Hexanedioic acid, bis(2-ethylhexyl) ester: Human health tier II assessment

28 June 2013

CAS Number: 103-23-1

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted

and published separately, using information available at the time, and may be undertaken at different tiers.

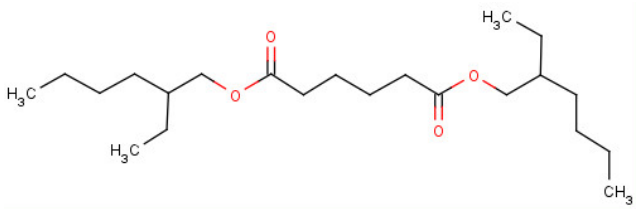
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:www.nicnas.gov.au

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Di(2-ethylhexyl) adipate Dioctyl adipate Bis(2-ethylhexyl)hexanedioate Diethylhexyl adipate (DEHA)
Structural Formula	
Molecular Formula	C22H42O4
Molecular Weight (g/mol)	370.57
Appearance and Odour (where available)	Colourless to light coloured liquid.
SMILES	C(=O) (CCCCC(=O)OCC(CCCC)CC)OCC(CCCC)CC

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information.

The chemical has reported commercial use including:

- manufacturing other chemicals;
- Polyvinyl chloride (PVC) films, PVC compounds for wire cable tubing and footwear;
- resins for tooling and for other adhesive purposes; and
- softeners.

The chemical is also listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of 1000–9999 tonnes.

International

The following international uses have been identified through the European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD SIAR); Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Substances and Ingredients (CosIng) database; and the United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) directory.

The chemical has reported cosmetic use as:

- an emollient;
- a film-forming agent;
- a skin conditioning agent; and
- as a solvent for cosmetic ingredients.

The chemical has reported commercial use including:

- as a resin plasticiser, used primarily in food-contact wrapping;
- in construction materials and as fillers;
- in paints, lacquers and varnishes;
- as a cutting fluid;
- as an adhesive agent;
- as softeners;
- as hydraulic (lubricant) fluids and additives; and
- for surface treatment.

Restrictions

Australian

No known restrictions have been identified.

International

International restrictions include (Galleria Chemica):

The chemical is 'Listed in EU directives on plastics in contact with food' with a restriction and/or specification as follows (last update 20 October 2009): SML = 18 mg/kg.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Substances Information System (HSIS (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):

- an exposure limit time weighted average (TWA) of 400 mg/m³ has been stated for the chemical in Poland; and
- Temporary Emergency Exposure Limits (TEELs) of up to 500 mg/m³ (TEEL-3) has also been stated for the chemical by the US Department of Energy (DOE).

Health Hazard Information

Toxicokinetics

In a toxicokinetic study, six male human volunteers each received 46 mg of the chemical (deuterium labelled di-2-(ethylhexyl) adipate) formulated in corn oil (European Commission, 1999; OECD, 2005; Government of Canada, 2011). No volunteer showed any adverse effect and no significant changes in biochemical or haematological parameters were detected. The parent compound was not found in plasma, and 2-ethylhexanoic acid (2- EHA) was the only compound detected in plasma. This metabolite appeared soon after dosing with the peak concentrations occurring between one and two hours. The metabolite was rapidly eliminated from plasma with an elimination half-life of 1.65 hours, and was not detected in plasma after 31 hours. The dominant metabolite identified in urine was also 2-EHA, accounting for an average of 8.6 % of the administered dose. The other metabolites together accounted for a further 3.5 % of the dose.

Acute Toxicity

Oral

The chemical was reported to be of low acute toxicity when administered orally, with a median lethal dose (LD50) of 9110 mg/kg bw in rats (OECD, 2005).

Dermal

The chemical was reported to be of low acute toxicity through skin exposure with an LD50 > 8670 mg/kg bw in rabbits (OECD, 2005).

Inhalation

The chemical exhibits low acute toxicity in animal tests following inhalation exposure.

In an acute inhalation toxicity study (OECD, TG 403), rats were exposed to aerosols (nose/head only) of the chemical at 5.7 mg/L for four hours. The particle size distribution, expressed as mass median aerodynamic diameter (MMD), was calculated to be 1.4 µm. There were no deaths at the tested concentration during the study period of 14 days. Irregular and accelerated respiration, as well as attempts to escape and piloerection, were noticed following exposure. There were no clinical signs after five days following dosing. There were no deaths and the LC50 was determined to be > 5.7 mg/L (REACH).

