NIOSH ALERT

SEPTEMBER 1990

REQUEST FOR ASSISTANCE IN

Preventing Adverse Health Effects from Exposure to *Dimethylformamide (DMF)*

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health

CDC
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DHHS (NIOSH) Publication No. 90-105

Request for Assistance in

Preventing Adverse Health Effects from Exposure to Dimethylformamide (DMF)

WARNING!

Avoid skin contact with dimethylformamide (DMF)! This chemical is easily absorbed through the skin and can cause liver damage and other adverse health effects.

The National Institute for Occupational Safety and Health (NIOSH) requests assistance in reducing the health risks to workers exposed to the solvent dimethylformamide (DMF). This substance is readily absorbed through the skin and is known to be toxic to the liver; recent evidence shows that liver damage may occur in exposed workers who appear to be healthy. DMF is also known to cause skin problems and alcohol intolerance. Some reports also suggest an increase in cancer among workers exposed to DMF, but the evidence is not conclusive at this time. NIOSH and other organizations are working to determine whether exposure to DMF increases the risk of developing cancer.

This Alert describes engineering controls, good work practices, and personal protective equipment (PPE) recommended for controlling exposures to DMF by inhalation and skin contact. NIOSH requests editors of appropriate trade journals, safety and health officials, and employers to bring these recommendations to the attention of workers, supervisors, and managers.

BACKGROUND

Dimethylformamide (DMF) is a colorless, water-soluble liquid with a faint ammonia-like odor. This organic solvent is used in acrylic fiber spinning, chemical manufacturing, and pharmaceutical production; it is also present in textile dyes and pigments, paint stripping solvents, and coating, printing, and adhesive formulations [NIOSH/OSHA 1981]. The National Institute for Occupational Safety and Health (NIOSH) estimates that more than 100,000 workers may be exposed to DMF in the United States [NIOSH 1983]. Currently, there is only one producer of DMF in the United States; annual production is between 50 and 60 million pounds [Porta 1988].

CURRENT EXPOSURE LIMITS

The NIOSH recommended exposure limit (REL), the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL), and the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value (TLV®) are all 10 parts of DMF per million parts of air (10 ppm), or 30 milligrams of DMF per cubic meter of air (30 mg/m^3), as an 8-hour time-weighted average (TWA) with a "skin" notation [NIOSH 1988; 29 CFR* 1910.1000; ACGIH 1989]. These exposure limits are based on the acute effects of DMF (primarily injury to the liver). The "skin" notation refers to the potential for absorption of DMF through the skin. Standards in other countries include 20 ppm in West Germany, 3 ppm in the USSR, and 10 ppm in East Germany, Sweden, and Czechoslovakia.

POTENTIAL HEALTH EFFECTS OF DMF

Liver Injury

DMF has long been known to be toxic to the liver [Massmann 1956; Scailteur and Lauwerys 1987]. Redlich et al. [1988] recently investigated a fabric-coating plant and found workers exposed to DMF (and other solvents) in poorly ventilated areas without appropriate skin protection. Blood tests revealed elevated liver enzymes (suggesting liver injury) in 35 of the 46 production workers tested; this percentage of abnormal tests (76%) was unusually high. The enzyme levels generally returned to normal within 1 to 5 months after removal from this exposure. However, four workers whose tests remained abnormal underwent liver biopsies (i.e., removal of a small piece of liver tissue). Examination of the biopsied tissues revealed damage that could have been caused by a chemical exposure.

*Code of Federal Regulations. See CFR in references.

Cancer

In 1986, investigators published a report of three men with testicular tumors (expected number of cases was not reported) who worked at an airframe repair shop employing 153 men [Ducatman et al. 1986]. When two additional airframe repair shops were investigated, one was found to employ four workers with a history of testicular cancer (0.95 case was expected). At the two shops where cases of testicular cancer were found, workers were exposed to a particular solvent mixture containing 80% DMF. The shop reporting no cases of testicular cancer did not use this solvent mixture.

In 1987, investigators reported three additional cases of testicular cancer (0.07 case was expected) in a group of men who had worked as finishers in a leather tannery [Levin et al. 1987; CDC 1988]. These men were exposed to a number of chemicals, including DMF, by inhalation of spray aerosols and by skin contact as they leaned over a conveyer belt to spread dye mixtures. Since 1975, 83 men are known to have worked in the finishing department of this tannery. In June 1989, NIOSH offered medical examinations to these men. Fifty-one of these workers (61%) participated, but no additional cases of testicular cancer were found [NIOSH 1990a].

Another study considered groups of workers exposed to DMF, acrylonitrile, or a combination of both chemicals at a large plant that manufactured acrylic fibers [Chen et al. 1988]. Nine cases of cancer of the mouth or throat were found among workers exposed to DMF alone (1.6 cases were expected); all of these cancer victims were smokers. Although tobacco use alone can cause cancer of the mouth or throat, it is not known whether

exposure to DMF might increase this risk by increasing absorption of carcinogens such as those present in tobacco (DMF is known to increase the absorption of some substances [Reiss 1966]).

