Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

methyl oct-2-ynoate

EC Number: 203-836-6
CAS Number: 111-12-6

CLH-O-0000007360-81-01/F

Adopted

14 September 2023

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: methyl oct-2-ynoate
EC number: 203-836-6
CAS number: 111-12-6
Dossier submitter: Denmark

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
10.01.2023	Germany		MemberState	1
Comment received				
We appreciate the proposal of the DK CA to classify methyl oct-2-ynoate as a strong skin sensitiser as Skin Sens. 1A, H317 based on animal and human data. There is clear evidence from animal (LLNA, GPMT, Buehler) and human (diagnostic patch test) data that methyl oct-2-ynoate acts as a skin sensitiser. In two reliable LLNAs conducted according to OECD TG 429, the test substance induced skin sensitisation resulting in EC3 values of 0.45 % and < 0.5 %, thus demonstrating a strong sensitising potency of methyl oct-2-ynoate that justifies a classification to Category 1A. The listed GPMT study and the Buehler test were not conducted according to OECD TG, but support the strong potency of methyl oct-2-ynoate as a skin sensitiser, too. Furthermore, methyl oct-2-ynoate elicited skin sensitisation in selected and consecutive dermatitis patients, showing relatively low/moderate and relatively high frequencies of occurrence of skin sensitisation for both groups of patients. The total number of published cases is approximately ~30. However, the exposure to methyl oct-2-ynoate is expected to be relatively low (SCCS, 2012; exposure consideration by DS). The human patch test data consists of 11 datasets: seven with consecutive patients (frequency range 0 - 1.67 %); three with selected patients (frequency range 0.3 – 3 %); one occupational study on selected workers (frequency 25 %). The observed frequencies in the patch tests varied from high to low/moderate frequency. There were three case studies showing late patch test reactions (2 - 4 weeks), including two cases with positive re-testing indicating that the sensitisation was induced by the patch testing which supports the strong potency of methyl oct-2-ynoate as a skin sensitiser. Furthermore, the NOEL-HRIPT-induction of 118 µg/cm2 and the LOEL-HRIPT/Human Maximisation Test				

(HMT), induction of 194 µg/cm2 derived for methyl oct-2-ynoate (Api et al. 2019) was in the range of ≤ 500 µg/cm2 and supports the sub-categorisation of methyl oct-2-ynoate in category 1A.

Altogether, the available data support to classify methyl oct-2-ynoate as a strong skin sensitiser, applying sub-categorisation as Skin Sens. 1A. A concentration limit for skin sensitisers shall be set according to their sensitisation potency and a GCL of 0.1 % is recommended for strong sensitisers.

Of note, the OECD Expert Group on defined Approaches for Skin Sensitisation and methyl oct-2-ynoate as a reference substance and classified the substance as Skin Sens. 1 A based on both HMT/HRIPT and CCNA data.

Note: As described by the DS, methyl oct-2-ynoate has to be listed on the ingredient label of a cosmetic product if the concentration is ≥ 10 ppm (0.001 %) in leave-on products or ≥ 100 ppm (0.01 %) in rinse-off products (Cosmetic Regulation 1223/2009). These limits were set, based on a pragmatic administrative decision, because at the time of decision data were insufficient to allow for the determination of a dose-response relationship and/or thresholds (SCCNFP opinion, 2019).

In its opinion from 1999, the SCCNFP stated that methyl oct-2-ynoate is restricted to 0.01 % in consumer products (IFRA guideline), because of a strong sensitising potential. "This is based on a private communication to IFRA ".

More recent IFRA standard limits for methyl oct-2-ynoate (2020) for most (leave-on) product types are below 0.1 % (Table 10 of the CLH proposal).

Dossier Submitter's Response
Thank you for these additional informations and your support.
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
12.01.2023	France		MemberState	2

Comment received

Animal data: Although the lack of information may be unfortunate regarding the available GPMT study and the Buehler test (no information about the vehicle, whether skin irritation was observed at the induction phase…), we agree that these studies are supportive of the two positive LLNA which are the key studies showing a strong sensitising potency of methyl oct-2-ynoate (EC3 < 0.5%). Thus, based on animal data, methyl oct-2-ynoate fulfils criteria for classification Skin Sens. 1A according to the CLP guidance.

Human data: The estimated score of 1 for methyl oct-2-ynoate regarding repeated exposure in the table p20 is inconsistent with the score (e.g. 2) taken into account for setting the exposure index. In view of the information provided from the SCCS ("the exposure to […] methyl-2-octynoate […] may appear to be low"), it seems that a score of 1 is appropriate. In any case, a score of 1 or 2 regarding repeated exposure would not have changed the conclusion "relatively low exposure" as the exposure index would have remained between 1 and 4.
Based on human data showing relatively low exposure and relatively low frequency of occurrence of skin sensitisation, we agree with the conclusion "category 1 or case by case evaluation".

Weight of evidence: Animal and human data do not lead to the same proposal of classification (cat. 1A vs. cat 1). Nevertheless, they do not show conflicting results: as animal data, human data show sensitising effects of methyl oct-2-ynoate, in particular strong potency of the substance in three case studies showing late patch test reactions. Based on the positive LLNAs and these three case studies, both showing strong potency of methyl oct-2-ynoate, we agree with the DS' proposal of classification Skin Sens. 1A with no specific concentration limit and with the GCL of 0.1% w/v.
Dossier Submitter's Response
Thank you for your support.
RAC's response
Noted.