Corrosion / Irritation

Skin Irritation

The chemical was reported to be slightly irritating to the skin of rabbits following a prolonged (24 hours) exposure (OECD, 2005; REACH). However, there were no signs of irritation following a shorter (four hours) exposure in rabbits to the analogue chemical, Plastomoll DNA (REACH). Effects were not sufficient to warrant a hazard classification.

Eye Irritation

The chemical has been reported to be non-irritating or slightly irritating to the eye in animal studies (OECD, 2005; REACH). Effects were not sufficient to warrant a hazard classification.

Sensitisation

Skin Sensitisation

The chemical was not found to induce dermal sensitisation in an animal study.

The chemical was intracutaneously administered to guinea pigs at 0.1 % in olive oil, three times a week for three weeks that were subsequently challenged after a two week rest period (OECD, 2005; REACH). The reaction was measured 24 hours after the challenge dose. The average area and height of the reaction at challenge were smaller than during the induction, indicating that the chemical was not a skin sensitiser.

Repeated Dose Toxicity

Oral

Based on the treatment-related effects reported in various repeat dose toxicity studies, the chemical is not considered to cause serious damage to health from repeated oral exposure.

Results indicated that repeatedly feeding the chemical (up to 90 days) to rats and mice showed reduced body weight gains at approximately 400 mg/kg bw/day and higher in rats, and approximately 600 mg/kg bw/day and higher in mice (NOAELs of 189 mg/kg bw/day in rats and 451 mg/kg bw/day in mice). Dose-dependent changes also included increased relative liver and kidney weights as well as biochemical and morphological evidence of peroxisome proliferation in the liver, leading to hepatic hypertrophy (OECD, 2005; REACH; Government of Canada, 2011).

Dermal

Based on the treatment-related effects reported at high doses, the chemical is not considered to cause serious damage to health through repeated dermal exposure. The observed effects do not warrant a hazard classification.

In a dermal toxicity study, rabbits (four/group) were exposed to the chemical with dermal applications to the shaved skin of the abdomen, five days a week for two weeks, at doses of 410 and 2060 mg/kg bw/day. At the 410 mg/kg bw/day dose, one animal had diarrhoea and died after the first treatment during the second week. Animals in this group had slight to moderate erythema and slight desquamation. At the 2060 mg/kg bw/day dose, animals had laboured breathing and were lethargic. Only one animal gained weight, while the other three did not. Animals in this group had moderate erythema and desquamation. Slightly altered cytology of the liver parenchymal cells (basophilic granulation with enlarged and hyperchromatic nuclei) was noted in one animal in this group. No other microscopic changes were noted. The LOEL was determined to be 2060 mg/kg bw/day, based on decreased body weight gain, lethargy, and laboured breathing (OECD, 2005; Government of Canada, 2011).

Inhalation

No data are available.

Genotoxicity

The chemical is not genotoxic in both in vitro and in vivo studies as reported below.

The chemical has been reported to be not mutagenic in two bacterial reverse mutation assays (OECD, TG 471) with and without metabolic activation; a sister chromatid exchange (SCE) assay (OECD TG 473) conducted using Chinese hamster ovary cells with or without activation; an unscheduled DNA synthesis assay (OECD TG 482); and a mouse lymphoma cell forward mutation assay (OECD TG 476) conducted using mouse lymphoma cell L5178Y tk+/tk-, with and without metabolic activation (OECD, 2005; REACH).

In a micronucleus assay, mice were treated with the chemical (0 or 5000 mg/kg bw in corn oil via an intraperitoneal (i.p.) injection), and the bone marrow harvested 30 hours after injection. A second animal group was treated with two doses of the chemical 24 hours apart and bone marrow harvested 24 hours after the last injection. There were no deaths. The numbers of micronucleated erythrocytes and mitotic indices were not significantly different between the treated and negative control groups. The chemical was reported to be not clastogenic under the conditions of the assay (OECD, 2005; REACH).

