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Directorate C - Public Health and Risk Assessment
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SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS

SCCP

Opinion on

Toluene

(its use as a solvent in nail cosmetics)

Adopted by the SCCP
during the 9th plenary meeting of 10 October 2006

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1. BACKGROUND

The Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP) stated in its opinion of 25 September 2001 that substances classified pursuant to Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances as carcinogenic (except substances only carcinogenic by inhalation), mutagenic or toxic for reproduction, of category 1 or 2, and substances with similar potential, must not be intentionally added to cosmetic products, and that substances classified pursuant to Directive 67/548/EEC as carcinogenic, mutagenic or toxic for reproduction, of category 3, and substances with similar potential, must not be intentionally added to cosmetic products unless it can be demonstrated that their levels do not pose a threat to the health of the consumer.

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 category 3: toxic for reproduction. The substance is not regulated in an Annex to the Cosmetics Directive nor has it been evaluated by the SCCNFP/SCCP before. However, it has been evaluated by the Scientific Committee on Toxicology, Ecotoxicology and Environment (SCTEE) in its opinion of 12 June 2001.

Toluene is banned in glue and spray paint at concentrations above 0.1 % in products for the general public according to Directive 76/769/EEC on certain dangerous substances and preparations (Directive 2005/59/EC of the European Parliament and of the Council of 26 October 2005 amending for the 28th time Council Directive 76/769/EEC, OJ L 309, 25.11.2005, p. 13–14).

The European Commission received a submission from the European Cosmetic Toiletry and Perfumery Association (COLIPA) concerning the use of toluene as solvent in certain nail products.

2. TERMS OF REFERENCE

1. *Is toluene safe when used in cosmetic products for all groups of consumers independent of their age, taking into account the data provided?*

2. *Does the SCCP recommend any further restrictions with regard to its presence in cosmetic products or the use by different age (children) of consumers?*

3. OPINION

3.1. Scope of the present opinion

The present opinion is mainly based on the industry submission on Toluene in Cosmetic Nail products, and on other published scientific data.

In their letter of 13 June 2005, accompanying Submission I, COLIPA draws the attention to the following: *"This submission does not provide a full toxicological hazard characterization of toluene as would normally be required and expected for submissions of the SCCP. Such work has been done previously under the requirements of Directive 793/73/EEC. The resulting report which has been evaluated by the Scientific Committee for Toxicity and Ecotoxicity (CSTEE) is attached. The opinion by the CSTEE on this report as well as the Commission's recommendations for risk management of toluene are also included. It is important to note that these risk management recommendations do not foresee any action to reduce exposure from cosmetic products".*

COLIPA continues to explain that *"Rather than duplicating this work, the submission presented is focused:*

a) on reprotoxicity as the toxicological endpoint which necessitated a SCCP review,
b) on providing an exposure driven risk assessment for the particular use of interest to the cosmetic industry (i.e. as a solvent in nail products)."

SCCP agrees that important official reports have been issued recently on the toxicity profile and safety of toluene, and has considered the following (summary) documents:

3.1.1. Scientific Committee for Toxicity and Ecotoxicity (CSTEE) opinion 2001

In a document issued on 12 June 2001, the CSTEE commented on the results of the Risk Assessment of Toluene, carried out in the framework of Council regulation (EEC) 793/93 on the evaluation and control of the risks of existing substances.

In the General Comments on Human Health, the CSTEE stated:

> Human data as well as studies in rodents provide evidence of developmental effects, i.e. lower birth weight, delayed postnatal development and developmental neurotoxicity. The CSTEE agrees with the assessor that the compound is to be labelled reproductive category 3, R63 (Possible risk of harm to the unborn child).
> The results of neurotoxicity studies are extensively discussed in the report. The ototoxic effect is well described. The CSTEE supports the proposed classification and labelling R 67: vapours may cause drowsiness and dizziness.

