have been reported. However, given the active substance nature, physico-chemical properties and low potential for accumulation in mammals and the absence of adverse effects in 28-day study, the active substance is not expected to present concerns for adverse effects on or via lactation.

2.6.6.3.2 Comparison with the CLP criteria regarding effects on or via lactation

Not applicable.

2.6.6.4 Conclusion on classification and labelling for reproductive toxicity

No classification for reproductive toxicity is warranted.

2.6.7 Summary of neurotoxicity

Table 64: Summary table of animal studies on neurotoxicity

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results: - NOAEL/LOAEL - target tissue/organ -critical effect at LOAEL	Reference
Not applicable, the chemical structure of heptamaloxyloglucan is not structurally related to neurotoxicants and therefore, no studies were performed to assess a neurotoxicity.			

2.6.8 Summary of other toxicological studies

2.6.8.1 Toxicity studies of metabolites and impurities

Not applicable, based on metabolites nature (found in dietary).

2.6.8.2 Supplementary studies on the active substance

As no specific risk is expected from oligo/monosaccharides, no additional study was performed.

2.6.9 Summary of medical data and information

No data was available. As demonstrated in all previous sections, no toxicity is expected from heptamaloxyloglucan and its metabolites, which are oligo- and monosaccharides.

2.6.10 Toxicological end points for risk assessment (reference values)

As concluded in the Peer Review on heptamaloxyloglucan (EFSA Scientific Report (2009) 334, 1-52), “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.”

Table 65: Overview of relevant studies for derivation of reference values for risk assessment

Species	Study (method/type, length, route of exposure)	Test substance	Critical effect	NOAEL	LOAEL	Cross reference
Not applicable						

2.6.10.1Toxicological end point for assessment of risk following long-term dietary exposure – ADI (acceptable daily intake)

As indicated in the previous DAR evaluation 2007, the submitted toxicological studies i.e. acute oral and 28-day toxicity studies do not allow setting an ADI. However, the applicant submitted data regarding the presence of heptamaloxyloglucan in apple juice at levels as high as 9.44 mg/L. The actual exposure of the consumers to heptamaloxyloglucan through apple juice consumption is 1.2 mg/day for children and young adults and 0.8 mg/day for adults (based on apple juice consumption in France, INCA study, 1999).

Even though considering as an extreme worst case that the total amount of sprayed plant protection product would remain on grapes until harvest, the average heptamaloxyloglucan concentration of grapes would be 0.175 mg/kg fruit. Considering the 97.5 percentile of grape consumption of table grapes and wine for the French population (40g grapes and 423 g wine), the average exposure to heptamaloxyloglucan resulting from application of the plant protection product would be 0.006 mg/day + 0.106 mg/day = 0.11 mg/day, which is lesser than the average exposure through apple juice consumption.

In addition, it has been demonstrated that heptamaloxyloglucan is present in many food from plant origin, and if not present, produced in human colon during fermentation of Non Starch Polysaccharides absorbed when eating vegetable. Accordingly, human intake of heptamaloxyloglucan via the diet greatly exceeds the potential exposure through the plant protection product. Furthermore, heptamaloxyloglucan is devoid of acute toxicity. No specific effects or target organs were identified from the short-term toxicity study performed in the mouse. Heptamaloxyloglucan is not genotoxic. Since heptamaloxyloglucan is an otherwise plant signalling molecule, no toxicologically relevant residue will occur in plants. Since there is no risk for consumers from the intended use of heptamaloxyloglucan as plant protection product, allocation of an ADI is considered unnecessary.

2.6.10.2Toxicological end point for assessment of risk following acute dietary exposure - ARfD (acute reference dose)

Heptamaloxyloglucan is an oligosaccharide which is a component of vegetal cell walls and thus naturally present in food from plant origin; furthermore it is devoid of acute toxicity and has no mutagenesis potential. The clastogenic potential of heptamaloxyloglucan cannot be determined since no data has been submitted. Therefore allocating an ArfD is not relevant.

2.6.10.3Toxicological end point for assessment of occupational, bystander and residents risks – AOEL (acceptable operator exposure level)

Heptamaloxyloglucan is an oligosaccharide, which is devoid of acute toxicity. No specific effects or target organs were identified from the short-term toxicity study performed in the rat. Heptamaloxyloglucan is not irritating for the skin and eyes and not sensitising. Heptamaloxyloglucan has no mutagenesis potential. The clastogenic potential of heptamaloxyloglucan cannot be determined since no data has been submitted. Significant percutaneous absorption is excluded. Furthermore it is a xyloglucan which is naturally present in food from plant origin. Therefore allocating an AOEL is not relevant.

2.6.10.4Toxicological end point for assessment of occupational, bystander and residents risks – AAOEL (acute acceptable operator exposure level)

Heptamaloxyloglucan is an oligosaccharide, which is devoid of acute toxicity. No specific effects or target organs were identified from the short-term toxicity study performed in the rat. Heptamaloxyloglucan is not irritating for the skin and eyes and not sensitising. Heptamaloxyloglucan has no mutagenesis potential. The clastogenic potential of heptamaloxyloglucan cannot be determined since no data has been submitted. Significant percutaneous absorption is excluded. Furthermore it is a xyloglucan which is naturally present in food from plant origin. Therefore allocating an AAOEL is not relevant.

2.6.11 Summary of product exposure and risk assessment

PEL101GV is used as an agricultural frost-protecting agent on grapevines and is not intended to afford protection against any harmful organism. PEL101GV is formulated as a lyophilisate inside a flask, and contains 100% of the only ingredient heptamaloxyloglucan.

PEL101GV has no significant acute toxicity *via* the oral and dermal routes of exposure, is not a skin or eye irritant and is not a skin sensitizer. According to the Regulation (EC) No. 1272/2008, the product PEL101GV should be not classified these endpoints. There is no evidence that the product PEL101GV is unlikely to trigger inhalation toxicity (please refer to the section 2.6.2).

Due to the absence of reference values (see the point 2.6.10), no risk assessment could be conducted by comparison to exposure modelling. Moreover, as the compound is of low toxicity and is a normal part of the diet, no adverse effects are anticipated.

2.7 RESIDUE

2.7.1 Summary of storage stability of residues

No supervised residue trials have been conducted for heptamaloxyloglucan, and none is required. Therefore no storage stability data are necessary.
Furthermore, heptamaloxyloglucan is of low toxicity and a signal molecule (elicitor) naturally occurring at low levels in plant tissues and then, it will not be possible to distinguish between the natural one and the one from the application of plant protection product.

2.7.2 Summary of metabolism, distribution and expression of residues in plants, poultry, lactating ruminants, pigs and fish

Plant metabolism studies

No plant metabolism studies are available.

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.
Heptamaloxyglucan is then a plant protection product prepared from an edible plant which naturally contains it at low levels.

Heptamaloxyloglucan is a branched xyloglucan molecule extracted from apples. It is made of 7 glucidic monomer units, which are D-glucopyranosyl and terminal D-glucitol (in the main chain) and D-xylopyranosyl, D-galactopyranosyl and L-fucopyranosyl (in side-chains). All these hexose and hexol residues are natural components of the apple and of other dicotyledonous plants, where they are major constituents of cellulose and hemicellulose molecules, which are the principal components of cell walls. Consequently, if heptamaloxyloglucan is consumed it will be broken down to simple sugars naturally presents in fruits and vegetables and will be used as an energy source and will exhibit no toxic effects.

For these reasons, no plant metabolism studies are needed.

Livestock metabolism studies
No livestock metabolism studies are available and none are required as grapes or related by-products are not used as feed items. Furthermore, heptamaloxyloglucan is a natural plant compound and then a natural component of livestock diet.

2.7.3 Definition of the residue

Heptamaloxyloglucan is a signal molecule naturally occurring at low levels in plant tissues which is not expecting to exhibit toxic effect. Due to its low toxicity, no ADI and no ARfD are proposed for heptamaloxyloglucan.

Consequently, it is not necessary to propose residue definitions for the active substance heptamaloxyloglucan in plant or animal commodities.

2.7.4 Summary of residue trials in plants and identification of critical GAP

Heptamaloxyloglucan is a signal molecule naturally occurring at low levels in plant tissues and it will not be possible to distinguish between the natural one and the one that come from the application of plant protection product.
Furthermore, considering the intended use (total application rate of 1.75 g/ha up to BBCH 16) and the high solubility of active substance (558 g/l), it will certainly disappear from leaves surface as last application is achieved more than 4 months before harvest. Therefore, the use of heptamaloxyloglucan as protection plant product is not expected to result in an increase of glycans or xyloglucans naturally present in grapes.
Moreover, if heptamaloxyloglucan is consumed it will be broken down to simple sugars naturally presents in fruits and vegetables and will be used as an energy source and will exhibit no toxic effects.
Finally, due to its absence of toxicity (no ADI and no ARfD), heptamaloxyloglucan is currently included in Annex IV of EU Regulation 396/2005, which lists active substances for which no MRLs are required and in the framework of the renewal it is proposed to maintain heptamaloxyloglucan in the Annex IV of regulation 396/2005/EC

2.7.5 Summary of feeding studies in poultry, ruminants, pigs and fish

No feeding are available and none are required as grapes or related by-products are not used as feed items in Europe.
Furthermore, as heptamaloxyloglucan is a natural plant compound is therefore a natural component of livestock diet.

2.7.6 Summary of effects of processing

No study investigating the effect of processing on the nature and on the quantity of heptamaloxyloglucan is available.
Heptamaloxyloglucan is a natural plant compound of low toxicity and it will not be possible to distinguish between the natural one and the one that come from the application of plant protection product.

Additionally, heptamaloxyloglucan is a branched xyloglucan molecule extracted from apples. It is made of 7 glucidic monomer units, which are D-glucopyranosyl and terminal D-glucitol (in the main chain) and D-xylopyranosyl, D-galactopyranosyl and L-fucopyranosyl (in side chains). All these hexose and hexol residues are natural components of the apple and of other dicotyledonous plants, where they are major constituents of cellulose and hemicellulose molecules, which are the principal components of cell walls.
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. They are not susceptible to result in the formation of toxicologically relevant residues.
It can also be noticed that galacturonases (enzymes cocktail) used at the first step of heptamaloxyloglucan production, are also used in the process of wine clarification in order to solubilise long chain polysaccharides (pectins and xyloglucans) in soluble ones. So, this kind of enological treatment is susceptible to induce heptamaloxyloglucan production in wine produced from non treated grapes.

For the above reasons, studies investigating the effect of processing on the nature and on the quantity of heptamaloxyloglucan are not necessary.

2.7.7 Summary of residues in rotational crops

Grapes, the only representative use is a permanent crop. Consequently, studies investigating the nature and the quantity of residue in rotational crops are not necessary.

2.7.8 Summary of other studies

No others study are considered necessary.

2.7.9 Estimation of the potential and actual exposure through diet and other sources

Heptamaloxyloglucan is a natural component of dicotyledonous plant cell walls. This substance is already present in different food commodities of plant origin, among them apple juice, and dietary supplement, and then the consumer is already exposed to this active substance.

Furthermore, considering the intended use (total application rate of 1.75 g/ha up to BBCH 16) and the high solubility of the active substance (558 g/l), it will certainly disappear from leaves surface as last application is achieved more than 4 months before harvest. Therefore, the use of heptamaloxyloglucan as protection plant product is not expected to result in an increase of glycans or xyloglucans naturally present in grape.

Additionally, heptamaloxyloglucan is a branched xyloglucan molecule extracted from apples. It is made of 7 glucidic monomer units, which are D-glucopyranosyl and terminal D-glucitol (in the main chain) and D-xylopyranosyl, D-galactopyranosyl and L-fucopyranosyl (in side chains). All these hexose and hexol residues are natural components of the apple and of other dicotyledonous plants, where they are major constituents of cellulose and hemicellulose molecules, which are the principal components of cell walls. Consequently, if heptamaloxyloglucan is consumed it will be broken down to simple sugars naturally presents in fruits and vegetables and will be utilised as an energy source and will exhibit no toxic effects.

