MAYNE DACARBAZINE

ChemWatch Material Safety Data Sheet
CHEMWATCH 32603
Date of Issue: Sat 4-Oct-2003

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

MAYNE DACARBAZINE

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

SUPPLIER

Mayne Pharma (USA) Inc.
Mack Cali Centre II
650 From Rd.
Paramus, NJ 07652
USA
Phone: 1.888.606.2245
E-mail: medicalinformation@us.maynepharma.com

HAZARD RATINGS

Flammability: 1

Toxicity: 2

Body Contact: 2

Reactivity: 0

Chronic: 3

SCALE: Min/Nil=0 Low=1 Moderate=2 High=3 Extreme=4

PRODUCT USE

Antineoplastic agent which is thought to act as an alkylating agent after inactivation by the liver to diazomethane (in a manner similar to nitrogen mustards). Conversely dacarbazine is a structural analogue of 5-amino-imidazole-4-carboxamide, which is an intermediate in purine synthesis and may act as an anti-metabolite which inhibits DNA synthesis. The drug may also act as a sulfhydryl reagent. Possesses minimum immunosuppressive effect. Used in the treatment of malignant melanoma, sarcoma and Hodgkin's disease. Normally given by injection.

SYNONYMS

C6-H10-N6-O
4- (dimethyltriazeno) imidazole-5-carboxamide
4- (5) - (3,3-dimethyl-1-triazeno) imidazole-5 (4) -carboxamide
5- (3,3-dimethyl-1-triazeno) imidazole-4-carboxamide
Deticene
DTIC
NCI-C04717
antineoplastic/ immunosuppressive
(dimethyltriezeno) imidazolecarboxamide
4- (3,3-dimethyl-1-triazeno) imidazole-5-carboxamide
5- (dimethyltriazeno) imidazole-4-carboxamide
1H-imidazole-4-carboxamide, 5- (3,3-dimethyl-1-triazenyl) -
DIC
DTIC-Dome
NSC-45388

Section 2 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
dacarbazine	4342-03-4	>98

Section 3 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW

RISK

May cause CANCER.
Ingestion may produce health damage*.
May be harmful to the fetus/ embryo*.
* (limited evidence).

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

Accidental ingestion of the material may be damaging to the health of the individual; animal experiments indicate that ingestion of less than 150 gram may be fatal.

EYE

Although the material 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

The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.

INHALED

The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.

CHRONIC HEALTH EFFECTS

There is ample evidence that this material can be regarded as being able to cause cancer in humans based on experiments and other information.

Principal routes of exposure are usually by skin contact/absorption and inhalation of generated dust
Blood disorders (leucopenia, thrombocytopenia) may be severe and delayed.
Anorexia, nausea and vomiting occur frequently. Other side effects include a flu-like syndrome, facial flushing and paraesthesia.
Hepatic toxicity accompanied by hepatic vein thrombosis and hepatocellular necrosis has resulted in death.
When administered orally in the diet dacarbazine induced thymic and splenic lymphosarcomas and mammary adenosarcomas in rats of both sexes and cerebral ependymomas and pulmonary alveolar carcinomas in female rats.
Intravenous injection induced lung tumours, lymphomas and splenic haemangiomas in male mice and lung tumours and uterine tumours in female mice. A single case of acute leukaemia after treatment with dacarbazine in combination with other cytotoxics has been reported.
· CAUTION: May produce immunosuppression in individuals occupationally exposed to the material.
Exposure to immunosuppressives may aggravate infectious diseases.
Chronic exposure to therapeutic doses of compounds which produce immunosuppression has been associated with development of lymphomas,(occasionally malignant) and mammary tumours. These may be secondary effects induced by activation of endogenous retroviruses,
Increased incidences of neoplasms, in mice and humans, have been reported after long-term immunosuppression by azathioprine and cyclosporin. Cyclosporin has been classified as a human carcinogen, by IARC, based on development of lymphomas after repeated and prolonged exposures to therapeutic doses.
Anti-cancer drugs used for chemotherapy can depress the bone marrow with reduction in the number of white blood cells and platelets and bleeding. Susceptibility to infections and bleeding is increased, which can be life-threatening. Digestive system effects may include inflammation of the mouth cavity, mouth ulcers, esophagus inflammation, abdominal pain and bleeds, diarrhea, bowel ulcers and perforation. Reversible hair loss can result and wound healing may be delayed. Long-term effects on the gonads may cause periods to stop and inhibit sperm production. Most anti-cancer drugs can potentially cause mutations and birth defects, and coupled with the effects of the suppression of the immune system, may also cause cancer.

Section 4 - FIRST AID MEASURES

SWALLOWED

If poisoning occurs, contact a doctor or Poisons Information Center.
· If swallowed do NOT induce vomiting.
· If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.
· Observe the patient carefully.
· Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconsciousness
· Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink.
· Seek medical advice.

