

MATERIAL SAFETY DATA SHEET

Prepared to U.S. OSHA, CMA, ANSI, Canadian WHMIS, and European Union Standards.

1. PRODUCT IDENTIFICATION

TRADE/MATERIAL NAME: Mustargen®

DESCRIPTION: Mechlorethamine hydrochloride for Injection

NDC DESIGNATIONS: NDC# 55292-911-51

CHEMICAL NAME: 2-Chloro-N-(2-chloroethyl)-N-methylethanamine Hydrochloride

CHEMICAL FAMILY: Substituted Amine

HOW SUPPLIED: 100 mg Vials for Intravenous Use

FORMULA: C₅H₁₁Cl₂N•HCl

PRODUCT USE:

Antineoplastic Pharmaceutical for Human Use

SUPPLIER:

RECORDATI RARE DISEASES INC.

ADDRESS:

100 Corporate Drive

Lebanon, NJ 08833 United States

BUSINESS PHONE/GENERAL MSDS INFORMATION:

1 (888) 575-8344 (8:00 A.M. to 5:00 P.M. CST)

EMERGENCY PHONE (U.S./NORTH AMERICA):

CHEMTREC: 1-800-424-9300 (US and CANADA)

EMERGENCY PHONE (Outside U.S.):

CHEMTREC INTERNATIONAL: +1-703-527-3887

EMAIL ADDRESS:

info@recordatirarediseases.com

2. HAZARD IDENTIFICATION

EU LABELING/CLASSIFICATION: This product meets the definitions of Carcinogenic Category 2, Mutagenic Category 2, Toxic for Reproduction Category 2, Very Toxic, and Irritant, as defined by the European Union Council Directive 67/548/EEC and subsequent directives. (See Section 15 for details on classification)

Classification: Carcinogenic Category 2; Mutagenic Category 2; Toxic for Reproduction Category 2; Very Toxic; Irritant

Risk Phrases: [R: 26/28]; [R: 36/38]; [R: 45]; [R: 46]; [R: 48]; [R: 61]

EMERGENCY OVERVIEW:

Product Description: This product is supplied as a light yellow-brown crystalline powder with a faint, fishy odor.

Health Hazards: This product is a cytotoxic antineoplastic agent. This product can cause cancer, reduced fertility and reproductive effects in both men and women, and birth defects. This product may be fatal if swallowed or inhaled. Contact can severely irritate the eyes, skin, and respiratory system.

Flammability Hazards: When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including e.g., carbon oxides, nitrogen oxides, and hydrogen chloride).

Reactivity Hazards: This product is not reactive.

Environmental Hazards: This product may be harmful if released into aquatic and terrestrial environments.

Emergency Considerations: Emergency responders should wear Level A protection appropriate for highly toxic or potent compounds.

3. COMPOSITION and INFORMATION ON INGREDIENTS

| CHEMICAL NAME | CAS # | EINECS # | AICS INVENTORY STATUS | % w/v | EU CLASSIFICATION FOR COMPONENTS |
|-------------------------------|-----------|-----------|-----------------------|-------|---|
| Mechlorethamine hydrochloride | 55-86-7 | 200-246-0 | Not on Inventory | 10% | HAZARD CLASSIFICATION: T+ Very Toxic; Corrosive RISK PHRASES: R: 26/28; R: 34; R: 45; R: 46; R: 48; R: 61 SYMBOL: T+; C |
| Sodium Chloride | 7647-14-5 | 231-598-3 | On Inventory | 90% | HAZARD CLASSIFICATION: Not applicable. RISK PHRASES: Not applicable. |

4. FIRST-AID MEASURES

Persons developing hypersensitivity reactions to preparations containing Mechlorethamine hydrochloride should receive immediate medical attention. If breathing is difficult, give oxygen. If not breathing, give artificial respiration. Take a copy of container label, Product Insert and MSDS to physician or health professional with the affected individual.

SKIN EXPOSURE: If skin contact occurs, rinse immediately and thoroughly with copious amounts of running water, followed by 2% sodium thiosulfate solution. Remove contaminated clothing, taking care not to contaminate eyes. Seek immediate medical attention. Contaminated clothing or shoes should be destroyed.

EYE EXPOSURE: If eye contact occurs, rinse eyes thoroughly with copious amounts of running water. Open victim's eyes while under gently running water. Use sufficient force to open eyelids and then "roll" while flushing eyes. Minimum flushing is for 15 minutes. Seek medical attention.

INHALATION: In unlikely event that inhalation occurs, remove victim to fresh air. If necessary, use artificial respiration to support vital functions. Seek immediate medical attention.

INGESTION: If this product is swallowed, CALL PHYSICIAN OR POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. If professional advice is not available, do not induce vomiting. Never induce vomiting or give diluents (milk or water) to someone who is unconscious, having convulsions, or unable to swallow. If victim is convulsing, maintain an open airway and obtain immediate medical attention.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: There is no information on pre-existing medical conditions that may be aggravated by occupational exposure to this product. With therapeutic use, pre-existing infections and kidney, bone marrow, gastrointestinal, liver, neurological, and infertility conditions may be aggravated.

RECOMMENDATIONS TO PHYSICIANS: This product should only be given to patients by persons experienced in management of patients receiving the type of therapy intended for this product.

