Scientific Committee on Consumer Safety

SCCS

SCIENTIFIC ADVICE ON on the threshold for the warning 'contains formaldehyde' in Annex V, preamble point 2 for formaldehyde-releasing substances

The SCCS adopted this scientific advice
by written procedure on 7 May 2021

ACKNOWLEDGMENTS

Members of the Working Group are acknowledged for their valuable contribution to this Opinion. The members of the Working Group are:

SCCS members:
Dr U. Bernauer
Dr L. Bodin
Prof. Q. Chaudhry (SCCS Chair)
Prof. P.J. Coenraads (SCCS Vice-Chair and Chairperson of the WG)
Prof. M. Dusinska
Dr J. Ezendam
Dr E. Gaffet
Prof. C. L. Galli
Dr B. Granum
Prof. E. Panteri
Prof. V. Rogiers (SCCS Vice-Chair)
Dr C. Rousselle
Dr M. Stepnik
Prof. T. Vanhaecke
Dr S. Wijnhoven

SCCS external experts:
Dr A. Koutsodimou
Prof. W. Uter (Rapporteur)
Dr N. von Goetz

All Declarations of Working Group members are available on the following webpage: Register of Commission expert groups and other similar entities (europa.eu)

This scientific advice is not subject to a commenting period.

1. ABSTRACT

The SCCS concludes the following:

1. In light of the data provided and taking under consideration the available scientific literature, does the SCCS consider the 0.05% threshold for labelling formaldehyde releasing substances adequate to protect consumers?

The SCCS considers that the present threshold does not sufficiently protect consumers sensitised to formaldehyde from exposure to free formaldehyde from formaldehyde releasers.

2. Does the SCCS consider necessary to change the 0.05% threshold and at which level?

Reducing the present threshold by a factor of 50, that is, to 0.001% (10 ppm), will protect the vast majority of consumers sensitised to formaldehyde. This threshold applies to the total free formaldehyde irrespective of whether a product contains one or more formaldehyde releaser(s).

Keywords: SCCS, scientific advice, formaldehyde, Regulation 1223/2009, CAS No. 50-00-0, EC No. 200-001-8, SCCS/1632/21

Document to be cited as: SCCS (Scientific Committee on Consumer Safety), Scientific advice on the threshold for the warning 'contains formaldehyde' in Annex V, preamble point 2 for formaldehyde-releasing substances, final version of 7 May 2021, SCCS/1632/21

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Two independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.
They are: the Scientific Committee on Consumer Safety (SCCS) and the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) and are made up of scientists appointed in their personal capacity.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Agency (EMA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCCS

The Committee shall provide Opinions on questions concerning all types of health and safety risks (notably chemical, biological, mechanical and other physical risks) of non-food consumer products (for example: cosmetic products and their ingredients, toys, textiles, clothing, personal care and household products such as detergents, etc.) and services (for example: tattooing, artificial sun tanning, etc.).

Scientific Committee members

Ulrike Bernauer, Laurent Bodin, Qasim Chaudhry, Pieter Jan Coenraads, Maria Dusinska, Janine Ezendam, Eric Gaffet, Corrado Lodovico Galli, Berit Granum, Eirini Panteri, Vera Rogiers, Christophe Rousselle, Maciej Stepnik, Tamara Vanhaecke, Natalie von Götz, Susan Wijnhoven

Contact

European Commission
Health and Food Safety
Directorate C: Public Health
Unit C2: Health information and integration in all policies
L-2920 Luxembourg
SANTE-SCCS@ec.europa.eu

PDF ISSN 1831-4767 ISBN 978-92-76-54758-7 doi:10.2875/269855 EW-AQ-22-009-EN-N

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2. MANDATE FROM THE EUROPEAN COMMISSION

Background

Formaldehyde (CAS No. 50-00-0, EC No. 200-001-8) was classified as carcinogen (category 1B) by Commission Regulation (EU) No 605/2014; in addition, the substance is also classified as skin sensitizer Cat. 1 (H317 May cause an allergic skin reaction).

In November 2014, the SCCS concluded in its opinion SCCS/1538/14[1] that nail hardeners with a maximum concentration of about 2,2 % of free formaldehyde can be used safely to harden or strengthen nails.

However, the discussions in the Working Group on Cosmetic Products concluded that suitable alternative substances were available and hence a derogation request under Art. 15(2) was rejected. Consequently, the Commission Regulation (EU) No 831/2019 delisted formaldehyde from Annex V (preservatives) and added to the list of substances prohibited in cosmetic products in Annex II (entry 1577).

Annex V contains a number of substances that are releasing formaldehyde in order to achieve a preserving function on the final cosmetic product (so called formaldehyde releasers). In addition, point 2 of the preamble of Annex V requires that:

"*All finished products containing substances in this Annex and which release formaldehyde must be labelled with the warning 'contains formaldehyde' where the concentration of formaldehyde in the finished product exceeds 0.05 %".*

This labelling had been introduced by the *Eighth Commission Directive 86/199/EEC* of 26 March 1986 with the intention to inform/warn consumers on the presence of a substance that could trigger an allergic reaction (e.g. in people sensitised to formaldehyde).

