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Integrated Exposure for Risk Assessment in Indoor Environment (INTERA)

Dimethyl fumarate (DMF) case study

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SUMMARY

Dimethyl fumarate (DMF) is a fungicide used to prevent mould growth in leather and textiles. It may be applied by spraying over the product or via slow evaporation from sachets inside the product. In 2006, an outbreak of allergic dermatitis was observed in some European Union (EU) countries, which was later attributed to dermal exposure to DMF in sofa cushions and footwear (Susitaival *et al.*, 2009; Gimenez-Arnau *et al.* 2009; Lammintausta *et al.* 2009). This led to a ban of DMF in products at concentrations in excess of 0.1 ppm in 2009, first in France and Belgium and then EU wide.

The INTERA methodology as previously described was tested to assess the intake of DMF through dermal exposure. Peer-reviewed and grey literature was reviewed to collate the necessary input data for the INTERA modelling platform. Far from complete, the data were particularly lacking on numbers of the exposed and DMF concentrations in the contact materials. We estimated the concentration of DMF in sofas to be in the order of 1 ppm and in footwear of 58 ppm. These values were used for all the EU countries. Therefore, the distribution of doses across the EU was based on body weight as the other parameters (DMF concentration in product and modifying factors: clothes, material density) were the same for all the countries.

Clothing thickness of 0.5 mm was assumed to reduce DMF migration to the skin by 10% and 0.1 mm by 1%. Other modifiers (e.g. environmental temperature, perspiration rate) were not considered due to the limited data on how they affect the migration of DMF and ultimately the exposure concentration. The uptake dose ($\mu\text{g kg}^{-1}\text{ day}^{-1}$) was calculated from the concentration in the material, exposure time, clothing, weight and the exposed skin area. We assumed all the product in contact with the skin was transferred to the skin and 100% absorption as recommended by the EC (2004) for substances with a molecular weight of < 500 and octanol-water partition coefficient (K_{ow}) of $-1 < \log K_{ow} < 4$. The largest source of uncertainty is the concentration of DMF in the product.

For an exposure scenario of a woman from Spain (aged 15-64 years) sitting 3 hours on a DMF contaminated sofa, wearing thick, thin clothing or bare skin being exposed experiences intake doses of 0.30, 0.33 and 0.34 $\mu\text{g kg}^{-1}\text{ day}^{-1}$, respectively, which are within the range of doses that result in a reaction in the patch-test allergy studies (Zimerson, 2011).

DMF has not been included in any national or European biomonitoring programmes. Internal doses could not be estimated by Physiologically based Pharmacokinetic modelling (PBPK). No independent data was available to validate the modelling outputs. This current assessment is based on limited data and a number of assumptions were needed. However had this limited (based on data availability) assessment been done proactively, it would have correctly warned both industry and regulatory authorities, and may have potentially prevented thousands of cases of serious dermatitis and eczema occurring.