EUROPEAN COMMISSION

Health & Consumer Protection
Directorate-General

Scientific Committee on Health and Environmental Risks

SCHER

Risk Assessment Report on Hexachlorocyclopentadiene (HCCP)

Human Health Part

CAS No.: 77-47-4
EINECS No.: 201-029-3

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

The SCHER adopted this opinion at its 16th plenary on 23 April 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.

Scientific Committee members

Herman Autrup, Peter Calow, Wolfgang Dekant, Helmut Greim, Colin Janssen, Bo Jansson, Hannu Komulainen, Ole Ladefoged, Jan Linders, Inge Mangelsdorf, Marco Nuti, Jerzy Sokal, Anne Steenhout, Jose Tarazona, Emanuela Testai, Marco Vighi, Matti Viluksela, Hanke Wojciech

Contact:

European Commission
Health & Consumer Protection DG
Directorate C: Public Health and Risk Assessment
Unit C7 - Risk Assessment
Office: B232 B-1049 Brussels

Sanco-Sc8-Secretariat@ec.europa.eu

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http://ec.europa.eu/health/ph_risk/risk_en.htm

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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 hexachlorocyclopentadiene (HCCP).

3.2 Specific comments

3.2.1 Exposure assessment

Only inhalation and dermal exposures are considered relevant for the occupational exposure scenarios. Since HCCP is not used in applications with potential consumer exposures and only a low bioconcentration factor has been determined, indirect exposures from the environment are predicted to be very low. The occupational exposure assessment develops four scenarios, and detailed assessments are made for three of these scenarios. The forth scenario is formation and release of HCCP during fires, which has to be considered as accidental release, and is not covered further. Occupational exposure by inhalation is in part based on measured data, in part on modelling; dermal exposures are modelled. The SCHER agrees with this approach.

3.2.2 Effect assessment

The effects assessment includes a very detailed assessment of ADME studies. The description of the study, however, is unclear since air concentrations are given in microg/kg bw (which are doses). If these are the estimated received doses, the approach to calculate these doses from air concentrations of HCCP should be given in the description. Given the inability to make firm conclusions based on the available ADME-studies, the SCHER supports the conclusion that 100 % absorption of HCCP after dermal or inhalation exposure should be used in risk characterisation.
SCHER also agrees that HCCP should be considered as skin, eye and respiratory tract irritant and as a potent skin sensitizer.
From the available repeated dose toxicity studies, no NOAEC for inhalation exposures could be derived and a LOAEC of 0.11 mg/m^3 regarding inflammatory effects on the respiratory tract was derived. Systemic effects reported after inhalation exposures were

ovarian inflammation, with a NOAEC of 0.11 mg/m^3. After oral administration, HCCP caused dose related increases in kidney to body weight ratios in mice and rats with an NOAEL of 10 mg/kg bw/day in rats. No NOAEL could be derived for mice. As a remark, received doses in inhalation studies can only be calculated with a detailed knowledge of extent of pulmonary retention and the tables describing these studies in the RAR should use the term "exposure concentration" or "air concentration" instead of giving "doses" in mg/m^3. The no effect concentrations are NOAECs and not NOAELs.
In genotoxicity studies in bacteria, HCCP was negative in the studies considered suitable for hazard assessment. In mammalian cells, weakly positive results were observed in chromosomal aberration assays. However, inhalation of HCCP for 13 weeks at maximal tolerated doses in mice did not increase the incidence of micronuclei in peripheral erythrocytes in mice. The SCHER agrees that HCCP should not be considered as a genotoxic agent in vivo.
In a 2-year carcinogenicity studies performed following the typical NTP study protocol, inhalation of HCCP at concentrations up to 2.28 mg/m^3 did not cause an increased incidence of tumours in rats and mice. The SCHER agrees that no concern regarding carcinogenicity can be derived on the basis of the negative carcinogenicity study in two species and the absence of genotoxicity of HCCP in vivo.
Regarding reproductive and developmental effects, the SCHER agrees with the conclusion of an overall NOAEL of 25 mg/kg bw/day used in the risk characterisation.

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 repeated inhalation and dermal exposures due to low MOS. Conclusion iii) is also supported regarding skin sensitisation. A potential for respiratory sensitisation by HCCP should be considered in the RAR and the minimal MOS may require adjustment for this endpoint with regard to conclusions on scenario 3 with a MOS of only 58. Regarding consumer exposure, due to absence of exposure, conclusion ii) is accepted. The SCHER also supports conclusion ii) regarding carcinogenicity and reproductive and developmental toxicity

4. LIST OF ABBREVIATIONS

ADME	Absorption, Distribution, Metabolism, Excretion
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
NTP	National Toxicology Program
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.*