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

Opinion on the results of the Risk Assessment of:

2-ETHYLHEXYL ACRYLATE

CAS N° : 103-11-7

EINECS N° : 203-080-7

HUMAN HEALTH

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

Adopted by the CSTEE during the 40th plenary meeting of 12-13 November 2003

[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.

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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.

1. Introduction

Six companies are known to produce or import 2-ethylhexyl acrylate within the EU. In 1999 the total production volume was 70,000 tonnes per year, the import volume was approximately 30,000 tonnes per year and 10,000 tonnes per year were exported. 2-Ethylhexyl acrylate is used as a monomer in the chemical industry for the production of polymers and copolymers, which are mainly processed further to aqueous polymer dispersions. The polymers and polymer dispersions are used in adhesives (60% of total use) and as binders for paints (25% of total use). Other applications include coatings of raw materials, and uses in the plastics and industries. In addition, it is used as a monomer in construction-industry chemicals in concentrations between 0.1-21%. In 2002, 426 products containing 2-ethylhexyl acrylate were registered in the Danish Product Register and 575 products in the Norwegian Products Register, respectively.

2. General Comments

The RAR with respect to the human health part of the report is of good quality. The CSTEE is in agreement with most of the proposed risk characterisation conclusions, except for respiratory sensitisation where the Committee proposes the conclusion (iii).

3. Specific Comments

Exposure assessment

Occupational exposure

Occupational exposure to 2-ethylhexyl acrylate may occur according to the following scenarios: 1) Production of 2-ethylhexyl acrylate and polymerisation, 2) formulation of preparations containing up to 21% 2-ethylhexyl acrylate, 3) use of formulations containing monomeric 2-ethylhexyl acrylate in the building trade, and 4) use of dispersions with residual monomeric 2-ethylhexyl acrylate. Assessment of inhalation exposure has mainly been based on measured exposure levels. Dermal exposure has been estimated using the EASE model.

The reasonable worst case of 2.8 mg/m^3 has been assessed for inhalation exposure during production of 2-ethylhexyl acrylate and polymerisation. Because of the highly irritative effect of 2-ethylhexyl acrylate, daily dermal exposure has been considered to be negligible. Occasional dermal exposure of up to 10.5 mg/person/day is possible.

For inhalation exposure during formulation of preparations of up to 21% 2-ethylhexyl acrylate, measurements are not available. Exposure of 19 mg/m^3 for a shift average has been estimated based on the EASE model. For dermal exposures occasional levels of 10.5 mg/person/day has been calculated.

For assessing the risk of inhalation exposure in the building trade, an exposure level based on measurements of methyl methacrylate has been used, since the latter may be contained in the formulations as a copolymer. For flooring works, the inhalation exposure level of 3 mg/m^3 has been used, recognising that this does not occur daily. For the same exposure scenario not occurring daily, dermal exposure of 880 mg/person/day has been modelled.

Inhalation exposure during use of dispersions with residual monomeric 2-ethylhexyl acrylate is considered to be negligible. Dermal exposure in these situations has been assessed to be up to 3 mg/person/day, here the exposure is also considered not to occur daily.

Consumer exposure

With respect to consumer use categories, dermal exposure may occur to lubricants and greases (0.08% residual monomer content), inhalation and dermal exposure to paints and lacquers (0.08% residual monomer content), and potential oral exposure to plastic articles coming into contact with food.

Dermal exposure to lubricants and greases has been estimated to be 11.2 µg/kg bw per event. For paints, the dermal exposure would lead to 1.3 µg/event. Inhalation exposure to 1 ppm (7,5 mg/m^3) of 2-ethylhexyl acrylate in indoor air has been taken as a worst case for short-term scenarios when using dispersion paints. The oral exposure of 2-ethylhexyl acrylate from exposure to articles coming into contact with food is estimated to be negligible, based on comparison with plastic material containing other acrylates.

Indirect exposure via the environment

Worst case exposures have been estimated for emissions from production sites, mainly via air, resulting in total daily doses of 2 µg/kg bw. Total exposure related to formulation of polymer dispersions (via fish consumption) has been estimated to be 0.4 µg/kg bw/day.

Effects assessment

Toxicokinetics

No specific studies are available on 2-ethylhexyl acrylate metabolism. Based on comparison with other acrylates, it may be assumed that it is metabolised via carboxylesterase-catalysed hydrolysis of the ester function to release acrylic acid and alcohol. The half-life of the hydrolysis reaction using tissue preparations is quite short. It may be assumed that the urinary excretion products are predominantly glucuronides of the oxidised metabolites. The acrylic acid is decarboxylated and degraded to carbon dioxide. Some of the 2-ethylhexyl acrylate may react with glutathione and excreted as thioethers. After an oral dose of the substance to rats, 50% of the dose was eliminated via the expired air and about 38% via the urine within the first 24 hours, whereas a small portion was excreted via the faeces. No specific studies using dermal administration or inhalation exposure are available.

Acute toxicity

Human data on the acute toxicity of 2-ethylhexyl acrylate are not available. In animal studies, 2-ethylhexyl acrylate possesses slight acute toxicity.

Irritation/corrosion

Animal studies have documented that 2-ethylacrylate is an irritant, but not a corrosive substance. On the basis of eye irritating studies, 2-ethylhexyl acrylate should not be classified as an eye irritant. Studies of repeated inhalation of 2-ethylhexyl acrylate in animals have revealed a serious respiratory irritation potential.

