EUROPEAN COMMISSION

Health & Consumer Protection
Directorate-General

Scientific Committee on Consumer Products

SCCP

OPINION ON

Toluene

(its use as a solvent in nail cosmetics)

Scientific Committees
on consumer products
on emerging and newly identified health risks
on health and environmental risks

The SCCP adopted this opinion at its 15th plenary of 15 April 2008

About the Scientific Committees
Three 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 Products (SCCP), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and are made up of external experts.

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

SCCP
Questions concerning the safety of consumer products (non-food products intended for the consumer).
In particular, the Committee addresses questions related to the safety and allergenic properties of cosmetic products and ingredients with respect to their impact on consumer health, toys, textiles, clothing, personal care products, domestic products such as detergents and consumer services such as tattooing.

Scientific Committee members
Claire Chambers, Gisela Degen, Ruta Dubakiene, Bozena Jazwiec-Kanyion, Vassilios Kapoulas, Jean Krutmann, Carola Lidén, Jean-Paul Marty, Thomas Platzek, Suresh Chandra Rastogi, Jean Revuz, Vera Rogiers, Tore Sanner, Günter Speit, Jacqueline Van Engelen, Ian R. White

Contact
European Commission
Health & Consumer Protection DG
Directorate C: Public Health and Risk Assessment
Unit C7 - Risk Assessment
Office: B232 B-1049 Brussels
Sanco-Sc6-Secretariat@ec.europa.eu

(ISSN)

http://ec.europa.eu/health/ph_risk/risk_en.htm

ACKNOWLEDGMENTS

Dr. C. Chambers
Prof. G. Degen (rapporteur)
Dr. B. Jazwiec-Kanyion
Prof. V. Kapoulas
Prof. J.-P. Marty
Prof. T. Platzek
Dr. S.C. Rastogi
Prof. J. Revuz
Prof. V. Rogiers
Prof. T. Sanner (Chairman)
Dr. J. van Engelen
Dr. I.R. White

Keywords: SCCP, scientific opinion, toluene, directive 76/768/ECC, CAS 108-88-3, EINECS 203-625-9

Opinion to be cited as: SCCP (Scientific Committee on Consumer Products), Opinion on toluene, 15 April 2008

TABLE OF CONTENTS

1. BACKGROUND

Council Directive 2003/15/EEC amended Directive 76/768/EEC introducing Article 4b. It states that "*the use in cosmetic products of substances classified as carcinogenic, mutagenic or toxic for reproduction, of category 1, 2 and 3, under Annex I to Directive 67/548/EEC shall be prohibited. To that end the Commission shall adopt the necessary measures in accordance with the procedure referred to in Article 10(2). A substance classified in category 3 may be used in cosmetics if the substance has been evaluated by the SCCNFP and found acceptable for use in cosmetic products*."

Toluene is classified as a CMR[1] category 3 substance, toxic for reproduction. The substance is not regulated in any Annex to the Cosmetics Directive nor has it been evaluated before for cosmetic usage.

A dossier for the continued use of toluene as a solvent in certain nail products was submitted by COLIPA[2].

The Scientific Committee on Consumers products (SCCP) adopted by its 9th plenary meeting on 10 October 2006 an opinion (SCCP/1029/06) on toluene with the following conclusion:

"For the present evaluation, measurements for two situations of nail product use were available:

- *Home use conditions (non-ventilated rooms): toluene air levels of 1 - 4 ppm*
- *Client exposure in (ventilated) professional nail studios: 0.26 ppm*

The duration of exposure is less than 30 min (typical application times 10-20 min). This exposure situation has been viewed in comparison to:

a) consumer exposure as characterized in the EU report on toluene (for two scenarios [U1 and U3A], for which there are at present no restrictions), and
b) occupational exposure limits (OEL) set for continuous 8 hour exposures where risks from levels of 25 to 50 ppm are considered as acceptable.

This comparison demonstrates that occasional consumer exposure to toluene present in nail cosmetics where the exposure may be within the range of 1 to 4 ppm can be considered as safe.

Although specific information related to the effects in children is limited and because of the low and occasional exposure, the SCCP is of the opinion that the presence of toluene as a solvent in nail cosmetics does not pose a risk to the health of all groups of consumers, independent of their age.

