EUROPEAN COMMISSION

Health & Consumer Protection
Directorate-General

Scientific Committee on Health and Environmental Risks

SCHER

Risk Assessment Report on styrene

Human Health Part

CAS No.: 100-42-6

EINECS no.: 202-851-5

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

SCHER adopted this opinion at its 23rd plenary on 6 May 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).

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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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ACKNOWLEDGMENTS

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Keywords: SCHER, scientific opinion, risk assessment, Regulation 793/93, styrene, human health, CAS 100-42-6

Opinion to be cited as:

SCHER, scientific opinion on the risk assessment report on styrene human health part, CAS 100-42-6, 6 May 2008

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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 SCHER is invited to examine the following issues:

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

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

(3) If 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 human health part of the document is very detailed and of good quality; the risk assessment methods used are in compliance with the requirements of the Technical Guidance Document. The most relevant studies and publications are all included in the RAR. SCHER generally agrees with the conclusions made in the RAR.
Abbreviations should be explained when they are first introduced (e.g. GRP, NAEL, RWC, SBR, SB, UP-resin). It would make the document more reader-friendly if a list of abbreviations and their explanations or a glossary could be added.

3.2 Specific Comments

3.2.1 Exposure assessment

Styrene is used mainly in the manufacture of polystyrene resins and of copolymers with acrylonitrile or 1,3-butadiene. Five occupational exposure scenarios were identified with highest exposures occurring within the glass-reinforced plastics (GRP) industry, partly because of the use of open moulding techniques and hand laminating (1.6 to 167 ppm 8hr TWA).

Consumer exposure may result from emissions of building materials and carpets, from food and food packaging, and from styrene-containing resins used for repair works and boat building as well as from tobacco smoke. The combined exposure (excluding tobacco smoke) was estimated to be at the level of about 90 micrograms per day.

SCHER agrees with the exposure assessment as proposed in the RAR.

3.2.2 Effect assessment

SCHER agrees with the Member State's Rapporteur on the key health effects of styrene (acute toxicity; skin, eye and respiratory tract irritation; repeated dose toxicity and developmental toxicity). SCHER also agrees that there are no concerns for sensitisation, or effects on fertility. However, SCHER disagrees with the conclusion, that there is no concern for human carcinogenicity.

SCHER agrees with the proposed NOAEC of 100 ppm (433 mg/m3) for acute exposure, based on human data. Local irritation signs included slight, transient effects on the

human eye (dryness) at 100 ppm (7 hours exposure); at 216 ppm (1 hour exposure) nasal irritation occurred.

Target organs of repeated styrene exposure include the central and peripheral nervous system (in humans and rodents), liver and lung (in mice) and the nose (mice and rats). In humans, styrene may cause a transient decrease in colour discrimination (at exposure levels of 50 ppm and higher) and effects on hearing. The 4-week NOAEC in rats for ototoxicity, the most sensitive endpoint, was at 300 ppm. A 2-year oral NOAEL of 150 mg/kg bw/day was identified for mice. Taking into account the well demonstrated species differences between mice, rats and humans the SCHER agrees that 50 ppm can be considered as NOAEC in humans because of the mildness and reversibility of the effects at this exposure level observed in mice and rats..

Styrene is not genotoxic in the vast majority of *in vitro* and *in vivo* standard mutagenicity tests, but was tested positive *in vitro* indicator tests for SCEs, DNA stand breaks and DNA adducts. Based on the interpretation of the relevance of the positive findings provided by the Member State's Rapporteur, SCHER agrees with the overall conclusion that "There is no convincing evidence that styrene possesses significant mutagenic/clastogenic potential *in vivo*" from the available data in experimental animals".

No causal association between occupational styrene exposure and lung cancer have been demonstrated in a variety of epidemiological studies. Styrene was not carcinogenic in rats (five oral studies, two inhalation studies), but induced lung tumours in mice in one inhalation study and in two out of four gavage studies. SCHER agrees with the proposed non-genotoxic mechanism of tumour induction in mice and the notion that this mechanism, which involves as a key step the metabolism of styrene to cytotoxic metabolites in Clara cells, is not operational in human lungs to any significant extent. This agrees with the conclusion of IARC (2002).

However, although the RAR clearly describes the metabolic formation of the genotoxic and carcinogenic styrene oxide, its possible contribution to the carcinogenic risk of styrene exposure in other organs than lung is also considered negligible. This is insufficiently justified. Therefore, SCHER agrees with the conclusion of IARC (2002), that, based on the observations in human workers regarding blood styrene 7,8-oxide, DNA adducts and chromosomal damage, it cannot be excluded that this and other mechanisms are important for other organs.

Styrene caused no effects on fertility and reproduction in a 2-generation inhalation study. Increased prenatal deaths were found at dose levels causing decreased maternal weight gain. SCHER agrees with the conclusion of a NOAEC of 150 ppm for the risk characterisation.

3.2.3 Risk characterisation

The risk characterisation performed in the RAR used the margin-of-safety approach and was performed for inhalation and dermal exposures.

SCHER agrees with the method of converting human NOAECs into (extrapolated) internal no adverse effect levels (NAELs), and on the conversion of animal NOAECs into NAELs based on a PBPK model.

SCHER agrees with conclusion iii)[1] for some occupational scenarios regarding acute and repeated exposures, and developmental toxicity because of low MOS.

[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.*

For consumers, SCHER agrees with conclusion iii) for acute and repeated exposures arising from boat building and for the use of styrene containing liquid resins in relation to eye and respiratory tract irritation, effects on the hearing and on colour vision following repeated exposure and developmental toxicity, and to the use of styrene-based paste in relation to developmental toxicity. However, SCHER points out that conclusion iii) also applies for carcinogenicity. SCHER agrees with conclusion ii) for all remaining consumer scenarios.

4. LIST OF ABBREVIATIONS

EASE	Estimation and Assessment of Substance Exposure Physico-chemical properties
MOS	Margin of Safety
NAEL(s)	No Adverse Effect Levels
NOAEC	No Observed Adverse Effect Concentration
RAR	Risk Assessment Report
TGD	Technical Guidance Document