Toxicology 325 (2014) 209–216

Contents lists available at ScienceDirect

Toxicology

journal homepage: www.elsevier.com/locate/toxicol

Short communication

The National Library of Medicine's (NLM) Hazardous Substances Data Bank (HSDB): Background, recent enhancements and future plans

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ARTICLE INFO

Article history:
Received 17 July 2014
Accepted 3 September 2014
Available online 16 September 2014

Keywords:
Information
Databases
Online
National Library of Medicine

ABSTRACT

The National Library of Medicine's (NLM) Division of Specialized Information Services (SIS) Toxicology and Environmental Health Information Program is responsible for the management of the online Hazardous Substances Data Bank (HSDB). HSDB, a part of NLM's Toxicology Data Network (TOXNET®), is a file of chemical/substance information with one record for each specific chemical or substance, or for a category of chemicals or substances. Like the rest of TOXNET's databases and other resources, HSDB is available online at no cost to global users. HSDB has approximately 5600 chemicals and substances, with a focus on toxicology information and also on human exposure, industrial hygiene, emergency handling procedures, environmental fate, regulatory requirements, and related areas of likely interest to HSDB users. All data are from a core set of books, government documents, technical reports, selected primary journal literature, and other online sources of information, with a goal of linking the HSDB content to as much publicly available information as possible. HSDB's content is peer-reviewed by the Scientific Review Panel, a group of experts in the areas covering the scope of HSDB content. Recent enhancements include the addition of chemical structures to HSDB records, the addition of new subfields such as age groups for human data, more occupational exposure standards, and the addition of information on numerous nanomaterials. Examples of future plans include providing more exposure-related information, e.g., uses of a chemical or substance in consumer products; the addition of information summaries aimed towards consumers and other members of the public wanting to learn about a chemical or substance; more visual content such as diagrams (images) of the pathways of metabolism of a substance; and enhanced search features and navigation.

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1. Introduction

HSDB is available for free 24 h a day (www.toxnet.nlm.nih.gov). It was established over 40 years ago at NLM to assist the United States Agency for Toxic Substances and Disease Registry (ATSDR) and the United States Environmental Protection Agency (EPA) in collecting, documenting and making available online information about the chemical substances found at National Priority Listing Sites (NPL) throughout the United States. The initial selection, building and review of specific chemical records were accomplished via meetings of representatives from the three organizations. Chemicals found at NPL sites included pollutants such as heavy metals and their salts, biocides, herbicides, insecticides, radionuclides, solvents, gases and intermediates, complex mixtures and pharmaceutical preparations. The information placed into a chemical specific record was extracted from books, government documents, technical reports, selected primary journal literature, and other sources of online information (National Library of Medicine, 2009, 2014a,b).

HSDB's information has a broad scope as shown in the names of the HSDB data fields: Human Health Effects, Emergency

Abbreviations: ATSDR, Agency for Toxic Substances and Disease Registry; CPSC, Consumer Product Safety Commission; DEA, Drug Enforcement Agency; DHS, Department of Homeland Security; EPA, Environmental Protection Agency; ECHA, European Chemicals Agency; FDA, Food and Drug Administration; HSDB, Hazardous Substances Data Bank; IARC, International Agency for the Research on Cancer; IPCS, International Programme on Chemical Safety; NIEHS, National Institute of Environmental Health Sciences; NIOSH, National Institute of Occupational Safety and Health; NLM, National Library of Medicine; OSHA, Occupational Safety & Health Adminstration; QC, quality control; TOXNET®, Toxicology Data Network; WHO, World Health Organization.

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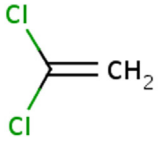
http://dx.doi.org/10.1016/j.tox.2014.09.003
0300-483X/Published by Elsevier Ireland Ltd.

1,1-DICHLOROETHYLENE

CASRN: 75-35-4



Human Health Effects:

Toxicity Summary:

