



NICNAS Existing Chemicals Information Sheet

Diethylene Glycol (DEG) CAS No: 111-46-6

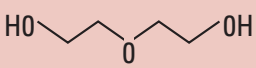
June 2009

Introduction

Diethylene glycol (DEG) is a widely used chemical with many industrial and household applications. It is also used in cosmetics for topical application.

In 2007, DEG was identified as a constituent in certain brands of imported toothpaste. In response to concerns over possible health effects from use of such toothpastes, NICNAS conducted a review of the human health hazards of DEG and of current regulatory controls. This Information Sheet contains the main findings from the human health hazard assessment report on DEG. The health hazard assessment report is available at the NICNAS website¹.

Chemical Identity

| | |
|----------------------|---|
| Common name: | Diethylene glycol (DEG) |
| Structural formula: |  |
| CAS registry number: | 111-46-6 |
| IUPAC chemical name: | 2,2'-oxybisethanol |

DEG is a clear syrupy liquid totally miscible (able to be mixed) in water.

Import, Manufacture and Use of Diethylene Glycol in Australia

DEG is widely used as a chemical intermediate and solvent for industrial and consumer applications.

In 2007, DEG was identified as a constituent in particular imported toothpastes. In response, NICNAS sought information from Australian industry on the use of DEG in oral cosmetic products (eg. toothpaste and mouthwash). There were no reports indicating the manufacture or importation of oral cosmetic products intentionally containing DEG.

Although DEG is not an allowable ingredient in foods or medicines, it is a known impurity in polyethylene glycol (PEG), an allowable ingredient for these applications. PEG is also used in cosmetics. Therefore, there is potential for very low levels of DEG to be present in cosmetics, including oral cosmetics such as toothpastes and mouthwashes.

¹ http://www.nicnas.gov.au/Publications/CAR/Other/DEG_Hazard_Assessment_Report_PDF.pdf

NICNAS Existing Chemicals Information Sheet

Exposure to Diethylene Glycol

From late May 2007, several countries including Australia issued safety warnings to consumers to avoid using certain toothpastes known to, or suspected of, containing DEG (used as a solvent replacing or being mislabelled as glycerine). Major recalls of imported toothpastes containing DEG were also issued. A few toothpaste brands were recalled. With advice from NICNAS, the Australian Competition and Consumer Commission (ACCC) banned the supply of toothpastes containing more than 0.25% w/w of DEG, effective 3 August 2007 for a period of 18 months.

Summary of Key Health Issues

DEG is of low acute oral toxicity in animals, however, calculation of lethal doses in humans indicates a higher sensitivity to toxic effects in humans compared to animals. Acute or chronic exposure to DEG can affect the nervous system, the kidneys and, to a lesser extent, the liver. Lethal doses are associated with renal failure and uraemic coma. DEG produces no or only minimal skin or eye irritation and no evidence of sensitisation in animals. From repeat dose toxicity studies in animals, mild renal effects (increases in urine volume) have been observed in experimental animals at doses of 230 mg/kg bw/d, with renal hydropic degeneration at 1.6 g/kg bw/d. Reproductive and developmental effects have also been observed in rodents but at significantly higher doses. Similar data for repeated exposure to the chemical are not available for humans.

Current Regulatory Status

DEG IS listed in:

- the Australian Inventory of Chemical Substances (AICS),
- the Adopted National Exposure Standards for Atmospheric Contaminants in the Occupational Environment [NOHSC:1003(1995)] with a time weighted average (TWA) of 100 mg/m³,
- the Hazardous Substances Information System (HSIS)² in accordance with the Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)] 3rd Edition. The classification and labelling details are: Xn: Harmful (cut-off \geq 25%); R22: Harmful if swallowed; S2: Keep out of the reach of children, and S46: If swallowed, seek medical advice immediately and show this container or label, and
- the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP)³. DEG for use in toothpastes and mouthwashes is now included in Appendix C of the SUSDP, with an exemption cut-off of 0.25 per cent. Appendix C lists substances, other than those included in Schedule 9 (prohibited substances), considered to be of such danger to health as to warrant prohibition of sale, supply and use.

Health and Safety Information

Health information for DEG was derived predominantly from the OECD SIDS Initial Assessment Report on the Ethylene Glycols Category and the Dutch Expert Committee on Occupational Standards report - Health-Based Recommended Occupational Exposure Limit for Diethylene Glycol. Additional literature searches provided relevant supplementary information.

Animal Data

DEG is rapidly and almost completely absorbed via the oral route. It is slowly and incompletely absorbed via the skin.