Sensitisation

In various tests with guinea pigs, a moderate sensitisation potential of 2-ethylhexyl acrylate has been revealed both without and with adjuvants. Dermal sensitisation in humans has also been reported. Information on potential for respiratory sensitisation in humans is not available.

Repeated-dose toxicity

2-Ethylhexyl acrylate induced dose-related degeneration of the olfactory epithelium after 90-day inhalation exposure of rats. The NOAEL for local effects on the respiratory tract was 75 mg/m^3. The animals showed lethargy, ptosis and reduced body weight gain at 225 mg/m^3, but no toxic effects on internal organs were identified. Minimal liver damage was indicated at 750 mg/m^3. Valid studies with dermal or oral routes are not available.

Mutagenicity

2-Ethylhexylacrylate (2-EHA) did not induce point mutations in bacterial tests, but there are positive assays with mammalian cells (mouse lymphoma assays, HPRT test in CHO cells). The positive results were, however, obtained at test concentrations which also caused clear cytotoxicity. There is no convincing evidence of chromosomal damage from an *in vitro*

chromosomal aberration study in mouse lymphoma cells, using a non-validated method. In this study aberration frequencies between 5 and 9% were reported as compared to 4% in the negative control cultures. An *in vitro* UDS test was negative.

A chromosomal aberration frequency of 2.2% was found in an *in vivo* bone marrow test on mice. This rate was higher than the concurrent controls, but within the historical range of the laboratory. An *in vivo* UDS test was negative (performed in accordance with OECD Testing Guideline 486).

Acrylic acid and 2-ethylhexanol, the hydrolysis products of ethylhexyl acrylate did not induce chromosomal aberrations *in vivo*.

Based on the available data for ethylhexyl acrylate and related compounds, it was concluded that ethylhexyl acrylate is not to be considered as a mutagenic compound *in vivo.*

Carcinogenicity

Human carcinogenicity data

Data on carcinogenicity in humans are not available.

Animal data

The carcinogenic potential of 2ethylhexylacrylate was investigated in lifetime studies in two strains of mice after dermal exposure. In two studies on C3H/HeJ mice, ethylhexyl acrylate increased the incidence of benign and malign skin tumours at concentrations that were highly irritating to the skin of the animals (= 21% ethylhexyl acrylate in acetone). Increases in neoplasias were not observed in the groups treated with 2.5% ethylhexyl acrylate, or treated for only 24 weeks with 43% ethylhexyl acrylate.

No skin tumours were found in NMRI mice treated dermally with ethylhexyl acrylate in concentrations of up to 85%, with or without subsequent application of 12-O-tetradecanoylphorbol 13-acetate (TPA).

Acrylic acid, the hydrolysis product, was not tumorigenic in mice treated dermally or orally. According to the RAR there is also “no concern from cancer data on 2-ethylhexanol”, although it is noted that 2ethylhexanol is nominated by the US National Toxicology Program for further cancer studies.

Based on the available data, it was concluded that ethylhexyl acrylate can induce skin tumours by a non-genotoxic mechanism through skin irritation.

Reproductive toxicity

There are no human data available on the reproductive toxicity of 2-ethylhexyl acrylate. There also are no fertility studies on this substance. No adverse effects on reproductive organs or on embryo-/foetal development have been revealed from 3-month repeated dose and developmental toxicity studies by the inhalation route in rats.

Risk characterisation

Workers

Acute toxicity

The CSTEE is in agreement with conclusion (ii).

Irritation/corrosion

The CSTEE is in agreement with conclusion (ii), since control measures exist which can minimise dermal exposure. It is important that such controls must be implemented and complied. The CSTEE also agrees that there does not appear to be a concern for respiratory irritation based on a comparison of exposure and effect levels.

Sensitisation

The CSTEE supports the conclusion (iii) for the occupational dermal exposure scenarios, except for the fourth scenario with very low 2ethylhexyl exposure (use of dispersions with residual monomer). With respect to the potential for respiratory sensitisation, the Committee does not support the conclusion (ii), but concludes with (iii) since 2-ethylhexyl acrylate both is a dermal sensitising agent and a strong respiratory irritant.

Repeated-dose toxicity

The CSTEE agrees that there is a concern for local effects related to inhalation exposures involving formulation of preparations containing up to 21% 2-ethylhexyl acrylate (conclusion iii). There are no concerns for systemic effects related to inhalation (conclusion ii). Also, the CSTEE agrees to the conclusion (ii) for both local and systemic effects for dermal exposure and combined inhalation and dermal exposure.

Genotoxicity

Based on the available data on ethylhexyl acrylate there is little evidence for a relevant genotoxic effect in experimental systems. The CSTEE agrees with the conclusion of the RAR that ethylhexyl acrylate is not to be considered as an *in vivo* mutagen. The CSTEE agrees with conclusion (ii).

Carcinogenicity

Based on the available data on animals, ethylhexyl acrylate can induce skin tumours by a non-genotoxic effect through strong skin irritation. Exposures with repeatedly strong skin irritation are however not expected to occur in the scenarios as described in the RAR. The CSTEE is in agreement with conclusion (ii).

Reproductive toxicity

Although the database on fertility is limited, the CSTEE is in agreement with conclusion (ii) since no effects on reproductive organs were noted at doses considerably higher than those that induce general toxic effects. The Committee also agrees that developmental toxicity is not expected as a specific effect, independent of general toxicity (conclusion ii).

Consumers

The CSTEE is in agreement with conclusion (ii).

Man exposed indirectly via the environment

The CSTEE is in agreement with conclusion (ii).