Regulatory Toxicology and Pharmacology 127 (2021) 105052

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

The SCCS Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation, 11th revision, 30–31 March 2021, SCCS/1628/21

SCCS members, Other experts

ARTICLE INFO

Handling editor: Dr. Lesa Aylward

Keywords:
SCCS
SCCS Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation
11th revision
SCCS/1628/21
Alternative method
NAM
New approach methodology
Risk assessment
NGRA
Next generation risk assessment
Cosmetics
Guidance

ABSTRACT

The "SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation, 11 th Revision" (SCCS/1628/21) contains relevant and updated information on the different aspects of testing and safety evaluation of cosmetic substances in Europe. The emphasis is on cosmetic ingredients for which a concern has been expressed for human health. Indirectly, the Guidance also provides some advice on the safety of finished products. A general aim is to improve harmonised compliance with the current cosmetic EU legislation, Regulation (EC) No 1223/2009, for which animal testing and marketing bans fully apply from 2013 onwards. This means that no *in vivo* testing of ingredients or finished products is allowed in Europe for the purpose of cosmetics. For this reason, the SCCS has closely followed the progress made in regard to the development and validation of alternative replacement methods, also referred to as new approach methodology (NAM). The "SCCS Notes of Guidance" are regularly revised and updated in order to incorporate progress made and experience gained over time, in particular on the use of NAMs, and the new methods and data that became available since previous revision (SCCS/1602/18) formed the basis of the current (11 th) Revision.

The "SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation, 11th Revision" (SCCS/1628/21SCCS/1628/21) is a document compiled by the members of the Scientific Committee on Consumer Safety (SCCS). It contains relevant information on the different aspects of testing and safety evaluation of cosmetic substances in Europe. The emphasis of this guidance document is on cosmetic ingredients, in particular those substances for which some concern has been expressed for human health. These regulated substances are the so-called Annex substances since they are listed in dedicated Annexes to the cosmetic legislation, Regulation (EC) No 1223/2009. There are 2 negative lists (Annexes II and III) and 3 positive lists (Annexes IV, V and VI). Annex II contains forbidden substances, usually pharmaceutical ingredients. Annex III substances are in general forbidden and only allowed at certain concentrations and in specific applications (e.g. hair dyes). Annexes IV, V and VI contain permitted colorants, preservatives and UV-filters, respectively. If one of these functions is necessary in a cosmetic product, the ingredient must be taken from one of these lists according to the needed functionality. Otherwise, the use of such ingredients in a cosmetic product would be illegal and could even be harmful to health.

Although the SCCS Notes of Guidance are designed to provide guidance on the ANNEX substances to public authorities and to the cosmetic industry, to improve harmonised compliance with the current cosmetic EU Regulation, they also provide some guidance indirectly for the safety assessment of finished cosmetic products. According to the Cosmetic Regulation, animal testing and marketing bans fully apply from 2013 onwards. The *in vivo* testing of finished products was banned after 11 March 2004, and in vivo testing for local toxicity after 11 March 2009. Subsequently, a complete ban on in vivo testing was placed from 11 March 2013 – including for repeated dose toxicity, toxicokinetics and developmental toxicity. For this reason, the SCCS has closely followed the progress made in regard to the development and validation of alternative methods, with emphasis on "replacement" methodologies, which essentially means only 1 "R" is allowed under to the cosmetics Regulation out of the "3R-principle" of Russell and Burch (Refinement, Reduction, Replacement of animals used in laboratory procedures).

The "SCCS Notes of Guidance" are regularly revised and updated to incorporate the progress of scientific knowledge in general, and the experience gained over time, in particular on the use of New Approach Methodologies (NAMs) and the Next Generation Risk Assessment (NGRA) framework. The SCCS Notes of Guidance take both new concepts into consideration and these are applied whenever the information accompanying a Commission's mandate to the SCCS on safety evaluation of cosmetic ingredient(s) is not comprised of in vivo data, but only results from *in vitro* assays, *in silico* modelling, and read-across.

