Opinion of the Panel on Food Additives, Flavourings, Processing Aids, Materials in contact with Food and Cosmetics of the Norwegian Scientific Committee for Food Safety

Adopted 20 December 2005

Risk assessment of diethyl phthalate (DEP) in cosmetics

SUMMARY

The Norwegian Food Safety Authority (Mattilsynet) has asked the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) to evaluate if the use of diethyl phthalate (DEP) in cosmetics can be considered safe for human health based on the present scientific data related to the toxicological profile of DEP. The case was evaluated by the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics.

Diethyl phthalate (DEP) (CAS no. 84-66-2) is used as a plasticizer in a wide variety of consumer products, including plastic package films, cosmetic formulations, toiletries, toothbrushes, and in medical treatment tubing. DEP is frequently used in cosmetics as a solvent and vehicle for fragrance and cosmetic ingredients, as well as an alcohol denaturant.

In this opinion, earlier evaluations of DEP adopted by the SCCNFP, WHO and the Norwegian Institute of Public Health have been used as a basis. In the latest opinion adopted by SCCNFP in 2003, it was concluded that the safety profile of DEP supports its use in cosmetic products at current levels.

The human exposure to DEP, based on recently reported urinary concentrations of the metabolite monoethyl phthalate (MEP) in the U.S. population, has been compared with the systemic exposure dose of DEP estimated in the worst case scenario in the SCCNFP opinion from June 2002. These calculations show that the average and high exposure found in the U.S. population are approximately 150 and 10 times lower than the theoretical systemic exposure dose used by SCCNFP.

Further, the Panel has evaluated new relevant epidemiological studies, which indicate a correlation between urinary phthalate levels and possible health effects. These new epidemiological studies do not provide sufficient information to decide whether the observed associations are true causal-relationships or whether they are fortuitous. Lifestyle practices such as smoking and consumption of alcohol, that are both associated with DEP exposure and adverse health effects, are possible confounders in these studies.

In conclusion, the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of the Norwegian Scientific Committee for Food Safety is of the opinion that new studies on DEP published later than 2003 and reviewed in this assessment, do not provide sufficient new information to change the conclusions given in the safety assessments of the use of DEP in cosmetics adopted by SCCNFP on 4 June 2002 and 9 December 2003.

The national ban on all phthalates in toys and childcare articles is a risk management decision based on the precautionary principle and risk assessments of selected phthalates (DEHP, DBP, BBP, DINP, DIDP, DNOP). Although DEP is included in this ban, the substance was not included in the toxicological evaluation of phthalates in toys and childcare articles performed by the CSTEE. DEP is not regulated in toys and childcare articles by the European Commission, and the use of DEP is probably very limited as it is not suitable in such products.

BACKGROUND

Diethyl phthalate (DEP) (CAS no. 84-66-2) is used as a plasticizer in a wide variety of consumer products, including plastic package films, cosmetic formulations, toiletries, toothbrushes, and in medical treatment tubing. DEP is frequently used in cosmetics as a solvent and vehicle for fragrance and cosmetic ingredients, as well as an alcohol denaturant. The use of DEP as an alcohol denaturant is very common in most countries in Europe as it makes the alcohol unfit to drink, and the acute oral toxicity of DEP is considered to be low.

In 1995, DEP was reported as an ingredient in 67 cosmetic formulations in USA at concentrations from less than 0.1% to 50% (1). Perfumes and fragrance preparations like eau de Cologne, eau de toilette and aftershave contain a high percentage of alcohol. It is therefore mainly in such preparations that the highest concentrations of DEP can be found. Trace amounts of DEP could also be detected in a wide range of other cosmetics (eye-shadows, hair sprays, wave sets, nail polish, enamel removers, bath soaps, detergents and skin care preparations), as most products are perfumed.

The use of different phthalates in consumer products has been the subject of great public concern in recent years. In laboratory animals, several phthalates seem to be hormonally active and show reproductive toxicity. Because a large proportion of the general population is exposed to phthalates, indicated by the levels in urine (2), these effects are a matter of concern. Especially, there is concern whether industrial chemicals, such as phthalates, may be associated with the proposed declining sperm counts in developed countries (3).