Finally, due to its low toxicity neither ADI nor ARfD is set or proposed for this active substance.

For the above reasons, it is not necessary to estimate the potential and actual exposure through diet and other sources for heptamaloxyloglucan.

2.7.10 Proposed MRLs and compliance with existing MRLs

Heptamaloxyloglucan is currently included to the Annex IV of regulation 396/2005/EC which comprised active substances for which no MRL are required for the following reasons.

Heptamaloxyloglucan is a natural component of dicotyledonous plant cell walls. This substance is already present in different food commodities of plant origin, among them apple juice, and dietary supplement, and then the consumer is already exposed to this active substance.
Furthermore, due to its low toxicity neither ADI nor ARfD is set or proposed for this active substance.

According to guidance document on criteria for the inclusion of active substances into Annex IV of regulation (EC) N° 396/2005 (SANCO/11188/2013, Rev. 2, September 20151), if a compound is naturally occurring in food and if it has no identified hazardous properties, it is a candidate for inclusion in Annex IV of Regulation (EC) No 396/2005.
Consequently, in the framework of the renewal, it is proposed to maintain heptamaloxyloglucan in the Annex IV of regulation 396/2005/EC.

2.7.11 Proposed import tolerances and compliance with existing import tolerances

Not relevant.

2.8 FATE AND BEHAVIOUR IN THE ENVIRONMENT

2.8.1 Summary of fate and behaviour in soil

Heptamaloxyloglucan is a polysaccharide which leads to smaller-sized oligosaccharides and monosaccharides after degradation. No other relevant metabolites, degradation or reaction products are expected to appear.

The rate of degradation of xyloglucans is directly correlated to the soil biomass (which produces the various enzymes necessary to the degradation) and to the soil temperature, which controls the activity of the enzymes. In addition, short chain soluble xyloglucans, like heptamaloxyloglucan are more easily degraded than long-chain insoluble molecules, so the half-life of the active substance in soil is expected to be short. Furthermore heptamaloxyloglucan is readily biodegradable.

No experimental DT_{50} in soil value was made available. However, heptamaloxyloglucan has a negative log (Kow)

[1] European Commission, 2015. Guidance document on criteria for the inclusion of active substances into Annex IV of Regulation (EC) No 396/2005. SANCO/11188/2013-Rev.2, 14 September 2015.

value and is readily biodegradable. Therefore, according to ECHA guidance on the Biocidal Products Regulation, vol. IV[2] (10/2017), a DT_{50} in soil of 30 days can be used by default.

According to the nature of the active substance, no study is required. Indeed, heptamaloxyloglucan is part of the organic matter of the soil and therefore calculation of a Koc is not considered relevant.

2.8.2 Summary of fate and behaviour in water and sediment [equivalent to section 11.1 of the CLH report template]

A study demonstrates that heptamaloxyloglucan is readily biodegradable. It is expected that heptamaloxyloglucan (which is stable in sterile water) will be relatively stable in this non-sterile water, but will be readily degraded by the micro-organisms. Therefore no study has been conducted as the outcome would only depend on the equilibrium between the water phase and the soil phase.

No experimental DT_{50} in water value was made available. However, heptamaloxyloglucan is readily biodegradable. Therefore, according to ECHA guidance on the Biocidal Products Regulation, vol. IV[3] (10/2017), a DT_{50} in water of 15 days can be used by default.

2.8.2.1 Rapid degradability of organic substances

Table 66: Summary of relevant information on rapid degradability

Method	Results*	Key or Supportive study[1]	Remarks	Reference
Ready biodegradability, OECD 301B	Biodegradation after 28 days was 78%. EL101GV is set as a readily biodegradable compound.	Key study	-	L'Haridon, J. 2006 (see Vol. 3 B.8.2.2.1 (AS) for details)

2.8.2.1.1 Ready biodegradability

Please refer to 2.8.2 and to Vol. 3 B.8.2.2.1 (AS).

2.8.2.1.2 BOD5/COD

No data available.

2.8.2.2 Other convincing scientific evidence

Table 67: Summary of other relevant information

Method	Results	Key or Supportive study	Remarks	Reference
Literature study	Microorganisms able to degrade hemicellulose are present in rivers water.	Supportive study	-	Freixa et al. 2016 (see vol.3 B.8.2.2.3)
Literature study	Microorganisms able to degrade hemicellulose are present in rivers water.	Supportive study	-	Romani et al. 2012 (see vol.3 B.8.2.2.3)
Literature study	Hemicellulose is degraded by microorganisms present in peatland.	Supportive study	-	Younes et al. 2015 (see vol.3 B.8.2.2.3)

[2] Guidance on Biocidal Products Regulation: Volume IV Environment - Assessment and Evaluation (Parts B+C); Reference: ECHA-17-G-23-EN; Cat. Number: ED-01-17-897-EN-N ISBN: 978-92-9020-151-9 DoI: 10.2823/033935 Publ.date: October 2017

[3] Guidance on Biocidal Products Regulation: Volume IV Environment - Assessment and Evaluation (Parts B+C); Reference: ECHA-17-G-23-EN; Cat. Number: ED-01-17-897-EN-N ISBN: 978-92-9020-151-9 DoI: 10.2823/033935 Publ.date: October 2017

2.8.2.2.1 Aquatic simulation tests

Please refer to point 2.8.2.

2.8.2.2.2 Field investigations and monitoring data (if relevant for C&L)

No data available.

2.8.2.2.3 Inherent and enhanced ready biodegradability tests

Please refer to 2.8.2.1.1.

2.8.2.2.4 Soil and sediment degradation data

Please refer to point 2.8.1 for soil degradation and to 2.8.2 for sediment degradation (water/sediment systems).

2.8.2.2.5 Hydrolysis

Heptamaloxyloglucan is considered hydrolytically stable (see Vol.3 B.8.2.1.1.).

2.8.2.2.6 Photochemical degradation

According to the nature of the active substance, no study was performed. In Volume 3 – B2 (CA), heptamaloxyloglucan is photochemically stable as it has no peak absorption with molecular absorption coefficient higher than 10 L/mol/cm at wavelength > 290nm.

2.8.2.2.7 Other / Weight of evidence

No additional data available.

2.8.3 Summary of fate and behaviour in air

Heptamaloxyloglucan has negligible volatility and is considered not to be persistent in air. Any residues in the atmosphere are expected to be rapidly degraded.

2.8.3.1 Hazardous to the ozone layer

Based on the available data presented under 2.8.3, there is no evidence that heptamaloxyloglucan may present a danger to the structure and/or the functioning of the stratospheric ozone layer.

2.8.3.1.1 Short summary and overall relevance of the provided information on hazards to the ozone layer

Please refer to 2.8.3.1.

2.8.3.1.2 Comparison with the CLP criteria

Please refer to 2.8.3.1.

2.8.3.1.3 Conclusion on classification and labelling for hazardous to the ozone layer

Please refer to 2.8.3.1.

2.8.4 Summary of monitoring data concerning fate and behaviour of the active substance, metabolites, degradation and reaction products

There is no toxicologically or eco-toxicologically relevant residue of heptamaloxyloglucan in any environmental compartment. Therefore, monitoring is not relevant.

No data was submitted or deemed necessary by the RMS.

2.8.5 Definition of the residues in the environment requiring further assessment

The following residue definition for risk assessment in environmental compartments is proposed:

Soil:	Heptamaloxyloglucan
Groundwater:	Heptamaloxyloglucan
Surface water and sediment:	Heptamaloxyloglucan
Air:	Heptamaloxyloglucan

2.8.6 Summary of exposure calculations and product assessment

PEL101GV is a formulation containing 1000 g/kg heptamaloxyloglucan intended for use on vines as an elicitor of the crop's self-defence mechanisms against frost damage. The application rate is 4 × 0.56 g a.s./ha with an interval of 4 days.

Soil

Table 68: PEC_{soil} for heptamaloxyloglucan on vines

Number of applications	Total application rate (g/ha) (no degradation between aplications)	PECsoil (mg/kg soil)
1	0.56	0.0004
2	1.12	0.0009
3	1.68	0.0013
4	2.24	0.0018

Groundwater

The applicant did not provide any PECgw calculations for heptamaloxyloglucan. RMS reminds that heptamaloxyloglucan is naturally present in the environment. It is a xyloglucan-derived oligosaccharide, which is an intermediate compound of natural organic matter decomposition process. It undergoes degradation by endogenous soil microorganisms naturally occurring in soil. Due to the ready biodegradability of heptamaloxyloglucan and to its sensitivity to the attack from many bacteria strains in soil giving raise to monomeric sugars as transformation product, heptamaloxyloglucan is not expected to reach groundwater.
Therefore, in this specific case, it is agreed that no concern is expected for the groundwater and no PECgw calculations are deemed necessary.

Surface water / Sediment

Table 69: Input parameters related to active substance heptamaloxyloglucan for PECsw/sed calculations STEP 1

Parameter	Value	Reference
Name	Heptamaloxyloglucan	
Water solubility [mg/L]	558 000 at 20°C	Volume 3 – B2 (CA), point 2.5
K_{OC} [L/kg]	0 10 000	Worst-case value for PECsw Worst-case value for PECsed
Total system DT_{50} [days]	1000 at 20°C	Worst-case value

The maximum initial PECs for heptamaloxyloglucan in the surface water and in the sediment, calculated with FOCUS Step 1 are presented below (two simulations have been conducted separately for surface water and sediment):

Table 70: FOCUS Step 1 PEC_{sw} and PEC_{sed} for heptamaloxyloglucan multiple applications of PEL101GV to vines (early applications)

FOCUS Step	**Max PEC_{sw} (µg/L)**	**Max PEC_{sed} (µg/kg)**
	Single global application	**Single global application**
Step 1	0.77	5.35

Air

Heptamaloxyloglucan has negligible volatility and is considered not to be persistent in air. Any residues in the atmosphere are expected to be rapidly degraded. No PEC_{AIR} is relevant.

Other routes of exposure

No other route of exposure is expected.

2.9 EFFECTS ON NON-TARGET SPECIES

The technical active substance heptamaloxyloglucan (EL101GV) is identical to the representative formulation PEL101GV.

Litterature data have been submitted to demonstrate that xyloglucans, among which heptamaloxyloglucan, are natural constituents of cell wall of dicotyledons, in which they account for *ca.* 10% of the whole constituents. Xyloglucans are synthesized in the ER-Golgi apparatus as soluble polymers, they are modified by acetylation and remain soluble until they can be cross-linked at the cell surface (Buchanan et al, 2000, CA 8.1/1).

2.9.1 Summary of effects on birds and other terrestrial vertebrates

No studies have been conducted to determine the toxicity of heptamaloxyloglucan on birds.
Herbivorous animals such as birds ingest hemicelluloses (typical name of xyloglucan), which are fermented by the bacteria of the hindgut and caecum and transformed in short-chain fatty acids. Fatty acids are absorbed and provide a substantial amount of the maintenance energy required by these animals (Stevens C.E., and Hume I.D., 1998, CA 8.1/2). As hemicelluloses are relatively soluble and therefore more easily fermented than the large polymers of cellulose, they account for a major part of digestible fibers in these animals.
Three publications have been provided to characterise the effects of xylo-oligosaccharides on the growth performance and immune function of broiler chickens (Morgan *and al*. 2018 (CA 8.1/04); Suo Hai-qing and *all*, 2015 (CA 8.1/05) and Yuan *and al*, 2018 (CA 8.1/06)).

Mammalian toxicity studies used in ecotoxicology are reported in the table below.