With respect to the Effects Assessment (Hazard Identification), the CSTEE stated on:

a) Mutagenicity / Genotoxicity:
Toluene was not mutagenic in bacterial and mammalian cell gene mutation and chromosomal aberration assays in vitro. A few positive results were observed at cytotoxic concentrations. At non-cytotoxic doses it did not induce sister chromatid exchanges, micronuclei or DNA damage in vitro. It did not induce DNA repair in various bacteria or gene conversions in yeast and had no genotoxic effects in Drosophila.
No cytogenetic changes were seen in the bone marrow of rodents and no DNA damage was found in peripheral blood cells, bone marrow and liver of mice. Some positive results were seen in studies where benzene was present as a contaminant. Toluene was not mutagenic to the sperm of mice in a dominant lethal test.
Equivocal results were obtained in monitoring studies with peripheral blood lymphocytes from workers co-exposed to toluene; no induction of sister chromatid exchanges, however, were observed in peripheral blood of volunteers after prolonged exposure to 50 ppm.
The CSTEE agrees with the assessor that toluene can be considered to be non-genotoxic.

b) Carcinogenicity:
In F344 rats no increase in the incidence of tumours was found in a NTP 2-yr inhalation study after exposures to 600 and 1200 ppm. No effects were observed in another study after 2 years inhalation of 300 ppm; however, as the MTD was not achieved, this study is not considered valid for the assessment of a potential carcinogenic effect.
In mice exposed for 2 years to 120, 600 and 1200 ppm, non-malignant pituitary adenomas in the pars intermedia were found in all exposed groups without a dose-response relationship (1 adenoma each in all groups of females and 1 in the high dose male group).
An oral study in SD-rats (Maltoni, 1983/5), where haemolymphoreticular neoplasia and "an increase in the total number of malignant tumours" were reported, was considered invalid by the assessor due to inadequate reporting (e.g. no information on tumour types and incidences, no historical control data).
Toluene, used as a vehicle in various dermal carcinogenicity studies in mice, did not induce a clear increase in dermal tumours. One skin-painting study (Primate Research Institute, 1988) showed skin irritation and tumour development, the difference in tumour incidence was just below statistical significance.
Human data do not show an excess of tumours in toluene-exposed workers.
Though there will be no change in the conclusions, the RAR should take account of the latest IARC evaluation (1999). In particular, there is additional human carcinogenicity data presented in the IARC report that would further support the conclusions of the RAR.
The CSTEE agrees with the assessor in that it cannot be concluded that toluene is carcinogenic.

Ref.: 23

3.1.2. European Union Risk Assessment Report on Toluene

The final report was published in 2003; the Rapporteur was the Danish Environmental Protection Agency. A previous draft of this report was peer reviewed by CSTEE (see above 3.1.1.). The 320 page document assesses the risks associated with the production and use of the commercial product toluene and use of products containing the isolated commercial product toluene, both for the Environment and for Human health.

Ref.: 22

The overall conclusions have been published also as Commission Recommendation (2004/394/EC) in the Official Journal of the European Union (L 144/72) on 30 April 2004. (Ref AR2). The Commission (in the section Strategy for limiting risks) considered the legislation for worker's protection currently in force at the Community level (i.e. OELs) to give an adequate framework to limit the risks of toluene to the extent needed. With respect to Consumers, they recommend to consider use restrictions for the substance as such and in preparations for use in adhesives and spray paint.

COLIPA (letter of 13 June 2005) notes *"that these risk management recommendations do not foresee any action to reduce exposure from cosmetics"*. (Remark SCCP: this exposure scenario has not been considered in the EU risk assessment report.)

The EU Risk Assessment Report on toluene describes various model exposure scenarios for consumers, namely gluing, spray painting, car maintenance, carpet laying and filling gasoline at self-service gas stations (section 4.1.1.3; p.138f). It provides detailed risk characterizations with MOS values for both inhalation and dermal exposure resulting from these scenarios (section 4.1.3.3; p.249f). This assessment as well as the occupational exposure limits in force in various countries (Tab. 4.1 in Ref 22) provides a frame for judgements on consumer exposure resulting from the use of toluene in cosmetic nail products.

