EUROPEAN COMMISSION

Health & Consumer Protection
Directorate-General

Scientific Committee on Health and Environmental Risks

SCHER

Risk Assessment Report on 2,3-EPOXYPROPYLTRIMETHYLAMMONIUM CHLORIDE (EPTAC)

Human Health Part

CAS No.: 3033-77-0
EINECS No.: 221-221-0

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

The SCHER adopted this opinion at its 19th plenary on 20 September 2007

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).

SCHER

Questions relating to examinations of the toxicity and ecotoxicity of chemicals, biochemicals and biological compound whose use may have harmful consequences for human health and the environment.

In particular, the Committee addresses questions related to new and existing chemicals, the restriction and marketing of dangerous substances, biocides, waste, environmental contaminants, plastic and other materials used for water pipe work (e.g. new organics substances), drinking water, indoor and ambient air quality. It addresses questions relating to human exposure to mixtures of chemicals, sensitisation and identification of endocrine disrupters.

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TABLE OF CONTENTS

1. BACKGROUND

Council Regulation 793/93 provides the framework for the evaluation and control of the risk of existing substances. Member States prepare Risk Assessment Reports on priority substances. The Reports are then examined by the Technical Committee under the Regulation and, when appropriate, the Commission invites the Scientific Committee on Health and Environmental Risks (SCHER) to give its opinion.

2. TERMS OF REFERENCE

On the basis of the examination of the Risk Assessment Report the SCHER is invited to examine the following issues:

(1) Does the SCHER agree with the conclusions of the Risk Assessment Report?

(2) If the SCHER disagrees with such conclusions, it is invited to elaborate on the reasons.

(3) If the SCHER disagrees with the approaches or methods used to assess the risks, it is invited to suggest possible alternatives.

3. OPINION

3.1 General comments

The health part of the document is of good quality, it is comprehensive, and the exposure and effects assessment follow the Technical Guidance Document. The RAR covers all studies relevant for exposure and hazard assessment of 2,3-epoxypropytrimethylammonium chloride (EPTAC).

3.2 Specific comments

3.2.1 Exposure assessment

Only inhalation of EPTAC-containing dusts and dermal exposures are considered relevant for the occupational exposure scenarios. The occupational exposure assessment develops a number of scenarios. Occupational exposure by inhalation is in part based on measured data, in part on modelling; dermal exposures are modelled. While inhalation exposures are predicted to be very low, some of the scenarios predict dermal exposures of up to 300 mg/person/day at the workplace. It should be noted that the use of EASE for modelling of dermal exposures gives highly conservative results and other models may give a more realistic prediction of exposure (Creely, K.S. et al., 2005; Marquart, H. et al., 2006).

EPTAC is not used directly in applications with consumer exposures, but consumers may be exposed to residues of EPTAC in products. Based on four scenarios evaluated in more detail, the RAR concludes that consumer exposure to EPTAC both by dermal contact and by oral contact with EPTAC-residues migrated from food contact materials is very low.

Indirect exposures from the environment were modelled and it was concluded that drinking water exposures may be higher then exposures from consumer product when using a worst case assumption, but still remains very low. The SCHER agrees with this approach.

3.2.2 Effect assessment

The information on ADME available is limited to in vitro skin penetration studies. The RAR therefore assumes 75 % absorption after inhalation and a dermal uptake of 6 %. However, the SCHER questions the use of a 6 % value for dermal absorption.

SCHER also agrees that EPTAC should be considered as an eye, but not a skin irritant. Based on the results of animal and human studies, EPTAC also has to be regarded as a skin sensitizer.

In the only repeated dose toxicity study, EPTAC gavage in doses of up to 100 mg/kg bw/day caused adverse effects on the kidney even in the lowest dose administered (3.16 mg/kg bw/day and adverse effects in the testes and the ovaries at doses of 31.6 mg/kg bw/day giving an overall LOAEL of 3.16 mg/kg bw/day with no NOAEL.

As expected from the presence of an epoxide function in EPTAC, genotoxicity studies in bacteria and mammalian cells and in an in vivo mouse micronucleus test were positive. The SCHER agrees that EPTAC should be considered as genotoxic.

In a 2-year dermal carcinogenicity study, EPTAC caused an increased incidence of tumours at the application site, but also an increase in the incidence of some systemic tumours in mice. The SCHER agrees that concern regarding carcinogenicity can be derived on the basis of the carcinogenicity study and the genotoxicity of HCCP in vivo.

Regarding reproductive and developmental effects, the SCHER agrees with the conclusion of an overall NOAEL of 10 mg/kg bw/day used in the risk characterisation. SCHER also supports the conclusion that additional testing will not result in an improved basis for risk assessment since the risk reduction measures are already mandated by the genotoxicity and dermal tumour induction seen with EPTAC.

3.2.3 Risk characterisation

The risk characterization performed in the RAR uses the margin-of-safety (MOS) approach and is performed for inhalation and dermal exposures. The SCHER agrees with conclusions iii)[1] for some of the occupational exposure scenarios regarding dermal exposures due to low MOS. Conclusion iii) is also supported regarding skin sensitisation.

Since the mutagenicity and dermal carcinogenicity already result in conclusion iii) testing for reproductive toxicity will very unlikely modify the need for risk reduction and should therefore not be of high priority.

Regarding consumer exposure, due to the concluded very low exposure, conclusion ii) is accepted. The SCHER also supports conclusion ii) for consumers and exposures from the environment regarding carcinogenicity and reproductive and developmental toxicity due to very low risks as delineated in the RAR.

4. LIST OF ABBREVIATIONS

LOAEL	Lowest Observed Adverse Effect Level
LOAEC	Lowest Observed Adverse Effect Concentration
MOS	Margin of Safety
NOAEC	No Observed Adverse Effect Concentration
NOAEL	No Observed Adverse Effect Level
RAR	Risk Assessment Report
TGD	Technical Guidance Document

[1] *According to the Technical Guidance Document on Risk Assessment – European Communities 2003:*

- *conclusion i): There is a need for further information and/or testing;*
- *conclusion ii): There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already;*
- *conclusion iii): There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.*

5. REFERENCES

H Marquart, N. D. Warren, J..Laitinen, J.J. van Hemmen Default values for assessment of potential dermal exposure of the hands to industrial chemicals in the scope of regulatory risk assessments. Ann Occup Hyg; 2006, 50:469-89