Species	**Product**	**Exposure System**	**Results**	**Reference**
Rat	EL101GV (Heptamaloxyloglucan)	Oral 14 d Acute	LD_{50} > 5000 mg/kg bw	CA 5.5/01 ***** (2004), 20030812ST
Rat	EL101GV (Heptamaloxyloglucan)	Oral Short-term toxicity	NOAEL = 1000 mg/kg bw/d	CA 5.3.1/01 *******. (2006), 20060118TRB *

* This study is performed according to OECD Test 407– Repeated dose 28-day oral toxicity in rodents. It is part of the dataset to be considered when setting the NOAEL for reproductive risk assessment in the EFSA guidance for risk assessment on birds and mammals (2009).

2.9.2 Summary of effects on aquatic organisms [section 11.5 of the CLH report]

2.9.2.1 Bioaccumulation [equivalent to section 11.4 of the CLH report template]

Table 71: Summary of relevant information on bioaccumulation

Method	Species	Results	Key or Supportive study	Remarks	Reference
No study. Not required. Log Kow < 0.					

2.9.2.1.1 Estimated bioaccumulation

Log Kow is estimated to be less than 0. Please refer above under point 2.2 (more details in Vol. 3 CA B2, point B.2.7).

2.9.2.1.2 Measured partition coefficient and bioaccumulation test data

As the log K_{OW} of heptamaloxyloglucan is below 0 (see Vol. 3CA B2, point B.2.7), no study is required

2.9.2.2 Acute aquatic hazard [equivalent to section 11.5 of the CLH report template]

Table 72: Summary of relevant information on acute aquatic toxicity

Method	Species	Test material	Results[1]	Key or Supportive study	Remarks	Reference
OECD N° 203 (1992)	*Oncorhynchus mykiss*	Technical heptamaloxyloglucan	96-h LC_{50} > 150 mg a.s./L (nom.)	Key study		CA 8.2.1/01 L'Haridon J. 2006a Report N°. 30711 EAP
OECD N° 202 (2004)	*Daphnia magna*		48-h EC50 > 150 mg a.s./L (nom.)	Key study		CA 8.2.4/01 L'Haridon J. 2006b Report N°. 30710 EAD
OECD 201 (1984);	*Scenedesmus subspicatus*		72-h ErC50> 150 mg a.s./L (nom.) 72-h EbC50 > 150 mg a.s./L (nom.)	Key study		CA 8.2.6/01 L'Haridon J., 2006c Report N°. 30709 EAA

2.9.2.2.1 Acute (short-term) toxicity to fish

One group of 7 rainbow trouts (body length 40-46 mm, mean body weight 1.06 g) were exposed for 96 hours under semi-static conditions (renewal every 24 hours) to nominal technical EL101GV (batch No ANN0304, purity 78.2%) concentration of 150 mg/L at 13-17°C. There was one control group without any treatment. A photoperiod of 16/8 hour was applied during the test.

Temperature was recorded between 14.4 and 16.1°C, dissolved oxygen concentrations were comprised between 6.8 and 9.6 mg/L, pH between 7.76 and 8.46 and water hardness between 145 and 158 mg/L of CaCO3.

Concentrations of heptamaloxyloglucan (EL101GV) during the test were ranged from 157 mg/L (105%) and 165 mg/L (110%). Thus, the analytical results for the active substance concentrations in the test solution were within a range of + 20% of the nominal values throughout the test. Hence the results are based on nominal concentrations.

No mortality or clinical signs were observed in the control group at 150 mg/L. The pH of the control did not vary by more than 1 unit during the test and the dissolved oxygen concentration remained > 60% of the air saturation value throughout the test. The study validity criteria were therefore met.

No mortality was observed in the treated group during the 96-hour observation period. No test item related

effects were observed in the fish. The results are summarized in the table below.

Group	Control	Treated
Concentration [mg a.s./L] nominal	0	150
Mortality [%]	0	0
Symptoms	None	None
Endpoint [mg a.s./L nominal]		
LC_{50}	> 150	

-: not measured

The study is valid and reliable for classification and risk assessment purpose.

2.9.2.2.2 Acute (short-term) toxicity to aquatic invertebrates

Four replicates of 5 Daphnia magna (less than 24 hours old) were exposed for 48 hours under static conditions to nominal technical EL101GV (batch No ANN0304, purity 78.2%) concentration of 150 mg/L at 18-22°C. There was one control group of 20 daphnids (4 replicates of 5 daphnids) without any treatment. A photoperiod of 16/8 hour was applied during the test.
The test substance was dissolved in test water directly.

During the test, temperature was recorded between 19.6 and 20.6°C, dissolved oxygen concentrations were comprised between 8.4 and 8.7 mg/L (94-98%), pH between 8.08 and 8.55 and water hardness of 303 mg/L of CaCO3.

Concentration of heptamaloxyloglucan (EL101GV) at test initiation was 144 mg/L (96%) and 126 mg/L (84%) at test termination. Therefore toxicity results (immobilisation) are based on nominal concentration.

There were no mortalities or clinical signs at nominal concentration of 150 mg/L

Group	Control	EL101GV
Concentration (nominal) [mg a.s./L]	0	150
Immobile (24 h) [%]	0	0
Immobile (48 h) [%]	0	0
	Endpoints [mg a.s./L]	
EC_{50} (48 h)	> 150	
NOEC (48 h)	150	

All validity criteria were met.

The study is valid and reliable for classification and risk assessment purpose.

2.9.2.2.3 Acute (short-term) toxicity to algae or aquatic plants

One group of six replicates of Scenedesmus subsipacatus (cell density 104 cells/mL at test initiation) and one without alga was exposed for 72 hours under static conditions to nominal technical EL101GV (batch No ANN0304, purity 78.2%) concentration of 150 mg/L at 21-25°C. There was one control group with six replicates containing alga without any treatment. Continuous illumination was applied during the test.
The test substance was dissolved in test water directly.

Temperature was recorded between 23.5 and 24.0°C, pH from 7.74 to 9.89 in control and 7.41 to 10.15 in treatment group.

Concentrations of heptamaloxyloglucan (EL101GV) during the test were equal to 155 mg/L (103%) at 0h and 158 mg/L (105%) at 72h in replicate without algae, and at 165 mg/L (110%) in replicate with algae. Toxicity results were therefore expressed as nominal concentrations.

The table below summarised the main results obtained during the study.

Group	Min-max cell densities (x 10^4/mL)			Specific growth rate (% inhibition)			Biomass 0-72h cell x mL^{-1} x h [area under growth curve] (% inhibition)
	24h	48h	72h	24h	48h	72h	
0	7.4-9.1	50.0-65.5	261.0-297.0	0.0878	0.0848	0.078	4940.0
150 mg/L	7.0-10.0	54.0-72.0	272.0-373.0	0.0880 (-0.23%)	0.0862 (-1.65%)	0.080 (-2.6%)	5598.4 (-13.3%)

Heptamaloxyloglucan has no inhibition effects on growth rate or biomass.

The criteria of validity are fulfilled.

The study is valid and reliable for classification and risk assessment purpose.

The alga (*Scenedesmus subsipacatus*) 72h static ErC50 and ErC10 values are greater than 150 mg heptamaloxyloglucan/L.

2.9.2.2.4 Acute (short-term) toxicity to other aquatic organisms

No data.

2.9.2.3 Long-term aquatic hazard [equivalent to section 11.6 of the CLH report template]

Table 73: Summary of relevant information on chronic aquatic toxicity

Method	Species	Test material	Results[1]	Relevant study	Remarks	Reference
OECD 201 (1984);	*Scenedesmus subspicatus*	heptamaloxyloglucan	72-h ErC10> 150 mg a.s./L (nom.)	Key study	Same study than the one reported for acute hazard	CA 8.2.6/01 L'Haridon J., 2006c Report N°. 30709 EAA

2.9.2.3.1 Chronic toxicity to fish

4 publications have been submitted that characterise the effects of arabinoxylan-oligosaccharides on juvenile Siberian sturgeon (Geraylou and al., 2012; Geraylou and al., 2013) and the effects of fructo-oligosaccharide on common carp (*Cyprinus carpio*) (Hoseinifar and al., 2014) and on the Japanese flounder Paralichthys olivaceus (Ye and al., 2011). No adverse effects were found in these studies.
In environment, heptamaloxylglucan, a natural component, is degraded in smaller oligosaccharides, then to monomers and finally to CO2. It is soluble in water and is expected to be quickly degraded (see also Volume 3 CA B.8). Moreover, Heptamaloxyloglucan is a major natural component of dicotyledonous leaves and vegetal parts, which are constantly and naturally brought to surface waters and sediments. Overall, chronic exposure of fish to heptamaloxylglucan is not expected and thus chronic data on fish not necessary.

2.9.2.3.2 Chronic toxicity to aquatic invertebrates

According to Regulation EU No 283/2013, "a long-term or chronic toxicity study on aquatic invertebrates shall be provided for all active substances where exposure of surface water is likely and the substance is deemed to be stable in water, that is to say there is less than 90 % loss of the original substance over 24 hours via hydrolysis."

In environment, heptamaloxylglucan, a natural component, is degraded in smaller oligosaccharides, then to monomers and finally to CO2. It is soluble in water and is expected to be quickly degraded (see also Volume 1 point 2.8 and Volume 3 section B.8). Moreover, Heptamaloxyloglucan is a major natural component of dicotyledonous leaves and vegetal parts, which are constantly and naturally brought to surface waters and sediments. Heptamaloxyloglucan displays no acute toxicity to aquatic invertebrates.

Overall, chronic exposure of aquatic invertebrates to heptamaloxylglucan is not expected and thus chronic data on aquatic invertebrates not necessary.

2.9.2.3.3 Chronic toxicity to algae or aquatic plants

For algae, please see above under 2.9.2.2.3.

For aquatic plants, according to Commission Regulation (EU) No 283/2013, a "laboratory test with *Lemna* species shall be performed for herbicides and plant growth regulators and for substances where there is evidence from information submitted under point 8.6 of Part A of this Annex or point 10.6 of Part A of the Annex to Regulation (EU) No 284/2013 that the test substance has herbicidal activity."

Heptamaloxyloglucan is a plant elicitor and as such could be considered as a plant growth regulator. Nevertheless, no tests on aquatic plants have been submitted by the notifier. RMS agreed to consider that test on aquatic macrophytes are not deemed necessary as no phytotoxicity on terrestrial plants or on alga have been observed. Moreover in the environment, heptamaloxylglucan, a natural component, is degraded in smaller oligosaccharides, then to monomers and finally to CO2. It is soluble in water and is expected to be quickly degraded (see section B.8). Moreover, Heptamaloxyloglucan is a major natural component of dicotyledonous leaves and vegetal parts, which are constantly and naturally brought to surface waters and sediments. Heptamaloxyloglucan displays no acute toxicity to alga and terrestrials non target plants.
Data on aquatic plants are not considered necessary.

2.9.2.3.4 Chronic toxicity to other aquatic organisms

No data.

2.9.2.4 Comparison with the CLP criteria

2.9.2.4.1 Acute aquatic hazard

Table 74: Summary of information on acute aquatic toxicity relevant for classification

Method	Species	Test material	Results[1]	Remarks	Reference
OECD N° 203 (1992)	*Oncorhynchus mykiss*	Technical heptamaloxyloglucan	96-h LC_{50} > 150 mg a.s./L (nom.)		CA 8.2.1/01 L'Haridon J. 2006a Report N°. 30711 EAP
OECD N° 202 (2004)	*Daphnia magna*		48-h EC50 > 150 mg a.s./L (nom.)		CA 8.2.4/01 L'Haridon J. 2006b Report N°. 30710 EAD
OECD 201 (1984);	*Scenedesmus subspicatus*		72-h ErC50> 150 mg a.s./L (nom.) 72-h EbC50 > 150 mg a.s./L (nom.)		CA 8.2.6/01 L'Haridon J., 2006c Report N°. 30709 EAA

All $L(E)C_{50}$ values are greater than 150 mg a.s./L. Thus no acute hazard classification is required for heptamaloxyloglucan.