In another micronucleus assay, mice were treated with the chemical (0, 375, 750, 1500 or 2000 mg/kg bw) in corn oil via i.p. for three consecutive days. A second group of animals was treated with two doses of the chemical (24 hours apart) at the same dose level. The bone marrow was harvested 24 hours after the last injection in both treatment groups. There were no deaths. It was concluded that the chemical was negative for chromosomal aberration and is thus not clastogenic (OECD, 2005; REACH).

In a dominant-lethal study using mice, the chemical did not cause a decrease in litter size, suggesting no adverse effects on spermatogenesis (OECD 2005).

Carcinogenicity

Based on the data available, the chemical is not considered to be a carcinogen.

The increased incidence of liver tumours in mice treated with the chemical has been proposed as a result of peroxisome proliferation. The activation of peroxisome proliferation in rodent livers is mediated by activation of peroxisome proliferator-

activated receptor-a (PPARa). Expression of PPARa in humans is much lower than that observed in mice (OECD, 2005; Government of Canada, 2011). Humans appear to be refractory to the important events associated with the induction of liver tumours through peroxisome proliferation mechanism, even though they possess functional PPARa and its receptor can be activated by peroxisome proliferation (US EPA, 2003). It has also been proposed that the stimulation of DNA synthesis by peroxisome proliferation may be more important in the carcinogenic process than is the proliferation of peroxisomes (Government of Canada, 2011). In this context, it is noted that while peroxisome proliferation has been observed both in mice and rats in chronic studies with the chemical, tumours have only been noted in mice.

There was no evidence of carcinogenicity in rats following oral treatment with 12000 ppm (600 mg/kg bw/day) or 25000 ppm (1250 mg/kg bw/day) of the chemical for two years in feed (OECD, 2005). There was also no carcinogenic activity when the chemical was applied to the skin of mice. In a one year study with dogs orally administered 0.2 % of the chemical in the diet (equivalent to 50 mg/kg bw/day), there was no detection of tumours (Government of Canada, 2011).

A significantly higher incidence of hepatocellular neoplasms (carcinoma & adenoma) was found in female mice: 38 % and 37 % at dose levels of 12000 and 25000 ppm, respectively (estimated dose of 3222 and 8623 mg/kg bw/day for female mice) compared with 6 % in controls. An insignificantly higher incidence of hepatocellular neoplasms was observed in male mice at dose levels of 12000 and 25000 ppm in the diet (estimated dose of 2659 and 6447 mg/kg for male mice). A significantly higher incidence of hepatocellular adenomas was observed only in male mice administered 25000 ppm in the diet (6447 mg/kg) (OECD, 2005).

The US Environmental Protection Agency (US EPA) has classified the chemical as a Class C Carcinogen (possible human carcinogen), based on an observed increase in the incidence of liver tumours in female mice, and a dominant lethal assay. It was also noted that this chemical exhibits structural relationships to other non-genotoxic compounds classified as probable and possible human carcinogens. However, there was an absence of human data, no evidence of genotoxicity, and also no evidence of carcinogenicity in rats (US EPA, 1994). It has been noted that the chemical has been proposed to be reassessed under the IRIS program of the US EPA.

IARC (2000) stated that the chemical induces peroxisome proliferation and cell replication in the livers of mice and, to a limited extent, in rats. Activation of PPARa is a prerequisite for liver hypertrophy, hyperplasia and eventual hepatocarcinogenesis as a result of peroxisome proliferators. There was no significant response in the human liver to the induction of peroxisome proliferation and hepatocellular proliferation in response to peroxisome proliferators. Hence, the IARC (2000) concluded that the increased incidence of liver tumours in mice treated with the chemical is a result from a mechanism that does not operate in humans.

The European Commission (1999) also assessed the cancer risk from exposure to the chemical as minimal (European Commission, 1999).

Reproductive and Developmental Toxicity

Based on the weight of evidence considered in the studies below, a no observed adverse effect level (NOAEL) of 200 mg/kg bw/day can be derived for both reproductive and developmental toxicity. As the publicly available sources do not provide information with sufficient clarity to allow an assessment of the hazard classification, a Tier III assessment is proposed to consider studies in detail to determine whether HSIS/GHS classification is warranted.

