# *European Commission*

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

# Heptamaloxyloglucan

## Volume 3 – B.6 (PPP) – PEL101GV

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

# Version History

| When | What |
|---|---|
| 09/2020 | Initial RAR |
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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.

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# B.6. TOXICOLOGY AND METABOLISM DATA AND ASSESSMENT OF RISKS FOR HUMANS

## B.6.1. ACUTE TOXICITY OF PLANT PROTECTION PRODUCT

The plant protection product PEL101GV, a water soluble powder (SP), contains 100% technical grade active substance Heptamaloxyloglucan, the acute toxicity studies are detailed in the Volume 3CA B6.

No new study has been submitted by the applicant since the previous dossier evaluation (DAR 2007).

### B.6.1.1. Oral

The plant protection product PEL101GV exclusively contains 100% technical grade active substance Heptamaloxyloglucan, with no transformation. An acute oral toxicity study was performed with Heptamaloxyloglucan (see document KCA 5.2.1/01) and the acute LD50 > 5000 mg/kg b.w. based on toxic class method.
**In accordance with Regulation (EC) No.1272/2008, the active substance must not be classified. No signal word or hazard statement is required.**

**Assessment and conclusion by RMS 2020:**
**Acceptability/Reliability:** This study is considered acceptable.
**Outcome and conclusion of the study:** No change from the previous peer-reviewed evaluation. The plant protection product PEL101GV does not require classification for this toxicological endpoint.

### B.6.1.2. Dermal

The plant protection product PEL101GV exclusively contains 100% technical grade active substance Heptamaloxyloglucan, with no transformation. Kow of Heptamaloxyloglucan is < 10-4, its water solubility is > 500 g/L and its molecular weight is > 1000 g/mol, so the active substance is unable to penetrate through lipophilic membranes, and thus no dermal absorption is possible. An acute dermal toxicity study was however performed with Heptamaloxyloglucan (see document KCA 5.2.2/01) and the acute LD50 > 2000 mg/kg b.w.
**In accordance with Regulation (EC) No.1272/2008, the active substance must not be classified. No signal word or hazard statement is required.**

**Assessment and conclusion by RMS 2020:**
**Acceptability/Reliability:** This study is considered acceptable.
**Outcome and conclusion of the study:** No change from the previous peer-reviewed evaluation. The plant protection product PEL101GV does not require classification for this toxicological endpoint.

### B.6.1.3. Inhalation

According to Section 7.1.3 of Part A of the Regulation (EU) No.284/2013, an acute inhalation toxicity study is not relevant if the plant protection product:
- is not a gas or a liquefied gas (solid at ambient temperature),
- is not a smoke generating formulation or a fumigant (granule formulation),
- is not to be used with fogging equipment,
- is not a vapour releasing plant protection preparation,
- is not an aerosol,
- is not a powder containing more than 1 % (w/w) of particles with a diameter < 50 µm (but a product Cat.1 - nearly dust free),
- is not to be applied from aircraft in cases where inhalation exposure is relevant,
- does not contain an active substance with a vapour pressure > 1*10-2 Pa and is not to be used in enclosed spaces such as warehouses or glasshouses (cypermethrin: vapour pressure value of 2.3*10-7 Pa at 20°C),
- is not applied by spraying.

In the present assessment, no study was performed. Since the active substance Heptamaloxyloglucan has a vapour pressure < 10-2 Pa, the plant protection product doesn't encounter any criteria described above, except the application by spraying. However by taking into consideration the product will be used as a solution with droplets of a diameter > 50 µm (see annex point KCP 3.5/01 and KCP 3.5/02) and its absence of toxicity, it appears useless to perform unnecessary testing in mammals.

**The plant protection product is not expected to present acute toxicity by inhalation exposure.**

**In accordance with Regulation (EC) No.1272/2008, the active substance must not be classified. No signal word or hazard statement is required.**

**Assessment and conclusion by RMS 2020:**

As mentioned by the applicant spraying is the mode of application of the active substance. Spraying is one of the criteria described under Regulation No. 283/2013. Section 5.2.3 stipulates *"The acute inhalation toxicity of the active substance shall be reported where any of the following apply: - the active substance has a vapour pressure > 1 × 10–2 Pa at 20 °C; - the active substance is a powder containing a significant proportion of particles of a diameter < 50 µm ( > 1 % on weight basis); - the active substance is included in products that are powders or are applied by spraying.".*

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

In light of the above remark and lack of ADME data on 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.

### B.6.1.4. Skin irritation

The plant protection product PEL101GV exclusively contains 100% technical grade active substance Heptamaloxyloglucan, with no transformation. A skin irritation study was performed with Heptamaloxyloglucan (see document KCA 5.2.4/01) and minimal and transient erythema (at 1 h post-application only) was the only skin reaction.

