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Scientific Committee on Toxicity, Ecotoxicity and the Environment

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SCIENTIFIC COMMITTEE ON TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE)

Opinion on the results of the Risk Assessment of:

Dimethyldioctadecylammonium chloride (DODMAC)

CAS No.: 107-64-2
EINECS No.: 203-508-2

REPORT VERSION (Human Health)

Draft of 16.07.2001

Carried out in the framework of Council Regulation (EEC) 793/93 on the evaluation and control of the risks of existing substances[1]

Opinion expressed at the 30th CSTEE plenary meeting

Brussels, 22 February 2002

[1] Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of those substances if they are produced or imported into the Community in volumes above 10 tonnes per year. The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94, which is supported by a technical guidance document.

Terms of reference

In the context of Regulation 793/93 (Existing Substances Regulation), and on the basis of the examination of the Risk Assessment Report the CSTEE is invited to examine the following issues:

1. Does the CSTEE agree with the conclusions of the Risk Assessment Report

2. If the CSTEE disagrees with such conclusions, the CSTEE is invited to elaborate on the reasons for this divergence of opinion.

Introduction

Dimethyldioctadecylammonium chloride (DODMAC) is the major component in the technical product ditallowdimethylammonium chloride (DHTDMAC). DODMAC, due to its properties as a surfactant, is used in cleaning products, the cosmetics industry and in the production of organic clays. Human exposure may occur during production and processing of DODMAC-containing products and by skin exposure of workers and consumers by use of cosmetics and detergents. Occupational exposure to DODMAC may occur by inhalation of DODMAC-containing dusts when handling a dry powder or by skin contact when handling aqueous emulsions or paste-like preparations of DODMAC. Annual production of DODMAC in the EU has declined from > 65 000 t/a in 1990 to approximately 400 t/a in 1998.

General comments

The health part of the document is of excellent quality. The CSTEE agrees with the general conclusions for most exposure scenarios that there is at present no need for further testing and for risk reduction measures beyond those already applied.

Specific comments

Despite the high production volumes, the database on DODMAC toxicity is limited and most of the information on DODMAC exposures of workers and consumers are based on expert judgement or modelling, only very actual measurements of exposures exist.

HUMAN HEALTH

1. Exposure assessment

Human occupational exposure to DODMAC may occur during production of DODMAC-containing products, during mixing of formulations containing DODMAC such as production of fabric softeners, car cleaning agents and organic clays, and during formulation and application of cosmetic products containing DODMAC. As pointed out in the RAR, the main human routes of exposure to DODMAC are inhalation of DODMAC-containing dusts during handling of powdered DODMAC-containing products and dermal contact during production,

formulation and application. The assessor assumption that the dermal exposure is low during production is not very convincing. Since only few measured data on the actual DODMAC-exposures are available, actual DODMAC-exposures under different scenarios were estimated by modelling. The highest occupational exposures (skin contact of up to 110 mg/person/day) are predicted for the use of hair care production and car polishing products containing DODMAC.

2. Effects assessment

Acute toxicity
The acute oral and dermal toxicity of DODMAC has been studied in rats and rabbits. The available data from the studies show that the acute toxicity of DODMAC is low with LD_{50}-values > 2000 mg/kg. Limited data on toxicity after inhalation of a poorly characterised « mist » containing DODMAC suggest that toxicity after inhalation is also low.

Irritation and corrosivity
Pure DODMAC has only a low potential for skin irritation and is not to be labelled according to the Classification and labelling Directive (67/548/EEC). However, technical grade DODMAC containing 11.3 % isopropanol and 11.7 % water causes corrosion of the skin. Pure DODMAC is a potent eye irritant.

Sensitising properties
A guinea pig maximisation test on DODMAC did not indicate a potential for DODMAC to act as sensitiser ; however, the study is considered inadequate to draw conclusions. Results of a repeated insult test with a preparation containing 78 % DODMAC and a multi-centered study with application of a DODMAC to individuals with contact dermatitis suggest that DODMAC is not a sensitizer in humans. However, DODMAC is reported to enhance significantly skin allergies to chemical substances in tests with guinea pigs and mice. According to the CSTEE, this finding is of relevance for the overall health risk of the chemical.

Repeated dose toxicity
There is only limited information on the toxicity of DODMAC after repeated administration to animals by the oral route and by skin contact. The CSTEE agrees with the derived NOAEL of 100 mg/kg bw per day for 28 day exposures.

Genotoxicity
DODMAC, tested as a 90 % preparation in 5 % isopropanol, was not mutagenic in a standard Ames test with Salmonella strains TA98, 100, 1535, 1537, 1538 and *E. coli* WP2uvrA, both in the absence and in the presence of S-9 mix. A further Ames test (not included in the RAR) with Salmonella typhimurium TA98 and TA100 was also negative both after activation with various liver homogenates (S-9) from rats, hamsters and guinea pigs and in the presence of norharman (Sunakawa T. *et al.*, 1981).

In a test performed according to current guidelines, DODMAC (90 % preparation in 5 % isopropanol) did not induce chromosome aberrations in V79 cells, both with and without metabolic activation. A further cytogenetic study in V79 cells was also negative.

There are no in-vivo genotoxicity studies available.

The CSTEE agrees with the RAR conclusion that there are no hints on mutagenic properties of DODMAC.

Carcinogenicity
No experimental data are available on the carcinogenicity of DODMAC or DHTDMAC, which contains DODMAC as a major component.

Based on the consistently negative *in vitro* studies on the genotoxicity of DODMAC, the CSTEE agrees with the RAR conclusion that there are no indications for a carcinogenic potential of DODMAC by a genotoxic mechanism. Due to the limited data on DODMAC toxicity after repeated administration, no conclusions on carcinogenicity by a non-genotoxic mechanism may be made.

3. Risk characterisation

Genotoxicity
The CSTEE agrees with the view that there are no concerns for genotoxicity and with the overall conclusion ii) for this endpoint for all scenarios

Carcinogenicity
The CSTEE agrees with the view that there are no concerns for carcinogenicity by genotoxic mechanisms and with the overall conclusion ii) for this endpoint for all scenarios. Due to the limited data on the toxicity of DODMAC after repeated administration (only one well performed 28 day study available), the relevance of possible cancer induction by non-genotoxic mechanism for risk characterisation can not be assessed. However, since most of the MOS calculated for the different exposure scenarios (> 200 for systemic toxicity after dermal uptake, very high for systemic toxicity after inhalation uptake) are large and DODMAC is poorly absorbed through the skin and not accumulated in mammals, the lack of data on toxicity after long-term administration does not change the overall conclusions.

Workers
The CSTEE agrees with the overall results of the risk assessment report that there is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already. The MOS-values calculated by the extrapolation procedures applied for the worst-case occupational exposure scenario (skin exposure) are low (only 3–9). However, these MOS are based on extrapolation from an oral NOAEL using correction factors for exposure duration, metabolic scaling and the assumption that dermal absorption of DODMAC equals intestinal absorption. The use of these factors results in a large overestimation of internal exposure after skin contact to DODMAC; therefore, concern is not indicated by the low MOS.

Consumers
The CSTEE agrees with the overall results of the risk assessment report that there is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

References

SUNAKAWA T *et al.*: Mutagenicity of surfactants: Mutagenicity of surfactants following activation with various liver homogenates and mutagenicity in the presence of norharman., Eisei Kagaku 27, (1981), 204-211.