### Sources of Exposure

## Toxicokinetics and Biomonitoring

### Biomarkers/Environmental Levels

### **General Populations**

- The most likely routes of exposure for the general public to DEHP are through ingestion of food, inhalation or ingestion of house dust, and dermal contact with consumer products containing DEHP.
- DEHP is present in environmental media and in numerous consumer articles that are used world-wide.
- The highest exposures to DEHP result from medical procedures such as blood transfusions or hemodialysis, during which DEHP may leach from plastic equipment directly into the blood.
- People residing near hazardous waste disposal sites or municipal landfills may be subject to higher-than-average levels of DEHP in ambient air and drinking water.

### **Occupational Populations**

- Occupational exposures may be significant in some settings.
- Workers in facilities that make or use PVC-containing products may be exposed to higher levels of DEHP, mostly through inhalation.

### **Toxicokinetics**

- DEHP is absorbed via inhalation, oral, and dermal routes.
- No studies have been identified that provide reliable information about the distribution of DEHP in tissues (other than blood) in humans.
- Animal studies indicate that for all routes of exposure, the initial distribution is to liver, intestine, muscle, kidney, and fat (and lung during inhalation exposure).
- DEHP has been detected in placenta, amniotic fluid, fetal liver, and other fetal tissues in exposed rats. Mammary milk contains and transfers DEHP and mono-(2-ethylhexyl)phthalate (MEHP) to nursing rat pups.
- Tissue lipases, esterases, and gut microflora hydrolyze DEHP. DEHP metabolites are further metabolized by cytochrome P450s, alcohol dehydrogenase, and aldehyde dehydrogenase.
- Most elimination of DEHP metabolites occurs by excretion in urine and feces (biliary secretion).

### **NHANES Biomonitoring**

NHANES (2013–2014) did not calculate the geometric mean (GM) of MEHP (% detection too low). The urinary GMs, corrected for creatinine (Cr), for other metabolites were MEHHP (mono-2-ethyl-5-hydroxyhexylphthalate): 6.49 μg/g Cr; MEOHP (mono-2-ethyl-5-hydroxyhexylphthalate): 4.25 μg/g Cr; and MECPP (mono-2-ethyl-5-carboxypentylphthalate): 10.6 μg/g Cr.

### **Biomarkers**

- DEHP and/or its metabolites (MEHP, MEHHP, MEOHP, and MECPP) can be detected in urine, blood, and other biological fluids.
- Urinary DEHP metabolites are the preferred biomarker of exposure.

### **Environmental Levels**

Air

There are no recent monitoring data for air levels of DEHP in the United States. Studies indicate that outdoor levels for the United States in the 1980s were very low, having units of ng/m<sup>3</sup>. Indoor air typically measured in μg/m<sup>3</sup>.

### Water

There are no recent monitoring data for water levels of DEHP in the United States. Studies completed in decades past revealed DEHP levels in the ppb range for surface water, rainwater, and groundwater.

### Sediment and Soil

■ There are no recent monitoring data for levels of DEHP in the sediment or soil in the United States. A 1990s study indicated levels in the ppm range.

### Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2022. Toxicological Profile for Di(2-ethylhexyl)phthalate. Atlanta, GA: U.S. Department of Health and Human Services, Public Health

# ToxGuide<sup>TM</sup> for

# Di(2-ethyl-hexyl)phthalate

 $C_{24}H_{38}O_4$ 

CAS # 117-81-7

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U.S. Department of Health and Human Services Public Health Service Agency for Toxic Substances and Disease Registry www.atsdr.cdc.gov



### Chemical and Physical Information

referred to as DEHP, is a manufactured

It is a colorless liquid with a slight odor.

flexible. Due to health concerns, DEHP

products, especially in the United States.

DEHP was once widely used as a

plasticizer to help make polyvinyl

chloride (PVC) products soft and

use has been discontinued in many

**DEHP** is a Liquid

chemical.

### Routes of Exposure

#### ■ Inhalation – Likely route of exposure for the occupational population. The general Di(2-ethylhexyl)phthalate, commonly population may also be exposed through

ambient air.

- Oral Predominant route of exposure for the general population through ingestion of contaminated foodstuffs, water, and dust.
- Dermal Likely route of exposure for the occupational population. The general population may also be exposed when handling products containing DEHP.
- Other Exposure via medical equipment (tubing, intravenous bags) in hospitalized individuals or those managing chronic conditions (e.g., dialysis).

### **DEHP** in the Environment

- DEHP enters the environment predominantly through disposal of wastes into landfills.
- It is ubiquitous in the environment, although usually at low levels.
- In the air, it exists in both a vapor and associated with particulates. It is subjected to both wet and dry deposition.
- In water, DEHP is predominantly adsorbed to suspended particulates and sediments; volatilization is not likely to occur.
- DEHP adsorb strongly to soils and sediments. The majority of DEHP in the environment is in soils and sediment.
- Biodegradation of DEHP can occur under aerobic conditions.
- It tends to bioconcentrate in aquatic organisms.

### Relevance to Public Health (Health Effects)

Health effects are determined by the dose (how much), the duration (how long), and the route of exposure.

### Minimal Risk Levels (MRLs)

Inhalation

- No acute- (≤14 days) or chronic-(≥365 days) duration inhalation MRLs were derived for DEHP.
- An intermediate-duration (15–364 days) inhalation MRL of 0.0002 ppm was derived for DEHP.

### Oral

- An acute-duration (≤14 days) oral MRL of 0.003 mg/kg/day was derived for DEHP.
- An intermediate-duration (15–364 days) oral MRL of 0.0001 mg/kg/day was derived for DEHP.
- No chronic-duration (≥365 days) oral MRL was derived for DEHP.

### **Health Effects**

- Human studies suggest an association between DEHP exposure and decreased serum testosterone and diminished sperm quality in males; an association with decreased fertility has not been observed.
- In animals, adverse effects to the male reproductive system were observed after oral and inhalation exposure. Decreased fertility was also observed following oral exposure.

- Evidence for potential associations between DEHP exposure and risk of allergy and asthma in humans is conflicting. Some animal studies indicate that DEHP is an immune adjuvant in presensitized animals.
- In rodents, high DEHP doses resulted in hepatic and renal damage.
- Animals chronically exposed to DEHP had increased incidence of liver adenomas and carcinomas, pancreatic adenomas, and benign Leydig cell tumors.
- DEHP has been classified by the U.S. Department of Health and Human Services as reasonably anticipated to be a human carcinogen, by the U.S. Environmental Protection Agency (EPA) as a probable human carcinogen (Group B2), and by the International Agency for Research on Cancer as possibly carcinogenic to humans (Group 2B).

### Children's Health

- Epidemiological and/or animal studies indicate that younger organisms may have greater susceptibility to DEHP.
- Prenatal exposure in humans has been associated with pre-term labor, altered development of male genitalia, early puberty, and delayed mental and psychomotor development in children.
- Studies in animals indicate that the developing organism is a sensitive target of DEHP toxicity. Effects of gestational or early life exposure include altered glucose homeostasis and impaired development of the reproductive, renal, hepatic, or nervous systems.