Treatment of overdosage should be repeated blood product transfusions, antibiotic treatment of complicating infections, and general supportive measures.

5. FIRE-FIGHTING MEASURES

FLASH POINT: Not applicable.

AUTOIGNITION TEMPERATURE: Not applicable.

FLAMMABLE LIMITS (in air by volume, %):

Lower (LEL): Not applicable. *Upper (UEL):* Not applicable.

FIRE EXTINGUISHING MATERIALS: Use extinguishing media appropriate for surrounding fire. Fire extinguishing materials that can be used against fires of this product include carbon dioxide, dry chemical powder, halon, 'ABC' Class, or appropriate foam.

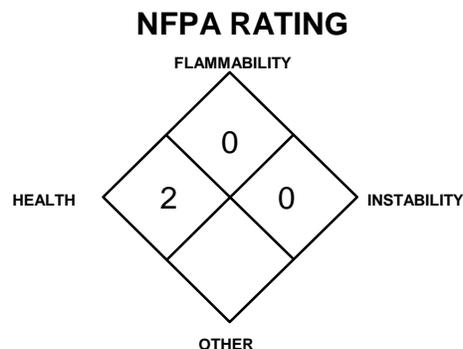
FIRE EXTINGUISHING MATERIALS NOT TO BE USED: None known.

UNUSUAL FIRE AND EXPLOSION HAZARDS: This product is cytotoxic and severely irritating and so presents a contact hazard to firefighters. When involved in a fire, the products of combustion or thermal decomposition can include irritating fumes and toxic gases (e.g., carbon oxides, nitrogen oxides, and hydrogen chloride).

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

SPECIAL FIRE-FIGHTING PROCEDURES: Firefighters should use Level A protection and follow precautions for highly toxic or potent compounds in the mustard gas family. Avoid all contact with Mustargen[®] and protect eyes and breathing passages at all times. All non-porous personal protective gear and contaminated fire-response equipment should be thoroughly decontaminated with soapy water and rinsed with a solution containing 5% sodium thiosulfate and 5% sodium bicarbonate before being returned to service. In the event of significant contamination, clothing and porous equipment may need to be discarded.



Hazard Scale: 0 = Minimal 1 = Slight 2 = Moderate
3 = Serious 4 = Severe

6. ACCIDENTAL RELEASE MEASURES

SPILL AND LEAK RESPONSE: Proper protective equipment should be used. In the event of a spill, clear the area and protect people. Avoid all exposure to Mustargen. Respiratory protection will likely be necessary if Mustargen spills outside a glove box in powder form. The atmosphere must have at least 19.5% oxygen before personnel can be allowed into the area without Self-Contained Breathing Apparatus (SCBA).

Small Spills: For small releases of this compound that is within containment such as glove box or cytotoxic hood (1 vial), wear protective gown, double latex or butyl rubber gloves, and safety glasses. Wipe up spilled material with damp sponge or wipe wetted with 5% sodium thiosulfate solution, which after a 45-minute contact time, inactivates the cytotoxic compound to a mildly irritating aqueous solution that can be collected and disposed of as normal hazardous waste. Place in a cytotoxic compound bag and hold for waste disposal. The spill areas then should be cleaned (three times) using a detergent solution

6. ACCIDENTAL RELEASE MEASURES (Continued)

SPILL AND LEAK RESPONSE (continued):

Large Spills: In case of a larger or uncontained spill, evacuate and isolate the affected area and protect people from all exposure. Trained personnel using pre-planned procedures should respond to large or uncontrolled releases. A hazmat response team may be necessary. Proper protective equipment would be a minimum of a Full hood PAPR with HEPA and charcoal filter and full body gown, long double gloves and shoe covers. Level A Protective Gear would be appropriate for firefighters or other external responders. Block drains and avoid release of spill or clean-up solutions to the environment. HEPA-vacuum spilled solids, or carefully place into sodium thiosulfate solution, and allow to stand for 45 minutes. Decontaminate the area of the spill thoroughly using an aqueous solution containing equal volumes of sodium thiosulfate (5%) and sodium bicarbonate (5%) followed by a triple detergent then a water rinse. Place all spill residue in an appropriate hazardous waste container and seal. Ventilate space well, and monitor the spill area and confirm contamination has been removed before non-response personnel are allowed back into the space.

Place all spill residues in an appropriate hazardous waste or cytotoxic compound container, seal, and hold for waste disposal. Dispose of in accordance with applicable International, National, and local procedures (see Section 13, Disposal Considerations).

7. HANDLING and USE

NOTE: Consistent with the OSHA Bloodborne Pathogen regulation (29 CFR 1910.1030), ensure that work practices involving medical sharps are followed. All open work should be conducted in a containment device such as a cytotoxic hood or other sealed/enclosed containment system appropriate for highly toxic/cytotoxic compounds.

SAFE WORK AND HYGIENE PRACTICES: This material is a cytotoxic agent; all exposures must be prevented.

As with all chemicals, avoid getting this material ON YOU or IN YOU. Do not eat, drink, smoke, or apply cosmetics while handling this product. Wash hands thoroughly after removing double gloves, which should be used for all handling of Mustargen® or contaminated equipment and containers. Post hazard and warning information in the work area. Communication of health and safety hazards of this compound must be given to employees before they work with it. Follow SPECIFIC USE INSTRUCTIONS supplied with compound.