1,1-Dichloroethene, or 1,1-DCE, does not occur naturally. It is produced commercially by the dehydrochlorination of 1,1,2-trichloroethane in the presence of excess base or by thermal decomposition of methyl chloroform (1,1,1-trichloroethane). 1,1-DCE is used as a captive intermediate in the production of hydrochlorofluorocarbons (HCFC-141b and HCFC-142b), in the production of chloroacetyl chloride, and in the production of homo-, co-, and terpolymers (latex and resin). The polymers are used in a variety of consumer products, including food packaging, textiles, and outdoor furniture. ...1,1-DCE is rapidly absorbed following inhalation and oral exposure. Because of its low relative molecular mass and hydrophobic nature, dermal absorption is also likely, but there are no relevant published data. Although 1,1-DCE is rapidly distributed to all tissues, most of the free 1,1-DCE, its metabolites, and covalently bound derivatives are found in the liver and kidney. 1,1-DCE is rapidly oxidized by cytochrome P450-dependent monooxygenase 2E1 (CYP2E1) to 1,1-dichloroethene oxide (DCE-epoxide), 2-chloroacetyl chloride, and 2,2-dichloroacetaldehyde. The major metabolites, DCE-epoxide and 2-chloroacetyl chloride, can react with glutathione (GSH), water, or tissue macromolecules. It is not known if the metabolism of 1,1-DCE is the same in humans, although in vitro microsomal preparations from human liver and lung form the same initial products. The only existing epidemiological study is inadequate to assess the cancer or non-cancer health effects of 1,1-DCE. Following high-dose exposure by the oral or inhalation route, the target organs in experimental animals are the liver, the kidney, and the Clara cells of the lung. Following low-dose, long-term exposure, the liver is the major target organ in rats following oral or inhalation exposure, but the kidney is the major target organ in mice following inhalation exposure. Bioassays for cancer by the oral route of exposure have been conducted in rats, mice, and trout. Although these bioassays have protocol limitations, none provides any significant evidence that 1,1-DCE is a carcinogen by the oral route of exposure. Bioassays for cancer by the inhalation route of exposure have been conducted in rats, mice, and hamsters. Most of these bioassays also have protocol limitations. One bioassay in male mice showed an increase in the incidence of kidney adenocarcinomas at one exposure level. There is evidence that the induction of kidney adenocarcinomas is a sex- and species-specific response related to the expression of CYP2E1 in the kidney of male mice. The results of the one bioassay showing an increase in tumours in one sex and at one exposure level in a single rodent species are not sufficient to justify an exposure-response assessment. 1,1-DCE causes gene mutations in microorganisms in the presence of an exogenous activation system. Most tests with mammalian cells in vitro or in vivo show no evidence of genotoxicity. There is no evidence that reproductive toxicity or teratogenicity is a critical effect for 1,1-DCE. No reproductive or developmental toxicity was observed at an oral exposure that caused minimal toxicity in the liver of the dams. There is some evidence of developmental variations in the heart after oral exposure, but it is not clear if these effects are directly caused by exposure to 1,1-DCE. There is evidence of fetal toxicity (delayed ossification) following inhalation exposure in the absence of maternal toxicity. One study shows no evidence that 1,1-DCE causes skin sensitization. The toxicity of 1,1-DCE is associated with cytochrome P450-catalysed metabolism of 1,1-DCE to reactive intermediates that bind covalently to cellular macromolecules. The extent of binding is inversely related to loss of GSH, so that severities of tissue damage parallel the decline in GSH. Thus, the responses to 1,1-DCE at low doses with little depletion of GSH are expected to be very different from the responses at high doses causing substantial GSH depletion. The critical effect from oral exposure is minimal hepatocellular mid-zonal fatty change in female Sprague-Dawley rats. Based on a BMDL10 (the lower 95% confidence limit on the benchmark dose (BMD) for a 10% response) of 4.6 mg/kg body weight per day and a total uncertainty factor of 100, the tolerable intake is 0.05 mg/kg body weight per day. The critical effect from inhalation exposure is minimal hepatocellular mid-zonal fatty change in female Sprague-Dawley rats. Based on a BMCL10 (the lower 95% confidence limit on the benchmark concentration (BMC) for a 10% response) of 6.9 mg/cu m and a total uncertainty factor of 30, the tolerable concentration is 0.2 mg/cu m. ... There are only limited data on the effects of 1,1-DCE in the aquatic and terrestrial environments. In studies conducted in closed systems, the EC50 for inhibition of the growth of a mixed methanotrophic culture was 0.05 mg/L; the 72-hr EC50 for inhibition of growth of green alga Chlamydomonas reinhardtii was 9.12 mg/L; and the 96-hr LC50 for bluegill (Lepomis macrochirus) was 74 mg/L. The limited data on occurrence of 1,1-DCE in surface water suggest that concentrations are in the microgram per liter range, indicating that acute toxic risks from 1,1-DCE for the aquatic environment are minimal. There are no long-term toxicity data with which to assess sublethal effects of 1,1-DCE on any organisms. However, because of the rapid volatilization of 1,1-DCE from the aquatic and terrestrial environments, no significant risk is expected.

[WHO; Concise International Chemical Assessment Document 51; 1,1-Dichloroethene (Vinylidine Chloride) (2003). Available from, as of September 2, 2008: http://www.inchem.org/documents/cicads/cicads/cicad51.htm **PEER REVIEWED**

Fig. 1. Human Toxicity Excerpts.

Medical Treatment, Animal and Human and Ecotoxicity Excerpts, Metabolism/Pharmacokinetics, Pharmacology, Environmental Fate/Exposure, Environmental Standards & Regulations, Chemical and Physical Properties, Manufacturing/Use Information, Laboratory Methods (analytical and clinical determinations), Synonyms and Formulations, and Safety Procedures. HSDB data fields are also referred to as “data elements”.

2. Chemical and substance selection

Chemicals, drugs, dietary supplements, venoms, heavy metals and other candidate compounds are evaluated and selected by the HSDB chemical selection team, an internal NLM group. Candidate chemicals are nominated by members of NLM’s staff, the public, scientific and regulatory agencies, and advisory groups.