Research has also suggested a possible association between DMF and prostate cancer [Chen et al. 1988; Walrath et al. 1989]. However, many of the DMF-exposed subjects with prostate cancer were also exposed to acrylonitrile, which is known to cause cancer in humans [NIOSH 1978].

The reports described above suggest an increase in cancer among workers exposed to DMF, but the evidence is not conclusive at this time. The reports indicate that workers were exposed to many different chemicals (including DMF) as well as tobacco. Therefore, the excess cancer observed could have resulted from exposure to one of these agents or to a combination of them; or the cancers could have been due to chance alone.

Animal studies published to date have failed to establish a link between DMF and cancer [Druckrey et al. 1967; Carnaghan 1967; Herrold 1969]. The International Agency for Research on Cancer (IARC) recently classified the evidence associating DMF with cancer in animals as "inadequate" [IARC 1989]. However, on the basis of the published literature reviewed above, IARC [1989] found "limited evidence" that DMF causes cancer in humans and classified DMF as "possibly carcinogenic to humans" (IARC Group 2B).

Other Health Effects

DMF is known to cause skin problems and alcohol intolerance (anxiety, palpitations, headache, flushing of the face and trunk, nausea, and vomiting) [Lauwerys 1986; Reinl and Urban 1965]. One study suggests that alcohol intolerance may occur in some workers even if exposures to DMF are below 10 ppm and there is no skin contact [Lauwerys et al. 1980].

The reproductive effects of DMF in humans have not been adequately studied. However, DMF is known to have induced malformations in the offspring of mice [Scheufler and Freye 1975] and rabbits [Merkle and Zeller 1980].

Although several studies have failed to establish that DMF is a mutagen (a substance that alters genetic material in cells) [Antoine et al. 1983; McGregor 1981; Martin and McDermid 1981], other reports have suggested that DMF may be mutagenic in some cell lines [Koudela and Spazier 1979, 1981]. It is also possible that DMF could enhance the mutagenicity of other substances [Arimoto et al. 1982].

Workers exposed to DMF have also reported weakness, dizziness, headache, abdominal pain, nausea and vomiting, and constipation.

CONCLUSIONS

On the basis of the information outlined in this Alert, NIOSH concludes the following:

- DMF is readily absorbed through the skin, inhaled, or ingested.
- DMF is a potent liver toxin.
- DMF may cause abdominal pain, constipation, nausea and vomiting, headache, weakness, dizziness, skin problems, and alcohol intolerance.
- Current evidence associating DMF with cancer in humans is not conclusive. The excess cancer observed could have resulted from exposure to other chemicals or tobacco, or from chance alone.
- The reproductive effects of DMF in humans have not been adequately studied.

RECOMMENDATIONS

NIOSH recommends the following measures to reduce exposure to DMF in the workplace.

Hazard Awareness. Workers should be informed about the potential health effects of DMF. A material safety data sheet (MSDS) should be made available to any worker who may be exposed to DMF.

Training. Workers should receive training in

—the importance of avoiding skin contact with DMF,

—the use of appropriate protective equipment (including protective clothing and respiratory protection), and

—specific work practices necessary to work safely with DMF.

Engineering Controls. Employers should use appropriate engineering controls to ensure that exposure to DMF in the workplace does not exceed the current NIOSH REL or OSHA PEL of 10 ppm as an 8-hr TWA [29 CFR 1910.1000; NIOSH 1988]. As with all toxic chemicals, exposures should be kept as far below this limit as practical.

Engineering controls that should be considered include

—substitution of less toxic materials,

—use of enclosed processes,

—separation of the worker from the processes, and

—design and installation of appropriate ventilation.

Biological Monitoring. Biological monitoring should be instituted if skin contact with liquid DMF might occur. Such monitoring may be accomplished by collecting urine at the end of the exposure period and analyzing it for certain metabolites of DMF. The method used by Lauwerys [1986] has not been validated by NIOSH but may be useful. Biological monitoring can provide additional information regarding the effectiveness of engineering controls, work practices, and personal protective equipment.

Medical Screening. Medical screening of workers (including blood tests to evaluate liver function) should be performed if one or more of the following are true:

- The concentration of DMF in workplace air exceeds 5 ppm as an 8-hr TWA (half the NIOSH REL or OSHA PEL).
- Biological monitoring reveals that excessive exposures are occurring.[†]
- One or more workers suffer an adverse health effect associated with exposure to DMF (for example, if a worker exposed to DMF develops toxic liver injury) [Redlich et al. 1988].
- Exposed workers show evidence of alcohol intolerance, which is an early sign of excessive exposure (symptoms of intolerance include anxiety, palpitations, headache, flushing of the face and trunk, nausea, and vomiting) [Lauwerys 1986, Reinl and Urban 1965].

[†]Although NIOSH has not independently evaluated the data, some researchers have suggested that urine concentrations of certain DMF metabolites below 40 mg/g creatinine (measured as n-methylformamide by gas chromatography) are not associated with signs of acute liver toxicity [Lauwerys 1986].