STORAGE AND HANDLING PRACTICES: Employees must be trained to properly use this product. Special attention must be paid in avoiding releasing airborne particles of this material. Potentially hazardous operations associated with the use of this product include withdrawal of needles from drug vials, drug transfers using syringes and needles, and expulsion of air from drug-filled syringes. Store this product away from incompatible materials (see Section 10, Stability and Reactivity). Store at controlled room temperature of 15-30°C (59-86°F) according to Package Labeling instructions. Store in secondary containment to minimize risk of spill or breakage, and to protect the environment.

SPECIFIC USE(S): This product is a human antineoplastic agent pharmaceutical. Follow all industry standards for use of this product.

PRODUCT PREPARATION INSTRUCTIONS FOR MEDICAL PERSONNEL: Handle this material following medical practices for cytotoxic compounds and the recommendations presented on the Package Labeling.

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear protective gear appropriate for the level of contamination and containment, taking care to avoid all exposure to Mustargen®. At a minimum, this would consist of double latex or butyl rubber gloves, goggles, and lab coat. Soak contaminated items for 45 minutes in an aqueous solution containing equal volumes of sodium thiosulfate (5%) and sodium bicarbonate (5%). Equipment can be wiped down with this solution, with damp sponge or polypad, followed by a water rinse. All needles, syringes, vials, and other disposable items should be collected and disposed of as cytotoxic/sharps or cytotoxic waste.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

VENTILATION, ENGINEERING, AND OCCUPATIONAL EXPOSURE CONTROLS: Admixtures or manipulations of this drug should be carried out in a cytotoxic drug safety cabinet to prevent all exposure to powders or aerosols. The cabinet should be regularly cleaned following the manufacturer's recommendations. All surfaces should be thoroughly washed with water and detergent and triple rinsed. During decontamination, workers should wear the same equipment recommended in Section 6 (Accidental Release Measures) of this MSDS for the cleanup of a large spill. HEPA filters on the cytotoxic drug safety cabinet should be changed per the manufacturer's instructions. The safety cabinet should be tested and certified as recommended by the National Sanitation Foundation in Standard Number 49.

EXPOSURE LIMITS/GUIDELINES:

| CHEMICAL NAME | CAS # | EXPOSURE LIMITS IN AIR | | | | | | | |
|--|-----------|---|---------------------------|--------------------------|---------------------------|--------------------------|---------------------------|---------------------------|-------------------|
| | | ACGIH-TLVs | | OSHA-PELs | | NIOSH-RELs | | NIOSH | OTHER |
| | | TWA mg/m ³ | STEL mg/m ³ | TWA mg/m ³ | STEL mg/m ³ | TWA mg/m ³ | STEL mg/m ³ | IDLH mg/m ³ | mg/m ³ |
| Mechlorethamine hydrochloride (active ingredient) | 55-86-7 | MECHLORETHAMINE HYDROCHLORIDE IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL. | | | | | | | |
| Sodium Chloride | 7647-14-5 | NE | NE | NE | NE | NE | NE | NE | NE |

NE = Not Established. See Section 16 for Definitions of Terms Used.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

RESPIRATORY PROTECTION: A full hood Powered Air Purifying Respirator (PAPR) with HEPA and charcoal filters should be used as a minimum for situations where containment is not achieved with a cytotoxic hood or other containment system. A respirator is not required for routine conditions of use with a Biological Safety Cabinet or glove box. If respiratory protection is needed, use only protection authorized in the U.S. Federal OSHA Respiratory Protection Standard (29 CFR 1910.134) and equivalent U.S. State standards, Canadian CSA Standard Z94.4-02, or the European Standard EN 529:2005 and Respiratory Protection Standards of EU member states. Oxygen levels below 19.5% are considered IDLH by OSHA. In such atmospheres, use of a full-facepiece pressure/demand SCBA or a full facepiece, supplied air respirator with auxiliary self-contained air supply is required under U.S. Federal OSHA's Respiratory Protection Standard (1910.134).

EYE PROTECTION: Safety glasses or chemical splash goggles should be used to prevent all contact with the eyes. For situations in which airborne dusts or splashes of reconstituted product can be anticipated wear chemical splash goggles, or regular splash goggles. If necessary, refer to U.S. OSHA 29 CFR 1910.133, the Canadian CSA Standard Z94.3-07, *Industrial Eye and Face Protectors*, or the European Standard CR 13464:1999.

HAND PROTECTION: Double glove, using latex, nitrile, or rubber gloves (powderless) or other appropriate gloves. Check gloves for leaks. Wash hands before putting on gloves and after removing gloves. Gloves should cover the gown cuff. Because all gloves are to some extent permeable and their permeability increases with time, they should be changed regularly (hourly is preferable) or immediately if they are torn or punctured. If necessary, refer to U.S. OSHA 29 CFR 1910.138, the European Standard CEN/TR 15419:2006, or appropriate Standards Canada or Israel for further information.