3.1.3. U.S. EPA: Toxicological Review of Toluene; Washington D.C., September 2005

The document (EPA/635/R-05/004) was prepared to provide scientific support and rationale for the hazard and dose-response assessment in IRIS pertaining to chronic exposure to toluene. The relevant literature was reviewed through January 2005. The report and the accompanying IRIS Summary have been reviewed by EPA scientists and by independent external scientists. The report (AR 1; 179 pp) was published after the COLIPA submission I on toluene to SCCP; it has been added by SCCP to the references because of its most recent review of published data.

Major conclusions in the characterization of hazard and dose response reached by EPA (page 87ff; AR 1) are in accordance with evaluations in other official reports by European committees.

Some of the EPA conclusions are cited here as background information:

- A number of occupational studies have examined the effects of toluene exposure via inhalation. The most sensitive effects observed in humans following inhalation exposure are neurologic effects, including altered colour vision, dizziness, fatigue, headache, and decreased performance in neurobehavioral tests. Exposure to higher levels in humans and animals has resulted in respiratory tract irritation. Animal studies have also demonstrated effects on other organ systems at high exposure levels (generally 600 ppm or greater).
- In mothers who inhaled very high levels of toluene as an addictive euphoric during pregnancy, the children showed a number of physical (small mid face, deep-set eyes, micrognathia, and blunting of the fingertips) and clinical (microcephaly, CNS dysfunction, attention deficits, and developmental delay/mental deficiency) changes attributed to toluene. Animal studies of toluene inhalation have revealed delayed neurodevelopment and decreased offspring weight at levels that also resulted in maternal toxicity. Gross malformations were not noted at any exposure level.
- A number of studies examining the toxicity of toluene following inhalation exposure in humans exist. The available data indicate that neurological effects are the most sensitive

effect of chronic inhalation exposure to toluene. A subset of studies was chosen from which to derive a point of departure for the derivation of the RfC. A value of 34 ppm (128 mg/m^3) was chosen as the point of departure. This value is the arithmetic mean of the available NOAELs as identified in Section 5.2.1. This value is lower than the LOAELs identified under human exposure conditions. An RfC of 5 mg/m^3 was derived by adjusting the average NOAEL for continuous exposure and application of a 10-fold UF for intra-human variability. Confidence in the database is high; multiple chronic studies in humans are available that examine neurotoxic effects and numerous animal reproductive and developmental studies, as well as a two-generation reproductive toxicity study, exist. There is high confidence in the resulting RfC.

The rationale provided for the Choice of Principal Study and Critical Effect (page 70; AR 1) is the following:

- A substantial database examining the effects of toluene in subchronic and chronic occupationally-exposed humans exists. The weight of evidence from these studies indicates neurologic effects (i.e., impaired colour vision, impaired hearing, decreased performance in neurobehavioral analysis, changes in motor and sensory nerve conduction velocity, headache, dizziness) as the most sensitive endpoint. Numerous case studies in humans exposed to high concentrations of toluene for abusive purposes have also indicated neurological effects in adults as critical effects of concern. Human studies indicating the potential for adverse effects from toluene exposure other than neurological effects are also available. None of these studies indicated effects at doses lower than those observed for neurological effects. Animal studies (NTP, 1990) have also suggested respiratory irritation as a sensitive effect, but this effect in humans appears to occur at higher exposure concentrations than those resulting in neurologic effects.

With respect to developmental and reproductive toxicity, the review states the following (page 56f; AR 1):

