N-Methylformamide



SYNONYMS

C2-H5-NO, HCONHCH3, "formamide, N-methyl-", EK-7011, methylformamide, monomethylformamide, NSC-3051, X-188

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS



CANADIAN WHMIS SYMBOLS



RISK

Harmful in contact with skin. May cause harm to the unborn child.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

Accidental ingestion of the material may be damaging to the health of the individual.

■ N-methylformamide is an investigational anticancer drug.

Oral doses of 0.

EYE

Although the liquid is not thought to be an irritant, direct contact with the eye may produce transient discomfort characterized by tearing or conjunctival redness (as with windburn).

SKIN

Skin contact with the material may be harmful; systemic effects may resultfollowing absorption.

- There is some evidence to suggest that this material can cause inflammation of the skin on contact in some persons.
- Open cuts, abraded or irritated skin should not be exposed to this material.
- Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects.

Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

■ Inhalation of vapours may cause drowsiness and dizziness.

This may be accompanied by narcosis, reduced alertness, loss of reflexes, lack of coordination and vertigo.

There is some evidence to suggest that the material can cause respiratory irritation in some persons.

The body's response to such irritation can cause further lung damage.

■ Inhalation hazard is increased at higher temperatures.

Inhalation of high concentrations of gas/vapor causes lung irritation with coughing and nausea, central nervous depression with headache and dizziness, slowing of reflexes, fatigue and inco-ordination.

CHRONIC HEALTH EFFECTS

■ Ample evidence exists, from results in experimentation, that developmental disorders are directly caused by human exposure to the material.

There has been some concern that this material can cause cancer or mutations but there is not enough data to make an assessment.

Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

In the rat, i.p. administration of 1 gm/kg N-methylformamide on day 7 or 11 of gestation destroyed 90% of the foetuses. doses of 400 mg/kg. p.o. or 100 mg/kg i.p. daily on 3 consecutive days caused extensive foetal loss and malformations. Cutaneous application of 600 mg/kg daily on two days after the tenth day of gestation was teratogenic and embryotoxic in rats and rabbits. Divided doses applied to the skin of rats, in six portions, were more toxic to mother and embryo than that observed after a single daily dose.

N-methylformamide possesses anti-neoplastic properties against a number of mouse tumors and human xenograft tumors grown in mice. Chronic hepatic necrosis (liver damage) is of the periacinar type.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
N-methylformamide	123-39-7	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

 \cdot If swallowed do NOT induce vomiting. \cdot If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

EYE

■ If this product comes in contact with the eyes: · Wash out immediately with fresh running water. · Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN

■ If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED

· If fumes or combustion products are inhaled remove from contaminated area. · Other measures are usually unnecessary.

NOTES TO PHYSICIAN

■ Treat symptomatically.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):

Not available

Upper Explosive Limit (%):	19.7
Specific Gravity (water=1):	0.997
Lower Explosive Limit (%):	1.8

EXTINGUISHING MEDIA

· Water spray or fog.

· Foam.

FIRE FIGHTING

· Alert Emergency Responders and tell them location and nature of hazard.

· Wear full body protective clothing with breathing apparatus.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

· Combustible.

 \cdot Slight fire hazard when exposed to heat or flame.

Combustion products include: carbon dioxide (CO2), nitrogen oxides (NOx), other pyrolysis products typical of burning organic material. May emit poisonous fumes.

May emit corrosive fumes.

FIRE INCOMPATIBILITY

Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION

Glasses: Chemical goggles. Gloves: Respirator: Type A Filter of sufficient capacity

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- · Remove all ignition sources.
- · Clean up all spills immediately.

MAJOR SPILLS

Moderate hazard.

- · Clear area of personnel and move upwind.
- · Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

- · DO NOT allow clothing wet with material to stay in contact with skin.
- · Avoid all personal contact, including inhalation.
- · Wear protective clothing when risk of exposure occurs.
- · Avoid all personal contact, including inhalation.
- · Wear protective clothing when risk of exposure occurs.

RECOMMENDED STORAGE METHODS

· Metal can or drum

· Packing as recommended by manufacturer.

STORAGE REQUIREMENTS

- · Store in original containers.
- · Keep containers securely sealed.
- \cdot No smoking, naked lights or ignition sources.
- · Store in a cool, dry, well-ventilated area.
- \cdot Store away from incompatible materials and foodstuff containers.
- · Protect containers against physical damage and check regularly for leaks.
- · Observe manufacturer's storing and handling recommendations.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

N-methylformamide: CAS:123-39-7

PERSONAL PROTECTION



RESPIRATOR

• type a filter of sufficient capacity.

EYE

· Safety glasses with side shields.

· Chemical goggles.

HANDS/FEET

■ Wear chemical protective gloves, eg. PVC.

Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

frequency and duration of contact,

· chemical resistance of glove material,

 \cdot glove thickness and

dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

• When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.

