



NTP
National Toxicology Program

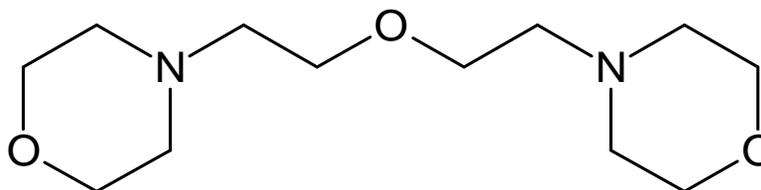
2,2-Dimorpholinodiethyl ether

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Concept Review
Board of Scientific Counselors
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Nomination



- DMDEE was Nominated by NCI
- Current production in excess of 1 million pounds but not part of HPV
- Significant potential for occupational exposure
- No data on toxicity, metabolism, carcinogenic potential
- Potential for the formation of N-nitrosomorpholine, a known carcinogen, as a metabolite



Human exposure

- DMDEE is used as a catalyst in polyurethane foams, in hot melt urethane adhesives, and in other warm melt adhesives.
- During production at elevated temperatures, fugitive catalyst may escape.
- Exposure to un-reacted catalyst may also occur during machining of foams into finished products:
 - Slabstock foam products are used in furniture seat cushions and bedding materials;
 - moulded foam is used in automotive seats, packaging, and a wide range of specialty products
- Dermal and inhalation exposure are the predominant routes of occupational exposure



Background

- No information in peer reviewed literature
- The Material Safety Data Sheet lists DMDEE as a skin, eye, and respiratory irritant
- Oral LD 50 of greater than 2000mg/kg in the rat
- low vapor pressure (0.578mmHg @ 123°C)
- Freezing point -280°C; boiling point 320°C
- Miscible with water
- DMDEE has a pH = 10.4



Key Issue

- The key issue addressed in the nomination and in this concept proposal is examination of the absorption, distribution, metabolism, and elimination of DMDEE with specific monitoring for formation N-nitrosomorpholine during the metabolism of DMDEE
- Metabolic formation of N-nitrosomorpholine would indicate a significant risk associated with exposure to DMDEE.



Specific Aim #1: ADME studies

- Conduct ADME studies by the oral and dermal routes of exposure with specific monitoring for the formation of N-nitrosomorpholine and N-nitroso(2-hydroxyethyl)glycine

Specific Aim #2: mutagenicity and DNA reactivity

- Examine bacterial mutagenicity
- Evaluate DNA reactivity in mammalian cells
 - DNA adducts
 - Comet assay



Significance

- DMDEE is a high production volume chemical with wide use in the manufacture of a number of products and significant potential for occupational exposure.
- If N-nitrosomorpholine is formed as a by product of metabolism then occupational exposure to DMDEE must be greatly minimized and the possibility of consumer exposure must be carefully examined.