Since the previous revision (SCCS/1602/18), several new addenda,

https://doi.org/10.1016/j.yrtph.2021.105052
Received 10 September 2021; Accepted 29 September 2021
Available online 13 October 2021

opinions and memoranda of importance to the content of this guidance document have been adopted and they form the basis of the 11th revision. Changes and updates are in particularly implemented covering the following aspects:

(i) Different inhalation models for cosmetic substances that can be inhaled in the form of powder, vapor, aerosolised droplets or aerosolised particles are described.
(ii) *In silico* methodology, covering Quantitative Structure Activity Relationship (QSAR) as well as Read-across are described, including pros and cons and examples of free-access software platforms. For the specific case of genotoxicity and carcinogenicity, the available programs that are free downloadable are indicated.
(iii) A general update is included on the available and validated NAMs. Also, robust values for the concept of Threshold of Toxicological Concern (TTC) are given for genotoxic and non-genotoxic compounds.
(iv) A comprehensive list of scientific concerns for the safety of nanomaterials has been added, and a reference is made to a separate SCCS updated Guidance on the Safety Assessment of Nanomaterials in Cosmetics (SCCS/1611/19).
(v) The section on endocrine disruptors has been extended and the important limitations of the use of NAMs in this critical domain have been highlighted.
(vi) A discussion on the necessity of introducing uncertainty factors in a number of specific cases has been included (dermal and oral absorption, extrapolation of the Point of Departure (PoD) derived from a 28-day repeated dose toxicity study towards the potential value of a 90-day subchronic toxicity study, etc).
(vii) A number of appendices to the SCCS Notes of Guidance have been added (microbiological quality of the finished product; free access to *in silico* mutagenicity/genotoxicity databases; inhalation parameterisation; Lifetime Cancer Risk Approach; PoD used for TTC derivation).

The SCCS Notes of Guidance remains a living document and will be regularly updated in the future. Any observation on this Guidance may be sent to SCCS mailbox (SANTE-C2-SCCS@ec.europa.eu) for further consideration by the SCCS.

Funding body information

None.

CRediT authorship contribution statement

Ulrike Bernauer: Writing – original draft, Writing – review & editing, SCCS member. **Laurent Bodin:** Writing – original draft, Writing – review & editing, SCCS member. **Qasim Chaudhry:** Writing – original draft, Writing – review & editing, SCCS member. **Pieter Jan Coenraads:** Writing – original draft, Writing – review & editing, SCCS member. **Maria Dusinska:** Writing – original draft, Writing – review & editing, SCCS member. **Janine Ezendam:** Writing – original draft, Writing – review & editing, SCCS member. **Eric Gaffet:** Writing – original draft, Writing – review & editing, SCCS member. **Corrado L. Galli:** Writing – original draft, Writing – review & editing, SCCS member. **Berit Granum:** Writing – original draft, Writing – review & editing, SCCS member. **Eirini Panteri:** Writing – original draft, Writing – review & editing, SCCS member. **Vera Rogiers rapporteur:** Writing - original draft, Writing - review and editing, SCCS member (rapporteur). **Christophe Rousselle:** Writing – original draft, Writing – review & editing, SCCS member. **Maciej Stepnik:** Writing – original draft, Writing – review & editing, SCCS member. **Tamara Vanhaecke:** Haecke, Writing – original draft, Writing – review & editing, SCCS member. **Susan Wijnhoven:** Writing – original draft, Writing – review & editing, SCCS member. **Aglaia Koutsodimou:** Writing – original draft, Writing – review & editing, SCCS external expert. **W. Uter:** Writing – original draft, Writing – review & editing, SCCS external expert. **Natalie von Goetz:** Writing - original draft, Writing - review & editing, SCCS external expert.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Reference

The SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation 11th Revision, March 2021, pp. 30–31. SCCS/1628/21, may be read in full on the website of the European Commission's independent Scientific Committees: sccs_o_250.pdf (europa.eu).