EYE

· If this product comes in contact with the eyes:
· Immediately hold the eyes open and wash continuously for at least 15 minutes with fresh running water.
· Ensure irrigation under eyelids by occasionally lifting the upper and lower lids.
· Transport to hospital or doctor without delay.
· Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

If product comes in contact with the skin:
· Immediately remove all contaminated clothing, including footwear (after rinsing with water).
· Wash affected areas thoroughly with water (and soap if available).
· Seek medical attention in event of irritation.

INHALED

· If dust is inhaled, remove from contaminated area.
· Encourage patient to blow nose to ensure clear passage of breathing.
· If irritation or discomfort persists seek medical attention.

NOTES TO PHYSICIAN

Treat symptomatically.

Section 5 - FIRE FIGHTING MEASURES

Flash Point (°F): Not available
Lower Explosive Limit (%): Not available
Upper Explosive Limit (%): Not available.
Autoignition Temp (°F): Not available

EXTINGUISHING MEDIA

Foam. Dry chemical powder. BCF (where regulations permit). Carbon dioxide. Water spray or fog - Large fires only.

FIRE FIGHTING

Alert Emergency Responders and tell them location and nature of hazard. Wear full body protective clothing with breathing apparatus. Prevent, by any means available, spillage from entering drains or water course. If safe, switch off electrical equipment until vapor fire hazard removed. Use water delivered as a fine spray to control fire and cool adjacent area. Avoid spraying water onto liquid pools. DO NOT approach containers suspected to be hot. Cool fire exposed containers with water spray from a protected location. If safe to do so, remove containers from path of fire.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

WARNING: May EXPLODE on heating!!!
· Solid which exhibits difficult combustion or is difficult to ignite.
· Avoid generating dust, particularly clouds of dust in a confined or unventilated space. Dust may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion.
· Dry dust can be charged electrostatically by turbulence, pneumatic transport, pouring, in exhaust ducts and during transport.
· Build-up of electrostatic charge may be prevented by bonding and grounding.
· Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting.
Combustion products include carbon monoxide (CO) and nitrogen oxides (NOx)
Heat may cause containers to explode.

FIRE INCOMPATIBILITY

Avoid contamination with strong oxidizing agents as ignition may result

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

· Clean up all spills immediately.
· Avoid contact with skin and eyes.
· Wear impervious gloves and safety glasses.
· Use dry clean up procedures and avoid generating dust.
· Vacuum up or sweep up.
· Place spilled material in clean, dry, sealable, labeled container.

MAJOR SPILLS

· Clear area of personnel and move upwind.
· Alert Emergency Responders and tell them location and nature of hazard.
· Wear full body protective clothing with breathing apparatus.
· Prevent, by any means available, spillage from entering drains or water course.
· Stop leak if safe to do so.
· Contain spill with sand, earth or vermiculite.
· Collect recoverable product into labeled containers for recycling.
· Neutralize/decontaminate residue.
· Collect solid residues and seal in labeled drums for disposal.
· Wash area and prevent runoff into drains.
· After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using.
· If contamination of drains or waterways occurs, advise emergency services.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

· Avoid all personal contact, including inhalation.
· Wear protective clothing when risk of exposure occurs.
· Use in a well-ventilated area. Avoid contact with moisture.
· Avoid contact with incompatible materials.
· When handling, DO NOT eat, drink or smoke.
· Keep containers securely sealed when not in use.
· Avoid physical damage to containers.
· Always wash hands with soap and water after handling.
· Work clothes should be laundered separately.
· Launder contaminated clothing before re-use.
· Use good occupational work practice.
· Observe manufacturer's storing and handling recommendations.
· Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.

RECOMMENDED STORAGE METHODS

Polyethylene or polypropylene container. Plastic carboy Plastic drum Polyliner drum Packing as recommended by manufacturer Check all containers are clearly labeled and free from leaks.

STORAGE REQUIREMENTS

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

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

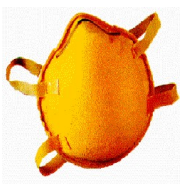
SUMMARY:

NTP - Anticipated as a carcinogen.
IARC Group 2B Possible human carcinogen.

DETAILS:

CEL TWA: 0.001 mg/m³

PERSONAL PROTECTION

EYE

No special equipment needed when handling small quantities of substance.
For bulk handling wear:
Chemical goggles or
Face shield.

HANDS/FEET

Rubber gloves
PVC gloves
Protective shoe covers
Head covering.

OTHER

No special equipment when handling small quantities of substance otherwise:
Coveralls
For Emergencies:
Vinyl suit
Safety shower

RESPIRATOR

High Efficiency Dust Respirator (P2, P3)
For non-routine emergencies wear full face mask self-contained breathing apparatus.