In a one-generation reproduction toxicity study (OECD, TG 415), the chemical was administered to Wistar rats in their feed at doses of 0, 300, 1800 or 12000 ppm (equivalent to 0, 28, 170 and 1080 mg/kg bw/day). Maternal toxicity was observed at 12000 ppm with increased absolute liver weights and reduced body weight gain in females. At the same dose level, mean pup weight gain and total litter weight were reduced throughout the post partum phase. The mean litter size was also slightly reduced at the highest dose. The NOAEL for maternal and reproductive toxicity was determined to be 170 mg/kg bw/day (US EPA, 1999; REACH).

In a pre- and postnatal toxicity study, the chemical was administered by oral gavage to rats at doses of 0, 200, 400, or 800 mg/kg bw/day from gestational day (GD) seven to postnatal day (PND) 17. There were no clinical signs of toxicity in the dams during the dosing period; maternal weight gains during pregnancy were similar across the four groups. The chemical induced a significantly prolonged gestation period (by approximately one day) at 800 mg/kg bw/day (22.3 ± 0.6 vs 23.2 ± 0.6). The body weights of both male and female pups were significantly reduced at birth at 800 mg/kg bw/day and remained significantly lower at PND three and 13. The NOAEL for reproductive toxicity was determined to be 400 mg/kg bw/day. The study also concluded that even though the chemical and di(2-ethylhexyl) phthalate have structural similarities and have a common metabolite, the

toxicology profiles of the two chemicals differ markedly as antiandrogenic endpoints were not affected in this study (Dalgaard et al. 2003).

In a repeat-dose fertility toxicity study (enhanced OECD TG 407), the chemical was administered (by gavage) to rats at doses of 0, 40, 200, and 1000 mg/kg bw/day for at least 28 days. There was no effect on food consumption, body weight, haematology, clinical biochemistry, and hormonal analysis during the study. Spermatological analysis did not reveal any abnormalities. Follicle atresia was increased in 4/10 rats in the high dose group; two of those four rats had a prolonged oestrous cycle, suggesting that the chemical disturbed the ovarian function. Histological changes were also detected in kidneys (male animals only) and ovaries of animals at the highest dose of 1000 mg/kg bw/day. A NOAEL of 200 mg/kg bw/day was established in this study (Miyata et al., 2006).

In a study to determine the effect of the chemical on female fertility, the chemical was orally administered to female rats at doses of 0, 200, 1000, and 2000 mg/kg bw/day for two or four weeks in a repeat-dose toxicity study, and for two weeks before mating, throughout mating and until gestation day seven. In the repeat-dose toxicity studies, chemical-related effects were observed in the ovaries in treatment groups at 1000 mg/kg bw/day and above, suggesting that the chemical disturbed ovulation and large follicle growth. In the fertility study, mean oestrus cycle length and post-implantation loss rate were significantly increased at 1000 mg/kg bw/day and above. In addition, a significant decrease in the implantation rate and number of live embryos, and a significant increase in pre-implantation loss rate were observed at 2000 mg/kg bw/day. A NOAEL of 200 mg/kg bw/day was derived based on the effects to the ovary in the repeat-dose toxicity study, and increased mean oestrus cycle length and post-implantation loss rate in the female fertility study (Wato et al., 2009).

In a dominant lethal study in male mice, a single dose of 5 mL/kg (4610 mg/kg) and 10 ml/kg (9220 mg/kg) of the chemical administered in an i.p. injection, resulted in a decrease in fertility, fewer implants, and higher foetal mortality compared with the control group. A dose level of 922 mg/kg had no effect (OECD, 2000). The effects observed were at high doses and the route of administration is not directly relevant to human exposure.