- A number of developmental effects, particularly neurodevelopmental changes, have been reported in children of women who abused toluene during pregnancy. Effects reported in children exposed *in utero* to toluene include microcephaly, CNS dysfunction, attention deficits, developmental delay/mental deficiency, small mid face, deep-set eyes, micrognathia (smallness of the jaws), and blunting of the fingertips (Byrne et al., 1991; Devathasan et al., 1984; Hunnewell and Miller, 1998; King et al., 1981; Maas et al., 1991; Meulenbelt et al., 1990; Miyagi et al., 1999; Ryu et al., 1998; Suzuki et al., 1983). Several studies in rats have reported altered neurobehavioral parameters in offspring following exposure of pregnant dams to high (≥ 800 ppm) concentrations of toluene (Da Silva et al., 1990; Hass et al., 1999; Hougaard et al., 1999). Significant changes in other developmental endpoints have also been reported in animal studies, including increases in spontaneous abortions, resorptions, altered pup body and organ weights, and altered pup development, but generally only at high doses (≥ 1000 ppm) (Dalgaard et al., 2001; Ono et al., 1995, 1996; Thiel and Chahoud, 1997; Ungvary and Tatrai, 1985). A two-generation inhalation reproduction study in rats did not report alterations in any indices of fertility, though decreased pup weight in the F1 generation exposed to 2000 ppm toluene was reported during the first 15 weeks of life, after which weights did not significantly differ from controls (API, 1984; Roberts et al., 2003).

In summary
On the basis of (these) official documents which have been issued recently on the toxicity profile and safety of toluene, the SCCP considers it feasible to conduct an exposure driven risk assessment for toluene in cosmetic nail products.

3.2. General substance Information

3.2.1. Physicochemical properties

At room temperature, toluene is a clear-to-amber colourless liquid with a pungent, benzene-like odour. Although it is a liquid at room temperature, toluene's low vapour pressure results in extensive volatilization. It is flammable with a flash point of 4°C.

Empirical formula: C_7H_8
Molecular weight: 92.15
Conversion factor: 1 mg/m^3 = 0.266 ppm at 25°C and 1 atm
1 ppm$_v$ = 3.75 mg/m^3 at 25°C and 1 atm
1 ppm$_v$ = 3.83 mg/m^3 at 20°C and 1.013 hPa

Ref.: AR1, AR2

Comment
In countries with the same OEL (Occupational Exposure Limit) of 50 ppm toluene, air concentration conversion factors for two temperatures lead to slightly different values in mg/m^3.

3.2.2 Function and Uses (for the present evaluation)

Toluene is used in nail cosmetics (nail lacquer, nail enamel, nail polish, top coat, base coat and nail treatments) as a diluent and solvent.

Ref.: AR3

Comment
Data on typical toluene concentrations in currently marketed nail products were not provided in the dossier submitted by COLIPA. A study conducted in 1991 to assess consumer exposure used nail products formulated with 25% (v/v) toluene (see below 3.3.1).

3.3 Exposure Scenarios

3.3.1 Cosmetic Exposure Levels

Exposure to toluene from cosmetics can occur in consumers using toluene containing nail products or by professional nail technicians applying toluene containing nail products to their clients.
A study of consumer exposure to toluene from the application of nail polish at home was conducted in 1991. The objective of this study was to calculate the concentration of toluene in the breathing zone of female subjects before, during and after nail polish application. A total of 15 subjects completed the study. The study was run in triplicate to confirm the calculations which did not vary from any of the three studies on these subjects. The nail products used in the

study were formulated with 25 % (v/v) toluene. The subjects applied one layer of base coat, two layers of enamel and one layer of top coat. The total amount of nail polish applied per usage was 0.53 gm on average. The application times were recorded and varied from 10.5 min to 20.3 min. The toluene concentrations, measured by an infrared gas analyzer in a 16 m^3 room with an air flow of approximately 1.0 change per hour, were also documented. Based on air concentration, application time and breathing constant for women, the mean exposure to toluene from the home application of nail polish was calculated to be 0.6 mg (measured air concentration 1- 4 ppm or 4-14 mg/m^3).

Ref.: 28

A study of professional nail technicians exposed to toluene over an eight hour work day (TWA) was conducted in 1999. This study was submitted to the State of California to support the safety of professional nail technicians and eliminate the need for official hazard warnings about toluene on professional nail product labels.

Industrial hygiene assessments were conducted by analytical air measurements of toluene content on one hundred seventy eight (n=178) professional nail technicians who were working with toluene containing cosmetic nail products with their clients.