BODY PROTECTION: During patient administration, use of lightweight cotton gown or other medical attire is recommended. If necessary, refer to the European Standard CEN/TR 15419:2006 for further information. Additional body garments should be used based upon the task being performed (e.g. sleevelets, apron, gauntlets, disposable suits) to avoid exposing skin surfaces. Appropriate techniques should be used to remove potentially contaminated clothing.

9. PHYSICAL and CHEMICAL PROPERTIES

PRODUCT AS SUPPLIED:

APPEARANCE, ODOR AND COLOR: Light yellow-brown crystalline powder with a faint fishy odor.

HOW TO DETECT THIS SUBSTANCE (warning properties): The appearance may be a manner to identify spills. Reconstituted product will be a clear, gold-colored solution, which is highly irritating to eyes and mucous membranes and may cause a burning sensation.

MOLECULAR WEIGHT (active ingredient): 192.52

BOILING POINT: Not established.

FREEZING/MELTING POINT: 108–111°C (226–232°F)

FLASH POINT: Not applicable.

FLAMMABILITY: Not flammable.

EXPLOSIVE PROPERTIES: Not explosive

OXIDIZING PROPERTIES: Not an oxidizer.

VAPOR PRESSURE (air = 1): Not applicable.

SPECIFIC GRAVITY (water = 1): Not established.

SOLUBILITY: Not established.

SOLUBILITY IN WATER: Soluble.

EVAPORATION RATE (nBuAc = 1): Not established.

ODOR THRESHOLD: Not applicable.

COEFFICIENT WATER/OIL DISTRIBUTION: Log K_{OW} = 0.91 (for pure Mechlorethamine hydrochloride)

PRODUCT AS PREPARED FOR ADMINISTRATION:

pH: 3–5

10. STABILITY and REACTIVITY

STABILITY: This product is stable when properly stored (see Section 7, Handling and Storage). This product is highly unstable when in neutral or alkaline solution.

DECOMPOSITION PRODUCTS: Combustion: Carbon oxides, nitrogen oxides, and hydrogen chloride. Hydrolysis: None known.

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: This product is generally compatible with other common materials in a medical facility. Acids, caustics, and other chemicals that could affect its performance should be avoided.

HAZARDOUS POLYMERIZATION: Will not occur.

CONDITIONS TO AVOID: Avoid heat, light, moisture and contact with incompatible chemicals.

11. TOXICOLOGICAL INFORMATION

SYMPTOMS OF OVEREXPOSURE BY ROUTE OF EXPOSURE: The health hazard information provided below is pertinent to employees using this product in an occupational setting. The following information describes the symptoms of exposure by route of exposure.

11. TOXICOLOGICAL INFORMATION (Continued)

ACUTE TOXICITY - DERMAL: Not determined.

ACUTE TOXICITY - INHALATION: This product may be fatal if inhaled. Inhalation of airborne dusts can severely irritate the respiratory system, causing coughing, wheezing, and difficulty breathing.

DERMAL IRRITATION: Skin contact can severely irritate contaminated skin, causing redness, discomfort, and pain. Severely irritating to soft tissues.

EYE IRRITATION: Eye contact can severely irritate contaminated eyes, causing tearing, blurred vision, and pain.

SENSITIZATION: Persons who are hypersensitive to this product may have an allergic reaction to this drug.

SKIN ABSORPTION: Not determined.

INGESTION: Ingestion, caused by poor hygiene practices, may be a potential route of occupational exposure. Acute ingestion of this product may cause burning sensation, nausea, vomiting, diarrhea, and symptoms described under "Other Potential Health Effects".

INJECTION: If accidentally injected, symptoms of acute injection overexposure can include severe leucopenia, anemia, thrombocytopenia, a hemorrhagic diathesis with subsequent delayed bleeding, and death. Persons who are hypersensitive to this product may have an allergic reaction to this drug.

OTHER POTENTIAL HEALTH EFFECTS-Therapeutic Doses: Employees administering the product should not experience adverse effects if handled properly. Adverse effects from therapeutic doses have included the following:

Local Toxicity: Thrombosis and thrombophlebitis may result from direct contact of the drug with the intima of the injected vein.

General: Hypersensitivity reactions, including anaphylaxis; nausea; vomiting; depression of formed elements in the circulating blood; jaundice; alopecia; vertigo; tinnitus; diminished hearing; hemolytic anemia associated with such diseases as the lymphomas and chronic lymphocytic leukemia; and chromosomal abnormalities.

Gastrointestinal: Nausea, vomiting, anorexia, weakness, and diarrhea.

Hematologic: Lymphocytopenia, granulocytopenia, agranulocytosis, leucopenia, thrombocytopenia, persistent pancytopenia, and hemorrhagic complications may be due to hyperheparinemia.

Integumentary: Maculopapular skin eruption, erythema multiforme, and herpes zoster.

Reproductive: Catamenia, oligomenorrhea, temporary or permanent amenorrhea, impaired spermatogenesis, azoospermia, and total germinal aplasia.

HEALTH EFFECTS OR RISKS FROM EXPOSURE: An Explanation in Lay Terms. Overexposure to this product may cause the following health effects:

Acute: The primary health effects that may be experienced by personnel exposed to this product is severe irritation of contaminated tissues or symptoms described under "Ingestion" if swallowed. In the event of acute exposures to therapeutic doses of this product, effects described in "Other Potential Health Effects" may result.