In a study to determine the effect of the chemical on developmental toxicity, the chemical was orally administered to female rats at doses of 0, 28, 170, and 1080 mg/kg bw/day, from GD one until termination on GD day 22 (OECD, 2005; REACH). The NOAEL for maternal toxicity was determined to be 170 mg/kg bw/day, based on a small, but statistically significant, reduction in bodyweight gain, and statistically significantly reduced maternal food consumption (US EPA, 1999; OECD, 2005; REACH). Although the incidence of minor external and visceral defects was unaffected, two visceral variants were increased at the top two dose levels: increased incidence of kinked ureters in the 170 mg/kg bw/day and 1080 mg/kg bw/day groups, and the incidence of slightly dilated ureters increased in the 1080 mg/kg bw/day group. It was suggested that minor skeletal defects were increased in a dose-related manner at the 170 and 1080 mg/kg bw/day doses, while skeletal variants were increased at the top dose only. These findings indicated slightly poorer ossification at the mid and top dose levels. Reduced ossification and increases in the incidence of visceral variants are considered to be due to slight foetotoxicity. Therefore, a developmental NOAEL of 28 mg/kg bw/day was established (OECD, 2005; REACH). However, since the changes at 170 mg/kg were not statistically significant, this dose level was considered more appropriate for a developmental NOAEL (US EPA, 1999; OECD, 2005). This study is not considered as a critical study given the study is poorly described and is cited differently by different authors (Government of Canada, 2011).

In a reproductive and developmental toxicity study (reported as above), the chemical was fed (gavage) to pregnant rats from GD seven through to PND 17 at doses of 0, 200, 400, or 800 mg/kg bw/day (Dalgaard et al., 2003). The NOAEL for developmental toxicity was established at 200 mg/kg bw/day, based on a dose related decrease in postnatal survival.

The chemical is hydrolysed to adipic acid and 2-ethylhexanol, the latter of which is oxidised to ethylhexanoic acid (OECD, 2005; Government of Canada, 2011). Ethylhexanoic acid is a known potent developmental toxin. Hence, the chemical can be expected to cause some developmental toxicity.

Other Health Effects

Endocrine Disruption

The chemical was evaluated for its effect on the endocrine system in several in vitro and in vivo bioassays. The chemical tested negative in these bioassays and, based on this information, the chemical is not expected to affect endocrine functions (Government of Canada, 2011).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are reproductive and developmental toxicity. The NOAEL for reproductive and developmental toxicity is 200 mg/kg bw/day, which is much higher than that seen for diethylhexyl phthalate (see the DEHP PEC report, NICNAS, 2010). The toxicology results also indicated that the chemical does not have similar antiandrogenic developmental toxicology, demonstrating that the chemical is very different toxicologically to DEHP.

Public Risk Characterisation

Although the chemical has no reported cosmetic use in Australia, the chemical has reported cosmetic use overseas as an emollient, a film-forming agent, a skin conditioning agent, and as a solvent for cosmetic ingredients. The chemical has also reported overseas use as a plasticiser in the flexible vinyl industry and is used widely as plasticiser in food contact wrapping (cling film). Dermal and oral routes are the likely routes of exposure for the public through the consumer use of products containing this chemical.

The OECD (2005) reported that public exposure to the chemical could occur through migration from the cling film wrapping to food. This migration is sensitive to the food's fat content and temperature. Public exposure also occurs from consumer products, particularly through personal care products (Government of Canada, 2011).

The Government of Canada (2011), for risk characterisation, also identified a critical NOAEL of 200 mg/kg bw/day for developmental toxicity. The Government of Canada (2011) concluded that there is adequate protection for human health from the use of cling film wrapping on food, based on the highest upper-bound intake estimate of 0.14 mg/kg bw/day, and a calculated margin of exposure (MOE) of 1400. However, it was also concluded that exposure to the chemical through daily use of cosmetic and personal care products in Canada could be a potential public health risk considering the MOE ranged from 91 to 3300.

A mandatory survey of the Australian industry in 1999 found that the chemical is not used in cosmetic and personal care products in the country. Based on these data, there is no risk to the Australian public from cosmetic and personal care products. However, considering the conclusion of the Canadian risk assessment, and that the Australian survey was undertaken over a decade ago, a Tier III assessment to quantify the risk should be undertaken if the chemical is currently found to be used in cosmetic and personal care products. In order to quantify the risk detailed exposure information from industry is required.

Occupational Risk Characterisation

During product formulation, dermal and ocular exposure of workers to the chemical may occur, particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations may also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices.

Given the critical systemic long-term health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise dermal exposure to the chemical are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU), has adequate information to determine appropriate controls.