Personal Protective Equipment. Before engineering controls are installed or when they are not technologically feasible, workers should use the following personal protective equipment to reduce exposures to DMF:

- Chemical Protective Clothing (CPC) such as gloves and aprons should be worn by workers using DMF to reduce skin contact and absorption. The most protective materials for gloves are butyl rubber, Teflon®, and polyethylene/ethylene (e.g., 4H® or Silver Shield®) [Forsberg and Mansdorf 1989]. Nitrile or neoprene gloves may be used for short-duration tasks that require more durable, abrasion-resistant material [Forsberg and Mansdorf 1989]. Note, however, that the quality of these gloves may vary significantly among glove producers [Mickelsen and Hall 1987]. Product-specific permeation data should therefore be obtained from the glove manufacturer. Saranex®/Tyvek® clothing may be used to protect parts of the body other than the hands during short-duration tasks.

- Respirators may be required by workers in certain situations such as emergencies and maintenance operations. The NIOSH recommendations for respiratory protection are based on the established health effects of DMF [NIOSH/OSHA 1981] and its inadequate warning properties (the odor threshold for DMF is 0.47 to 100 ppm) [Hooper 1988].

Table 1 lists the types of respiratory protection recommended for DMF under various exposure conditions. For additional information on the selection and use of respirators, refer to the *NIOSH Respirator Decision Logic* [NIOSH 1987b] and the *NIOSH Guide to Industrial Respiratory Protection* [NIOSH 1987a]. Respirators should be approved by NIOSH and the Mine Safety and Health Administration (MSHA) [NIOSH 1990b].

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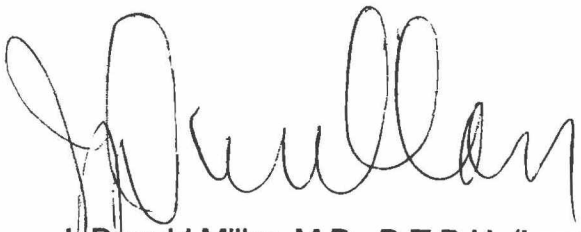

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Table 1.—Respiratory protection recommended for DMF

Condition	Minimum respiratory protection
Airborne concentration:	
Less than 100 ppm	Any SAR,*,† or any SCBA†,§
Less than 250 ppm	Any SAR with a helmet or hood
Less than 500 ppm	Any SAR with a full facepiece, or any SCBA with a full facepiece
Less than 3,500 ppm	Any SAR with a full facepiece operated in a pressure-demand or other positive-pressure mode
3,500 ppm ** or more, or planned or emergency entry into unknown concentrations	Any SAR equipped with a full facepiece and operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary SCBA operated in a pressure-demand or other positive-pressure mode, or any SCBA equipped with a full facepiece and operated in a pressure-demand or other positive-pressure mode
Firefighting	Any SCBA equipped with a full facepiece and operated in a pressure-demand or other positive-pressure mode
Escape only	Any air-purifying, full-facepiece canister respirator providing protection against organic vapors and equipped with an end-of-service-life indicator (ESLI), or Any SCBA equipped with a full facepiece and operated in a pressure-demand or other positive-pressure mode

* Supplied-air respirator.
† If eye irritation occurs, full-facepiece respiratory protective equipment should be used.
§ Self-contained breathing apparatus.
** The concentration of DMF that is immediately dangerous to life and health (IDLH).

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NIOSH ALERT

Dimethylformamide (DMF)

WARNING!

Avoid skin contact with dimethylformamide (DMF)! This chemical is easily absorbed through the skin and can cause liver damage and other adverse health effects.

Dimethylformamide is associated with the following health effects:

- ***Liver damage***
- ***Alcohol intolerance***
- ***Skin problems***

Exposed workers have also reported the following symptoms:

- ***Weakness***
- ***Nausea and vomiting***
- ***Abdominal pain***
- ***Dizziness***
- ***Headache***
- ***Constipation***

Some reports suggest an increase in cancer among workers exposed to DMF, but the evidence is not conclusive at this time. The excess cancer observed could have resulted from exposure to other chemicals or tobacco, or from chance alone.

Take the following precautions if you are exposed to DMF on the job:

1. Obtain and read the material safety data sheet (MSDS) for DMF and the NIOSH Alert on DMF (see ordering information at right).

2. Avoid skin contact with DMF: Use chemical protective clothing such as gloves and aprons made from butyl rubber, Teflon®, or polyethylene/ethylene (for example, 4H® or Silvershield®).

3. Use respiratory protection when concentrations of DMF in workplace air may exceed 10 ppm as an 8-hour time-weighted average (for example, during emergencies or maintenance operations).

4. Participate in your company's medical screening program if you qualify.

For additional information, see the NIOSH Alert on DMF [DHHS (NIOSH) 90-105], or call 1-800-35-NIOSH. Single copies are available free from the following:

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