List of phthalates and their metabolites mentioned in this opinion

Phthalate	**Metabolites**
diethyl phthalate (DEP)	monoethyl phthalate (MEP)
dibutyl phthalate (DBP)	monobutyl phthalate (MBP)
di-2-ethylhexyl phthalate (DEHP)	mono-(2-ethylhexyl) phthalate (MEHP)
benzylbutyl phthalate (BzBP)	monobenzyl phthalate (MBzP)
dimethyl phthalate (DMP)	monomethyl phthalate (MMP)
butylbenzyl phthalate (BBP)	monobutyl phthalate (MBP) monoisobutyl phthalate (MiBP)
di-isononyl phthalate (DINP)	
di-isodecyl phthalate (DIDP)	
dioctyl phthalate (DNOP)	
dioctyl tere-phthalate (DOTP)	

Earlier opinions and evaluations concerning DEP

Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP) 2002 and 2003

In light of the extensive use of DEP in different cosmetic formulations and the general concerns raised regarding the safety of phthalates, the EU Commission requested the Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP) to review the safety of DEP and consider if the safety profile of DEP supports its use in cosmetic products at current levels.

An opinion concerning diethyl phthalate was adopted by SCCNFP during the 20th Plenary meeting of 4 June 2002 (1). It was concluded that:

"DEP shows a low level of toxicity. Testing for dermal irritation and sensitisation in humans as well as in animals, and for photo-toxicity and photo sensitisation in human volunteers, has demonstrated its safety of use. Even undiluted the effects observed were minimal or moderate. The results of sub-chronic, and reproduction studies did not show any adverse effects attributable to treatment. The marginal increase of combined hepatocellular adenomas and carcinomas in high-dose male mice was considered as an uncertain finding due to the absence of effect on females and the low incidence observed in controls. In rats no effect was noted on that endpoint. Though all the genotoxicity end-points were not fully covered, the weight of evidence supports a low level of concern in carcinogenicity of DEP under the normal conditions of use, based also on borderline effects observed in some genotoxicity tests."

Based on this conclusion, the SCCNFP gave the following opinion:

"The SCCNFP is of the opinion that the safety profile of Diethyl-phthalate supports its use in cosmetic products at current levels.

At present the SCCNFP does not recommend any specific warnings or restrictions under the currently proposed conditions of use."

Due to new relevant scientific data on phthalates published in 2003 (4,5), the SCCNFP was requested by the EU Commission to review the new publications and answer the following questions:

> * *Does the data provided in the attached publications change the overall assessment of diethyl phthalate as stated in the opinion of SCCNFP (SCCNFP/0411/01)?*
>
> * *If yes, what does the SCCNFP recommend on the basis of the new data provided?*

A new and updated opinion concerning DEP was adopted by the SCCNFP during the 26th Plenary meeting of 9 December 2003 (6). In this opinion it was concluded:

"The SCCNFP is of the opinion that the data provided in the above-mentioned publications do not change the overall assessment of diethyl phthalate as stated in its opinion on diethyl phthalate of 4 June 2002 (doc. n° SCCNFP/0411/01)."

World Health Organisation (WHO), 2003

The World Health Organisation evaluated the health effects and environmental effects of DEP in 2003 (7). A tolerable intake (TDI) of 5 mg/kg body weight/day was established based on a NOAEL (no observed adverse effect level) of 1600 mg/kg body weight/day for developmental effects in mice to which an uncertainty factor of 300 was applied.

Norwegian Institute of Public Health, 2004

At the same time as the last evaluation of DEP by SCCNFP, the Norwegian Institute of Public Health was requested by the Norwegian Food Safety Authority to evaluate a new epidemiological study from Duty *et al.* (4), which suggested an association between human exposure of DEP at environmental levels and male reproductive effects. The evaluation performed by the Norwegian Institute of Public Health was finished 26 March 2004 and their main conclusions were (8):

- *The new study (4) does not provide evidence for a causal-relationship between exposure to diethyl phthalate (DEP), measured as urinary monoethyl phthalate (MEP), and DNA damage in sperm.*
- *The study (4) does not provide new information on the human DEP exposure.*

New report from Greenpeace

Recently, a new report called "An investigation of chemicals in perfumes" from Greenpeace in 2005 again raised concerns regarding the use of DEP as a cosmetic ingredient by claiming that "…there is evidence to suggest that phthalates and synthetic musks in common use may present us with diverse health and environmental hazards." In the study from Greenpeace 36 brands of eau de toilette and eau de parfum had been tested for levels of different phthalates. The results confirmed that DEP was detected in almost every product analysed in concentrations ranging from not detected to 2.2 %. The average value found was 0.27 % (9).