2.9.2.4.2 Long-term aquatic hazard (including bioaccumulation potential and degradation)

Table 75: Summary of information on long-term aquatic toxicity relevant for classification

Method	Species	Test material	Results[1]	Remarks	Reference
OECD 201 (1984);	*Scenedesmus subspicatus*	heptamaloxyloglucan	72-h ErC10> 150 mg a.s./L (nom.)	Same study than the one reported for acute hazard	CA 8.2.6/01 L'Haridon J., 2006c Report N°.

					30709 EAA

In view of the nature of the active substance (branched xyloglucan molecule, part of hemicellulose extracted from apple pomace), its mode of action (plant elicitor action as anti-freezing), its rapid degradation expected in the environment (see Volume 1 point 2.8), and the available results on algae, no chronic hazard classification is required for heptamaloxyloglucan.

2.9.2.5 Conclusion on classification and labelling for environmental hazards

No acute and chronic hazard classification proposed.

2.9.3 Summary of effects on arthropods

- **Effects on bees**

Acute oral and contact toxicity tests are available with technical active substance heptamaloxyloglucan coded EL101GV which is identical to the representative formulation PEL101GV.

Species	Test item	Exposure System	Endpoint	Reference
Apis mellifera L. (honey bee, adult)	Technical heptamaloxyloglucan (EL101GV)	Acute, 48h contact	LD_{50} > 100 µg a.s./bee	CA 8.3.1.1/01 Servajean E. *et al.*, 2006
		Acute, 48h oral	LD_{50} > 100 µg a.s./bee	
	Galactose	Chronic, feeding	LDD50 > 1620 µg/bee/d	CA 8.3.1/03 Barker R.J. *et al.*, 1977

No chronic test on adult and larvae bees are available.

Exposure of bees (adults, and larvae) to xyloglucan, polysaccharides, or monosaccharides occurred naturally. Being derived from apple, the composition of heptamaloxyloglucan is a combination of sugars monomers that occurred naturally in plants, nectar/pollen or honey. As such bees are naturally exposed to xyloglucans, including heptamaloxyloglucan. Thus no chronic toxicity tests were considered necessary in this particular case. Furthermore, from the literature studies provided, galactose, which is one of the monomers of heptamaloxyloglucan was found to have lethal effects on bees after 16 days of oral administration. Thus a risk assessment was proposed for this monomer.

- **Effects on non-target arthropods other than bees**

No tests on non-target arthropods other than bees are available with technical active substance heptamaloxyloglucan.

Heptamaloxyloglucan is a branched xyloglucan molecule extracted from apples and composed of 7 hexose residues (glucopyranosyl, fucopyranosyl, xylopyranosyl and galactopyranosyl). All these hexose are natural components of the apple and of other dicotyledonous plants, where they are major constituents of cellulose and hemicellulose molecules, which are the principal components of cell walls. As such, heptamaloxyloglucan takes part of usual food on arthropods. Heptamaloxyloglucan is not toxic to honey bees (oral and contact LD50 > 100 µg/bee). For these reasons, no test on non-target arthropods was deemed necessary of heptamaloxyloglucan.

Considering the type of component (xyloglucan extracted from apple), its mode of action (plant elicitor to protect vine from freezing), its natural occurrence in plants, the low dose applied (0.560 g/ha), testing on non-target arthropods was not required in this particular case.

2.9.4 Summary of effects on non-target soil meso- and macrofauna

No tests on non-target soil meso- and macrofauna are available with technical active substance heptamaloxyloglucan.

Earthworms ingested micro-organisms together with soil that are able to degrade oligosaccharides into

monomeric sugars. Glucose, xylose, fucose, galactose and glucitol, the monomeric sugars expected to result from degradation of heptamaloxyloglucan, are naturally occuring into organic matter of soil (see Volume 1 point 2.8 and Volume 3 point B.8.1 on fate and behaviour in soil).

Based on literature data (see Volume 3 CA B.9.4.2 for details), it was considered that oligosaccharides such as heptamaloxyloglucan, which is a xyloglucan-derived oligosaccharide, could be degraded in soil by enzymatic action of the microorganisms (see also Volume 1 point 2.8 and Volume 3 point B.8.1). The assimilation and degradation of xyloglucan-like molecules by soil macro-organisms such as earthworms is facilitated by soil microorganisms that they ingest together with soil (see also Vol. 3 CA B.9.7).

Overall, considering the type of component (xyloglucan extracted from apple), its mode of action (plant elicitor to protect vine from freezing), its natural occurrence in plants (estimated around 1.1 g/ha in apple field, see Volume 3 CA B.8.1.1.1.4), the low dose applied (0.56 g/ha), no unacceptable effects are expected following application of heptamaloxyloglucan in vine as intended.

2.9.5 Summary of effects on soil nitrogen transformation

No tests on non-target soil nitrogen transformation are available with technical active substance heptamaloxyloglucan.

Heptamaloxyloglucan is a possible degradation product of plant cell walls as it can be produced from xyloglucan by enzymatic degradation naturally occurring in plant or in soil by micro-organsims. Plant decay is a natural substrate for soil micro-organism growth.

In an apple field, heptamaloxyloglucan natural level was estimated to be 1.1 g/ha (see Volume 3 CA B.8.1.1.1.4 for details). This value is similar to the intended application rate on vines (0.56 g/ha). Additionally, the initial PECsoil of heptamaloxyloglucan were calculated after the 4th application of PEL101GV to be 0.0018 mg/kg dry soil. Such low concentrations are not susceptible to change the qualitative composition of the organic matter which reaches the soil.

Furthermore, based on literature data, it is considered that oligosaccharides such as heptamaloxyloglucan, which is a xyloglucan-derived oligosaccharide, could be degraded in soil by enzymatic action of the microorganisms (also refer to Volume 3 CA B.8.1.1.1.4). The assimilation and degradation of xyloglucan-like molecules by soil macro-organisms such as earthworms is facilitated by soil microorganisms that they ingest together with soil (see also Vol. 3 CA B.9.7).

Veras *et al*., 2017 (CA 8.5/02) showed that yeasts (*Scheffersomyces stipitis*, *Spathaspora passalidarum*, *Spathaspora arborariae* and *Candida tenuis*) were able to use xylose as substrate of fermentation to produce ethanol.

Considering the type of component (xyloglucan extracted from apple), its mode of action (plant elicitor to protect vine from freezing), its natural occurrence in plants, the low dose applied (0.56 g/ha), heptamaloxyloglucan is not expected to have any adverse effects on the function of soil micro-organisms ecosystems.

2.9.6 Summary of effects on terrestrial non-target higher plants

A non-GLP test on effects on vegetative vigor of non-target plants has been conducted with technical heptamaloxyloglucan (which is the only component of the representative formulation PEL101GV).

Substance	Tested species	Endpoint	Reference
Technical heptamaloxyloglucan	*Triticum aestivum* (wheat) *Sinapis alba* (mustard) *Trifolium pratense* (red cover)	No adverse effects up to 20.0 g a.s./ha	Servajean E., (2006b) (CA 8.6/01)

2.9.7 Summary of effects on other terrestrial organisms (flora and fauna)

No data.

2.9.8 Summary of effects on biological methods for sewage treatment

Heptamaloxyloglucan is a xyloglucan molecule and made of 7 glucidic monomer units, which are all natural components of cell walls of the apple (from which it is extracted) and of other dicotyledonous plants. Moreover it could be produced by degradation of xyloglucan by enzymes naturally occurring in plant or soil micro-organisms. It is not expected to have any detrimental effect on biological methods for sewage treatment.

Considering the type of component (xyloglucan extracted from apple), its mode of action (plant elicitor to protect vine from freezing), its natural occurrence in plants, the low dose applied (0.56 g/ha), RMS is still of the opinion that testing on effects on biological methods for sewage treatment is not required in this particular case.

2.9.9 Summary of product exposure and risk assessment

No test has been performed with the representative formulation PEL101GV as the only component is the technical active substance heptamaloxyloglucan.

2.9.9.1 Risk assessment to birds

See Volume 3 B.9.2.1

No data on toxicity of heptamaloxyloglucan to birds is available. Theoretical toxicity values below which no acceptable risk is expected has been calculated instead of standard risk assessment.

Acute risk assessment:
Considering the acute theoretical DDD of 0.11 mg/kg bw resulted from the 4 applications on vine at a maximum application rate of 0.560 g a.s./ha, the acute LD50 should be lower than 1.1 mg/kg bw to reach an unacceptable acute risk (trigger = 10). Given the nature of the active substance that is extracted from apple pomace, this is considered unlikely. Therefore no unacceptable acute risk of heptamaloxyloglucan to birds can be concluded.
Furthermore, Morgan and al. 2018; Suo Hai-qing and al, 2015 and Yuan and al, 2018 showed a beneficial effect on growth and immune performance of broiler chickens when they are supplemented in diet with xylo-oligosaccharides. Summaries of these publications are presented in RAR Vol3. CA B9.1.1.
Overall, no acute risk on birds is expected following applications of PEL101GV on vine.

Chronic risk assessment:
In environment, heptamaloxylglucan is degraded in smaller oligosaccharides, then to monomers and finally to CO2. It is soluble in water and is expected to be quickly degraded in soil and water/sediment system (see Volume 3 CA B.8). Chronic risk of birds to heptamaloxylglucan is not expected due to the nature of the compound and the expected low level in the environment following use of PEL101GV. Overall, no long term dietary risk on birds is expected following applications of PEL101GV on vine.

Risk from drinking water:
In view of the intended uses, risk assessment for puddle scenario should be performed.
Considering the acute theoretical AReff of 1.57 g a.s./ha, the LD50 should be lower than 0.031 mg/kg bw to meet the trigger for performing risk assessment for less sorptive substance. Given the nature of the active substance, this is considered unlikely. Therefore risk of heptamaloxyloglucan to birds through drinking water from puddle is not necessary.

Risk from secondary poisoning:
The Log Pow of heptamaloxyloglucan (<0) is below the limit of 3. A risk assessment for secondary poisoning is not required and the risk of food chain bioaccumulation to fish-eating and worm-eating birds is negligible.

2.9.9.2 Risk assessment to wild mammals

Acute risk assessment:

Screening step: Acute risk (TER_A) of Heptamaloxyloglucan to mammals

Intended use	Vines
Active substance	Heptamaloxyloglucan
Application rate	4 × 0.000560 kg of EL101GV/ha
Acute toxicity (mg a.s./kg bw)	> 5000

TER criterion	10

Scenario	**Indicator species**	**Shortcut value (SV_{90})**	**MAF_{90}**	**Daily dietary dose (DDD) (mg/kg b.w.)**	**TER_A**
Vineyard	Small herbivorous mammal	136.4	2.1	0.16	> 31 170.8

The TERA value for heptamaloxyloglucan is greater than the trigger value of 10, indicating that application of PEL101GV is considered to pose no unacceptable acute risk to mammals when applied according to Good Agricultural Practice on vineyard.

Chronic risk assessment:

Screening step assessment for the long-term risk of heptamaloxyloglucan to mammals

Intended use	Vines
Active substance/product	heptamaloxyloglucan
Application rate	4 × 0.000560 kg of heptamaloxyloglucan /ha
Reproductive toxicity (mg/kg bw/d)	NOAEL = 1000 (based on short term study performed according to OECD 407)
TER criterion	5

Scenario	**Indicator species**	**Shortcut value (SV) for assessment**	**MAF_{90}**	**Daily dietary dose (DDD) (mg/kg b.w.)**	**TER**
Vineyard	Small herbivorous mammal	72.3	2.8	0.11	8821

The TERLT value for heptamaloxyloglucan is greater than the trigger value of 5, indicating that application of PEL101GV poses no unacceptable long-term risk to mammals when applied according to Good Agricultural Practice on vineyard.