The results of the air sampling for the presence of toluene showed that the mean toluene exposure from inhalation was 0.236 ppm or 0.260 ppm at the 90% upper confidence level (Annex III of ref. AR4, taken from ref. 29).

In this same study, the results of air sampling for the clients or customers of the professional nail technicians were 0.149 ppm toluene for the mean or 0.166 ppm at the 90% upper confidence level.

Ref.: 29

Comment

The air concentrations for toluene in the industrial hygiene assessment (ref. 29) are much lower for both professional nail technicians and their clients than those measured under simulated (home) use conditions in the breathing zone of consumers (ref. 28). Higher values obtained for home use can be explained by less ventilation and also closer proximity to the source. To cover a realistic scenario, the values for simulated home use conditions will be used for further considerations.

3.3.2. Other (Incidental) Exposure

Exposure to toluene can be *(i)* occupational, *(ii)* environmental or *(iii)* from the use of toluene containing products by either professionals or consumers.

Occupational exposures can occur from the synthesis and manufacturing of toluene, the delivery and storage of gasoline and the professional application of paints and coatings containing toluene. Another professional exposure to toluene containing products occurs in technicians working in professional cosmetic nail salons. However, ventilation is recommended for professional cosmetic nail salon settings by the suppliers of professional nail products.

Environmental exposure to toluene occurs from spills or waste disposal.

Consumer exposure to toluene can occur from the use of paints and coatings containing toluene in the home. It can occur also from gluing (hobbyist) and do-it-yourself carpet laying with toluene containing materials. Consumer exposure can also occur from the application of cosmetic nail products in the home. Typically, there is little or no ventilation when consumers apply cosmetic nail products in the home.
Incidental exposures can be uncontrolled or controlled by appropriate ventilation procedures.

3.3.3. Intentional Exposure

Intentional exposure to toluene can occur from individuals inhaling toluene vapours to produce a state of euphoria. These exposures are purposely uncontrolled.

3.4 Quantitative Exposure (from Cosmetic Nail products and Other Scenarios)

3.4.1 Cosmetic exposure

The results of the air sampling for the presence of toluene showed that exposure from inhalation was 1 – 4 ppm under simulated home use conditions or 0.26 ppm at the 90% upper confidence level in clients of professional nail studies (see above, section 3.3.1). In both settings the duration of exposure for the application of cosmetic nail products is less than 30 min, typically between 10 and 20 min. Although products are in contact to the keratin of the nail plate, penetration through the nail plate is nil or minimal. Also contact with the skin is usually nil or minimal. Therefore, toluene exposure by the dermal route is not relevant for further considerations.

For consumer exposure from cosmetic nail products, SCCP decided on 1-4 ppm toluene,
i.e. ***a range similar to that for two scenarios (U1 and U3A, i.e. gluing and car maintenance; see below 3.4.2) assessed in the EU Report on Toluene (Ref. 22).***

To facilitate a comparison between consumer exposure scenarios assessed in the EU Report on Toluene and exposure arising from the use of cosmetic nail products, exposure values given as mg/m^3 in the above Table for various scenarios (U1 – U5) are converted to ppm:
(Conversion factor: 1 mg/m^3 = 0.266 ppm at 25°C and 1 atm)

U1:	**7.1**	**mg/m^3**	**=**	**1.888 ppm**
U2:	1000	mg/m^3	=	266 ppm
U3A:	**10**	**mg/m^3**	**=**	**2.66 ppm**
U4:	195	mg/m^3	=	51.87 ppm
U5:	63	mg/m^3	=	16.758 ppm

3.4.2 Other consumer exposures

The EU Risk Assessment Report on toluene considered various model exposure scenarios for consumers, namely gluing, spray painting, car maintenance, carpet laying and filling gasoline at self-service gas stations (section 4.1.1.3; p.138f, ref 22). Only for illustrative purposes, table 4-46 (from the risk characterization part) of this report is included here along with some comments on the margin of safety (MOS) values for the scenarios considered.