With reference to this report from Greenpeace and with reference to the use of DEP in toys and rainwear being banned in Norway, a member of the Norwegian Parliament has asked the Norwegian Minister of Environment if he will also consider banning the use of DEP in cosmetic products like creams, soaps, shampoo and fragrance. The question has since been forwarded to the Minister of Health as cosmetics are regulated under that ministry in Norway.

The Minister of Health has asked the Norwegian Food Safety Authority, in cooperation with the Norwegian Scientific Committee for Food Safety, to evaluate new scientific research and data relevant for the toxicological profile of DEP to make sure that the cosmetic products on the Norwegian market are safe for the consumer.

Regulations

Cosmetics

DEP can be used in cosmetic products without any limitations in the field of application and/or use. However, as for other unregulated cosmetic ingredients, the manufacturer is obliged to prove the safety for human health of the finished product through a safety assessment (10).

Toys and childcare articles

According to the Norwegian regulation relating to restrictions on the marketing and use of certain dangerous substances and preparations (11), phthalates shall not be used in toys and childcare articles intended for children under three years of age, and which can be placed in the mouth of them. Such toys and childcare articles shall not be placed on the Norwegian market.

The Norwegian ban on all phthalates, including DEP, in toys and childcare articles is a risk management decision based on the precautionary principle. The regulation banning all phthalates is not EU harmonised, however, other countries in EU (e.g. Sweden and Denmark) follow the same principle as Norway. The EU Commission has introduced a temporary ban on six other phthalates (DEHP, DBP, BBP, DINP, DIDP, DNOP) used to soften the plastic parts of toys and childcare articles. DEP, however, is not restricted for use in toys and childcare articles by the European Commission, but the use of DEP is probably very limited as it is not suitable in such products.

Recently, the European Commission has submitted a proposal for amendments of Directive 76/769/EEC relating to restrictions on the marketing and use of certain dangerous substances and preparations (phthalates) and Council Directive 88/378/EEC concerning the safety of toys. The proposed amendments concern the marketing and use of toys and childcare articles containing these six phthalates that the EU Commission already has a temporary ban on.

TERMS OF REFERENCE

The Norwegian Food Safety Authority (Mattilsynet) refers in its letter of 15 March 2005 to new scientific data related to the toxicological profile of diethyl phthalalte (DEP) published after the last opinion adopted by the SCCNFP during the 26th Plenary meeting of 9 December 2003.

Based on the present scientific data on DEP, the Norwegian Food Safety Authority (Mattilsynet) has asked the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) to evaluate whether the use of DEP in cosmetics can be considered safe for human health.

Due to the political interest in the assessment, VKM is requested to give the task high priority.

ASSESSMENT

The Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of the Norwegian Scientific Committee for Food Safety has evaluated new scientific data on DEP published after the last opinion adopted by the SCCNFP during the 26th Plenary meeting of 9 December 2003. The earlier opinions adopted by the SCCNFP, WHO and the Norwegian Institute of Public Health have been used as a basis for our assessment. Since the two opinions by the SCCNFP were adopted in June 2002 (1) and December 2003 (6) some new relevant epidemiological studies have been published (4,12,13,14,15). These studies, which may indicate an association between urinary phthalate levels and possible health effects, have also been evaluated in this opinion.

Current safety evaluation by SCCNFP – exposure calculations

In 2002, the safety of DEP as a cosmetic ingredient was evaluated by the SCCNFP (1). Due to the widespread use of DEP in different cosmetic products they made a calculation based on a worst case dermal intake from cosmetics in their safety assessment (1) by using the following premises:

Usage volume of 10 ml containing 10 % DEP per day		
Maximum amount of ingredient applied	I (mg)	= 1120 mg
Body weight		= 60 kg
Maximum absorption through the skin	A (%)	= 5 %
Dermal absorption per treatment	I x A	= 56 mg/day
Systemic exposure dose (SED)	I x A/60kg	= 0.93 mg/kg bw/day
No observed adverse effect level (mg/kg)	NOAEL	= 150 mg/kg bw/day
Margin of Safety (MOS)	NOAEL/SED	= 150

SCCNFP concluded that normal use of cosmetics is safe by estimating a margin of safety (MOS) = 150. SCCNFP based their assessment on a NOAEL = 150 mg/kg body weight/day (1) from a sub-chronic oral toxicity study in rats: "*toxic signs after 16 weeks of exposure of DEP in the diet consisted of an increase in relative liver weight (without significant abnormal histological findings) in females at concentrations at 1 % and 5 % and in a lesser extent at 0.2 % (corresponding to 150 mg/kg body weight/day).*"