· When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.

· Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

· Neoprene gloves.

OTHER

- · Overalls.
- · P.V.C. apron.
- · Barrier cream.
- · Skin cleansing cream.
- · Eye wash unit.

ENGINEERING CONTROLS

General exhaust is adequate under normal operating conditions. Local exhaust ventilation may be required in special circumstances.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Liquid. Mixes with water.			
State	Liquid	Molecular Weight	59.07
Melting Range (°F)	25	Viscosity	Not Available
Boiling Range (°F)	387	Solubility in water (g/L)	Miscible
Flash Point (°F)	246	pH (1% solution)	Not applicable.
Decomposition Temp (°F)	Not available.	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Not available
Upper Explosive Limit (%)	19.7	Specific Gravity (water=1)	0.997
Lower Explosive Limit (%)	1.8	Relative Vapor Density (air=1)	2.04
Volatile Component (%vol)	Not available	Evaporation Rate	Not available

APPEARANCE

Clear, colourless hygroscopic liquid with faint odour; mixes with water, alcohols, chloroform, acetone, ethyl acetate.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

 \cdot Presence of incompatible materials.

· Product is considered stable.

STORAGE INCOMPATIBILITY

· Avoid oxidizing agents, acids, acid chlorides, acid anhydrides.

· Avoid strong bases.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

N-methylformamide

TOXICITY AND IRRITATION

N-METHYLFORMAMIDE:

unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOXICITY

Intraperitoneal (Rat) LD50: 3500 mg/kg

Oral (Mouse) LD50: 2600 mg/kg

Intraperitoneal (Mouse) LD50: 802 mg/kg

Subcutaneous (Mouse) LD50: 3100 mg/kg

Intravenous (Mouse) LD50: 1580 mg/kg

■ Dimethylformamide (DMF) is closely structurally related to N-methylformamide (MMF), in that both contain an N-substituted formamide moiety. The substances differ only in the degree of substitution on the nitrogen atom; MMF contains one methyl group and DMF contains two. Review of the toxicologic databases for MMF and DMF indicates that the two substances have generally similar toxicity profiles.

The pathways for biotransformation of DMF and MMF have been extensively investigated. Qualitatively, the pathways of metabolism for DMF and MMF are quite similar. The major pathway for primary metabolism of DMF is the P450-mediated oxidation to form N-(hydroxymethyl)-N-methylformamide (HMMF). An alternative pathway for biotransformation of DMF is formal demethylation to yield MMF. MMF is further metabolized by hydroxylation of the remaining methyl group to form N-(hydroxymethyl) formamide, or by oxidation of the formyl carbon, leading to formation of a reactive carbamoylating intermediate. The reactive intermediate can react with cellular glutathione (GSH) to yield SMG, which is eventually excreted in the urine as the corresponding mercapturic acid.

Mammalian Acute Toxicity: MMF has slight acute oral toxicity with an LD50 in rats of 4000-7077 mg/kg and an LD50 in mice of approximately 2600 mg/kg. MMF was moderately toxic by skin absorption in the pregnant rabbit with an ALD of 1500 mg/kg and exhibited very low toxicity by skin absorption in the pregnant rat with an ALD of 11,000 mg/kg. The ALD studies were conducted in pregnant rats and rabbits .

MMF was irritating to rabbit eyes.

Repeated Dose Toxicity: The primary target organ in repeated dose studies appears to be the liver for both MMF and DMF. These effects appear at similar doses/exposures to the 2 chemicals. In a two-week inhalation study with MMF, no adverse effects were seen in rats exposed to 50 ppm. Higher concentrations (132 and/or 402 ppm) produced compound-related biochemical and microscopic pathology changes in the liver. Longer term repeated dose studies of MMF were not available; however, data were available on the structurally similar compound, DMF. In a two-week inhalation study in rats with DMF, increased liver weights were observed at 91 ppm. In a 90-day inhalation stud y with DMF, evidence of hepatocellular injury was seen as early as day 4 on increases in the activities of liver-specific enzymes at concentrations of 200 ppm and above. Relative liver weights were increased in males at 100 ppm and above and in females at 50 ppm and above. Pathologic changes of the liver (minimal to moderate centrilobular hepatocellular necrosis) were observed at 400 ppm and above. Developmental Toxicity: For both MMF and DMF, the fetus appears to have the same sensitivity to the test chemicals as the maternal animal

MMF did not produce developmental effects at maternally non-toxic doses when given by inhalation to rats, dermally to rats, and orally to rats and rabbits. Developmental effects were observed in mice when treated with MMF orally and dermally. In studies in which both maternal and fetal effects were carefully examined, the effects of MMF appeared at the same dose levels in maternal and fetal animals. In the inhalation study in rats, maternal lethality and toxicity was demonstrated at 150 ppm MMF and maternal toxicity remained evident as mild respiratory distress in the 50 ppm treated dams. Decreased fetal weight and fetal malformations and variations were observed at 150 ppm. Developmental toxicity, expressed as slight depression in fetal weight, was evident at 50 ppm. The NOEL for both the dam and the fetus was 15 ppm. In an oral study in rats and rabbits, maternal toxicity was evidenced as decreased body weight and food consumption at 75 mg/kg in rats and 50 mg/kg in rabbits. The NOEL for maternal and fetal weight, was 10 mg/kg in both rats and rabbits.

