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Unit C2 – Management of Scientific Committees; scientific co-operation and networks
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:

Bis(pentabromophenyl)ether

Human Health Part

CAS No.: 1163-19-5

EINECS No.: 214-604-9

REPORT VERSION:

Final draft report, October 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.

GENERAL COMMENTS

The acronym in the report is DBDPO, more common is DBDE. The risk assessment of decabromodiphenyl ether (DBDE) is difficult for several reasons. The compound is extremely lipophilic and has a low volatility, this is why available exposure models are of limited value. It is also difficult to analyse and therefore there are few measured exposure data. It can also contain and form extremely toxic brominated dioxins and furans (PBDD/F). The properties also make it necessary to critically look at test results as *e.g.* the dose may not be compatible with its low solubility.

The exposure assessment in the report is anyhow mainly based on predicted values, which may be less accurate than for other substances. Where these predicted values can be compared with measured data they seem to agree reasonably well.

The CSTEE agrees with the overall conclusion ii) for all endpoints for DBDE for consumers and inhalation exposure for workers. Regarding dermal exposure for workers it is not clear from the report how the body burden is calculated from the exposure predictions. The exposure for the PBDD/F may be a problem. In an Appendix this is mentioned, but not in the conclusions in the main report. The used TDI values are also higher than those recommended today for these substances.

Possible effects of indirect exposure to lower brominated degradation products of DBDE are not covered in the report.

SPECIFIC COMMENTS

Exposure assessment

The major occupational exposure to DBDE will probably appear during the handling of the substance itself. As it is produced as fine particles the major exposure will be to the dust during bagging operations. There are only few measured data available describing the exposure to DBDE and the assessor has used the EASE model to predict the levels, and the results are comparable with the scarce data that have been measured. It is mentioned in several places that the substance in the final product will be included in the polymer and that DBDE is immobile in the polymer. The concentration of the flame retardant is, however, up to 30% and the amount attached to the surface must be considerable. Furthermore the substance is

probably not dissolved in the polymer, and if so, there will be particles of pure DBDE on the surface.

Consumers may be exposed to DBDE from flame retarded materials, but the few studies are difficult to interpret, and the assessor *feels that the consumer exposure to DBDE is likely to be negligible*. The levels found in the general US population may be the result of an indirect exposure via the environment. EUSES has been used to predict this pathway. This model is not reliable for substances as lipophilic as DBDE, and the predicted concentration in *e.g.* root tissues of plants is probably grossly overestimated. This does not influence the final conclusions as the estimated occupational exposure is much higher than the consumer exposure. In the environment, DBDE may yield lower brominated diphenylethers with higher bioavailability and toxicity by photolysis and microbial degradation, congeners not found in technical products of PBDEs. These lower brominated congeners may be a source for indirect exposure of man.

The half-life of DBDE in man has recently been estimated to about one week [Hagmar *et al.*, Organohalogen Compounds, 47 (2000) 198] and the levels found in the general population indicate a continuous exposure. This is not referenced in the report and is surprising considering the properties of the compound; this is data that needs to be confirmed.

The presence and formation of polybrominated dioxins and furans also has to be taken into account in an assessment of DBDE. This is done in Appendix D of the RAR, which is difficult to follow as it deals both with OBDE and DBDE. It is assumed that the commercial DBDE products are not contaminated with these substances. This is probably not true, although the levels may be low. The Annex also refers to a report on levels of PBDD/F in *fumes collected during extrusion of a commercial blend of polybutyleneterephthalate and DBDE*, where 760 pg TEQ/m3 were found. If this concentration is inhaled over 8 h it will cause an exposure of concern.

Effects assessment

Samples used for toxicity testing differed in purity, samples containing only 75 % DBDE were often used in the older studies. In the more recent carried out in accordance with GLP procedures, purity was > 97%.

