

COMPILED COMMENTS ON CLH CONSULTATION

Comments provided during consultation are made available in the table below as submitted through the web form. Please note that the comments displayed below may have been accompanied by attachments which are listed in this table and included in a zip file if non-confidential. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Last data extracted on 26.10.2020

Substance name: 1-phenylethan-1-one (1-phenylethylidene)hydrazone

CAS number: 729-43-1

EC number: 211-979-0

Dossier submitter: France

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
16.10.2020	Germany		MemberState	1
Comment received				
<p>We support the classification of 1-phenylethan-1-one (1-phenylethylidene)hydrazone (CAS no. 729-43-1) as skin sensitiser. Four human cases (children and adult) are reported, showing that the substance elicited positive patch test reactions. The well-conducted studies show a relationship between sports equipment (shin pads, sneakers)-induced contact dermatitis and the role of 1-phenylethan-1-one (1-phenylethylidene)hydrazone in skin sensitisation. Classification is supported by positive results from in vitro studies for skin sensitisation and alerts for skin sensitisation based on QSAR modelling. In contrast, in an LLNA (Klimish score 1) ace-topnenone azine did not show a sensitisation potential at concentrations of 1 %, 2.5 % and 5 % (SI values: 0.7, 0.4, and 0.5), challenging a strong skin sensitising potential of 1-phenylethan-1-one (1-phenylethylidene)hydrazone. However, 1-phenylethan-1-one (1-phenylethylidene)hydrazone was identified as a new emerging substance to cause skin allergies in humans (more case reports have been published recently) with to some extent high severities of responses (hospitalisation and generalised dermatitis).</p> <p>Based on the available data, we support the classification of 1-phenylethan-1-one (1-phenylethylidene)hydrazone as Skin Sens.1, without sub-categorisation. A recommendation for the GCL or SCL should be given.</p>				

Date	Country	Organisation	Type of Organisation	Comment number
22.10.2020	Belgium		Individual	2
Comment received				
<p>Bonjour,</p> <p>Mon fils (10 ans) développe un eczéma allergique très sévère au contact avec une substance chimique particulière (acétophénone azine) qui est en consultation actuellement sur le site de l'ECHA.</p> <p>Propositions CLH: 5</p> <ul style="list-style-type: none">• Date de début: 24/08/2020• Date limite: 23/10/2020 <p>Il est suivi par le service dermatologie des cliniques universitaires St Luc à BRUXELLES (Docteurs <confidential> et <confidential>) Cette substance est présente dans les</p>				

équipements sportifs. Il est important qu'elle puisse être identifiée par un étiquetage spécial afin que les consommateurs puissent l'éviter en cas d'allergie.
D'avance, je vous remercie.

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment photos GL.docx

Date	Country	Organisation	Type of Organisation	Comment number
23.10.2020	Sweden		MemberState	3

Comment received

In the CLH-proposal the dossier submitter presents 4 case reports of 3 children and one adult with allergic skin reactions to 1-phenylethan-1-one (1-phenylethylidene)hydrazone from shin pads and shoes. Some of the cases report severe reactions (one case with hospitalization and one with generalized dermatitis) indicating that 1-phenylethan-1-one (1-phenylethylidene)hydrazone is a potent skin sensitizer. Following the submission of the CLH-dossier at least 2 more case reports have been published (see references below).

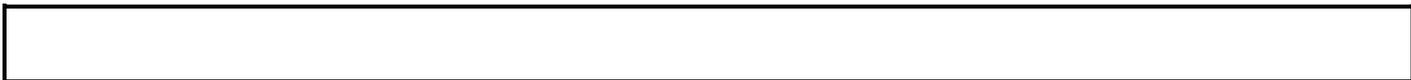
The human data is supported by two positive in vitro test results from key events 2 (OECD TG 442D; Keratinosens) and 3 (h-CLAT; OECD TG 442E) in the AOP for skin sensitisation. These two in vitro tests are included in the "2 out of 3" defined approach that is not yet accepted by the OECD for assessing skin sensitisation potential, but since the results of the two tests are concordant the SE CA considers that the outcome can be used to indicate such potential. Moreover, the available data is further supported by alerts for skin sensitisation potential by QSAR modeling (Derek Nexus and Caesar). QSAR modeling is a widely accepted in silico tool for prediction of health hazards of substances.

The dossier submitter also presents results from a negative LLNA test in mice, including a discussion on findings that could point to that it may be a false negative. The SE CA agrees that a SI>3 could not be excluded since the maximum concentration tested was low (only 5%) and that the results from the positive and negative controls are somewhat conflicting. On the other hand, from the lack of clear dose response (SI values of 0.7, 0.4 and 0.5 at concentrations of 5, 2.5 and 1% (w/v)) there is little indication that using a higher concentration would result in a much higher SI value. It would be helpful if the dossier submitter could elaborate on the rationale behind the dose selection in the study.

The evidence of the skin sensitizing properties of 1-phenylethan-1-one (1-phenylethylidene)hydrazone presented by the dossier submitter is in our view limited. However, there are positive findings from at least 4 human patch tests that cannot be negated by the LLNA test results. Moreover, it cannot be excluded that the low number of current cases could reflect that the substance has not yet been used for a sufficient period for more cases to emerge, and/or underreporting. The in vitro/silico data presented in the CLH-report supports the skin sensitizing properties demonstrated by the human patch tests and additional new studies in the scientific literature could be used as further evidence. Overall, the SE CA concurs with the dossier submitter that the substance is a skin sensitizer in Category 1 based on a weight of evidence assessment and using expert judgement. Sub-categorization is not possible based on the reported results.

1) Koumaki D, Bergendorff O, Bruze M, Orton D. Allergic Contact Dermatitis to Shin Pads in a Hockey Player: Acetophenone Is an Emerging Allergen. *Dermatitis*. 2019 Mar/Apr;30(2):162-163.

2) Besner Morin C, Stanciu M, Miedzybrodzki B, Sasseville D. Allergic contact dermatitis from acetophenone azine in a Canadian child. *Contact Dermatitis*. 2020 Jul;83(1):41-42.



CONFIDENTIAL ATTACHMENTS

1. photos GL.docx [Please refer to comment No. 2]