This conclusion is based on an exposure driven evaluation of both, acute inhalation effects and reproductive toxicity."

As part of the implementation of this opinion a discussion took place with stakeholders. From this discussion some questions were raised:

1. It is stated that "penetration through the nail plate is nil or minimal" (3.4.1. Cosmetic exposure p. 10). However, this assumption was questioned by member states and industry was asked to provide documentation to support this statement.

[1] CMR: carcinogenic, mutagenic or toxic to reproduction
[2] COLIPA: European Cosmetic Toiletry and Perfumery Association

2. From the consumer exposure scenarios (U1 = gluing and U3A = car maintenance (car polishing)) in the EU Risk Assessment Report on toluene, which were used to compare the actual consumer exposure, when toluene is used as a solvent in nail products the exposure was 1.89 ppm and 2.66 ppm respectively. These exposures resulted in a MOS of 21 and 15 for acute effects such as headache and dizziness, and of 40 and 28 for functional performance. For the same scenarios the MOS for reproductive toxicity by inhalation were 317 and 225, respectively. Questions were raised as to whether the MOS should be higher also for acute effects such as headache, dizziness and functional performance.
3. Whether a content of 25% really was technical needed.

The current submission from industry is a response to questions 1 and 3 above.

2. TERMS OF REFERENCE

1. Does the SCCP consider that the penetration through the nail plate is practically nil taking into account the data provided or does the SCCP have any other information that can document this assumption?

2. Considering that toluene is a CMR 3 substance and assuming also a MOS of 100 or above for the acute effects like headache, dizziness and functional performance, is it possible for the SCCP to calculate a concentration for the specific use in cosmetic products?

3. OPINION

3.1. Penetration through the nail plate

With regard to the possibility of ungual penetration of toluene from nail products, two factors have to be considered: *absorption* though nail plate and/or skin horny layer and *evaporation* of the volatile chemical.

Absorption through the nail plate:

In vitro subungual penetration testing using human fingernail was first published by Walters using a closed reservoir system in 1981 (1); and by Franz using an open reservoir system in 1992 (2). This methodology was adapted from the in vitro percutaneous absorption test using human skin (3).

In the scientific literature, there is only one published study on subungual penetration of solvents; the solvents studied were water and a series of alkanols (4). Data from this study suggest that the nail behaves like a hydrogel of high ionic strength to the polar and semipolar alcohols. The more hydrophobic a compound is, the lower are the permeability rates, apparently linked to decreased partitioning into the complex matrix of the nail plate. This was supported by research by Mertin et al. on subungual penetration of drug substances (5), also indicating that nail plates constitutes a hydrophilic gel membrane rather than a lipophilic partition membranes as it is the case for the stratum corneum.
Another recently published study with regard to nail permeability is on the hydrophobic substance dibutylphthalate (6); it reports ungual penetration at the limit of chemical detection upon application of neat product for several days (max. mean flux 3 µg/cm^2/h).
Experimental data on the subungual penetration of toluene itself are lacking, yet it can be concluded from the experimental data available on other chemical substances that such a study would also produce little or no subungual penetration due to the hydrophobicity of the substance.

Considering this low potential of hydrophobic chemicals for nail penetration, the values obtained in a study on toluene absorption through human skin (7) can be regarded as a *worst case* for ungual penetration; it revealed that toluene is absorbed slowly through human skin, with absorption rates ranging from 14 to 23 mg/cm^2-hour. In studies where comparisons between different exposure routes were made (e.g. 8), the amount of toluene absorbed through the skin was considerably less than the amount absorbed following inhalation exposure.

Evaporation:
The assumption that penetration of toluene through the nail plate is nil or minimal, is further supported by consideration of its physicochemical properties. Toluene has a low vapour pressure (28.4 mm Hg at 25°C) that will result in extensive volatilization (9) upon application of toluene-containing nail products, thereby rapidly reducing the fraction of the substance available for ungual penetration.

3.2. Acute effects of toluene

With regard to effects of Toluene (classified toxic to reproduction, Cat. 3) on reproductive toxicity, a MOS value of ≥ 100 is needed to account for uncertainty in laboratory animal-to-human extrapolation as well as intra-individual variations. Based on a NOAEC of 600 ppm or 2,250 mg/m^3 for fertility and development (see SCCP Opinion on Toluene of 10 October 2006, ref. 10) and the worst case of consumer exposure to toluene from nail products (4 ppm), a MOS of 150 is calculated and considered to be clearly sufficient in light of the fact

that use of such products only leads to short-term exposure.

