

2016 Children's Safe Products - Reporting Rule update Draft Chemical Evaluation

CAS	1241-94-7
Substance Name	Ethylhexyl diphenyl phosphate (EHDPP) or Diphenyl (2-ethylhexyl) phosphate (DPEHP)

Toxicity

Toxicity data for Ethylhexyl diphenyl phosphate (EHDPP) was reviewed by the UK Environmental Agency in 2009 [1]. Dose-related changes to the blood, liver, kidney, adrenal glands, testes and ovaries were observed in laboratory rats exposed to 375-425 mg/kg-day of commercial EHDPP in their food over 90 days [1, 2]. The LOAEL¹ from three 90-day feeding experiments, was 15 mg/kg/day for increase in liver enzymes in male rats (NOAEL¹ was 6 mg/kg-day). A fertility and reproductive toxicity study in rats reported that mating and reproductive performance were unaffected by treatment (up to 0.8% EHDPP in food). Reduced pup weight and survival were noted at mid- and high-doses, respectively. Relative and absolute liver and adrenal weight were increased in a dose-dependent manner in both sexes and both generations. Liver and adrenal pathology was also reported. The reproductive NOAEL for both parental and pup generations was 0.2 percent EHDPP in the diet: equivalent to 144 mg/kg/day [1].

UK assessors judged EHDPP to have a low potential to cause cancer in humans based on negative results in *in vitro* and *in vivo* mutagenicity and genotoxicity assays and an absence of proliferative lesions in repeat-dose studies [1].

Investigators at the National Toxicology Program have used high-throughput assays and rapidly developing whole organisms, such as zebrafish and the nematode *C. elegans*, to screen for potential developmental toxicity and neurotoxicity of a number of organophosphorus flame retardants [3, 4]. Based on results, EHDPP was prioritized for additional testing of neurodevelopmental testing. Briefly, EHDPP reduced firing rate in a neural network assay and inhibited larval development in the nematode *C. elegans* [3, 4]. EHDPP caused significant inhibition of mitochondrial activity which may partly explain the observed developmental arrest in *C. elegans* [4]. In two developmental rat studies, no clearly treatment-related developmental effects were seen at oral doses of up to 3,000 mg/kg-day [1].

Exposure

EHDPP is primarily used as a flame retardant and plasticizer in flexible PVC. It is used in food-wrapping films such as those used to wrap meats and skinless sausages [1, 2]. According to a 2009 assessment by the UK, other current uses are in PVC plastics, rubber, polyurethanes, photofilms, paints, pigment dispersions, adhesives, and PVC coatings on textiles and fabrics [1]. These are materials that could be in children's products. It is also used in inflammable hydraulic fluids like those used in large aircraft [2]. U.S. national volume production was reported to be one million to ten million pounds/year in 2012 [5].

¹ LOAEL Low Observed Adverse Effect Level and NOAEL No Observed Adverse Effect Level

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EHDPP has been detected in U.S. house dust; levels ranged from 140 to 3,000 ng/g [6]. EHDPP has been detected in U.S. diet studies, primarily in fats and oily foods [1, 2]. A sample of margarine for example had 20 ppm. Estimates of mean daily dietary intake in the U.S. by Gunderson et al. 1995, were 339 ng/kg bodyweight for infants and 1236 ng/kg body weight for toddlers based on data from 1986-1991 surveys [2].

Biomonitoring studies have measured EHDPP or metabolites in breast milk, urine, and blood. EHDPP was detected in breast milk of Swedish women and women from three Asian counties [7, 8]. It was recently detected in blood of Chinese adults at a median level three times higher than TPHP [9]. A urinary metabolite of EHDPP called DPHP has also been measured in human urine. It is not specific to EHDPP as it can be generated from at least two other flame retardants, TPHP and RDP² [10]. The DPHP metabolite has been detected in urine of California adults, 91% of children in a German day care study, and 93% of the infants in a North Carolina study [11-13]. Urinary levels of DPHP in children were higher than their mothers in two studies [14, 15]. Two studies looked for evidence that household sources of TPHP flame retardant contributed to children's exposure. No correlations with indoor dust or air concentrations of TPHP were detected in the German study [12]. No correlations between DPHP in infant urine and the number of infant products in the home were detected in the North Carolina infants [11]. Either another flame retardant is contributing to this metabolite (for example EHDPP) or there are more important sources of exposure.

If EHDPP is released into the environment, biodegradation is expected to occur with conservative estimated half-lives of 50 days in surface water and 300 days in soil and sediment [1]. It has potential to build up in aquatic organisms [2]. A 2009 review for measurements in environmental media located some soil, water, and air studies conducted in the 1980s but no positive detections, including in samples collected near industrial production sites [1].

References

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² A variety of hydrolysis products of resorcinol bis(diphenylphosphate) (RDP) and its oligomers were identified by Ballesteros-Gomez, et al. 2015. These metabolites include DPHP. (see ref #10 Ballesteros-Gomez et al.)

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