Chronic: Persons who are hypersensitive to this product may have an allergic reaction to this drug. In the event of chronic exposures to therapeutic doses of this product, effects described in "Other Potential Health Effects" may result.

TARGET ORGANS: **Acute:** Occupational Exposure: None known. Therapeutic Doses: Blood system, gastrointestinal system. **Chronic:** Occupational Exposure: None known. Therapeutic Doses: Blood system, gastrointestinal system, reproductive system.

GENERAL TOXICITY INFORMATION: Mechlorethamine hydrochloride, a biologic alkylating agent, has a cytotoxic action that inhibits rapidly proliferating cells. In water or body fluids, Mechlorethamine hydrochloride undergoes rapid chemical transformation and combines with water or reactive compounds of cells, so that the drug is no longer present in active form a few minutes after administration.

TOXICITY DATA: The calculated LD₅₀ (oral-rat) for Mustargen® is 111 mg/kg. The following are toxicity data for the active component of this product. The data given are Human, LD₅₀ (oral-rat), and LD₅₀ (oral-mouse) data. Other data are available but are not presented in this MSDS. Contact Recordati Rare Diseases Inc. for additional information.

MECHLORETHAMINE HYDROCHLORIDE:

TDLo (Intravenous-Human) 400 µg/kg; Gastrointestinal:- nausea or vomiting;
Blood: leukopenia, thrombocytopenia
LD₅₀ (Oral-Rat) 10 mg/kg
LD₅₀ (Oral-Mouse) 20 mg/kg
DNA Inhibition (Human-Lymphocyte) 10 µmol/L

MECHLORETHAMINE HYDROCHLORIDE (continued):

DNA Inhibition (Human-HeLa cell) 1 µmol/L
DNA Damage (Human-HeLa cell) 8 mg/L
Cytogenetic Analysis (Human-Leukocyte) 10 µg/L
Cytogenetic Analysis (Human-Lymphocyte) 50 µg/L
Sister Chromatid Exchange (Human-Lymphocyte) 6250 µg/L

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

| | | |
|----------------------|--------|----|
| HEALTH HAZARD | (BLUE) | 2* |
|----------------------|--------|----|

| | | |
|----------------------------|-------|---|
| FLAMMABILITY HAZARD | (RED) | 0 |
|----------------------------|-------|---|

| | | |
|------------------------|----------|---|
| PHYSICAL HAZARD | (YELLOW) | 0 |
|------------------------|----------|---|

PROTECTIVE EQUIPMENT

| EYES | RESPIRATORY | HANDS | BODY |
|--|---------------|---|---------------|
|  | SEE SECTION 8 |  | SEE SECTION 8 |

For Routine Industrial Use and Handling Applications

Hazard Scale: 0 = Minimal 1 = Slight 2 = Moderate
3 = Serious 4 = Severe * = Chronic hazard

11. TOXICOLOGICAL INFORMATION (Continued)

CARCINOGENIC POTENTIAL: The International Agency for Research on Cancer has judged that Mechlorethamine is a probable carcinogen in humans. This is supported by limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in animals. Young-adult female RF mice were injected intravenously with four doses of 2.4 mg/kg of Mechlorethamine (0.1% solution) at 2-week intervals with observations for up to 2 years. An increased incidence of thymic lymphomas and pulmonary adenomas was observed. Painting Mechlorethamine on the skin of mice for periods up to 33 weeks resulted in squamous cell tumors in 9 of 33 mice. The National Toxicology Program has judged that Mechlorethamine hydrochloride is reasonably anticipated to be a carcinogen.

The remaining components of this product are not found on the following lists: U.S. EPA, U.S. NTP, U.S. OSHA, U.S. NIOSH, IARC, GERMAN MAK, and ACGIH, and is therefore not considered to be, nor suspected to be, a cancer-causing agent by these agencies. and therefore are neither considered to be nor suspected to be cancer-causing agents by these agencies.

REPRODUCTIVE TOXICITY INFORMATION: Listed below is information concerning the effects of this product and its components on the human reproductive system. This product is rated as POSITIVE EVIDENCE OR RISK, There is a risk to fetus after drug is administered, but under certain circumstances (e.g., treatment of life-threatening illnesses) the benefits can outweigh the risk.

Mutagenicity: Mechlorethamine induced mutations in the Ames test, in *E. coli* and *Neurospora crassa*. Mechlorethamine caused chromosome aberrations in a variety of plant and mammalian cells. Dominant lethal mutations were produced in ICR/Ha Swiss mice.

Embryotoxicity: No adequate animal studies have been conducted to determine embryotoxic effects of the active component, Mechlorethamine hydrochloride. No embryotoxic effects have been reported in humans.

Teratogenicity: Mechlorethamine can cause fetal harm when administered to a pregnant woman. Mustargen® has been shown to produce fetal malformations in the rat and ferret when given as single subcutaneous injections of 1 mg/kg (2–3 times the maximum recommended human dose).

