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4,4-DIAMINODIPHENYLMETHANE (DDM)

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The enclosed background material on 4,4'-diaminodiphenylmethane (DDM) has been prepared by the Office of Extramural Coordination and Special Projects, National Institute for Occupational Safety and Health to alert members of the occupational health community to new information on a potential occupational hazard.

Your comments and suggestions for changes to future reports are solicited.

Sincerely yours,

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Safety and Health

This office has prepared the following summary of information on the production, uses, exposure and health effects of 4,4'-diaminodiphenylmethane (DDM).

DDM, 4,4'-diaminodiphenylmethane, also known as p,p'-methylenedianiline (MDA), is an important chemical intermediate. Over 200,000,000 pounds per year of DDM are manufactured in the United States. A list of the manufacturers and producers of DDM is attached. DDM is produced by the condensation of aniline with formaldehyde in the presence of an acid catalyst.

Approximately ninety-nine percent of the DDM produced is consumed in its crude form (occasionally containing not more than 50% DDM and polyDDM) at its production site by reaction with phosgene in the preparation of isocyanates and polyisocyanates. These isocyanates and polyisocyanates are employed in the manufacture of rigid polyurethane foams which find application as thermal insulation. Polyisocyanates are also used in the preparation of the semiflexible polyurethane foams used for automotive safety cushioning.

DDM is also used as:

- an epoxy hardening agent
- a raw material in the production of polyurethane elastomers
- in the rubber industry
  - a curative for neoprene (1)
  - an anti-frosting agent (anti-oxidant) in footwear
- a raw material in the production of Qiana Nylon
- a raw material in the preparation of poly(amide-imide) resins (used in magnet wire enamels)

It is estimated that 2,500 workers are exposed to DDM. Many of these exposures to DDM are in the preparation of isocyanates and polyisocyanates and, on construction sites, in the application of epoxy coatings.

In 1965, the hepatotoxic effects of DDM in humans were first seen in the so-called "Epping Jaundice" outbreak in Great Britain. In this incident 84 people who had eaten DDM contaminated bread, experienced hepatocellular damage evidenced by elevated SGOT and SGPT levels (2,3). DDM has also been shown to produce liver lesions in a group of intragastrically fed rats (4) and has caused liver degeneration and spleen lesions in another group of DDM fed rats (5.)

DDM in the occupational environment has been implicated in a number of cases of toxic hepatitis. During an 18 month period beginning April 1972, six cases of hepatitis developed among about 300 men who used epoxy resins in the construction of a nuclear power plant in Alabama. Two chemicals, DDM and 2-nitropropane, were held suspect in this study (6,7). In another study, 13 cases of hepatitis developed between 1966 and 1972 among workers who added DDM to a mixture to produce a hard plastic insulating material. All of these men became ill within a few days of working intensively with DDM (8). One other case of hepatitis, possibly associated with DDM, was reported by a person who wrote to the Environmental Protection Agency describing an episode of acute hepatitis as well as CNS and pulmonary symptoms he experienced following exposure to a surfacing agent containing DDM.

The carcinogenic effects of DDM have also been studied. In one study, 16 rats were given 4 or 5-20 mg DDM doses by stomach tube over 8 months. A hepatoma and a haemangioma like tumor of the kidney were found in one rat after 18 months and an adenocarcinoma of the uterus was found in another after 24 months (9). In another report, of 48 rats given DDM intragastrically 5 times weekly, all developed liver cirrhosis, four developed hepatomas (2 benign) and others, miscellaneous tumors (10). In a third report, 50% of 50 DDM injected rats developed tumors (4 hepatomas) compared with 26% of a control group (11). There have been no reported human cancers associated with DDM.

If, as hypothesized in the Center for Disease Control study of nuclear power plant construction workers, not all workers are susceptible to liver injury after exposure to DDM, and if the 1-2% incidence of liver disease seen in this study were applied to all workers with possible exposure to DDM, we would expect to see 25 to 50 cases of DDM associated toxic hepatitis a year.

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LISTED MANUFACTURERS AND PRODUCERS OF
4,4'-Diaminodiphenylmethane

COMPANY	PLANT LOCATION
Allied Chemical Corporation Specialty Chemicals Division	Moundsville, West Virginia
Dow Chemical, U.S.A.	Midland, Michigan
Jefferson Chemical Company, Inc.	Port Neches, Texas
Mobay Chemical Corporation	New Martinsville, West Virginia Cedar Bayou, Texas
Rubicon Chemicals, Inc.	Geismar, Louisiana
Uniroyal, Inc. Uniroyal Chemical Division	Naugatuck, Connecticut
The Upjohn Company Polymer Chemicals Division	La Porte, Texas

Adapted from the following sources:

1975 Directory of Chemical Producers, Stanford Research Institute, Menlo Park, California, page 818, 1975.

Synthetic Organic Chemicals, U.S. Production and Sales, 1973, U.S. International Trade Commission, ITC Publication 728, U.S. Government Printing Office, Washington, D.C., pages 23, 41 and 139, 1975.

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