In 2020, the Commission services received additional information suggesting that formaldehyde exposure to levels below 0.05% could cause contact dermatitis in persons with formaldehyde allergy, questioning the current provisions concerning the labelling of such substances in Annex V.

Terms of reference

1. *In light of the data provided and taking under consideration the available scientific literature does the SCCS consider the 0.05% threshold for labelling formaldehyde releasing substances adequate to protect consumers??*

2. *Does the SCCS consider necessary to change the 0.05% threshold and at which level?*

[1] https://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_164.pdf

3. SCIENTIFIC ADVICE

3.1 FUNCTION AND USES

Formaldehyde as such has been added to the list of substances prohibited in cosmetic products in Annex II (entry 1577). However, formaldehyde is still present in cosmetic products via the so-called formaldehyde releasers (FRs). The FRs are quite commonly used in cosmetics, e.g. in 7.9% of 4680 cosmetic products surveyed 2006-9 in Germany, with large variation between different product types, including both leave-on and rinse-off products (1), or in 25% of 496 examined Dutch skin care products, and 23.8% of 8057 US products (2).

3.2 TOXICOLOGICAL EVALUATION

The toxicological evaluation of formaldehyde is covered under SCCS/1538/14, including acute toxicity, irritation of skin, eye and respiratory tract, skin sensitisation and repeat dose and developmental toxicity. Recently, a restriction of formaldehyde and FRs regarding inhalation exposure has been established by the RAC/SEAC (ECHA/RAC/RES-O-0000006740-76-01/F and ECHA/SEAC/RES-O-0000006931-71-01/F, respectively).

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This advice only addresses skin sensitisation to formaldehyde as liberated by FRs. Skin sensitisation induced by FRs themselves, and the amount of cross-reactivity between FRs and formaldehyde in patch tests or other tests is outside the scope of this advice.

Skin exposure

As a lower tier, conservative scenario for aggregate exposure to leave-on cosmetics, aggregate exposure of the hand by applying body lotion, face cream, and hand cream was selected. Assuming the daily quantities and respective surface areas as per Notes of Guidance, except for using the same dose per area for body lotion as for hand cream, this is estimated to result in about 7.75 mg/cm² cosmetic product per day on the palms. Assuming the current warning threshold concentration of free formaldehyde of 0.05% (500 ppm) in all of these cosmetic products as a result of the use of one or more FRs as preservative(s), such product exposure would translate to a dose per area (dose/area) of 3.9 µg/cm² formaldehyde per day, repetitively, day after day. Of note, this must be regarded as a lower limit exposure estimate, owing to additional every-day exposures e.g. via rinse-off cosmetic products, where FRs are commonly used (1).

Actual formaldehyde levels from FR were analysed using a modified HPLC method: Doi *et al*. detected > 30 mg/kg (> 30 ppm) in 83 of 89 cosmetic product samples containing different FRs, and > 250 ppm in 44/89 samples (3). As summarised in a review by de Groot *et al*. "… all releasers (with the exception of 2-bromo-2-nitropropane-1,3-diol, for which adequate data are lacking) can, in the right circumstances of concentration and product composition, release >200 ppm formaldehyde, which may result in allergic contact dermatitis." (4).

Contact allergy to formaldehyde released by FRs

The repeated open application test (ROAT) simulates, in a standardised fashion, actual (cosmetic) product use. In short, the procedure involves twice daily open application of a certain volume of matrix on a defined skin area (often 5x5 cm²) containing a defined amount (and correspondingly dose/area) of a substance examined for causing an elicitation reaction, i.e., allergic contact dermatitis (ACD). As in real life, application is continued day after day – in the ROAT normally for up to four weeks (or until ACD occurs) – to reflect cumulative exposure. Thereby, evidence contributed by such standardised ROAT studies is best suited to derive elicitation threshold doses, such as the "Eliciting Dose 10" (ED_{10}) leading to ACD in 10% of sensitised individuals, or a dose/area not leading to an elicitation reaction in the sensitised. This information can directly be related to consumer exposure, and used for objectives of secondary prevention.

A number of different ROAT studies using different FRs trying to elicit ACD in formaldehyde allergic individuals have been reviewed in 2010 by de Groot *et al.* (4). These studies illustrate that on normal skin, concentrations of free formaldehyde of 130-370 ppm, as released by different FRs, are clearly capable of eliciting ACD in formaldehyde-sensitised individuals (5–8).