Reproductive Toxicity: Mechlorethamine impaired fertility in the rat at a daily dose of 500 mg/kg intravenously for two weeks. Since the gonads are susceptible to Mechlorethamine, treatment may be followed by delayed catamenia, oligomenorrhea, or temporary or permanent amenorrhea. Impaired spermatogenesis, azoospermia, and total germinal aplasia have been reported in male patients treated with alkylating agents, especially in combination with other drugs. In some instances spermatogenesis may return in patients in remission, but this may occur only several years after intensive chemotherapy has been discontinued.

A mutagen is a chemical that causes permanent changes to genetic material (DNA) such that the changes will propagate through generation lines. An embryo toxin is a chemical that causes damage to a developing embryo (i.e. within the first eight weeks of pregnancy in humans), but the damage does not propagate across generational lines. A teratogen is a chemical that causes damage to a developing fetus, but the damage does not propagate across generational lines. A reproductive toxin is any substance that interferes in any way with the reproductive process.

ACGIH BIOLOGICAL EXPOSURE INDICES (BEIs): Currently, ACGIH Biological Exposure Indices (BEIs) have not been determined for the components of this product.

12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

MOBILITY: This product has not been tested for mobility in soil.

PERSISTENCE AND BIODEGRADABILITY: This product has not been tested for persistence or biodegradability. Solutions of Mechlorethamine HCL decompose on standing, and may form a variety of organic materials in the environment on contact with moisture and organic matter.

BIO-ACCUMULATION POTENTIAL: This product has not been tested for bio-accumulation potential.

ECOTOXICITY: This product has not been tested for aquatic or plant toxicity; it may be harmful to aquatic organisms and may cause long-term adverse effects in the aquatic environment.

OTHER ADVERSE EFFECTS: This product does not contain any component with known ozone depletion potential.

ENVIRONMENTAL EXPOSURE CONTROLS: Controls should be engineered to prevent release to the environment, including procedures to prevent spills, atmospheric release and release to waterways.

13. DISPOSAL CONSIDERATIONS

DISPOSAL METHODS: It is the responsibility of the generator to determine at the time of disposal whether the product meets the criteria of a hazardous waste per regulations of the area in which the waste is generated and/or disposed of. Waste disposal must be in accordance with appropriate International, National, and local regulations. This product, if unaltered by use, may be disposed of by treatment at a permitted facility or as advised by your local hazardous waste regulatory authority. Shipment of wastes must be done with appropriately permitted and registered transporters.

13. DISPOSAL CONSIDERATIONS (Continued)

DISPOSAL CONTAINERS: Waste materials must be placed in and shipped in appropriate 5-gallon or 55-gallon poly or metal waste pails or drums. Permeable cardboard containers are not appropriate and should not be used. Ensure that any required marking or labeling of the containers be done to all applicable regulations.

PRECAUTIONS TO BE FOLLOWED DURING WASTE HANDLING: Wear proper protective equipment when handling waste materials.

U.S. EPA WASTE NUMBER: Not applicable to wastes consisting only of this product.

EWC WASTE CODE: Wastes from Natal Care, Diagnosis, Treatment, or Prevention of Disease in Humans: Chemicals other than those consisting of or containing dangerous substances 18-01-07.

14. TRANSPORTATION INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION REGULATIONS: This product is classified as a hazardous material, per U.S. DOT regulations, under 49 CFR 172.101.

| | |
|--|--|
| <u>Proper Shipping Name:</u> | Medicine, solid, toxic, n.o.s. (Mechlorethamine Hydrochloride) |
| <u>Hazard Class Number and Description:</u> | 6.1 (Toxic Substance) |
| <u>UN Identification Number:</u> | UN3249 |
| <u>Packing Group:</u> | PG III |
| <u>Dot Label(s) Required:</u> | Toxic |
| <u>Emergency Response Guidebook Number (2004):</u> | 151 |

Marine Pollutant: No component of this product is classified by the U.S. DOT as a Marine Pollutant (as defined by 49 CFR 172.101, Appendix B).

Note: Shipping this product as Toxic solids, organic-excepted small quantity may be applicable per 49 CFR 173.4 (a).

TRANSPORT CANADA, TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: This product is classified as dangerous goods, per regulations of Transport Canada.

| | |
|---|--|
| <u>Proper Shipping Name:</u> | Medicine, solid, toxic, n.o.s. (Mechlorethamine Hydrochloride) |
| <u>Hazard Class Number and Description:</u> | 6.1 (Toxic Substance) |
| <u>UN Identification Number:</u> | UN 3249 |
| <u>Packing Group:</u> | III |
| <u>Hazard Label(s) Required:</u> | Toxic |
| <u>Special Provisions:</u> | 16 |
| <u>Explosive Limit & Limited Quantity Index:</u> | 5 |
| <u>ERAP Index:</u> | None |
| <u>Passenger Carrying Ship Index:</u> | None |
| <u>Passenger Carrying Road or Rail Vehicle Index:</u> | 5 |

Marine Pollutant: This product is not a Marine Pollutant under Transport Canada regulations.