In an assessment of DEP performed by WHO, another NOAEL of 1600 mg/kg body weight/day was used (7): "*In a standard NTP* (the National Toxicology Program, USA) *teratogenicity study with rats, no malformations, but rib number variation and a decrease in fetal weight were observed at an oral dose level of 3200 mg/kg body weight per day, which was also maternally toxic. In this study, the NOAEL for maternal and fetal toxicity was 1900 mg/kg body weight per day. In a dermal exposure study in mice, variation in rib numbers, but no fetotoxicity or teratogenicity, was observed at the highest dose tested, 5600 mg/kg body weight per day, which also was maternally toxic. The NOAEL for maternal and offspring effects in the mouse study was 1600 mg/kg body weight per day. This value, 1600 mg/kg body weight per day, is considered a NOAEL for reproductive toxicity. The NOAEL is supported by a single dose level study in which no adverse effects in dams or pups were observed (specifically, no malformations in male rat reproductive organs, which were observed after*

exposure to other phthalate esters) after perinatal exposure to diethyl phthalate at 750 mg/kg body weight per day in rats."

By using a NOAEL = 1600 mg/kg body weight/day and the estimated worst-case dermal exposure from cosmetics (0.93 mg/kg bw/day), as calculated by SCCNFP (1), the MOS would be 1720.

Exposure calculations based on recent surveys in the U.S. population

The National Health and Nutrition Examination Survey (NHANES) is a series of ongoing surveys conducted by the Center for Disease Control and Prevention's (CDC's) National Center for Health Statistics (NCHS) that are designed to collect data on the health and nutritional status of the U.S. population (16). Urinary phthalate data collected from 289 adults during 1988-1994 (NHANES III study) was presented by Blount *et al.* (2). Silva *et al.* (17) measured the urinary monoester metabolites of seven commonly used phthalates in approximately 2540 samples collected from participants of the continued NHANES survey (NHANES 1999-2000). Recently new updated data from the Center for Disease Control and Prevention was presented in July 2005 (16). In this report (NHANES 2001-2002) (n = 2782), the geometric mean for the urinary level of MEP was 178 µg/l, while the 95th percentile was 2500 µg/l (16). The human exposure of DEP based on the urinary MEP concentrations in the third report from CDC (NHANES 2001-2002) (16) can be estimated as follows:

Urine volume/day = 1.5 l

Body weight = 60 kg

70% of DEP is secreted as MEP in the urine within 24h (18)

Calculation based on geometric mean of MEP = 178 µg/l

MEP secreted/day = 178 µg/l x 1.5 l = 267 µg

DEP exposure = 267 µg x 100/70/60 kg /day = **6.4 µg/kg body weight/day**

Calculation based on 95th percentile of MEP = 2500 µg/l

MEP secreted/day = 2500 µg/l x 1.5 l = 3750 µg

DEP exposure = 3750 µg x 100/70/60 kg /day = **89 µg/kg body weight/day**

These calculations show that the most likely real exposure for average and high exposure are approximately 150 and 10 times lower than the systemic exposure dose (SED) used in the worst case scenario by SCCNFP, which was **930 µg/kg body weight/day.** The SED calculated by SCCNFP is based on a usage volume of 10 ml containing 10 % DEP. The average concentration of DEP of perfumed cosmetic products was recently found to be 0.27 % (9), which indicates that SCCNFP's worst case exposure estimate is far above that of the general population. The urinary MEP levels in the third report from CDC (NHANES 2001-2002) (16) accord very well with levels found in 406 men recruited from a fertility clinic (19). In this study, the excretion of MEP correlated with the number of personal products used, and in particular those who had used cologne or after shave within 48 hours before sampling. Current smokers had a median level of MEP about 70% higher than that of non-smokers.