² <http://hsis.ascc.gov.au>

³ <http://www.tga.gov.au/ndpsc/susdp.htm#susdp>

NICNAS Existing Chemicals Information Sheet

Acute Toxicity

In animals, the acute oral, dermal and inhalational toxicity of DEG are low. Oral toxicity is similar for both rats and mice with LD50 (Lethal Dose, 50%; ie. the dose that is lethal for half the animals tested) values ranging from 13-30 g/kg bw (body weight). A single study of dermal toxicity in rabbits derived a LD50 value of 13.3 g/kg bw. Acute inhalational toxicity has also been tested in rats and mice. The 4-hour LC50 in rats was 4600 mg/m³. (Lethal concentration, 50%)

Acute effects reported include narcosis, metabolic acidosis, increased urine volumes, anuria and degeneration of renal tubules following oral administration of DEG at various doses.

Irritation and Sensitisation

DEG causes no or only minimal skin and eye irritation in laboratory animals. Respiratory depression was reported in mice although the characteristics were reported as not typical of a pure airway irritant. DEG does not cause skin sensitisation in guinea pigs.

Repeated Dose Toxicity

In animals, repeated oral exposures to DEG are associated with effects mainly in the kidney (increased urine volumes, hydropic degeneration and tubular necrosis) and to a lesser extent the liver (vacuolar degeneration). From 98-day and 225-day studies in Wistar rats, a Lowest-Observed-Adverse-Effect-Level (LOAEL) for increases in urine volume was established at 230 mg/kg bw/d with the No-Observed-Adverse-Effect-Level (NOAEL) at 100 mg/kg bw/d. A LOAEL based on renal hydropic degeneration was established at 1.6 g/kg bw/day with the NOAEL at 300 mg/kg bw/d.

Genotoxicity

DEG is considered non-genotoxic. *In vitro* tests with DEG resulted in either the chemical being negative, or only weakly positive for mutagenicity. Some indications of chromosomal damage were seen in *in vivo* tests, but only at high doses.

Carcinogenicity

Carcinogenicity results are ambiguous. Urinary bladder calculus and tumour responses were recorded in some long-term oral studies in the rat, but these were considered to result from chronic irritation of the bladder wall by DEG-induced stones. Other studies showed no evidence of carcinogenic effects after oral administration. Several studies in mice also showed no carcinogenicity after dermal DEG application.

Reproductive and developmental toxicity

Reproduction toxicity studies in rats and mice indicate that DEG induces adverse effects on fertility and development, but only at doses higher than those associated with repeat dose effects and in the presence of maternal toxicity. From these studies, the LOAEL for fertility and developmental effects in mice was established at 6.1 g/kg bw/d based on reductions in litters/pair, live pups/litter and live pup weight. The NOAEL was 3.1 g/kg bw/d. Maternal toxicity (decrease in body weight) was noted at 6.1 g/kg bw/d.

NICNAS Existing Chemicals Information Sheet

Human Data

Oral Toxicity

A number of mass poisonings in humans involving substitution of DEG for more expensive, non-toxic glycols in medicinal preparations have been documented over the last 70 years. Typical features of toxicity include neurological impairment, metabolic acidosis and acute renal failure. Early mortality and morbidity are high, with most deaths occurring within the first 2 weeks post exposure.

Large overlaps in ranges of lethal and non-lethal doses have been observed for adults and children. A median lethal oral dose of 1.49 g/kg bw DEG (range 0.25-4.9 g/kg bw) was estimated from large-scale intoxication of Haitian children with a paracetamol syrup contaminated with DEG. On this basis, humans appear to be about ten times more sensitive to the toxic effects of DEG than the animal species used in toxicity studies.

Irritation and Sensitisation

DEG causes no or only minimal skin irritation in humans. Data for eye irritation in humans were not available. In humans, there is a single case study reporting skin sensitisation 2-4 weeks after a man started smoking a brand of cigarettes containing DEG. However, overall, available data indicate that DEG is not a skin sensitiser in humans.

International Regulatory Activities Related to the 2007 Incidents

Due to potential health concerns over ingestion of DEG in 2007, the USA and Canada took action (Import Alert IA6674) to prevent the importation of toothpaste containing DEG. The Chinese General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ) also announced on 11 July 2007 that it had banned the use of DEG in toothpaste. In Europe, the Italian and Spanish authorities ordered the seizure of toothpaste products and toothpaste samples handed out in hospitals, hotels and on airplanes on suspicion of being tainted with DEG.