Risk from drinking water:

In view of the intended uses, risk assessment for puddle scenario should be performed.

The Koc of heptamaloxyloglucan is equal to 0. The trigger for the ratio of effective application rate to acute and long term endpoints is less than 50.

Ratio of AReff to acute/short-term toxicity endpoint – heptamaloxyloglucan

AR_{eff} (g a.s./ha)	**Acute LD_{50} (mammals) (mg /kg b.w.)**	**$Ratio_{acute}$**	**Short-term NOED (mammals) (mg /kg b.w./d)**	**$Ratio_{short\text{-}term}$**
1.568	> 5000	0.00031	1000	0.0016

The acute and reproductive ratio are below the trigger value. Therefore, the acute and reproductive risk to mammals via drinking water, following application of heptamaloxyloglucan according to the proposed use pattern, is not triggered.

Risk from secondary poisoning:

The Log Pow of heptamaloxyloglucan (<0) is below the limit of 3. A risk assessment for secondary poisoning is not required and the risk of food chain bioaccumulation to fish-eating and worm-eating mammals is negligible.

2.9.9.3 Risk assessment to aquatic organisms

Aquatic organisms: acceptability of risk (PEC/RAC < 1) for heptamaloxyloglucan for each organism group based on FOCUS Steps 1 calculations for the use of PEL101GV in vines (early)

Group		**Fish acute**	**Inverteb. acute**	**Algae**
Test species		***Oncorhynchus mykiss***	***Daphnia magna***	***Scenedesmus subspicatus***
Endpoint (µg/L)		LC_{50} > 150 000	EC_{50} > 150 000	E_rC_{50} > 150 000
AF		100	100	10
RAC (µg/L)		> 1 500	> 1 500	> 15 000
FOCUS Scenario	**PEC $_{gl\text{-}max}$ (µg/L)**			
Step 1				
	0.77	< 0.000513	< 0.000513	< 0.0000513

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Risk assessment conducted under the worst case assumption with 1 application of 2.24 g a.s./ha (equivalent to no degradation of heptamaloxyloglucan after 4 applications of 0.560 g as/ha) show that no unacceptable acute risk on aquatic organisms are expected following applications of PEL101GV.

In environment, heptamaloxylglucan, a natural component, is degraded in smaller oligosaccharides, then to monomers and finally to CO2. It is soluble in water and is expected to be quickly degraded. Moreover, Heptamaloxyloglucan is a major natural component of dicotyledone leaves and vegetal parts, which are constantly and naturally brought to surface waters and sediments. Overall, chronic exposure of aquatic organsisms to heptamaloxylglucan is not expected. Thus, no chronic risk assessment was deemed necessary.

2.9.9.4 Risk assessment to bees

Several publications have been provided in Vol 3 CA B.9 that allow to consider that xyloglucans among which heptamaloxyloglucan can be found in the environment and can be used and assimilated by bees. Moreover literature data were provided that demonstrate that monomers constituting heptamaloxyloglucan can be found in nectar and honey.

Acute risk assessment based on SANCO/10329/2002 guidance document:

Acute hazard quotients for honey bees according to SANCO/10329/2002

Test substance	**Exposure route**	**Endpoint (µg a.s./bee)**	**Maximum single application rate (g a.s./ha)**	**Hazard quotient (HQ)**	**HQ assessment trigger**
Heptamaloxyloglucan	Oral	LD_{50} > 100	0.560	< 0.0056	50
	Contact	LD_{50} > 100	0.560	< 0.0056	50

For heptamaloxyloglucan, the oral and contact hazard quotient values are below the trigger value of 50 for acute oral and contact exposure indicating an acceptable acute risk to bees following application of PEL101GV in vineyard.

Acute risk assessment based on EFSA 2013 guidance document

Screening acute oral risk assessment for honey bees

Test substance	Exposure route	Endpoint (µg a.s./bee)	Maximum single application rate (kg a.s./ha)	SV	ETR acute adult oral	Trigger
Heptamaloxyloglucan	Oral	LD_{50} > 100	0.00056	10.6	< 0.00006	0.2

The ETRacute adult oral value is below the trigger of 0.2 indicating an acceptable acute oral risk for bees after applications of PEL101GV in vineyard.

Screening acute contact risk assessment for honeybees:

Test substance	Exposure route	Endpoint (µg a.s./bee)	Maximum single application rate (g a.s./ha)	Hazard quotient (HQ)	HQ assessment trigger
Heptamaloxyloglucan	Contact	LD_{50} > 100	0.560	< 0.0056	42

The HQ contact for Heptamaloxyloglucan is below the trigger values of 42 (for upwards and/or sideward spray), indicating an acceptable acute contact risk for adult bees exposed to heptamaloxyloglucan when applied as intended in vineyard.

Chronic risk assessment based on EFSA 2013 guidance document
No chronic data are available with the active substance. In view of the intended uses, chronic exposure of adult honey bees has been calculated. To obtain an acceptable risk for adult bees when exposed in chronic to heptamaloxyloglucan, the LDD50 oral should be ≥ 0.198 µg a.s./bee/d which seems realistic for such compound.

Case of galactose:
Galactose is an element constitutive of heptamaloxyloglucan. Based on Barker R.J. et al., 1977, (see CA 8.3.1/03 summarised under Vol 3 CA B.9.3.1.2), a 16d-LDD50 > 1.62 mg/bee/day has been determined.

Screening chronic risk assessment for honey bees (adults) exposed to galactose

Test substance	Exposure route	Endpoint (µg/bee/d)	Maximum single application rate (kg a.s./ha)	Type of spraying	SV	ETR chronic adult oral	Trigger
Galactose	Oral	LDD_{50} > 1620 µg/bee/d	0.00056	upwards and/or sideward	10.6	3.7×10^{-6}	0.03

The ETR is below the trigger of 0.03 indicating an acceptable chronic risk for adult bees exposed to galactose contained in heptamaloxyloglucan considering that heptamaloxyloglucan will be entirely converted in galactose as worst case exposure conditions.

Effects on honey bees development (Risk assessment to larvae)
To obtain an acceptable risk for larvae when exposed chronically to heptamaloxyloglucan, the NOEL should be ≥ 0.0171 µg a.s./bee/d which seemed realistic for such compound.

For chronic risk to adult bees and larvae, the applicant also proposed some evidence considering the exposure to monomers such as sucrose and fructose during standard OECD tests to demonstrate that no adverse effects are expected. For details, please refer to Volume 3 CP B.9.6.1.

2.9.9.5 Risk assessment to non-target arthropods

No tests on non-target arthropods other than bees are available with technical active substance heptamaloxyloglucan.

Heptamaloxyloglucan is a branched xyloglucan molecule extracted from apples and composed of 7 hexose residues (glucopyranosyl, fucopyranosyl, xylopyranosyl and galactopyranosyl). All these hexose are natural components of the apple and of other dicotyledonous plants, where they are major constituents of cellulose and hemicellulose molecules, which are the principal components of cell walls. As such, heptamaloxyloglucan takes part of usual food on arthropods. Heptamaloxyloglucan is not toxic to honey bees (oral and contact LD50 > 100 µg/bee). For these reasons, no test on non-target arthropods were deemed necessary of heptamaloxyloglucan.

Considering the type of component (xyloglucan extracted from apple), its mode of action (plant elicitor to protect vine from freezing), its natural occurrence in plants, the low dose applied (0.560 g/ha), no adverse effects on non-target arthropods are expected.

2.9.9.6 Risk assessment to soil macro- and meso fauna

Earthworms ingested micro-organisms together with soil that are able to degrade oligosaccharides into monomeric sugars. Glucose, xylose, fucose, galactose and glucitol, the monomeric sugars expected to result from degradation of heptamaloxyloglucan, are naturally occuring into organic matter of soil (see Volume 1 point 2.8 and Volume 3 point B.8.1 on fate and behaviour in soil).

Based on literature data (see Volume 3 CA B.9.4.2 for details), it was considered that oligosaccharides such as heptamaloxyloglucan, which is a xyloglucan-derived oligosaccharide, could be degraded in soil by enzymatic action of the microorganisms (see also Volume 1 point 2.8 and Volume 3 point B.8.1). The assimilation and degradation of xyloglucan-like molecules by soil macro-organisms such as earthworms is facilitated by soil microorganisms that they ingest together with soil (see also Vol. 3 CA B.9.7).

The natural concentration of heptamaloxyloglucan in the soil of an apple orchard has been estimated by the applicant (see Volume 3 CA B.8.1.1.1.4) to be 1.1 g/ha. This value is similar to the intended application rate on vines (0.56 g/ha). Thus, the very low amounts of residues due to the use of heptamaloxyloglucan (0.0018 mg a.s./kg soil) is not expected to change the qualitative composition of the organic matter which reaches the soil or to cause damage on soil macro-organisms.

Overall, considering the type of component (xyloglucan extracted from apple), its mode of action (plant elicitor to protect vine from freezing), its natural occurrence in plants (estimated around 1.1 g/ha in apple field, see Volume 3 CA B.8.1.1.1.4), the low dose applied (0.56 g/ha), no unacceptable effects are expected following application of heptamaloxyloglucan in vine as intended.

2.9.9.7 Risk assessment to soil nitrogen transformation

Heptamaloxyloglucan is a possible degradation product of plant cell walls as it can be produced from xyloglucan by enzymatic degradation naturally occurring in plant or in soil by micro-organsims. Plant decay is a natural substrate for soil micro-organism growth.

In an apple field, heptamaloxyloglucan natural level was estimated to be 1.1 g/ha (see Volume 3 CA B.8.1.1.1.4 for details). This value is similar to the intended application rate on vines (0.56 g/ha). Additionally, the initial PECsoil of heptamaloxyloglucan were calculated after the 4th application of PEL101GV to be 0.0018 mg/kg dry soil. Such low concentrations are not susceptible to change the qualitative composition of the organic matter which reaches the soil.

Considering the type of component (xyloglucan extracted from apple), its mode of action (plant elicitor to protect vine from freezing), its natural occurrence in plants, the low dose applied (0.56 g/ha), heptamaloxyloglucan is not expected to have any adverse effects on the function of soil micro-organisms ecosystems.

2.9.9.8 Risk assessment to non-target plants

Assessment of the risk for non-target plants due to the use of PEL101GV in vineyards

Intended use	**Vineyards**			
Active substance/product	Heptamaloxyloglucan / PEL101GV			
Application rate (g a.s./ha)	4 × 0.437			
MAF	2.7			
Test species	**ER_{50} (g a.s./ha)**	**Drift value (%)**	**$PER_{off\text{-}field}$ (g a.s./ha)**	**TER criterion: TER ≥ 5**
Triticum aestivum (wheat) *Sinapis alba* (mustard) *Trifolium pratense* (red cover)	> 20	2.70	0.041	> 487

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The risk to non-target plants following application of the product PEL101GV, containing only heptamaloxyloglucan is considered acceptable as TER is greater than the trigger value of 5. Therefore, the use of PEL101GV is not expected to pose unacceptable risk to non target plants.

2.10 ENDOCRINE DISRUPTING PROPERTIES

2.10.1 Assessment of endocrine disrupting properties for human health

Physico-chemical properties and ADME information demonstrate that no bioaccumulation potential relates to heptamaloxyloglucan as the unchanged molecule is not absorbed in the digestive tract, and all metabolites are glucids or short-chain fatty acids which are involved in a large variety of physiological metabolic pathways occurring in mammals.

The potential endocrine activity has not been investigated as per the new guidance Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009.

