



Scientific Committee on Health and Environmental Risks

SCHER

Opinion on

Risk Assessment Report on

NITROBENZENE

Human Health Part

CAS No: 98-95-3

EINECS No: 202-95-3



The SCHER adopted this opinion at its 25th plenary on 9 September 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 (EMA), 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, Hanke Wojciech, Colin Janssen, Bo Jansson, Hannu Komulainen, Ole Ladefoged, Jan Linders, Inge Mangelsdorf, Marco Nuti, Anne Steenhout, Jose Tarazona, Emanuela Testai, Marco Vighi, Matti Viluksela

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

© European Commission 2008

The opinions of the Scientific Committees present the views of the independent scientists who are members of the committees. They do not necessarily reflect the views of the European Commission. The opinions are published by the European Commission in their original language only.

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

ACKNOWLEDGMENTS

The rapporteur is acknowledged for his valuable contribution to this opinion:
Prof. W. Dekant Universität Würzburg, Germany

Keywords: SCHER, scientific opinion, risk assessment, Regulation 793/93, nitrobenzene, human health, CAS 98-95-3

Opinion to be cited as:

SCHER, scientific opinion on the risk assessment report on nitrobenzene, human health part, CAS 98-95-3, 9 September 2008

TABLE OF CONTENTS

ACKNOWLEDGMENTS	3
1. BACKGROUND.....	1
2. TERMS OF REFERENCE	5
3. OPINION	5
3.1 General comments	5
3.2 Specific comments	5
3.2.1 Exposure assessment	5
3.2.2 Effect assessment.....	5
3.2.3 Risk characterisation.....	6
4. LIST OF ABBREVIATIONS.....	6

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 nitrobenzene.

3.2 Specific comments

3.2.1 Exposure assessment

The almost exclusive use of nitrobenzene is as an intermediate in the synthesis of aniline; other uses are of low importance. Nitrobenzene seems not to be contained in consumer products. Regarding occupational exposure assessment, the RAR uses only one relevant occupational scenario (production and further processing of nitrobenzene) develops a detailed exposure assessment. Exposures by dermal contact and by inhalation are assessed by a combination of modelling and measured data on air concentrations of nitrobenzene for inhalation, and modelling for dermal exposures applying the defaults of the TGD. Consumer exposures and indirect exposures are expected to be very low due to the almost exclusive use of nitrobenzene as a chemical intermediate in industry. SCHER agrees with this assessment.

3.2.2 Effect assessment

The RAR describes all toxicity studies performed with nitrobenzene in sufficient detail. Regarding repeated-dose toxicity and carcinogenicity, a number of studies are available for evaluation and SCHER agrees with NOAECs/LOAECs resp. NOAELs/LOAELs derived from the evaluation of these studies. Methemoglobinemia and anemia are the most pronounced toxic effect of nitrobenzene in rodents.

Regarding toxicokinetics, SCHER agrees with the derived 100 % absorption factor for oral uptake and suggests to also use 100 % retention for inhalation. Based on the available contradictory data, concern regarding skin sensitisation is derived in the RAR and SCHER agrees with conclusion i) regarding the need for a local lymphnode assay to assess hazard for sensitisation. SCHER also agrees that there is concern regarding carcinogenicity due to the presence of structural alerts in the molecule and a number of long-term animal studies showing induction of a variety of tumour types after exposure

to nitrobenzene. However, nitrobenzene was negative in most of the available genotoxicity data in vivo and in vitro, but methodological issues with the experimental conduct were identified for many of the genotoxicity endpoints investigated. Therefore, absence of genotoxic effects cannot be completely ruled out. SCHER agrees with the RAR that there is an unclear genotoxic potential of nitrobenzene. SCHER also agrees that nitrobenzene is not a specific reproductive toxicant.

3.2.3 Risk characterisation

The risk characterization performed in the RAR uses the margin-of-safety (MOS) approach. The SCHER agrees conclusion i) regarding skin sensitisation due to absence of reliable studies and conclusion ii) regarding reproductive and developmental toxicity due to large MOS. SCHER also agrees to conclusion iii) regarding local and systemic effects after inhalation at the workplace after inhalation exposures. Regarding carcinogenicity, SCHER concludes that the human relevance of the positive carcinogenicity studies in animals cannot be assessed due to insufficient data on mechanism of carcinogenicity and therefore, conclusion iii) regarding carcinogenicity for both dermal and inhalation exposures as made in the RAR due to low MOS is further supported. SCHER also agrees with conclusion ii) for all endpoints regarding all toxicity endpoints in the risk assessments for humans due to environmental nitrobenzene exposures due to high MOS.

4. LIST OF ABBREVIATIONS

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