



EUROPEAN COMMISSION

Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs

Dir F: Ecosystems I: Chemicals, food, Retail

Unit F2: Bioeconomy, Chemicals & Cosmetics

SCIENTIFIC COMMITTEE ON CONSUMER SAFETY (SCCS)

Request for a scientific opinion **on Citral (CAS No. 5392-40-5, EC No. 226-394-6) on sensitisation endpoint**

Commission Department requesting the Opinion: Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs

1. Background on Quantitative Risk Assessment (QRA)

Skin allergies may arise from exposure to certain chemicals and may lead to Allergic Contact Dermatitis (ACD). This adverse health effect, especially from fragrance ingredients is a common and relevant problem from exposure to cosmetic and other household products. Therefore, it is a topic of high interest for consumers, industry and Regulatory Authorities.

A model for dermal sensitisation quantitative risk assessment (QRA) was developed and implemented by the International Fragrance Association (IFRA). The methodology relied on thresholds (no effect or low effect levels) established in healthy human volunteers and/or in animal experiments. A set of safety factors were applied to derive 'acceptable exposure level'. The QRA methodology was evaluated by the Scientific Committee on Consumer Products (SCCP) in 2008 (SCCP/1153/08)¹ stating that there was no confidence that the levels of skin sensitisers identified by QRA are safe for the consumer. However, the committee added that models like the QRA approach may, after refinement and validation, be applicable in the future for risk assessment of new substances. In 2012, the SCCS reiterated this position in the context of the opinion on Fragrance Allergens (SCCS/1459/11)².

Following the SCCS opinion of 2012, the International Dialogue for the Evaluation of Allergens (IDEA) was established to improve the risk assessment of fragrance allergens. The IDEA project focused on reviewing the uncertainty factors, introducing dermal aggregate exposure for fragrance ingredients resulting in the QRA2 methodology which was reviewed by the SCCS in 2018 (SCCS/1589/17)³. In that Opinion, SCCS concluded that *'a lot of progress has been achieved since the initial publication of the QRA. However, it is not yet possible to use the QRA2 to establish a concentration at which induction of sensitisation of fragrance is unlikely to occur...A number of additional considerations and refinements have been incorporated to the proposed methodology. However, explanation of certain methodological approaches and assumptions, as well as a description of uncertainties is lacking, the*

¹ https://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_135.pdf

² https://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_102.pdf

³ https://ec.europa.eu/health/sites/default/files/scientific_committees/consumer_safety/docs/sccs_o_211.pdf

provision of which would enhance understanding of the methodology. These aspects have been highlighted in the SCCS comments under each section with the aim to provide pointers for improvement. If shaped up properly, this could be a useful methodology not only for risk assessment of fragrance allergens, but potentially also for other cosmetic ingredients’.

The IDEA project continued its work in order to further improve and refine the QRA2 methodology resulting in a peer-reviewed publication⁴. In December 2021, IFRA submitted a dossier on derived safe use levels for the fragrance ingredient Citral by applying the refined QRA2 methodology based on the induction of skin sensitisation.

2. Background on Citral

Citral (CAS No. 5392-40-5, EC No. 226-394-6) with the chemical name ‘3,7-Dimethyl-2,6-octadienal’ is a mixture of neral and geranial, which are monoterpene aldehydes. It is widely used as both a fragrance and flavour ingredient in food, beverages and various cosmetic and household products due to its distinct, acceptable, and lemon-like pleasant odour. Citral is also a common constituent of many essential oils, such as lemongrass and *Litsea cubeba* oils.

Citral has been subject to a safety evaluation by SCCP in 2008 (SCCP/1153/08)⁵ using the QRA methodology and by the SCCS in 2012 (SCCS/1459/11)⁶ in the context of the opinion on Fragrance Allergens. Citral is currently regulated as a fragrance ingredient in cosmetic products in entry 70 of Annex III to the Cosmetics Regulation⁷. In particular, the presence of the substance must be indicated in the list of ingredients referred to in Article 19(1)g of the Cosmetics Regulation when its concentration exceeds 0.001% in leave-on products and 0.01% in rinse-off products.

In light of the information provided, the Commission requests the SCCS to assess whether the derived safe use levels for Citral by application of the QRA2 based on the induction of skin sensitisation is adequate to protect consumers.

3. Terms of reference

- (1) *In light of the data provided and taking under consideration the derived upper safe levels using QRA2 methodology for the sensitisation endpoint, does the SCCS consider Citral safe when used as a fragrance ingredient in cosmetic products up to the maximum concentrations provided in the dossier submission?*
- (2) *Does the SCCS have any further scientific concerns with regard to the use of QRA2 to derive safe upper levels for Citral or for fragrance allergens in general?*

⁴ Api et. al., Updating exposure assessment for skin sensitisation quantitative risk assessment for fragrance materials, Regul. Toxicol. Pharmacol. 118 (2020) 1 - 12).

⁵ https://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_135.pdf

⁶ https://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_102.pdf

⁷ <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02009R1223-20211001>

4. Deadline

9 months.

5. Supporting documents

Dossier submission on sensitisation endpoint for Citral using the QRA2 methodology.

The SCCS approved this mandate by written procedure on 16 February 2022.

→ Due to the reception of additional information in autumn 2023, the deadline has been postponed accordingly, in agreement with mandating DG GROW.