Two in vivo short-term toxicity studies providing data on adverse effects on endocrine endpoints are available:

- The oral 28-day study in rat was performed with heptamaloxyloglucan treated by gavage at dose levels of 50, 200 or 1000 mg/kg b.w./day. In this study, relevant endocrine organs were weighed and examined histologically included testes, epididymides, prostate, seminal vesicles, ovaries, uterus and oviducts, vagina, thymus, adrenals. There was no toxicological effect observed of heptamaloxyloglucan.
- The oral 90-day study in mice was performed with tamarind seed. The results demonstrate that tamarind seed had no short-term toxicity. However, even if the glucidic monomers structure of tamarind seed is similar to heptamaloxylogucan, the bridging is not considered acceptable based on the molecular weight difference (650,000 versus 1,078 g/mol for tamarind and heptamaloxyloglucan respectively).

The long-term toxicity and carcinogenicity studies provided are considered as supportive studies performed with tamarind seed or protein-bound xyloglucan. The bridging between tamarind seed and heptamaloxyloglucan based on the molecular weight difference could not be considered acceptable. Similarly the bridging between protein-bound xyloglucan and heptamaloxyloglucan is not supported based on the glucidic monomers structure.

No EATS mediated adversity has been observed but data are considered limited.

There is no indication of EATS mediated adversity of heptamaloxyloglucan observed in the oral 28-day study, which falls under level 4 of the OECD Conceptual Framework (CF) for endocrine disruptors. Considering its physico-chemical properties, lack of toxicity in the 28 day rat study and no potential for accumulation, no further investigation on the endocrine disrupting properties is considered necessary.

2.10.2 Assessment of endocrine disrupting properties for the environment

Effects on wild mammals

Based on human health conclusion, RMS considered that based on its physico-chemical properties and ADME information, and the unlikely potential for accumulation, it does not seem relevant to investigate further endocrine disrupting properties for wild mammals, as per Section 3.1 in “Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009”.

Effects on non-target species other than mammals

No study dedicated to assessment of endocrine disrupting properties has been submitted.

The applicant considered that taking into account the oligosaccharidic nature of the active substance and this absence of (eco)toxicological effects, in order to avoid unnecessary experiments in vertebrates, no further experimental investigations have been made. For fish, the applicant concluded that oligosaccharides seem to act as prebiotic in fish organisms.

Long term studies are limited to literature data provided for birds and fish relative to growth performance and immune function of broiler and different cultivated fish species (See Volume 3 CA B.9.1.1 for birds and Volume 3 CA B.9.2.2 for fish). No specific investigation of EATS mediated effects have been performed.

RMS conclusions for non-target organisms

Heptamaloxyloglucan has a molecular weight of >1078 daltons. According to EDSP of the US EPA, polymers with molecular weight greater than 1000 daltons are unlikely to interact with the hormone systems, as they are considered not able to cross biological membranes.

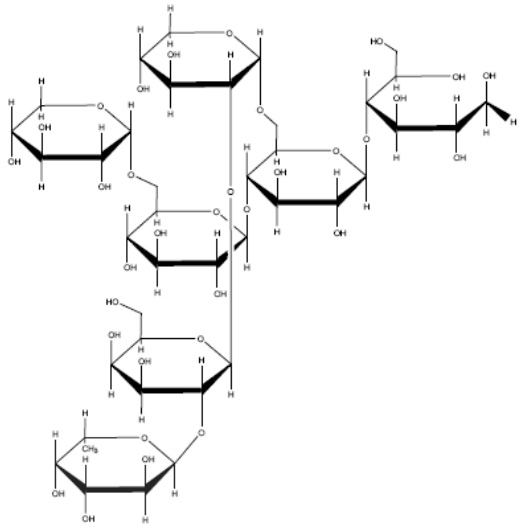
In addition, according to the Guidance for the identification of endocrine disruptors (EFSA, 2018): "There may be cases in which due to the knowledge on the physico-chemical and (eco)toxicological properties of the substance an ED assessment does not appear scientifically necessary or testing for this purpose not technically possible (BP Regulation1, Annex IV or PPP Regulation 2, Annex, Point 1.5)."
Therefore, as concluded for human health and as per Section 3.1 in "Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009", RMS considers that it does not seem relevant to investigate further endocrine disrupting properties for non target organisms.

2.11 PROPOSED HARMONISED CLASSIFICATION AND LABELLING ACCORDING TO THE CLP CRITERIA *[SECTIONS 1-6 OF THE CLH REPORT]*

2.11.1 Identity of the substance [section 1 of the CLH report]

2.11.1.1Name and other identifiers of the substance

Table 76: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	*{[α-D-Xyl p-(1→6)]-β-D-Glc p-(1→4)}{[α-L- Fuc p-(1→2)-β-D-Gal p-(1→2)-α-D-Xyl p-(1→6)]-β-D-Glc p-(1→4)}-D-Glc-ol* with: Xyl p: xylopyranosyl Glc p: glucopyranosyl Fuc p: fucopyranosyl Gal p: galactopyranosyl Glc-ol: glucitol
Other names (usual name, trade name, abbreviation)	Heptamaloxyloglucan
ISO common name (if available and appropriate)	/
EC number (if available and appropriate)	/
EC name (if available and appropriate)	/
CAS number (if available)	870721-81-6
Other identity code (if available)	/
Molecular formula	$C_{40}H_{70}O_{33}$
Structural formula	
SMILES notation (if available)	/
Molecular weight or molecular weight range	1078.96 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Homochiral (issued from naturally homochiral carbohydrates)
Description of the manufacturing process and identity of the source (for UVCB substances only)	NA
Degree of purity (%) (if relevant for the entry in Annex VI)	>780 g/kg, <1000 g/kg

2.11.1.2Composition of the substance

Table 77: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	**Concentration range (% w/w minimum and maximum in multi-constituent substances)**	**Current CLH in Annex VI Table 3.1 (CLP)**	**Current self-classification and labelling (CLP)**
Heptamaloxyloglucan	>780 g/kg	None	None

Table 78: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	**Concentration range (% w/w minimum and maximum)**	**Current CLH in Annex VI Table 3.1 (CLP)**	**Current self-classification and labelling (CLP)**	**The impurity contributes to the classification and labelling**
Patulin	≥ 0 mg/kg, < 50 mg/kg	NA	NA	No

Table 79: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	**Function**	**Concentration range (% w/w minimum and maximum)**	**Current CLH in Annex VI Table 3.1 (CLP)**	**Current self-classification and labelling (CLP)**	**The additive contributes to the classification and labelling**
/	/	/	/	/	/

Table 80: Test substances (non-confidential information)

Identification of test substance	**Purity**	**Impurities and additives (identity, %, classification if available)**	**Other information**	**The study(ies) in which the test substance is used**
Heptamaloxyloglucan	>780 g/kg	None	Refer to Vol. 4 for further information	Please refer to Vol. 3 and Vol. 4

2.11.2 Proposed harmonized classification and labelling

2.11.2.1Proposed harmonised classification and labelling according to the CLP criteria

Table 81: Proposed harmonised classification and labelling according to the CLP criteria

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry		*{[α-D-Xyl p-(1→6)]-β-D-Glc p-(1→4)}{[α-L-Fuc p-(1→2)-β-D-Gal p-(1→2)-α-D-Xyl p-(1→6)]-β-D-Glc p-(1→4)}-D-Glc-ol*	/	870721-81-6							
Dossier submitters proposal		*{[α-D-Xyl p-(1→6)]-β-D-Glc p-(1→4)}{[α-L-Fuc p-(1→2)-β-D-Gal p-(1→2)-α-D-Xyl p-(1→6)]-β-D-Glc p-(1→4)}-D-Glc-ol*	/	870721-81-6	No change proposed						
Resulting Annex VI entry if agreed by											

RAC and COM											

2.11.2.2Additional hazard statements / labelling

Not applicable

Table 82: Reason for not proposing harmonised classification and status under CLH public consultation

Hazard class	Reason for no classification	Within the scope of CLH public consultation
Explosives	Data conclusive but not sufficient for classification	Yes
Flammable gases (including chemically unstable gases)	Hazard class not applicable	Yes
Oxidising gases	Hazard class not applicable	Yes
Gases under pressure	Hazard class not applicable	Yes
Flammable liquids	Hazard class not applicable	Yes
Flammable solids	Data conclusive but not sufficient for classification	Yes
Self-reactive substances	Data conclusive but not sufficient for classification	Yes
Pyrophoric liquids	Hazard class not applicable	Yes
Pyrophoric solids	Data conclusive but not sufficient for classification	Yes
Self-heating substances	Data conclusive but not sufficient for classification	Yes
Substances which in contact with water emit flammable gases	Data conclusive but not sufficient for classification	Yes
Oxidising liquids	Hazard class not applicable	Yes
Oxidising solids	Data conclusive but not sufficient for classification	Yes
Organic peroxides	Data conclusive but not sufficient for classification	Yes
Corrosive to metals	Data conclusive but not sufficient for classification	Yes
Acute toxicity via oral route	Conclusive but no sufficient for classification	Yes
Acute toxicity via dermal route	Conclusive but no sufficient for classification	Yes
Acute toxicity via inhalation route	Data lacking	Yes
Skin corrosion/irritation	Conclusive but no sufficient for classification	Yes
Serious eye damage/eye irritation	Conclusive but no sufficient for classification	Yes
Respiratory sensitisation	Conclusive but no sufficient for classification	Yes
Skin sensitisation	Conclusive but no sufficient for classification	Yes
Germ cell mutagenicity	Data lacking	Yes
Carcinogenicity	Conclusive but no sufficient for classification	Yes
Reproductive toxicity	Conclusive but no sufficient for classification	Yes
Specific target organ toxicity-single exposure	Conclusive but no sufficient for classification	Yes
Specific target organ toxicity-repeated exposure	Conclusive but no sufficient for classification	Yes
Aspiration hazard	Hazard class not applicable	Yes

Hazard class	Reason for no classification	Within the scope of CLH public consultation
Hazardous to the aquatic environment	Data conclusive but not sufficient for classification: acute E(L)C_{50} on fish, daphnia and alga greater than 150 mg active substance/L and active substance considered rapidly degradable.	Yes/No
Hazardous to the ozone layer		Yes/No

2.11.3 History of the previous classification and labelling

Previous classification was proposed for the first inclusion of heptamaloxyloglucan. No CLH report was submitted to ECHA. The active substance is currently not reported in C&L inventory of the ECHA website.

2.11.4 Identified uses

Heptamaloxyloglucan will be used as plant protection products as anti-freezing.

2.11.5 Data sources

For current classification please refer to the table above and Volume 1 point 2.2 to 2.9.

2.12 RELEVANCE OF METABOLITES IN GROUNDWATER

Not relevant.

2.13 CONSIDERATION OF ISOMERIC COMPOSITION IN THE RISK ASSESSMENT

2.13.1 Identity and physical chemical properties

Heptamaloxyloglucan is constituted of several sugar derivatives from vegetal origin, which are naturally homochiral. The active substance is therefore a single isomer (enantiomer).

2.13.2 Methods of analysis

The method of determination of the active substance and its impurities cannot discriminate enantiomers. However as sugars are naturally homochiral, the active substance is also homochiral and the available analytical method is considered sufficient.

2.13.3 Mammalian toxicity

Not relevant.

2.13.4 Operator, Worker, Bystander and Resident exposure

Not relevant.

2.13.5 Residues and Consumer risk assessment

Not relevant.

2.13.6 Environmental fate

Not relevant.

2.13.7 Ecotoxicology

Not relevant.