NICNAS Recommendation

The chemical is recommended for Tier III assessment to determine whether the chemical is used in cosmetic and personal care products in Australia. If the chemical is used in the country, a quantitative risk assessment should be undertaken to characterise the risk.

All other human health risks are considered to have been sufficiently assessed at the Tier II level.

Regulatory Control

Public Health

Considering the available information that indicates low public exposure from this chemical, no regulatory controls are recommended.

Work Health and Safety

The chemical is recommended for Tier III assessment to examine whether the chemical warrants hazard classification for reproductive and developmental toxicity. No classification is proposed for the other endpoints. This does not consider classification of physical hazards and environmental hazards.

Advice for consumers

Products containing the chemical should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing Risks of Hazardous Chemicals in the Workplace—Code of Practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of Safety Data Sheets for Hazardous Chemicals— Code of Practice* and *Labelling of Workplace Hazardous Chemicals—Code of Practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

References

Cosmetics Directive (CosIng). Hexanedioic acid, bis(2-ethylhexyl ester (103-23-1). http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details&id=74283. Accessed April 2013

Dalgaard M, Hass U, Vinggaard AM, Jarfelt K, Lam HR, Sorensen IK, Sommer HM & Ladefoged O 2003. Di(2-ethylhexyl) adipate (DEHA) induced developmental toxicity but not antiandrogenic effects in pre- and postnatally exposed Wistar rats. Reproductive Toxicology 17(2) pp. 163-170.

European Commission (1999). Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). Opinion of the toxicological characteristics and risks of certain citrates and adipates used as a substitute for phthalates as plasticisers in certain soft PVC products. 2/JCD/csteep/cit28999.D(99). September 1999

Galleria Chemica. Accessed March 2013. http://jr.chemwatch.net/galleria/

Government of Canada 2011. Hexanedioic acid, bis(2-ethylhexyl) ester (DEHA), Batch 11 Challenge Substances. Accessed March 2013 at http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/index-eng.php

Miyata K, Shiraishi K, Houshuyama S, Imatanaka N, Umano T, Minobe Y, Yamasaki K 2006. Subacute oral toxicity study of di(2-ethylhexyl)adipate based on the draft protocol for the “Enhanced OECD test guideline no. 407.” Archives Toxicology 80, pp.181–186.

NICNAS 2006. Australian High Volume Industrial Chemicals List (AHVICL). Accessed March 2013 at http://www.nicnas.gov.au/Industry/Australian_High_Volume_Industrial_Chemicals/NICNAS_AHVICL_2006_PDF.pdf

NICNAS 2010. Priority Existing Chemical Assessment Report No. 32: Diethylhexyl phthalate (DEHP). National Industrial Chemicals Notification and Assessment Scheme, Commonwealth of Australia.

OECD 2005. SIAR category assessment for hexanedioic acid, bis(2-ethylhexyl) ester. Accessed February 2013 at http://webnet.oecd.org/hpv/UI/handler.axd?id=c0edaa0e-2885-4ebe-a102-135ed2bc2da3

REACH. Hexanedioic acid, bis(2-ethylhexyl) ester (103-23-1). Accessed May 2013. http://apps.echa.europa.eu/registered/data/dossiers/DISS-9c7edc7d-d043-56b3-e044-00144f67d249/DISS-9c7edc7d-d043-56b3-e044-00144f67d249_DISS-9c7edc7d-d043-56b3-e044-00144f67d249.html

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed March 2013 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

Substances in Preparations in Nordic Countries (SPIN). Accessed March 2013 at http://fmp.spin2000.net/fmi/xsl/spin/SPIN/maininfo.xsl?-db=SPINstof&-lay=SPINnavn&-view

US EPA 1992. Di(2-ethylhexyl)adipate (CASRN 103-23-1). Accessed March 2012 via the USA EPA Integrated Risk Information System (IRIS) at: http://www.epa.gov/iris/search_human.htm

Wato E, Asahiyama M, Suzuki A, Funyu S, Amano Y 2009. Collaborative work on evaluation of ovarian toxicity. 9) Effects of 2- or 4-week repeated dose studies and fertility study of di(2-ethylhexyl)adipate (DEHA) in female rats. Journal of Toxicological Sciences 34(1) pp 101-109.

Last update 28 June 2013

Share this page