INTERNATIONAL AIR TRANSPORT ASSOCIATION SHIPPING INFORMATION (IATA): This product is classified as dangerous goods, as follows.

| | |
|--|--|
| <u>Proper Shipping Name:</u> | Medicine, solid, toxic, n.o.s. (Mechlorethamine Hydrochloride) |
| <u>Hazard Class Number and Description:</u> | 6.1 (Toxic Substance) |
| <u>UN Identification Number:</u> | UN 3249 |
| <u>Packing Group:</u> | III |
| <u>Hazard Label(s) Required:</u> | Toxic |
| <u>Passenger & Cargo Aircraft Packing Instruction:</u> | 613 |
| <u>Passenger & Cargo Aircraft Maximum Net Quantity/Pkg.:</u> | 5 kg |
| <u>Cargo Aircraft Only Packing Instruction:</u> | 615 |
| <u>Cargo Aircraft Only Maximum Net Quantity/Pkg.:</u> | 5 kg |
| <u>Special Provisions:</u> | A3 |
| <u>ERG Code:</u> | 6L |

INTERNATIONAL MARITIME ORGANIZATION SHIPPING INFORMATION (IMO): This product is classified as dangerous goods, as follows.

| | |
|---|--|
| <u>Proper Shipping Name:</u> | Medicine, solid, toxic, n.o.s. (Mechlorethamine Hydrochloride) |
| <u>Hazard Class Number and Description:</u> | 6.1 (Toxic Substance) |
| <u>UN Identification Number:</u> | UN 3249 |
| <u>Packing Group:</u> | III |
| <u>Label(s) Required:</u> | Toxic |
| <u>Special Provisions:</u> | 221, 223, 944 |
| <u>Packing Instructions:</u> | P002, LP02 |
| <u>EmS:</u> | F-A, S-A |
| <u>Stowage and Segregation:</u> | Category C. Clear of living quarters. |

Marine Pollutant: The components of this product are not listed as marine pollutants by the IMO.

14. TRANSPORTATION INFORMATION (Continued)

EUROPEAN AGREEMENT CONCERNING THE INTERNATIONAL CARRIAGE OF DANGEROUS GOODS BY ROAD (ADR): This product is classified by the United Nations Economic Commission for Europe to be dangerous goods, as follows.

| | |
|--------------------------------------|--|
| <u>Substance Identification No.:</u> | 3249 |
| <u>Name of Substance:</u> | Medicine, solid, toxic, n.o.s. (Mechlorethamine Hydrochloride) |
| <u>Class:</u> | 6.1 |
| <u>Classification Code:</u> | T2 |
| <u>Packing Group:</u> | III |
| <u>Label:</u> | Toxic |
| <u>Special Provisions:</u> | 221, 274, 601 |
| <u>Limited Quantities:</u> | LQ9 |
| <u>Packing Instructions:</u> | P002, LP02, R001 |
| <u>Mixed Packing Provisions:</u> | MP10 |
| <u>Hazard Identification No.:</u> | 60 |

EUROPEAN UNION COUNCIL DIRECTIVE 96/49/EC OF 23 JULY 1996 ON THE APPROXIMATION OF THE LAWS OF THE MEMBER STATES WITH REGARD TO THE TRANSPORT OF DANGEROUS GOODS BY RAIL (RID) AND SUBSEQUENT DIRECTIVES: This product is classified to be dangerous goods, as follows.

| | |
|--------------------------------------|--|
| <u>Substance Identification No.:</u> | 3249 |
| <u>Name of Substance:</u> | Medicine, solid, toxic, n.o.s. (Mechlorethamine Hydrochloride) |
| <u>Class:</u> | 6.1 |
| <u>Classification Code:</u> | T2 |
| <u>Packing Group:</u> | III |
| <u>Label:</u> | Toxic |
| <u>Special Provisions:</u> | 221, 274, 601 |
| <u>Limited Quantities:</u> | LQ9 |
| <u>Packaging Instructions:</u> | P002, LP02, R001 |
| <u>Packaging Special Provisions:</u> | PP6 |
| <u>Mixed Packing Provisions:</u> | MP10 |
| <u>RID Tank Code:</u> | SGAH, L4BH |
| <u>RID Tank Special Provisions:</u> | TU15, TE1, TE15 |
| <u>Transport Category:</u> | 2 |
| <u>Colis Express:</u> | CE11 |
| <u>Hazard Identification No.:</u> | 60 |

15. REGULATORY INFORMATION

U.S. REGULATIONS:

U.S. SARA REPORTING REQUIREMENTS: The components of this product are not subject to the reporting requirements of Sections 302, 304, and 313 of Title III of the Superfund Amendments and Reauthorization Act.

U.S. SARA THRESHOLD PLANNING QUANTITY: There are no specific Threshold Planning Quantities for any component of this product. The default Federal MSDS submission and inventory requirement filing threshold of 10,000 lb (4,540 kg) therefore applies, per 40 CFR 370.20.

U.S. CERCLA REPORTABLE QUANTITIES (RQ): Not applicable.

U.S. TSCA INVENTORY STATUS: This product is regulated under Food and Drug Administration standards; it is not subject to requirements under TSCA.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT (PROPOSITION 65): WARNING! The Mechlorethamine hydrochloride component of this product is on the California 65 Proposition Lists as a chemical known to the State to cause cancer and developmental toxicity.

OTHER U.S. FEDERAL REGULATIONS: Manufacturers, packers, and distributors of drug and drug products for human use are responsible for complying with the labeling, certification, and usage requirements as prescribed by the Federal Food, Drug, and Cosmetic Act, as amended (sections 201-902, 52 Stat. 1040 et seq., as amended; 21 U.S.C. 321-392).