New epidemiological studies on possible health effects of DEP
Recently, a series of human studies have indicated associations between urinary MEP levels similar to that found in the general population (2,13) and possible health effects related to

- Lung function parameters
- Male reproductive effects

Lung function parameters
Hoppin *et al*. (12) used urinary phthalate data from the 289 participants in the Third National Health and Nutrition Examination Survey (NHANES III) to examine whether there was any correlation between urinary phthalate levels and lung function parameters. Although common in other studies on the effects of environmental exposures other than smoking, on respiratory health effects, they were not able to limit their analysis to never smokers because of small sample size. When their linear regression models controlled for race, age, age squared, standing height, body mass index, cumulative smoking, and current smoking they found that monobutyl phthalate (MBP, the metabolite of DBP) was significantly associated with decrement in forced vital capacity (FVC), forced expiratory volume at 1 sec (FEV_1) and peak expiratory flow (PEF), in males but not in females. MEP (the metabolite of DEP) was associated with lower FVC and FEV_1 in men. Mono-(2-ethylhexyl) phthalate (MEHP, the metabolite of DEHP) was not adversely associated with any of the pulmonary function parameters.

Male reproductive effects
Duty *et al.* (13) reported that among men coming for treatment to an infertility clinic (n=168); those with higher urinary metabolites of specific phthalates were more likely to have low sperm count and impaired sperm quality. After adjusting for age, abstinence time, and smoking (current, former and never) they found positive dose-response relationships for urinary monobutyl phthalate (MBP) and monobenzyl phthalate (MBzP, the metabolite of BzBP) with one or more semen parameters, and a suggestive association for monomethyl phthalate (MMP, the metabolite of DMP) with abnormal sperm morphology. No correlations were found for other phthalates, such as monoethyl phthalate (MEP).

In another study, Duty *et al.* (4) investigated whether urinary levels of phthalate metabolites were associated with DNA strand breaks in sperm cells, measured by the neutral comet assay. The subjects (n=168) were apparently the same as in the study presented above (13). Urinary metabolites of eight phthalates were analysed and the neutral comet assay was used to measure DNA integrity in sperm. After adjusting for age and smoking status they found a statistically significant positive association between urinary levels of MEP and mean comet extent (DNA migration) in sperm. However, no significant associations were found between comet assay parameters and other urinary phthalate metabolites, including MBP, MBzP, MEHP and MMP. This pattern of correlation between DNA migration and urinary phthalate levels did not accord with the pattern of correlation observed between various other sperm parameters and urinary phthalate levels (13).

In a preliminary study, Duty *et al*. (14) found a preliminary association between urinary concentrations of MBP and MBzP, altered levels of inhibin B and follicle stimulating hormone (FSH) and a suggestive association between urinary MEP and increased serum levels of testosterone. The data was collected from 295 men recruited from Massachusetts

General Hospital between 1999 and 2003. In this material, there were also apparent associations between smoking status and urinary MEP, MBP and MMP concentrations. Median MEP levels were higher in current smokers (236 ng/ml) and former smokers (231 ng/ml) than in never smokers (135 ng/ml). This pattern was similar also for MMP and MBP.

In a very recent study, Swan *et al.* (15) examined the relationship between testicular function and the anogenital distance (AGD) of 134 boys 2-36 month of age and the prenatal urinary levels of phthalate metabolites of their mothers. AGD, the distance from the anus to the insertion of the genital tubercle, is androgen dependent, and about twice as long in males as in females, and has been shown to be a sensitive measure of prenatal antiandrogen exposure in animal experiments. Since AGD was measured at different ages, the anogenital index (AGI = AGD/weight) was used for regression analysis. They found a significant correlation between AGI and penile volume and incomplete testicular descent. They found that MBP and monoisobutyl phthalate (MiBP) (both metabolites of BBP), MBzP (the metabolite of BzBP), as well as MEP were inversely related to AGI. The strongest association to decreased AGI was obtained with the total urinary phthalate score. They examined several potentially confounding factors including mother's ethnicity and smoking status, time of day and season when the urine sample was collected, gestational age at sample collection, and baby's weight at examination. Other than age and age squared, no covariates altered regression coefficients for the phthalates metabolites by more than 15 %, and none were included in the final models of regression analyses. However, it was not described how these potential confounding factors varied among the participants.

Discussion and implications of new epidemiological studies on possible health effects of DEP

Phthalate concentrations of human urines reported in several studies show that the general population is exposed at a low level to a spectrum of phthalates (2,16,17,19). A series of new epidemiological studies demonstrate statistical correlations between some of the phthalates found in urine and possible adverse changes on lung function, semen parameters, DNA strand breaks in sperm, male reproductive hormones, testicular function and the anogenital distance (AGD) (4,12,13,14,15).

