**Committee for Risk Assessment**

**RAC**

Annex 2

**Response to comments document (RCOM)**

to the Opinion proposing harmonised classification and labelling at EU level of

# Sodium 3-(allyloxy)-2-hydroxypropanesulphonate

**EC Number: 258-004-5**
**CAS Number: 52556-42-0**

CLH-O-0000007154-78-01/F

**Adopted**

**15 September 2022**

**ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON SODIUM 3-(ALLYLOXY)-2-HYDROXYPROPANESULPHONATE**

## COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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**Substance name: sodium 3-(allyloxy)-2-hydroxypropanesulphonate**
**EC number: 258-004-5**
**CAS number: 52556-42-0**
**Dossier submitter: France**

## GENERAL COMMENTS

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 01.12.2021 | Germany | | MemberState | 1 |
| Comment received | | | | |
| The Comments are provided in the confidental attachment<br><br>ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment DE-CA Comments CLH_Sodium 3-(allyloxy)-2-hydroxypropanesulphonate.pdf | | | | |
| Dossier Submitter's Response | | | | |
| NaOH is a starting material of the substance. It is used to form the sodium salt of 3-(allyloxy)-2-hydroxypropanesulphonate.<br>Furthermore, the substance is defined as a salt while the solution tested is a solution. Therefore the direct comparison is not possible as the pH of the solution is not known.<br><br>In addition, in the tested material, NaOH is a constituent resulting of the dissolution of HAPS in water (to obtain an aqueous solution of 38.2% of HAPS to be tested) as well as the two other impurities (3- (alloxy)propane-1,2-diol and disodium-2- hydroxy-3-sulphonatopropyloxypropane sulphonate). The interpretation is that the NaOH is spontaneously formed in the aqueous solution by dissolution, the test material being an aqueous solution of the substance HAPS.<br><br>Therefore, in both cases, FR does not consider NaOH as an additive but as an impurity. To be noted that the registrants were contacted regarding these uncertainties on the nature of the substance tested in the toxicity studies, but their answer did not provide much more clarity. | | | | |
| RAC's response | | | | |
| RAC takes note of this issue. | | | | |

## TOXICITY TO REPRODUCTION

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 30.11.2021 | Sweden | | MemberState | 2 |
| Comment received | | | | |
| Fertility<br>The Swedish CA support the proposed classification of sodium 3-(allyloxy)-2-hydroxypropanesulphonate (HAPS) as Repr. 1B for effects on sexual function and fertility (H360F) based on the findings in the OECD 421 study. Clear effects on fertility were observed, resulting in fewer implants and pups (live and stillborn) at the low dose (62,5 mg/kg/d) and virtually no implants in the mid-dose (250 mg/kg/d) and a complete lack of born pups, in the absence of described general maternal toxicity. Although no implants and born pups was observed at the high dose (1000 mg/kg/d), this dose was associated with substantial maternal toxicity, manifested as mortality in 5/12 dams dosed initially, and we therefore do not consider the effects observed at this dose as reliable to include as a basis for the classification.<br><br>Developmental toxicity<br>Based on the lack of developmental effects in the OECD 414 studies (dose-range and main study) we support no classification for effects on development. | | | | |
| Dossier Submitter's Response | | | | |
| Thank you for your support. | | | | |
| RAC's response | | | | |
| RAC takes note of the comments. | | | | |

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 01.12.2021 | Germany | | MemberState | 3 |
| Comment received | | | | |
| The Comments are provided in the confidental attachment<br><br>ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment DE-CA Comments CLH_Sodium 3-(allyloxy)-2-hydroxypropanesulphonate.pdf | | | | |
| Dossier Submitter's Response | | | | |
| Effects on fertility: thank you for your support.<br><br>Effect on development:<br><br>Dossier submitter agrees that developmental toxicity cannot be completely excluded from the OECD 421 study based on the following:<br>- presence of corpora lutea after the first pairing (satellite group)<br>- some developmental effects in the low dose group<br>  o stillborn: 6.9% versus 5% in the control group<br>  o post-implantation loss: 3% versus 1% in the control group<br>  o dose response can not be investiguated since this is the only dose with females achieving pregnancy.<br><br>However, some information rather point to an effect on fertility:<br>- high reduction / absence of implants per dam<br>- histopathological effects on ovaries of infertile treated females of the high dose group (examination not performed in the medium and low dose groups) | | | | |

- absence of corpora lutea after second mating (medium and high dose groups)
- no effect reported in the prenatal developmental toxicity study

Regarding your question on the method to detect implantation site: The numbers of implantation sites per uterus horn and corpora lutea per ovary were counted and recorded. Implantation sites were counted on the day of necropsy, corpora lutea were usually counted under a microscope after at least one day of fixation in a formalin solution.

Please note that access to individual data of the study report for more details was not available.

Overall, the interpretation made is that the data rather point to a fertility effect as the cause of the reduction of pregnancy although a developmental effect during the gestation cannot be ruled out. The evidence that these effects are due to an impairment of the development is not sufficient to consider a classification for developmental effect.

RAC's response

RAC takes note of the comments.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 01.12.2021 | Germany | C.S.B. GmbH | Company-Importer | 4 |

Comment received

C.S.B. GmbH has no comments on the proposed classification:
Repr. 1B – H360F

Dossier Submitter's Response

Noted.

RAC's response

RAC takes note.

**OTHER HAZARDS AND ENDPOINTS – Eye Hazard**

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 01.12.2021 | Germany | C.S.B. GmbH | Company-Importer | 5 |

Comment received

C.S.B. GmbH agrees with the proposed classification:
Eye Dam. 1 – H318

Dossier Submitter's Response

Thank you for your support.

RAC's response

RAC takes note.

| Date | Country | Organisation | Type of Organisation | Comment number |
|---|---|---|---|---|
| 01.12.2021 | Germany | | MemberState | 6 |

Comment received

The Comments are provided in the confidental attachment

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment DE-CA Comments CLH_Sodium 3-(allyloxy)-2-hydroxypropanesulphonate.pdf

| Dossier Submitter's Response |
| --- |
| Thank you for your support. |
| RAC's response |
| RAC takes note of the comments. |

CONFIDENTIAL ATTACHMENTS
1. DE-CA Comments CLH_Sodium 3-(allyloxy)-2-hydroxypropanesulphonate.pdf [Please refer to comment No. 1, 3, 6]