With regard to the *acute* effects of toluene, the SCCP does not see the need to set an MOS of 100 or above for the following reasons:

- Such a MoS would contain an uncertainty factor to account for laboratory animal-to-human interspecies differences, which is not necessary because the evaluation is based on human data.
- These human data were used to set occupational exposure limits (OEL) to protect against the most sensitive endpoint, *i.e.* effects on the central nervous system under regular prolonged exposure. OELs for toluene of 25 and 50 ppm are now in force in various countries for an 8-hour work-shift (time weighted average). Exposure to toluene in nail products is infrequent and short by comparison, and toluene levels during home use of such products containing 25% Toluene do not exceed 4 ppm.
- There are no recommendations for restrictions of consumer exposure made in the EU report on toluene (11) for two scenarios [U1 for gluing and U3A for car maintenance/polishing]. These exposures of 7.1 and 10 mg/m³ [corresponds to 1.9 and 2.7 ppm] resulted in a MOS of 21 and 15 for acute effects such as headache and dizziness, and of 40 and 28 for functional performance and where not considered to be of concern.

As a consequence, the short term exposure from nail products containing 25% toluene is not considered to be of concern with regard to acute neurological effects.

4. CONCLUSION

1. Taking into account the available data on ungual penetration of chemical substances and the physico-chemical properties of toluene, the SCCP is of the opinion, that the penetration of toluene can reasonably be expected to be practically nil .

2. Taking into account the available scientific data, the short-term exposure to toluene from nail products containing 25% toluene is not considered to be of concern with regard to acute neurological effects. Since the risk assessment is based on human data, a MoS of ≥10 is acceptable.

In summary, the SCCP is of the opinion that inclusion of toluene up to 25% is safe from the general toxicological view in nail cosmetics used as intended in adults and children. However, the SCCP would like to point out that there is a foreseeable risk of increased inhalation by children as part of the normal playing behaviour from cosmetics promoted as children's toys. Therefore, the use of toluene in such products is not considered appropriate.

5. MINORITY OPINION

Not applicable

6. REFERENCES

1. Walters KA et al. (1981) Physicochemical characterization of the human nail: I. Pressure sealed apparatus for measuring nail plate permeabilities. J Invest. Dermatol. 76: 70-79.

2. Franz TJ (1992) Absorption of amorolfine though human nail. Dermatol. 184 (suppl 1): 18-20.
3. Franz TJ (1975) Percutaneous absorption: on the relevance of in vitro data. J Invest. Dermatol. 64: 190-195
4. Walters KA et al. (1983) Physicochemical characterization of the human nail: permeation pattern for water and the homologous alcohols and differences with respect to the stratum corneum. J Pharm Pharmacol 35: 28-33.
5. Mertin D, Lippold BC (1997) In-vitro permeability of the human nail and of a keratin membrane from bovine hooves: influence of the partition coefficient octanol/water and the water solubility of drugs on their permeability and maximum flux. J Pharm Pharmacol. 49: 30-34
6. Jackson EM (2008). Subungual penetration of dibutyl phthalate in human fingernails. Skin Pharmacol Physiol. 21(1):10-14.
7. Dutkiewicz T, Tyras H (1968) Skin absorption of toluene, styrene and xylene by man. Br J Ind Med 25:243.
8. Sato A, Nakajima T (1978) Differences following skin or inhalation exposure in the absorption and excretion kinetics of trichlorethylene and toluene. Br J Ind Med 35:43-49.
9. EPA: TOXICOLOGICAL REVIEW OF TOLUENE (CAS No. 108-88-3) In Support of Summary Information on the Integrated Risk Information System (IRIS) September 2005, U.S. Environmental Protection Agency, Washington D.C., EPA/635/R-05/004
10. SCCP opinion on Toluene (its use as a solvent in nail cosmetics), 10. October 2006

European Union Risk Assessment Report. Toluene. Final report. Volume 30. Institute for Health and Consumer Protection, European Chemicals Bureau, EUR 20539, 2003