

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

SUMMARY STATEMENT ON RESTRICTION REPORT: PROPOSAL FOR A RESTRICTION - BIS(2-ETHYLHEXYL)PHTHALATE (DEHP), BENZYL BUTYL PHTHALATE (BBP), DIBUTYL PHTHALATE (DBP) AND DIISOBUTYL PHTHALATE (DiBP).

Introduction

1. The Committee on Toxicity (COT) was asked by the UK Health and Safety Executive (HSE) to give an opinion on a Restriction Report drafted by the Danish Environmental Protection Agency (EPA) on risks from combined exposures to four phthalate esters (DEHP, DBP, DiBP and BBP). This summary statement reports our conclusions, which we reached at a meeting held on 1st November 2011.
2. We had previously completed a review of the toxicology of phthalate esters and published a statement on this in May 2011.¹
3. We reviewed the Restriction Report² and also considered new toxicological data on DEHP³ and DiBP⁴ and four biomonitoring studies.⁵⁻⁸ We did not undertake a detailed review of published epidemiological studies or consider the available toxicological data on alternative plasticisers.
4. We reached the following conclusions on the Restriction Report;

Reference Doses

5. We agree the reference doses for DEHP, DiBP and BBP established in the Restriction Report. In respect of DBP, we agree that the dose of 2 mg/kg bw/day in the study by Lee *et al.* (2004)⁹ should be the point of departure for establishing a reference dose. However, we noted that the effects on mammary glands in male rats, which were observed at this dose, would most likely reflect androgenic activity, whereas DBP is anti-androgenic. Moreover, the testicular effects, which were observed at the same dose, were reversible with continued dosing and lacked clear dose-dependence. Also, this apparent lowest observed adverse effect level (LOAEL) is much lower than the no observed adverse effect levels (NOAELs) observed in other developmental studies of the compound in which reproductive outcomes were investigated. Taking these reservations into account, we consider that an assessment factor of 300 is unduly conservative, and that the tolerable daily intake (TDI) for DBP of 0.01 mg/kg bw/day established by the Scientific Panel on Food Additives, Flavours, Processing Aids and Materials in Contact with Food

(AFC) of the European Food Safety Authority (EFSA)¹⁰ is a more appropriate reference dose for DBP than the DNEL proposed in the Restriction Report.

6. Although the reference doses for the four compounds are derived from studies of developmental toxicity, we agree that it is reasonable to apply them to all population groups, including infants and children. However, we note that whereas during pregnancy adverse effects might conceivably arise from over-exposure on a single day, in other circumstances it is the average exposure over at least several days which would be relevant. Thus when deriving risk characterisation ratios (RCRs) for population groups other than women of child-bearing age, estimates should be made of potential average exposures over several days, and not of the highest exposures that might occur on a single day.

Absorption

7. We agree the values for gastro-intestinal absorption that were used in the Restriction Report. However, empirical evidence indicates that the default values assumed for dermal absorption of DBP and DEHP are likely to be overestimates.

Exposure assessment

8. As acknowledged by the authors of the Restriction Report, there is much uncertainty regarding their exposure estimates. We recognise that the estimates do not take account of all possible sources of exposure. Nevertheless, we consider them to be highly conservative. This is because: a) they assume that on a single day an individual is highly exposed to each compound from each of the sources considered, which is unrealistic; and b) they focus on the highest exposures which might occur in a single day, whereas as argued above (paragraph 6), in population groups other than women of reproductive age, exposures over a longer period would be more relevant. Furthermore, a recently completed Total Diet Study undertaken by the Food Standards Agency (FSA) indicates that, in the UK, dietary intakes of the four phthalates under consideration are substantially lower than those assumed in the Restriction Report.

Biomonitoring

9. We agree that the studies selected in the Restriction Report⁵⁻⁷ were adequately conducted but note that the calculated intakes reflect historical exposures prior to the introduction of EU wide regulatory controls on the use of phthalates. Also, the risk assessment again focuses on the highest exposures which might occur in a single day, and makes the assumption that an individual will be simultaneously exposed to high levels of all four compounds.

Approach to Risk Characterisation

10. We agree that a dose addition approach to risk characterisation is appropriate.

Risk Characterisation Ratios (RCRs)

11. Bearing in mind the sources of conservatism outlined above, we view the RCRs reported in the Restriction Report as a first tier risk assessment. They are not so high that they necessarily require risk reduction measures, beyond those which are already in place. However, they do indicate a need for more refined risk assessment, and if necessary, more thorough consideration of the possible risks from use of alternative products, including estimation of potential exposures.

Refining Risk Characterisation Ratios

12. To refine the characterisation of risk, we suggest that it would be most useful to collect new biomonitoring data reflecting current exposures in representative populations. Such studies should look at: a) the distributions of estimated exposures in a single day; b) the variation of exposures in individuals from day to day; and c) the inter-relationship of individual exposures to different phthalates. As a secondary objective they might also collect information about participants' activities as a means of exploring the major determinants of high exposure.

Conclusion

13. The risk characterisation for combined exposure to DEHP, DBP, BBP and DiBP that is reported in the Restriction Report should be viewed as a first tier assessment. Given its conservatism and the levels of the RCRs calculated, it does not necessarily indicate a need for risk reduction measures beyond those that are already in place. To refine the risk assessment, it would be most useful to collect further biomonitoring data from representative populations. If necessary, there should also be a more thorough risk assessment for other products which might be used as substitutes should additional restrictions be imposed on DEHP, DHP, BBP and DiBP.

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References

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