In a more recent modified ROAT study by Hauksson *et al.* (9), an originally FR-free moisturiser was spiked with 0.6% (the maximum permitted concentration according to Annex V/33 of the Cosmetics Regulation), 0.33%, 0.06% vs. no DMDM hydantoin, releasing at least 40 ppm, 20-40 ppm, 2.5-10 ppm, and no formaldehyde, respectively, (9). NB: 40 ppm twice daily correspond to 0.16 µg formaldehyde/cm² per day, with 2 mg/cm² matrix application. This ROAT study had been modified by inducing slight, acute irritant contact dermatitis before twice daily applications of above-mentioned moisturiser were started. The usual twice daily open application was rendered more sensitive by pre-irritation, that is, represents a worst-case, but not uncommon scenario regarding the condition of the skin. As result, 9/15 formaldehyde allergic subjects vs. 0/12 non-allergic controls reacted to a moisturizer with at least 40 ppm free formaldehyde, and 6/15 to the range of 20-40 ppm; both comparisons yielding statistical significance (9). The lowest concentration level of 2.5-10 ppm formaldehyde did not elicit an allergic reaction. The certainty of this (0/15 reactions) can be quantified with an upper 95% confidence limit of 20% (10), which may be regarded as acceptable. This controlled clinical trial (9) can be regarded as key study, as it offers a direct transfer of results.

Elicitation threshold to formaldehyde

In the diagnostic patch test, with its single occlusive application of the hapten, the ED_{10} for formaldehyde has been estimated to be 20.1 µg/cm² (95% CI: 4.09-43.9 µg/cm²) (11), based on data from a previous study (7). In order to quantify the relationship between an ED_{xx} in the patch test and an ED eliciting the same proportion of sensitised individuals in a ROAT, with its twice daily open application, the eliciting doses have been modelled and compared between the two application methods for a few allergens for which such data were available (12). It has been suggested that for volatile compounds (like formaldehyde) the ED_{xx} is higher by a factor of ~ 10 in the patch test, compared to a ROAT (12). Hence, a dose per area capable of eliciting allergic reactions in 10% of sensitised persons via twice daily open application of formaldehyde could be estimated to be around 2 µg/cm² (95% CI: 0.41-4.4 µg/cm²). As a limitation, this approach relies on (i) one single patch test study (7), and (ii) a hitherto unvalidated putative "adjustment factor" of 10 for volatile compounds not based on results with formaldehyde, but with the fragrances isoeugenol and hydroxyisohexyl 3-cyclohexene carboxaldehyde (12).

SCCS conclusion
There is sufficient evidence that the present warning threshold limit of 500 ppm is insufficient to protect formaldehyde-sensitive subjects from elicitation of ACD by FR-containing cosmetic products. This is supported by several ROAT studies, all reporting elicitation by lower levels of free formaldehyde (4). Moreover, supplemental evidence is contributed by calculations, albeit based on a number of assumptions, comparing daily repeated exposure to 500 ppm free formaldehyde via FRs (at least 3.9 µg/cm²) to an extrapolation of open application from dose-response patch test data with 0.41 µg/cm² as the lower 95% confidence limit of an ED_{10}. This comparison indicates that a sufficiently protective threshold must be lower by at least a factor of ~ 10.

However, the conclusion by SCCS regarding a suitable threshold concentration for labelling is based on evidence from (9), as this ROAT study provides compelling, directly usable evidence that concentrations of 20-40 ppm still elicit a large share of formaldehyde-allergic subjects, while a concentration of up to 10 ppm was safe in this regard. Hence, the SCCS concludes that by reducing the present cut-off by a factor of 50, that is, to 10 ppm (0.001%), the vast majority of persons sensitised to formaldehyde will be protected.

While this can be derived for leave-on cosmetic products (as used in the study (9)), there is no direct evidence available concerning rinse-off cosmetic products, as all ROAT studies with FRs had been performed with leave-on cosmetics/preparations (4,9). However, evidence contributed from another allergen, methylisothiazolinone, indicates elicitation doses in ROAT studies with leave-on and rinse-off application, respectively, may indeed be very similar: 7/9 MI-sensitised patients developed ACD following exposure to 50 ppm MI via a cream (13), and 7/9 following rinse-off exposure to 50 ppm MI in another study with different patients (14). Therefore, it seems justified to also apply the recommended threshold level to rinse-off cosmetics.

4. CONCLUSION

1. *In light of the data provided and taking under consideration the available scientific literature, does the SCCS consider the 0.05% threshold for labelling formaldehyde releasing substances adequate to protect consumers?*

   The SCCS considers that the present threshold does not sufficiently protect consumers sensitised to formaldehyde from exposure to free formaldehyde from formaldehyde releasers.

2. *Does the SCCS consider necessary to change the 0.05% threshold and at which level?*

   Reducing the present threshold by a factor of 50, that is, to 0.001% (10 ppm), will protect the vast majority of consumers sensitised to formaldehyde. This threshold applies to the total free formaldehyde irrespective of whether a product contains one or more formaldehyde releaser(s).

5. MINORITY OPINION

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7. GLOSSARY OF TERMS

See SCCS/1628/21, 11th Revision of the SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation – from page 181

8. LIST OF ABBREVIATIONS

See SCCS/1628/21, 11th Revision of the SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation – from page 181

Additional abbreviations:

CI	Confidence interval
ED_{xx}	Eliciting dose for xx % of sensitised persons
FR	Formaldehyde releaser
ROAT	Repeated open application test