2.14 RESIDUE DEFINITIONS

2.14.1 Definition of residues for exposure/risk assessment

Food of plant origin: Not required

Food of animal origin: Not required

Soil: Heptamaloxyloglucan

Groundwater: Heptamaloxyloglucan

Surface water: Heptamaloxyloglucan

Sediment: Heptamaloxyloglucan

Air: Heptamaloxyloglucan

2.14.2 Definition of residues for monitoring

Food of plant origin: Not required

Food of animal origin: Not required

Soil: None

Groundwater: None

Surface water: None

Sediment: None

Air: None

Level 3

Heptamaloxyloglucan

3 PROPOSED DECISION WITH RESPECT TO THE APPLICATION

3.1 BACKGROUND TO THE PROPOSED DECISION

3.1.1 Proposal on acceptability against the decision making criteria – Article 4 and annex II of regulation (EC) No 1107/2009

3.1.1.1 Article 4				
		Yes	No	
i)	It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorisation in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses.	X		RMS considers that heptamaloxyloglucan can be renewed and that authorizations of PPP can be granted in at least one Member States.
3.1.1.2 Submission of further information				
		Yes	No	
i)	It is considered that a complete dossier has been submitted	X		RMS considers that a complete dossier was submitted. However, please refer to Table 3.1.4.
ii)	It is considered that in the absence of a full dossier the active substance may be approved even though certain information is still to be submitted because: (a) the data requirements have been amended or refined after the submission of the dossier; or (b) the information is considered to be confirmatory in nature, as required to increase confidence in the decision.			
3.1.1.3 Restrictions on approval				
		Yes	No	
	It is considered that in line with Article 6 of Regulation (EC) No 1107/2009 approval should be subject to conditions and restrictions.		X	
3.1.1.4 Criteria for the approval of an active substance				
Dossier				
		Yes	No	
	It is considered the dossier contains the information needed to establish, where relevant, Acceptable Daily Intake (ADI), Acceptable Operator Exposure Level (AOEL) and Acute Reference Dose (ARfD).	X		Not relevant (Please refer to Level 2.6)
	It is considered that the dossier contains the information necessary to carry out a risk assessment and for enforcement purposes (relevant for	X		Not relevant

	substances for which one or more representative uses includes use on feed or food crops or leads indirectly to residues in food or feed). In particular it is considered that the dossier: (a) permits any residue of concern to be defined; (b) reliably predicts the residues in food and feed, including succeeding crops (c) reliably predicts, where relevant, the corresponding residue level reflecting the effects of processing and/or mixing; (d) permits a maximum residue level to be defined and to be determined by appropriate methods in general use for the commodity and, where appropriate, for products of animal origin where the commodity or parts of it is fed to animals; (e) permits, where relevant, concentration or dilution factors due to processing and/or mixing to be defined.			
	It is considered that the dossier submitted is sufficient to permit, where relevant, an estimate of the fate and distribution of the active substance in the environment, and its impact on non-target species.	X		All representative uses
Efficacy				
		Yes	No	
	It is considered that it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use is sufficiently effective.	X		One Heptamaloxyloglucan based product is currently registered on the representative use in France. It will be re-assessed following the renewal of Heptamaloxyloglucan.
Relevance of metabolites				
		Yes	No	
	It is considered that the documentation submitted is sufficient to permit the establishment of the toxicological, ecotoxicological or environmental relevance of metabolites.	X		Not relevant.
Composition				
		Yes	No	
	It is considered that the specification defines the minimum degree of purity, the identity and maximum content of impurities and, where relevant, of isomers/diastereo-isomers and additives, and the content of impurities of toxicological, ecotoxicological or environmental concern within acceptable limits.	X		The active substance is considered as a technical material with a purity of min. 780 g/kg and several impurities that are structurally similar to the active substance. Instead, it could also have been considered as a UVCB substance of botanical origin, with a purity of 1000 g/kg.
	It is considered that the specification is in compliance with the relevant			Non applicable : no FAO specifications have been set

	Food and Agriculture Organisation specification, where such specification exists.			
	It is considered for reasons of protection of human or animal health or the environment, stricter specifications than that provided for by the FAO specification should be adopted			Non applicable : no FAO specifications have been set
Methods of analysis				
		Yes	No	
	It is considered that the methods of analysis of the active substance, safener or synergist as manufactured and of determination of impurities of toxicological, ecotoxicological or environmental concern or which are present in quantities greater than 1 g/kg in the active substance, safener or synergist as manufactured, have been validated and shown to be sufficiently specific, correctly calibrated, accurate and precise.	X		Validated analytical methods for the determination of the active substance, its significant impurities and its relevant impurity in the technical material are available.
	It is considered that the methods of residue analysis for the active substance and relevant metabolites in plant, animal and environmental matrices and drinking water, as appropriate, shall have been validated and shown to be sufficiently sensitive with respect to the levels of concern.	X		As no residue definition has been set, no analytical method for the determination of residues of this active substance is necessary. The active substance and its impurities are naturally occurring compounds and no residue definition is necessary in plant, animal and environmental matrices.
	It is confirmed that the evaluation has been carried out in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.	X		
Impact on human health				
Impact on human health - ADI, AOEL, ARfD				
		Yes	No	
	It is confirmed that (where relevant) an ADI, AOEL and ARfD can be established with an appropriate safety margin of at least 100 taking into account the type and severity of effects and the vulnerability of specific groups of the population.	X		ADI, AOEL, AAOEL and ARfD are considered not relevant (See Level 2.6.10).
Impact on human health – proposed genotoxicity classification				
		Yes	No	
	It is considered that, on the basis of assessment of higher tier genotoxicity testing carried out in accordance with the data requirements and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No 1272/2008, **as mutagen category 1A or 1B.**			Based on the results of *in vitro* genotoxicity studies, heptamaloxyloglucan is considered to have not mutagenic potential. However, the clastogenic potential of heptamaloxyloglucan cannot be determined since no data has been submitted (see Level 2.6.4).
Impact on human health – proposed carcinogenicity classification				

		Yes	No	
i)	It is considered that, on the basis of assessment of the carcinogenicity testing carried out in accordance with the data requirements for the active substances, safener or synergist and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No 1272/2008, **as carcinogen category 1A or 1B.**		X	Heptamaloxyloglucan is not considered to be carcinogenic (see Level 2.6.5).
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			
Impact on human health – proposed reproductive toxicity classification				
		Yes	No	
i)	It is considered that, on the basis of assessment of the reproductive toxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No 1272/2008, **as toxic for reproduction category 1A or 1B.**		X	Heptamaloxyloglucan is not considered to be toxic for reproduction (see Level 2.6.6).
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			
Impact on human health – proposed endocrine disrupting properties classification				
		Yes	No	

i)	It is considered that **the substance SHOULD BE identified as having endocrine disrupting properties** in accordance with the provisions of point 3.6.5 in Annex II of Regulation (EC) No 1107/2009		X	Heptamaloxyloglucan is not considered to have endocrine disrupting properties (see Level 2.10).
ii)	Linked to above identification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			
Fate and behaviour in the environment				
Persistent organic pollutant (POP)				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a persistent organic pollutant (POP) as laid out in Regulation 1107/2009 Annex II Section 3.7.1.		X	See level 2 section 2.8
Persistent, bioaccumulative and toxic substance (PBT)				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a persistent, bioaccumulative and toxic (PBT) substance as laid out in Regulation 1107/2009 Annex II Section 3.7.2.		X	See level 2 section 2.8
Very persistent and very bioaccumulative substance (vPvB).				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a a very persistent and very bioaccumulative substance (vPvB) as laid out in Regulation 1107/2009 Annex II Section 3.7.3.		X	See level 2 section 2.8
Ecotoxicology				
		Yes	No	
i	It is considered that the risk assessment demonstrates risks to be acceptable in accordance with the criteria laid down in the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) under realistic proposed conditions of use of a plant protection product containing the active substance, safener or synergist. The RMS is content that the assessment takes into account	X		Quantitative risk assessment performed for mammals, aquatic organisms, bees and plants allow concluding that the risk can be considered acceptable. For other organisms, weight of evidence considering the type of component (xyloglucan extracted from apple), its mode of action (plant elicitor to protect vine from freezing), its natural occurrence in plants, the low dose applied (0.56 g/ha), allow to conclude that no unacceptable risk is expected

	the severity of effects, the uncertainty of the data, and the number of organism groups which the active substance, safener or synergist is expected to affect adversely by the intended use.			following application of heptamaloxyloglucan on vineyard. See level 2 section 2.9 All representative uses
ii	It is considered that the substance **SHOULD BE identified as having endocrine disrupting properties** that may cause adverse effects on non-target organisms in accordance with the provisions of point 3.8.2 in Annex II of Regulation (EC) No 1107/2009.		X	Heptamaloxyloglucan has a molecular weight of >1078 Daltons and is considered unlikely to interact with the hormone systems, as it is considered not able to cross biological membranes. As concluded for human health and as per Section 3.1 in "Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009", RMS considers that it does not seem relevant to investigate further endocrine disrupting properties for non target organisms.
iii	Linked to the consideration of the endocrine properties immediately above. It is considered that the exposure of non-target organisms to the active substance in a plant protection product under realistic proposed conditions of use is negligible.	X		The amount of heptamaloxyloglucan applied is of 0.56 g /ha.
iv	It is considered that it is established following an appropriate risk assessment on the basis of Community or internationally agreed test guidelines, that the use under the proposed conditions of use of plant protection products containing this active substance, safener or synergist: — will result in a negligible exposure of honeybees, or — has no unacceptable acute or chronic effects on colony survival and development, taking into account effects on honeybee larvae and honeybee behaviour.	X		See level 2 points 2.9.3 and 2.9.9.4 No unacceptable risk to bees is expected. All representative uses.
Residue definition				
		Yes	No	
	It is considered that, where relevant, a residue definition can be established for the purposes of risk assessment and for enforcement purposes.	X		*Refer to level 2.7.3* Heptamaloxyloglucan is a signal molecule naturally occurring at low levels in plant tissues Due to its low toxicity no ADI and no ARfD is set for heptamaloxyloglucan and it is propose to maintain its inclusion in the Annex IV of regulation 396/2005/EC (active substances for which no MRL are required). Consequently, no residue definition is considered necessary for products of

				plant or animal origin.
Fate and behaviour concerning groundwater				
		Yes	No	
	It is considered that it has been established for one or more representative uses, that consequently after application of the plant protection product consistent with realistic conditions on use, the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater complies with the respective criteria of the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.	X		Due to the ready biodegradability of heptamaloxyloglucan and to its sensitivity to the attack from many bacteria strains in soil giving raise to glucose, there is no chance that heptamaloxyloglucan, will ever reach the ground water level. Therefore there is no need to consider PECgw

3.1.2 Proposal – Candidate for substitution

Candidate for substitution				
		Yes	No	
	It is considered that the active substance shall be approved as a candidate for substitution		X	Heptamaloxyloglucan does not meet the criteria to be considered as a candidate for substitution (as below): *— its ADI, ARfD or AOEL is significantly lower than those of the majority of the approved active substances within groups of substances/use categories,* **NO** *— it meets two of the criteria to be considered as a PBT substance,* **NO** *— there are reasons for concern linked to the nature of the critical effects (such as developmental neurotoxic or immunotoxic effects) which, in combination with the use/exposure patterns, amount to situations of use that could still cause concern, for example, high potential of risk to groundwater; even with very restrictive risk management measures (such as extensive personal protective equipment or very large buffer zones)* , **NO** *— it contains a significant proportion of non-active isomers,* **NO** *— it is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogen category 1A or 1B, if the substance has not been excluded in accordance with the criteria laid down in point 3.6.3,***NO** *— it is or is to be classified, in accordance with the provisions of Regulation*

				(EC) No 1272/2008, as toxic for reproduction category 1A or 1B if the substance has not been excluded in accordance with the criteria laid down in point 3.6.4, **NO** *— if, on the basis of the assessment of Community or internationally agreed test guidelines or other available data and information, reviewed by the Authority, it is considered to have endocrine disrupting properties that may cause adverse effects in humans if the substance has not been excluded in accordance with the criteria laid down in point 3.6.5.,* **NO**

3.1.3 Proposal – Low risk active substance

Low-risk active substances				
		Yes	No	
	It is considered that the active substance **shall be considered of low risk.** If the active substance is not a micro-organism, in particular it is considered that: (a) the substance **should NOT be classified or proposed for classification** in accordance to Regulation (EC) No 1272/2008 as any of the following: — carcinogenic category 1A, 1B or 2, — mutagenic category 1A, 1B or 2, — toxic to reproduction category 1A, 1B or 2, — skin sensitiser category 1, — serious damage to eye category 1, — respiratory sensitiser category 1, — acute toxicity category 1, 2 or 3, — specific Target Organ Toxicant, category 1 or 2, — toxic to aquatic life of acute and chronic category 1 on the basis of appropriate standard tests, — explosive, — skin corrosive, category 1A, 1B or 1C; (b) it has **not been identified as priority substance under Directive 2000/60/EC**; (c) it is **not deemed to be an endocrine disruptor** in accordance to Annex II of Regulation (EC) No 1107/2009; (d) it **has no neurotoxic or immunotoxic effects**; (e) it **is not persistent** (half-life in soil is more than 60 days) or its **bio-concentration factor is lower than 100**.	X		The relevant criteria relating to human health and environment are met given the nature of the active substance.