ENGINEERING CONTROLS

Enclosed local exhaust ventilation is required at points of dust, fume or vapour generation.
HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapours.
Barrier protection or laminar flow cabinets should be considered for laboratory scale handling.
The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated: Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied

respirators should be evaluated.
Fume-hoods and other open-face containment devices are acceptable when face velocities of at least 1 m/s (200 feet/minute) are achieved. Partitions, barriers, and other partial containment technologies are required to prevent migration of the material to uncontrolled areas. For non-routine emergencies maximum local and general exhaust are necessary. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.

Type of Contaminant:	Air Speed:
solvent, vapours, etc. evaporating from tank (in still air)	0.25-0.5 m/s (50-100 f/min.)
aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers (released at low velocity into zone of active generation)	0.5-1 m/s (100-200 f/min.)
direct spray, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)	1-2.5 m/s (200-500 f/min.)

Within each range the appropriate value depends on:

Lower end of the range	Upper end of the range
1: Room air currents minimal or favourable to capture	1: Disturbing room air currents
2: Contaminants of low toxicity or of nuisance value only.	2: Contaminants of high toxicity
3: Intermittent, low production.	3: High production, heavy use
4: Large hood or large air mass in motion	4: Small hood-local control only

Simple theory shows that air velocity falls rapidly with distance away from the opening of a simple extraction pipe. Velocity generally decreases with the square of distance from the extraction point (in simple cases). Therefore the air speed at the extraction point should be adjusted, accordingly, after reference to distance from the contaminating source. The air velocity at the extraction fan, for example, should be a minimum of 1-2.5 m/s (200-500 f/min.) for extraction of gases discharged 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.
Mixes with water.

Molecular Weight: 182.2
Boiling Range (°F): Not available
Melting Range (°F): 413.6 - 419
Specific Gravity (water=1): Not available
Solubility in water (g/L): Miscible
pH (as supplied): Not applicable
pH (1% solution): Not available
Vapor Pressure (kPa): Negligible
Volatile Component (%vol): Negligible
Evaporation Rate: Not applicable
Relative Vapor Density (air=1): >1
Flash Point (°F): Not available
Lower Explosive Limit (%): Not available
Upper Explosive Limit (%): Not available.
Autoignition Temp (°F): Not available
Decomposition Temp (°F): Not available
State: Divided solid

APPEARANCE

White to ivory-coloured solid; mixes with water.
A colour change of a reconstituted solution from pale yellow to pink indicates decomposition.

Section 10 - CHEMICAL STABILITY AND REACTIVITY INFORMATION

CONDITIONS CONTRIBUTING TO INSTABILITY

· Presence of incompatible materials.
· Product is considered stable.
· Hazardous polymerization will not occur.

STORAGE INCOMPATIBILITY

Avoid reaction with oxidizing agents

Section 11 - TOXICOLOGICAL INFORMATION

dacarbazine

unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances
TOXICITY IRRITATION
WARNING: This substance has been classified by the IARC as Group 2B Possibly Carcinogenic to Humans.
Tenth Annual Report on Carcinogens: Substance anticipated to be Carcinogen [National Toxicology Program: U.S. Dep. of Health & Human Services 2002]
Exposure to the material for prolonged periods may cause physical defects in the developing embryo (teratogenesis).

Section 12 - ECOLOGICAL INFORMATION

Section 13 - DISPOSAL CONSIDERATIONS

US EPA Waste Number & Descriptions

A. General Product Information

Reactivity characteristic: use EPA hazardous waste number D003 (waste code R).

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.
· Consult manufacturer for recycling options and recycle where possible .
· Consult Waste Management Authority for disposal.
· Incinerate residue at an approved site.
· Recycle containers where possible, or dispose of in an authorized landfill.

Section 14 - TRANSPORTATION INFORMATION

DOT Information
Shipping Name:
NONE
Hazard Class: None

UN/NA Number: None
Packing Group: None
Labels Required:
Additional Shipping Information:
International Transport Regulations:
IMO: None

Section 15 - REGULATORY INFORMATION

US Federal Regulations

A. General Product Information
In addition to Federal and State regulation, local regulations may apply. Check with your local regulatory authorities.

The substance (dacarbazine) appears on the TSCA Inventory

B. Component Information
This material contains one or more of the following chemicals required to be identified under SARA Section 302 (40 CFR 455 Appendix A) SARA Section 313 (40 CFR 372.65) and/or CERCLA (40 CFR 302.4):

State Regulations

A. General Product Information
No additional information

B. Component Information
The following components appear on one or more of the following state hazardous substance lists.

Component	CAS No	CA	FL	MA	MN	NJ	PA
dacarbazine	4342-03-4	Y	Y	Y	Y	Y	Y

The following statement(s) are provided under the California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65):

WARNING! This product contains a chemical known to the state of California to cause cancer.

Other Regulations

A. General Product Information
Component listed in the European Inventory of New and Existing Chemical Substances (EINECS)
B. Component Information
CANADA
Component found on the Canadian Domestic Substances List.

Section 16 - OTHER INFORMATION

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