Scientific Committee on Health and Environmental Risks

SCHER

Opinion on

Risk Assessment Report on TETRACHLOROETHYLENE Human Health Part

CAS No.: 127-18-4
EINECS No. 204-825-9

The SCHER adopted this opinion at its 22nd plenary on 12 March 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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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 tetrachloroethylene.

3.2 Specific comments

3.2.1 Exposure assessment

The occupational exposure assessment considers six different scenarios for the use of tetrachloroethylene with dry cleaning as the major application. Exposure assessment for inhalation regarding 8 h TWAs is based on measured data in many cases whereas short-term peak level exposures are based on modelling. Regarding dermal exposure, TGD defaults or scenario-specific information was introduced into the EASE model for prediction of dermal exposures. Both inhalation and dermal exposure assessment is presented as typical values and as realistic worst-case exposures and both assessments are forwarded into the risk assessment.

Consumer exposure mainly related to inhalation exposure of tetrachloroethylene from dry-cleaned clothes is also based on measured and modelled data. Regarding combined exposures, inhalation of tetrachloroethene in the vicinity of dry cleaning establishments is delineated as the most significant source; the assessment of the general exposure from food gives a realistic worst-case scenario of 14.5 µg/kg/day.

3.2.2 Effect assessment

The RAR describes in detail all the toxicity studies performed with tetrachloroethylene. Regarding repeated-dose toxicity, a number of studies are available for evaluation and SCHER agrees with NOAELs and NOAECs derived from the evaluation of these studies.

In the RAR, the available mutagenicity studies on tetrachloroethylene are evaluated. In summary, most of the studies using oxidative activation by cytochrome P450 gave negative results suggesting that this pathway in tetrachloroethylene biotransformation does not result in formation of genotoxic metabolites. As indicated in the RAR, the

glutathione S-conjugate of tetrachloroethylene and downstream products (cysteine S-conjugate, mercapturc acid) are mutagenic in bacteria and tetrachloroethylene itself has also been shown to be mutagenic in bacteria under conditions favouring the formation of these conjugates.

One in vivo mutagenicity study in mice using specific conditions (intraperitoneal administration of a high dose after partial hepatectomy) showed a marginal increase in the frequency of micronuclei in hepatocytes.

SCHER does not conclude that these results indicate a need for further mutagenicity testing. The small increase in micronucleus frequency may be due to secondary effects such as cytotoxicity or related to the mode-of-action of tetrachloroethylene for liver tumour induction in mice, which is peroxisome proliferation (not considered relevant for humans). Even a positive response in a repeat of this test will not affect the overall weight-of-evidence conclusion that tetrachloroethylene, under conditions of oxidative biotransformation as occurring in the liver, is not mutagenic.

However, the RAR will need to consider the relevance of the observed mutagenicity of tetrachloroethylene under conditions favouring glutathione S-conjugates for conclusions on mutagenicity.

These experiments gave a positive response, and the mutagenicity of metabolites formed by further metabolism of glutathione S-conjugates was also demonstrated. However, this pathway becomes relevant only after application of high doses in animals.

3.2.3 Risk characterisation

The risk characterization performed in the RAR uses the MOS approach for oral, inhalation and dermal exposures of consumers and dermal and inhalation exposures of workers. SCHER agrees with this approach and the absence of concern regarding sensitization. For the occupational exposure scenarios, the MOS regarding realistic worst-case scenarios result in conclusion iii)[1] for a number of exposure scenarios and endpoints. SCHER agrees with these conclusions. SCHER also agrees with conclusion iii) regarding consumer exposures from coin-operated dry-cleaning machines. Conclusion ii) for indirect and combined exposures is supported considering the justification for threshold approach to assess risk of renal tumour induction.

4. LIST OF ABBREVIATIONS

EASE	Estimation and Assessment of Substance Exposure
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.