	(f) it is a **semiochemical** and verifies points (a) to (d). Paragraph (e) doesn't apply to naturally occurring active substances. If the active substance is a micro-organism, in particular it is considered that at strain level the micro-organism has not demonstrated multiple resistance to anti-microbials used in human or veterinary medicine. If the active substance is a baculovirus, in particular it has not demonstrated adverse effects on non-target insects.			

3.1.4 List of studies to be generated, still ongoing or available but not peer reviewed

Data gap	Relevance in relation to representative use(s)	Study status		
		No confirmation that study available or on-going.	Study on-going and anticipated date of completion	Study available but not peer-reviewed
3.1.4.1 Identity of the active substance or formulation				
No further data required				
3.1.4.2 Physical and chemical properties of the active substance and physical, chemical and technical properties of the formulation				
Vapour pressure of the pure active substance	Although no value could be considered acceptable, the substance is considered as having a very low volatility. No particular concern is expected.	X		
Water/octanol partition coefficient of the active substance	Although no value could be considered acceptable, the substance clearly has a higher affinity towards water than to organic solvents. No particular concern is expected.	X		
3.1.4.3 Data on uses and efficacy				

3.1.4.4 Data on handling, storage, transport, packaging and labelling				
None				
3.1.4.5 Methods of analysis				
No further study required				
3.1.4.6 Toxicology and metabolism				
A read across evaluation with a suitable analogue that would have reliable acute inhalation data. If no suitable analogue is found inhalation route testing is required.	Relevant for all representative uses.	X		
A read across approach with suitable analogues having data for chromosomal aberration and/or micronucleus *in vitro* is required.	Relevant for all representative uses.	X		
3.1.4.7 Residue data				
No further data/studies required				
3.1.4.8 Environmental fate and behaviour				
None				
3.1.4.9 Ecotoxicology				
None				

3.1.5 Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) No 546/2011, and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

Area of the risk assessment that could not be finalised on the basis of the available data	**Relevance in relation to representative use(s)**
None	

3.1.6 Critical areas of concern

An issue is listed as a critical area of concern:
(a) where the substance does not satisfy the criteria set out in points 3.6.3, 3.6.4, 3.6.5 or 3.8.2 of Annex II of Regulation (EC) No 1107/2009 and the applicant has not provided detailed evidence that the active substance is necessary to control a serious danger to plant health which cannot be contained by other available means including non-chemical methods, taking into account risk mitigation measures to ensure that exposure of humans and the environment is minimised, or
(b) where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) 546/2011, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

Critical area of concern identified	**Relevance in relation to representative use(s)**
None	

3.1.7 Overview table of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in 3.3.1, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)
All columns are grey as the material tested in the toxicological studies has not been demonstrated to be representative of the technical specification.

Representative use		Vine
Operator risk	Risk identified	
	Assessment not finalised	
Worker risk	Risk identified	

	Assessment not finalised	
Bystander risk	Risk identified	
	Assessment not finalised	
Consumer risk	Risk identified	
	Assessment not finalised	
Risk to wild non target terrestrial vertebrates	Risk identified	
	Assessment not finalised	
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	
	Assessment not finalised	
Risk to aquatic organisms	Risk identified	
	Assessment not finalised	
Groundwater exposure active substance	Legal parametric value breached	
	Assessment not finalised	
Groundwater exposure metabolites	Legal parametric value breached	
	Parametric value of 10µg/L[(a)] breached	
	Assessment not finalised	
Comments/Remarks		

The superscript numbers in this table relate to the numbered points indicated within chapter 3.1.5 and 3.1.6. Where there is no superscript number, see level 2 for more explanation.
(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

3.1.8 Area(s) where expert consultation is considered necessary

It is recommended to organise a consultation of experts on the following parts of the assessment report:

Area(s) where expert consultation is considered necessary	**Justification**
None	

3.1.9 Critical issues on which the Co RMS did not agree with the assessment by the RMS

Points on which the co-rapporteur Member State did not agree with the assessment by the rapporteur member state. Only the points relevant for the decision making process should be listed.

Issue on which Co-RMS	**Opinion of Co-RMS**	**Opinion of RMS**

disagrees with RMS		
None		

3.2 PROPOSED DECISION

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3.3 RATIONAL FOR THE CONDITIONS AND RESTRICTIONS TO BE ASSOCIATED WITH THE APPROVAL OR AUTHORISATION(S), AS APPROPRIATE

3.3.1 Particular conditions proposed to be taken into account to manage the risks identified

Proposed condition/risk mitigation measure	**Relevance in relation to representative use(s)**
**********	**********

3.4 APPENDICES

GUIDANCE DOCUMENTS USED IN THIS ASSESSEMENT

General

European Food Safety Authority; Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (OJ L 309, 24.11.2009, p. 1-50). EFSA Journal 2011;9(2):2092. [49 pp.]. doi:10.2903/j.efsa.2011.2092. Available online: www.efsa.europa.eu

SANCO/2012/11251 rev.4: Guidance Document on the renewal of approval of active substances to be assessed in compliance with Regulation (EU) No 844/2012 (the Renewal Regulation)

SANCO/12580/2012: Guidance Document on preparing lists of test and study reports According to article 60 of Regulation (EC) No 1107/2009

Section identity, physical chemical and analytical methods

Section physico chemical properties

Manual on development and use of FAO and WHO specifications for pesticides - third revision of the First Edition, WHO, Rome 2016
Chemicals Regulation Directorate, DATA REQUIREMENTS HANDBOOK, (Version 2.2, June 2012)
Technical monograph N°17, 2nd edition, Guidelines for Specifying the Shelf Life of Plant Protection Products, June 2009
Evaluation Manual for the Authorisation of plant protection products and biocides according to Regulation (EC) No 1107/2009, EU part, Plant Protection Products, Chapter 2 Physical and chemical properties, version 2.0; January 2014, Board
Guidance ST/SG/AC 10/11/Rev.5 for the safety properties
CLP regulation 1272/2008

Section analytical methods

SANCO/3030/99 rev.4: Technical Material and preparations: guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414
SANCO/3029/99 rev .4: Residues: guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, section 4) and Annex III (part A, Section 5) of directive 91/414
SANCO/825/00 rev.8.1: Guidance document on pesticide residues analytical methods

Section Data on application and efficacy

Section Toxicology

Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009. SANCO/10597/2003-rev. 10.1 (2012)

Section Residue and consumer risk assessment

SANCO/11188/2013 - Rev. 2, 14 September 2015; Guidance document on criteria for the inclusion of active substances into Annex IV of Regulation (EC) N° 396/2005.

Section fate and behavior in environment

European Commission (2014) - Assessing Potential for Movement of Active Substances and their Metabolites to Ground Water in the EU" Report of the FOCUS Ground Water Work Group, EC Document Reference Sanco/13144/2010 version 3, 613 pp.

European Food Safety Authority, 2014 - EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662, 37 pp., doi:10.2903/j.efsa.2014.3662

FOCUS (1997) - Soil persistence models and EU Registration - The Final Report of the Soil Modelling Workgroup of FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use) – 29 February 1997.

FOCUS (2001) - FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.1. 221 pp.

FOCUS (2006) - Guidance document on estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU registration. Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005, version 2.0, 434 pp.

FOCUS (2007) - Landscape And Mitigation Factors In Aquatic Risk Assessment. Volume 1. Extended Summary and Recommendations. Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment, EC Document Reference SANCO/10422/2005 v2.0. 169 pp.

FOCUS (2008) - Pesticides in Air: Considerations for Exposure Assessment. Report of the FOCUS Working Group on Pesticides in Air, EC Document Reference SANCO/10553/2006 Rev 2 June 2008. 327 pp.

FOCUS (2014a) - Generic guidance for Tier 1 FOCUS groundwater assessments. Version 2.2, May 2014.

FOCUS (2014b) - Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration, version 1.1

FOCUS (2015) - Generic guidance for FOCUS surface water Scenarios, Version: 1.4, Date: May 2015

SANCO (2003) Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council directive 91/414/EEC. Sanco/221/2000-rev.10-final, 25 February 2003.

Section ecotoxicology

European Food Safety Authority; Guidance Document on Risk Assessment for Birds & Mammals on request from EFSA. EFSA Journal 2009; 7(12):1438. doi:10.2903/j.efsa.2009.1438. Available online: www.efsa.europa.eu

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 268 pp. doi:10.2903/j.efsa.2013.3290.

SANCO/10329/2002 rev 2 final (2002). Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC

European Food Safety Authority, 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). EFSA Journal 2013;11(7):3295, 268 pp., doi:10.2903/j.efsa.2013.3295

ECHA (European Chemicals Agency) and EFSA (European Food Safety Authority) with the technical support of the Joint Research Centre (JRC), Andersson N, Arena M, Auteri D, Barmaz S, Grignard E, Kienzler A, Lepper P, Lostia AM, Munn S, Parra Morte JM, Pellizzato F, Tarazona J, Terron A and Van der Linden S, 2018. Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009. EFSA Journal 2018;16(6):5311, 135 pp. https://doi.org/10.2903/j.efsa.2018.5311. ECHA-18-G-01-EN.

3.5 REFERENCE LIST

Directive 91/414/EEC concerning the placing of plant protection products on the market

Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC.

EFSA Scientific Report (2009) 334, Conclusion regarding the peer review of the pesticide risk assessment of the active substance heptamaloxyloglucan (finalised 17 July 2009).

Review report for the active substance heptamaloxyloglucan - SANCO/10502/09 - final, 27 October 2009

Regulation (UE) N°283/2013 (1st March 2013) setting out data requirements for active substances, in accordance with regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market

Regulation (UE) N°284/2013 (1st March 2013) setting out data requirements for plant protection products, in accordance with regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market

Commission Regulation (EU) No 500/2013 of 30 May 2013 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for acetamiprid, Adoxophyes orana granulovirus strain BV-0001, azoxystrobin, clothianidin, fenpyrazamine, heptamaloxyloglucan, metrafenone, Paecilomyces lilacinus strain 251, propiconazole, quizalofop-P, spiromesifen, tebuconazole, thiamethoxam and zucchini yellow mosaik virus - weak strain in or on certain products

Commission Implementing Regulation (EU) 2016/183 of 11 February 2016 amending Implementing Regulation (EU) No 686/2012 allocating to Member States, for the purposes of the renewal procedure, the evaluation of the active substances whose approval expires by 31 December 2018 at the latest

Section identity, physical chemical and analytical methods
None

Section data on application and efficacy
None

Section toxicology
None

Section residue and consumer risk assessment
None

Section fate and behavior in environment
None

Section ecotoxicology
None