Considerations on the *acute toxicity* of toluene are based on observations in humans experimentally exposed to toluene, where concentrations of 75 ppm (285 mg/m^3) and above caused headache, dizziness, and feeling of intoxication, irritation and sleepiness. A NOAEC of 40 ppm (150 mg/m^3) for these effects has been identified in the EU Risk Assessment Report and taken forward to the risk characterization (section 4.1.3.1; p.232, ref 22). Furthermore, toluene can cause impaired neuropsychological function, an acute effect demonstrated in performance tests. For impaired function in performance tests a LOAEC of 75 ppm (281 mg/m^3) has been taken forward to the risk characterization.

Table 4.46 MOSs and conclusions for acute effects by inhalation exposure for different consumer exposure scenarios

X. x)	Scenario sub-scenario	Headache, dizziness …			Functional performance		
		Exp.[a)]	MOS	Conclusion	Exp.[a)]	MOS	Conclusion
U1:	Gluing	7.1	21	ii	7.1	40	ii
U2:	Spray painting	1000	0.15	iii	1000	0.28	iii
U3A:	Car maintenance (car polishing)	10	15	ii	10	28	ii
U3B:	Car maintenance (cleaning hands)	neg.	-	ii	neg.	-	ii
U4:	Carpet laying	195	0.76	iii	195	1.4	iii
U5:	Filling gasoline at self-service stations	63			63		

[a)] mg/m^3

(Cited from ref. 22, page 250) *"For spray painting (scenario U2) and for carpet laying (scenario U4) MOSs are below the acceptable level. For these scenarios, there is concern for acute toxicity by inhalation:* ***conclusion (iii)***[1].
For gluing (scenarios U1) and for car maintenance (scenarios U3A and U3B), there is no concern for acute toxicity by inhalation: ***conclusion (ii)***[2].
No formal risk characterisation has been performed for filling gasoline at self service stations (scenario U5), since toluene exposures arising from the production and handling of gasoline are not formally a part of this risk assessment (cf. Section 0)."

Toluene is classified as a Reproductive Category 3, R63 (Possible risk of harm to the unborn child). Therefore, the pertinent part of the EU RAR on Toluene is included here for orientation (although toxicity for reproduction and development are observed at higher toluene doses than acute effects and with repeated exposure).

Regarding toxicity for reproduction, it is concluded (section 4.1.2.9.5; p.230 in ref. 22) that limited data in humans indicate an increased risk for late spontaneous abortions at dose levels around 88 ppm. Human data as well as studies in rats and limited data in mice provide evidence of similar developmental effects, i.e. lower birth weight, delayed postnatal development and developmental neurotoxicity. In animals, the NOAEC for lower birth weight and delayed postnatal development is 600 ppm. (A NOAEC for developmental neurotoxicity cannot be determined from the available studies. The LOAEC for this effect is 1,200 ppm.) The human LOAEC of 88 ppm (330 mg/m^3) and the rat NOAEC of 600 ppm (2,250 mg/m^3) were taken forward to the risk characterisation.

(Cited from ref. 22, page 253f) *"For scenario U1 to U4 the frequency of the exposure is assumed to be low (cf. Section 4.1.1.3). The exposure arising from these scenarios is therefore regarded as being short-term exposures. The available database on the toxicity for reproduction of toluene, however, arises from studies where exposure in all cases has been repeated. As there is no information on the relationship between the observed effects on reproduction and the duration of the exposure leading to these effects, it is not possible to exclude that even single exposures might produce effect on reproduction. However, a quantitative comparison of the estimated exposure levels for these particular scenarios and the NOAEC of 2,250 mg/m3 for fertility and development (see Table 4.49) is considered to be a cautious approach."*

[1] **Conclusion (iii)** There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

[2] **Conclusion (ii)** There is at present no need for further information or testing or for risk reduction beyond those which are being applied already.