The acute oral dermal toxicity was studied in rats and rabbits. The data show that the acute toxicity of DBDE is low. Data in rats indicate a low absorption (approximately 6%) of DBDE through the gastro-intestinal tract. Based on physicochemical properties and analogy with PCBs, a maximal dermal absorption of 1% may be assumed. Limited data on toxicity after inhalation also indicate low toxicity. Animal and human data indicate that DBDE is not an irritant for skin and eyes. From studies in rabbits it is concluded that DBDE has no “chloracnegenic” activity. Results of two large studies in humans and a Magnusson and Kligman test in guinea pigs did not indicate that DBDE is a skin sensitiser, although in the latter study commercial OBDE was used with less than 3 % DBDE. No information is available on respiratory sensitisation.

Repeated dose toxicity studies in rats and mice show that the subacute, subchronic and chronic toxicity of DBDE is low. The CSTEE agrees with a lowest NOAEL for systemic

toxicity of 1,120 mg/kg/day. Effects found were liver enlargement with centrilobular cytoplasmic enlargement and vacuolisation, renal hyaline degenerative cytoplasmic changes and follicular cell hyperplasia of the thyroid. In the chronic study in rats non-neoplastic changes included fibrosis of spleen, and hyperplasia in lymph nodes. Intratracheal administration of DBDE dust particles in rats resulted in focal aggregates of macrophages in the lung, the half-life of DBDE in the lung was determined to be 150 days.

From the negative results of the in vitro and in vivo mutagenicity assays there is no concern for mutagenicity.

In the carcinogenicity studies conducted by NTP equivocal evidence of carcinogenicity was obtained in male mice (increase of liver tumours in low dose group and thyroid gland follicular cell tumours in both dose groups); no evidence of carcinogenicity in female mice. In both male and female rats some evidence of carcinogenicity (dose-dependent increased incidence of neoplastic liver nodules); on this effect a LOAEL for carcinogenicity of 1,120 mg/kg/day is based. IARC (1990) has concluded a limited evidence for carcinogenicity in experimental animals; DBDE has been classified in group 3: “Not classifiable as to its carcinogenicity to humans”.

Toxicity for reproduction was examined in a one generation reproduction study in rats producing no signs of toxicity in dams and neonates at 100 mg/kg/day, the highest dose tested. In a developmental study carried out in the seventies with a commercial DBDE with 77.4 % purity, embryotoxicity was noted that included embryo/foetal death and subcutaneous oedema, indicating a LOAEL (conceptus) of 10 mg/kg/day. However, in a recent prenatal developmental GLP study with a composite of three lots of commercial DBDE with of purity 97.34%, no maternal or developmental toxicity was observed at 1,000 mg/kg/day. The high toxicity to neonates in combination with oedema formation observed in the older study are likely caused by dioxin-like impurities in the product of low purity. The CSTEE agrees that based on the recent study, no concern for adverse effects on development may be assumed.

The effects of PBDD/F have been evaluated using “dioxin equivalents” (TEQ). The assessor uses I-TEFs for the chlorinated analogues, but today WHO-TEFs are normally used. There is also an IPCS document (WHO Environmental Health Criteria Document 205, Polybrominated Dibenzo-*p*-dioxins and Dibenzofurans, 1998) which could be referenced, as this includes an estimate of the TEFs for the brominated compounds. The TDI that is used is the old WHO value of 10 pg TEQ/kg bw/day, but this has been revised and is today 1-4 pg TEQ/kg bw/day. The European Commission has also recently decided on a TWI (tolerable weekly intake) of 14 pg TEQ/kg bw.

Risk characterisation

The CSTEE agrees with the overall conclusion ii) for all endpoints for DBDE for consumers and inhalation exposure for workers. Regarding dermal exposure for workers it is not clear from the report how the body burden is calculated from the exposure predictions given in Table 4.1. The exposure for the PBDD/F may be a problem. In an Appendix this is mentioned, but not in the conclusions in the main report. The used TDI values are also higher than those recommended today for these substances.