Extensive testing has been conducted in rats and rabbits by inhalation, oral, and dermal routes of exposure which shows that DMF affects the embryo/fetus only under conditions which will affect the maternal animal. Rats exposed by inhalation to either 18 or 172 ppm during gestation showed no structural changes. Both maternal and fetal weights were reduced at 172 ppm. Similarly, no teratogenic effects were seen in rats inhaling either 30 or 300 ppm during gestation with weights affected in both maternal and fetal rats at 300 ppm. Oral studies in rats showed maternal toxicity at doses of 100 mg/kg or greater along with fetal toxicity at the same doses. No malformations were seen and the fetal effect consisted of weight depressions and skeletal developmental delays. DMF given orally to rabbits produced both maternal and fetal effects with fetal anomalies being produced at doses that had little maternal effect. Studies in other species and those involving dermal exposure supports the hypothesis that the maternal and foetal animals are equally sensitive to the toxic effects of DMF.

Reproductive Toxicity: No formal reproductive toxicity studies have been conducted on MMF. Data were available on the structurally similar compound, DMF. Rats given dermal applications of either 500, 1000, or 2000 mg/kg of DMF from 4 weeks pre-mating through the production and lactation of 1 litter showed no effects on reproductive endpoints. Administration of 2000 mg/kg resulted in a reduction in the number of viable pups per litter. Body weight effects were seen in the parents at 1000 and 2000 mg/kg. Foetal and weanling body weights were similar to controls. In a continuous breeding study in which mice were exposed to either 1000, 4000, or 7000 ppm of DMF in their drinking water, a decrease in fertility (reflected by a decrease in pups born alive and in live litter size) was seen at 4000 and 7000 ppm. Liver damage was produced in all parental animals (1000 to 7000 ppm) and body weight gains were affected at 4000 and 7000 ppm. Decreased fertility and foetal effects (decreased pup weight) paralleled the parental sensitivity observed at 4000 and 7000 ppm. No effects on fertility or foetal parameters were observed at 1000 ppm. In a 90-day inhalation study conducted in rats and mice, relative testes weights were increased at 400 ppm and above in the rats; however, no microscopic findings or adverse effects have been shown to occur at higher doses/exposures than hepatotxic effects). Based on its structural similar toxicity profile for developmental and repeated dose toxicity, it is expected that MMF is not a reproductive toxin.

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IRRITATION

Genetic Toxicity: MMF was not mutagenic in Escherichia coli. No data on the clastogenicity of MMF are available. However the genetic toxicity of the analog, DMF, has been extensively investigated. A review of the available literature indicates that although some positive findings have been observed, DMF does not induce chromosome aberrations or gene mutations in most of the systems tested. In in vitro bacterial mutation assays, 33/37 tests with DMF produced negative results. DMF was also negative in 14/14 unscheduled DNA synthesis assays (in vitro), negative in 19/22 clastogenicity assays (in vitro), negative in 8/9 in vivo micronucleus assays, negative in 11/11 in vivo dominant lethal tests, and negative in 17/17 other in vivo genetic toxicity assays. The weight of evidence suggests that DMF and, by analogy, MMF are not genotoxic.

Foetoxicity, foetolethality and specific development abnormalities recorded.

Section 12 - ECOLOGICAL INFORMATION

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
N-methylformamide	LOW	No Data Available	LOW	HIGH

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

Puncture containers to prevent re-use and bury at an authorized landfill.

Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- · Reuse
- · Recycling
- · Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. If it has been contaminated, it may be possible to reclaim the product by filtration, distillation or some other means. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

· Recycle wherever possible or consult manufacturer for recycling options.

· Consult Waste Management Authority for disposal.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

N-methylformamide (CAS: 123-39-7) is found on the following regulatory lists;

"Canada Toxicological Index Service - Workplace Hazardous Materials Information System - WHMIS (English)","International Chemical Secretariat (ChemSec) REACH SIN* List (*Substitute It Now!) 1.0","OECD Representative List of High Production Volume (HPV) Chemicals","US DOE Temporary Emergency Exposure Limits (TEELs)","US EPA High Production Volume Program Chemical List","US Toxic Substances Control Act (TSCA) - Inventory"

Section 16 - OTHER INFORMATION

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Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references. A list of reference resources used to assist the committee may be found at:

www.chemwatch.net/references.

■ The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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