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EXPLANATORY NOTE ON THE MODIFICATIONS OF THE SCCS OPINION ON NITROSAMINES AND SECONDARY AMINES FOLLOWING THE PUBLIC CONSULTATION ON THE PRE-CONSULTATION OPINION

This note sets out the rationale for the modifications made to the opinion of the European Commission Scientific Committee on Consumer Safety (SCCS) on **Nitrosamines and Secondary amines** following a public consultation conducted between 19 December 2011 and 10 February 2012.

Introduction

The European Commission requested the Scientific Committee on Consumer Safety to assess the potential risks to human health by the presence in cosmetics of nitrosamines or of chemicals with secondary amine groups which may give rise to N-nitroso compounds, and to provide guidance to the Commission in revising the relevant entries of Annexes II and III of the Cosmetics directive (76/768/EEC). A SCCS Working Group comprising of 2 members of the SCCS, 1 member of the SCHER and 3 experts from academia with experience on the subject was formed. The WG produced a draft opinion which was discussed and adopted by the SCCS plenary on 13-14 December 2011 as a preliminary opinion suitable for public consultation (pre-consultation opinion).

In line with its procedures for stakeholder dialogue, implemented in the Rules of Procedures of the new Scientific Committees set up by Commission Decision 2008/721/EC of 5 September 2008, the European Commission Health and Consumers Directorate General (DG SANCO) conducted a public consultation on the pre-consultation opinion of SCCS between 19 December 2011 and 10 February 2012.

Results/participation

By the deadline, DG SANCO received a total of 3 contributions of which the majority agreed or mostly agreed to the conclusions of the opinion. All of them were reviewed by the Working Group and appropriate modifications introduced into the opinion, which was then discussed and adopted as the final opinion by the SCCS at its plenary of 27 March 2012.

Modifications to the opinion

The opinion has been modified to take into account all submitted comments which were assessed by the Working Group to be pertinent and relevant for the subject matter and which were within the competences of the Scientific Committees and respected the clear separation between risk assessment and risk management that underpins the Scientific Advisory structure of the European Commission. Comments on policy, risk management, legal clarification, ethics, the precautionary principle, were not considered as, although pertinent to the subject matter, they are outside the competences of the Scientific Committees.

Detailed explanations of the way the comments received were treated by the SCCS are provided below. The numbering of pages and sections correspond to the final opinion adopted by the SCCS on the 27 March which is published together with this document.

Comment for which changes to the opinion were made

For the following comments submitted the opinion has been modified in the following manner:

- Background- page 5: The background of the opinion, entry 62, has been modified to reflect the text of the Cosmetic Regulation.
- Section 4.3.2 –page 12: the Apparent Total N-nitroso group Content (ATNC) has been modified to explain its reliability. This term has replaced the term TNOC in order to bring consistency in the nomenclature.
- Section 4.3.1 page 14, table 1: the chemical structure of hair dye A84 has been corrected.
- Section 4.7, page 23: the answer to the question "*Comment on the levels of 50 µg nitrosamine/ kg*" has been extended to address whether this limit refers also to finished products. The following answer has been added: *This limit (50 µg nitrosamine/ kg) does not apply to finished products. The secondary amine content in the finished product determines the content of nitrosamines potentially formed.*
- Section 4.8.1, page 23: the answer on the specific cases of spermidine, gerotine and dipropylenetriamine has been refined to clarify that the SCCS considers them under the *term secondary alkylamine.*
- Annexes – page 30, table1: figures from the table on T25 for NDELA have been recalculated according to the new information added to this table: *The experiment by Berger et al.(1990) has been excluded from the calculation of the mean as it is more than 7 times standard deviation above the mean.* As a consequence mean T25 and mean HT25 changed. See also changes in table 3, NDELA- page 21. page 44 changes were also made when calculating BMDL-10 values for NDELA and NMOR.

Comments for which no changes could be made

In addition to the comments received which resulted in the above changes, the following comments were received and evaluated by the SCCS but no changes were introduced in the opinion. The main reasons for this are: 1) comments were outside the scope of the terms of reference for this opinion; 2) comments were outside the competences of the

Scientific Committees (and SCCS in this case) as they concerned policy and risk management issues; 3) in the scientific judgement of the SCCS, the submitted scientific evidence and argumentation were not of sufficient quality and strength to support changes and modifications in the opinion and its conclusions. For reasons of clarity, a brief rationale underpinning the evaluation of each comment is provided for each comment.

- Regarding the comments on the **definition of the regulation** through their potential precursors and control the potential formation of nitrosamines of nitrosamines rather than limiting the use of amines, the SCCS considers this comment to be outside its remit as it concerns regulation and policy.
- The use of the term secondary amine in a regulatory context is too wide and that preference should be given to addressing potential precursors based on chemical categorization. This is, from the SCCS point of view, a regulatory question.
- Concerning the comment on the nitrosating **conditions of excess nitrous acid being unrealistic for cosmetics**, the SCCS takes the position that a scientific result on nitrosation obtained under well controlled laboratory conditions are relevant to judge compounds which may be nitrosated such as these three specific cases of spermidine, gerotine and dipropylentriamine. This is particularly true when information on conditions of production, storage and handling, which could narrow down the conditions to those factors which would enhance nitrosation, is not available.
- Concerning the comment received claiming that **no evidence is provided to show that topical N-nitrosamines are carcinogenic**, the SCCS considers that, given the high systemic bioavailability of nitrosamines (as shown e.g. for NDELA), there is no reason to believe that nitrosamines will not be subject to bioactivation to carcinogens and systemically induce malignant transformation regardless of the route of exposure as has been demonstrated (Hofmann 1983).
- As regards the comment that the **majority of N-nitrosamines to which humans are exposed are formed endogenously**, the SCCS is of the opinion that it is true that a considerable part of human exposure to N-Nitroso compounds (NOC) (not limited to nitrosamines) originates from endogeneous nitrosation in the organism. It is a valid suggestion to evaluate exposure to preformed nitrosamines from cosmetics and other sources from this perspective. At present, however, it is impossible to assess the contribution to human health risk of endogeneously formed NOC with the required degree of scientific confidence. Many of the NOC formed have been shown to be practically quantitatively excreted in the urine, to be non mutagenic and non carcinogenic. For this reason they have been developed and applied as biomarkers for endogenous nitrosation in humans by many research groups. SCCS is of the opinion that the proposed considerations are important for future developments in risk assessment. However this can only be done science based. Specifically, much more knowledge is needed concerning biological consequences of endogeneous nitrosation. Crude mass balances are not helpful. This is a complex task, requiring much more basic research than that referenced to. However, SCCS would not recommend to include in such evaluations exposures to tobacco specific nitrosamines, as suggested.