Table 4.49 ***MOSs and conclusions of reproductive toxicity by inhalation for different consumer exposure scenarios***

X. Scenario x) sub-scenario	Development	
	Exposure [a)]	MOS
U1: Gluing	7.1	317
U2: Spray painting	1000	2
U3A: Car maintenance (car polishing)	10	225
U3B: Car maintenance (cleaning hands)	neg.	-
U4: Carpet laying	195	12
U5: Filling gasoline at self-service stations	63	

[a)] mg/m³

(Cited from ref. 22, page 253f): „*For scenarios U1, U3A and U3B (Gluing, Car maintenance (car polishing) and Car maintenance (cleaning hands)) the MOSs are considered to be sufficiently high. This should be seen in the light of the assumed low frequency of these exposure scenarios. There is therefore no concern for toxicity for reproduction for these scenarios:* ***conclusion (ii)***[3].
For scenarios U2 and U4 (Spray painting and Carpet laying) the MOSs are 2 and 12, respectively. These MOSs are considered low even though the approach is regarded to be cautious. Hence, at present it cannot be excluded that these particular scenarios lead to concern for reproduction. However, the available information is insufficient, and further information on the relationship between the observed effects on reproduction and the duration of the exposure leading to these effects is needed: ***conclusion (i)***[4].
The issue of reproductive effects and short-term exposure is not normally dealt with in the ESR. The present testing and risk assessment methodology do not cover this problem. The approach applied in this report is in accordance with the recommendation of the 26th Technical Meeting on Existing Chemicals.

3.5 Occupational Exposure Limits (OEL) for toluene

Clearly, the regulatory basis for protecting consumers against undesirable health effects, *e.g.* from exposure to cosmetic products, differs from regulation for the protection of workers against adverse health effects.
Yet, since COLIPA (ref. AR4) has argued in Submission I that consumer exposure to toluene from cosmetic nail products is considerably ("orders of magnitude ") lower than occupational exposure limits (OEL) in various countries, these values are provided below. It seems worth to mention that OELs refer to air concentrations set for an 8-hour work-shift (time weighted average) and chronic exposure. They have been set to protect against the most sensitive endpoint, i.e. effects on the central nervous system.
OELs now in force in various countries range between 25 to 50 ppm toluene (Table 4.1 from ref. 22). The table below lists limits for an 8 hour work shift (TWA) and STEL values.

[3] **Conclusion (ii)** There is at present no need for further information or testing or for risk reduction beyond those which are being applied.

[4] **Conclusion (i)** There is need for further information and/or testing

The duration of toluene exposure for the application of cosmetic nail products is less than 30 min, typically between 10 and 20 min (see above, 3.3.1)

Country	Time weighted average		Short-term exposure limit		Reference
	mg/m³	ppm [1)]	mg/m³	ppm [1)]	
Belgium	191	50			
Denmark	95	25			Arbejstilsynet (1996)
France	375		550		
United Kingdom	190	50	560	150	
Germany	190	50	950 (30 min)		MAK und BAT-Werte Liste (1999)
The Netherlands	150	40	-	-	SZW (1999)
Norway	95	25			
Sweden	200	50	400	100	1993
EU	188	50			Hunter et al. (1997)
USA (ACGIH)	190	50	-		ACGIH (1999)

[1)] ppm: parts per million

3.6 Special Considerations (Children)

With regard to possible childhood susceptibility, the US EPA Report of 2005 (AR 1, page 62) states the following:

> *„Only limited data exist that examine the potential differences in susceptibility to toluene between children and adults. Children have been shown to have differences in levels of CYP enzymes and several phase II detoxification enzymes (e.g., N-acetyl transferases, UDP glucuronyl transferases, and sulfotransferases) relative to adults (Leeder and Kearns, 1997; Nakajima et al., 1992; Vieira et al., 1996), as well as other physiological differences (e.g., children have higher brain mass per unit of body weight, higher cerebral blood flow per unit of brain weight, and higher breathing rates per unit of body weight) (Snodgrass, 1992). However, data on the possible contributions of these differences to potential age-related differences with respect to toluene are lacking".*

4. 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.

5. MINORITY OPINION

Not applicable

6. REFERENCES

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