In men urinary MEP was associated with a decrease in FVC and FEV1, but not with other parameters such as peak expiratory flow (PEF), whereas no association was seen in women and non-smokers alone. This is a cross-sectional study and the decrease in lung function parameters are supposed to occur over a long time, the urinary MEP only reflects very recent exposure (12). This study is only suggestive as to the possible association between lung function parameters and urinary MEP and the hypothesis should be tested in a follow up study with proper control of DEP exposure and preferably in non-smokers as smoking is a confounder in that study.

The apparent association reported between urinary levels of MEP, which is the most abundant phthalate in human urine (4), and mean comet extent (DNA fragmentation) in sperm (4) was unexpected because DEP and MEP is considered to be non-genotoxic.

Another unexpected result was the inverse relationship between maternal prenatal urinary levels of MEP and AGI among boys 2-36 month of age (15). In male rodents, it has previously been demonstrated (20) that prenatal exposures at high doses of BzBP, DEHP and BBP impair testicular function and shorten AGD, whereas DEP, DMP and DOTP do not. Hence, DEP was not among the phthalates that after prenatal exposure at high doses impaired

testicular function and shortened AGD in rats (20). In other animal studies, DEP has not been considered to be a potent reproduction toxicant (1,7). Furthermore, a possible antiandrogen effect of DEP is not in accordance with the study of Duty *et al.* (14) reporting positive association between increased urinary levels of MEP and increased serum levels of testosterone in humans.

The new epidemiological studies (4,12,13,14,15) do not provide sufficient information to decide whether the observed associations are true causal-relationships or whether they are fortuitous. Lifestyle practices that are both associated with DEP exposure and the effect are possible confounders. In particular smoking is associated both with several reproductive effects in humans, i.a. reduced sperm count in males exposed to smoking *in utero* and estrogenic effects (21,22) and apparently also with urinary MEP (14,19). The median urinary concentration of MEP was higher in current smokers (236 ng/ml) and former smokers (231 ng/ml) than in never smokers (135 ng/ml) (14). The higher urinary MEP level in current smokers was recently confirmed in a study by the same authors (19). However, with regard to smoking status and DNA damage in sperm cells, they did not find a correlation (4), although correlations between smoking and DNA damage were found in several other studies (23,24). It is not clear how Swan *et al.* (15) have controlled for smoking. Further studies with proper control of different lifestyle practices such as smoking, diet and use of alcohol are needed to confirm or refute the observed associations. It is also important to examine whether human DEP exposure parallels the exposure of other phthalates that are more potent in animal experiments. More research is needed to explore the reproductive toxicity of phthalates in humans to decide whether humans are more susceptible to phthalates in general, and DEP in particular, than laboratory animals.

The new studies available do not provide sufficient evidence for a causal-relationship between exposure to DEP and possible health effects, and do therefore not change the conclusions in the safety assessment by SCCNFP on the use of DEP in cosmetics.

CONCLUSIONS

- The Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of the Norwegian Scientific Committee for Food Safety is of the opinion that new studies on DEP published later than 2003 and reviewed in this assessment, do not provide sufficient new information to change the conclusions given in the safety assessments of the use of DEP in cosmetics adopted by SCCNFP on 4 June 2002 (1) and 9 December 2003 (6).

- The national ban on all phthalates in toys and childcare articles is based on a risk management decision based on the precautionary principle and risk assessments of a selection of phthalates (DEHP, DBP, BBP, DINP, DIDP, DNOP). Although DEP is included in this ban, the substance was not included in the toxicological evaluation of phthalates in toys and childcare articles performed by the EU Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). DEP is not restricted for use in toys and childcare articles by the European Commission, and the use of DEP is probably very limited as it is not suitable in such products.

- Further human studies on the exposure to phthalates in general and DEP in particular and adverse reproductive effects in humans, properly controlled for potential life style confounders such as tobacco smoking, are needed to refute or confirm whether phthalates at current levels of exposure may cause adverse reproductive effects. Further research should be directed to clarify whether humans are more susceptible to phthalates in general, and DEP in particular, than laboratory animals.

ASSESSED BY

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ACKNOWLEDGEMENT

The Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food, and Cosmetics wishes to thank Jan Erik Paulsen and Jan Alexander for the contribution to the draft of this opinion.

The Panel also wishes to thank Marit Kopangen at the Norwegian Pollution Control Authority (SFT) for her contribution to the text regarding the regulation of phthalates in toys and childcare articles in the opinion.

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