**In accordance with Regulation (EC) No.1272/2008, the active substance must not be classified. No signal word or hazard statement is required.**

**Assessment and conclusion by RMS 2020:**

**Acceptability/Reliability:** This study is considered acceptable.

**Outcome and conclusion of the study:** No change from the previous peer-reviewed evaluation. The plant protection product PEL101GV does not require classification for this toxicological endpoint.

### B.6.1.5. Eye irritation

The plant protection product PEL101GV exclusively contains 100% technical grade active substance Heptamaloxyloglucan, with no transformation. An eye irritation study was performed with Heptamaloxyloglucan (see document KCA 5.2.5/01) and minimal and transient conjunctival redness (at 1 h post-application only) was the only finding.

**In accordance with Regulation (EC) No.1272/2008, the active substance must not be classified. No signal word or hazard statement is required.**

**Assessment and conclusion by RMS 2020:**

**Acceptability/Reliability:** This study is considered acceptable.

**Outcome and conclusion of the study:** No change from the previous peer-reviewed evaluation. The plant protection product PEL101GV does not require classification for this toxicological endpoint.

### B.6.1.6. Skin sensitization

The plant protection product PEL101GV exclusively contains 100% technical grade active substance Heptamaloxyloglucan, with no transformation. A skin sensitization study according to LLNA was performed with Heptamaloxyloglucan (see document KCA 5.2.6/01).

No skin reactions and no noteworthy increases in ear thickness were observed in the treated animals. No noteworthy lymphoproliferation and no dose-response relationship were noted at the tested concentrations. Heptamaloxyloglucan is not considered as a skin sensitizer.
**In accordance with Regulation (EC) No.1272/2008, the active substance must not be classified. No signal word or hazard statement is required.**

**Assessment and conclusion by RMS 2020:**
**Acceptability/Reliability:** This study is considered acceptable.
**Outcome and conclusion of the study:** No change from the previous peer-reviewed evaluation. The plant protection product PEL101GV does not require classification for this toxicological endpoint.

### B.6.1.7. Supplementary studies on the plant protection product
Not applicable as the preparation will not be used with other plant protection products or with adjuvants.

### B.6.1.8. Supplementary studies for combinations of plant protection products
Not applicable as the preparation will not be used with other plant protection products or with adjuvants.

## B.6.2. DERMAL ABSORPTION
As concluded in the Peer Review on heptamaloxyloglucan (EFSA Scientific Report (2009) 334, 1-52) since the operator, worker and bystander exposure estimates are not required, dermal absorption values are not required.

Furthermore, the formulation PEL101GV is strictly identical to the technical active substance heptamaloxyloglucan coded EL101GV. For dermal absorption, no study was performed. Indeed, $K_{ow}$ of EL101GV is low ($< 10^{-4}$) and molecular weight is high (> 1000 g/mol): the active substance is unable to penetrate through lipophilic membranes, and thus no dermal absorption is possible.

## B.6.3. AVAILABLE TOXICOLOGICAL DATA RELATING TO CO-FORMULANTS

There is no non-active substance of toxicological concern in PEL101GV
**CONFIDENTIAL information - data provided separately (Volume B4).**

## B.6.4. EXPOSURE DATA
### B.6.4.1. Operator exposure

As concluded in the Peer Review on heptamaloxyloglucan (EFSA Scientific Report (2009) 334, 1-52), there is no need to assess the operator exposure.

### B.6.4.2. Bystander and resident exposure

As concluded in the Peer Review on heptamaloxyloglucan (EFSA Scientific Report (2009) 334, 1-52), there is no need to assess the bystander and resident exposure.

### B.6.4.3. Worker exposure

As concluded in the Peer Review on heptamaloxyloglucan (EFSA Scientific Report (2009) 334, 1-52), there is no need to assess the worker exposure.

## B.6.5. EXPOSURE AND RISK ASSESSMENT

As concluded in the Peer Review on heptamaloxyloglucan (EFSA Scientific Report (2009) 334, 1-52), the active substance is “generally regarded as safe for human exposure, since it is an oligosaccharide, which is a component

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

**Assessment and conclusion by RMS 2020:**
Since reference values were not considered necessary based on the toxicological profile of the active substance as indicated in the EFSA Scientific Report (2009) 334, 1-52 , 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.
However, regarding the genotoxicity aspect of the active substance RMS disagrees with the applicant's statement on genotoxicity (absence of clastogenicity data), Refer to details in Volume B6.

## B.6.6. REFERENCES RELIED ON

The formulation PEL101GV is strictly identical to the technical active substance heptamaloxyloglucan coded EL101GV. Please refer to Volume 3 CA B.6.10.