CANADIAN REGULATIONS:

CANADIAN DSL/NDL INVENTORY STATUS: The components of this product are listed on the DSL.

CANADIAN ENVIRONMENTAL PROTECTION ACT (CEPA) PRIORITY SUBSTANCES LISTS: The components of this product are not on the CEPA Priority Substances Lists.

CANADIAN WHMIS CLASSIFICATION and SYMBOLS: Class D1B: Materials Causing Immediate and Serious Toxic Effects-Toxic Material (Based on calculated LD₅₀)



15. REGULATORY INFORMATION (Continued)

EUROPEAN UNION INFORMATION:

LABELING/CLASSIFICATION: This product is classified as dangerous according to current European Union Guidelines. This material meets the definition of EU hazard classes Carcinogenic Category 2, Mutagenic Category 2, Toxic for Reproduction Category 2, Very Toxic and Irritant.

Classification: Carcinogenic Category 2; Mutagenic Category 2; Toxic for Reproduction Category 2; Very Toxic; Irritant

Risk Phrases: [R: 26/28]: Very toxic if swallowed or by inhalation. [R: 36/38]: Irritating to eyes and skin. [R: 45]: May cause cancer. [R: 46] May cause heritable genetic damage. [R: 48]: Danger of serious damage to health by prolonged exposure. [R: 61]: May cause harm to unborn child.

Safety Phrases: [S:(1/2-)*]: Keep locked up and out of reach of children. *This safety phrase can be omitted from the label when the substance or preparation is sold for industrial use only. [S: 22]: Do not breathe dust. [S: 24/25]: Avoid contact with skin and eyes. [S: 26]: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. [S: 36/37/39]: Wear suitable protective clothing, gloves, and eye/face protection. [S: 45]: In case of accident or if you feel unwell, seek medical advice immediately (show label where possible). [S 53]: Avoid exposure-Obtain special instructions before use. [S: 60]: This material and its container must be disposed of as hazardous waste.

Annex II Hazard Symbol: T



16. OTHER INFORMATION

Disclaimer: The information and recommendations contained herein are based upon tests believed to be reliable. However, Recordati Rare Diseases Inc. does not guarantee their accuracy or completeness NOR SHALL ANY OF THIS INFORMATION CONSTITUTE A WARRANTY, WHETHER EXPRESSED OR IMPLIED, AS TO THE SAFETY OF THE GOODS, THE MERCHANTABILITY OF THE GOODS, OR THE FITNESS OF THE GOODS FOR A PARTICULAR PURPOSE. Adjustment to conform to actual conditions of usage may be required. The information contained herein relates only to this specific product. If this product is combined with other materials, all component properties must be considered. Recordati Rare Diseases Inc. assumes no responsibility for results obtained or for incidental or consequential damages, including lost profits, arising from the use of these data. No warranty against infringement of any patent, copyright or trademark is made or implied.

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DEFINITION OF TERMS

A large number of abbreviations and acronyms appear on a MSDS. Some of these, **CAS #:** This is the Chemical Abstract Service Number that uniquely identifies each constituent.

EXPOSURE LIMITS IN AIR:

CEILING LEVEL: The concentration that shall not be exceeded during any part of the working exposure.

DFG MAKs: Federal Republic of Germany Maximum Concentration Values in the workplace. Exposure limits are given as TWA (Time-Weighted Average) or PEAK (short-term exposure) values.

DFG MAK Germ Cell Mutagen Categories: **1:** Germ cell mutagens that have been shown to increase the mutant frequency in the progeny of exposed humans. **2:** Germ cell mutagens that have been shown to increase the mutant frequency in the progeny of exposed mammals. **3A:** Substances that have been shown to induce genetic damage in germ cells of human of animals, or which produce mutagenic effects in somatic cells of mammals *in vivo* and have been shown to reach the germ cells in an active form. **3B:** Substances that are suspected of being germ cell mutagens because of their genotoxic effects in mammalian somatic cell *in vivo*; in exceptional cases, substances for which there are no *in vivo* data, but that are clearly mutagenic *in vitro* and structurally related to known *in vivo* mutagens. **4:** Not applicable (Category 4 carcinogenic substances are those with non-genotoxic mechanisms of action. By definition, germ cell mutagens are genotoxic. Therefore, a Category 4 for germ cell mutagens cannot apply. At some time in the future, it is conceivable that a Category 4 could be established for genotoxic substances with primary targets other than DNA [e.g. purely aneugenic substances] if research results make this seem sensible.) **5:** Germ cell mutagens, the potency of which is considered to be so low that, provided the MAK value is observed, their contribution to genetic risk for humans is expected not to be significant.

DFG MAK Pregnancy Risk Group Classification: **Group A:** A risk of damage to the developing embryo or fetus has been unequivocally demonstrated. Exposure of pregnant women can lead to damage of the developing organism, even when MAK and BAT (Biological Tolerance Value for Working Materials) values are observed. **Group B:** Currently available information indicates a risk of damage to the developing embryo or fetus must be considered to be probable. Damage to the developing organism cannot be excluded when pregnant women are exposed, even when MAK and BAT values are observed. **Group C:** There is no reason to fear a risk of damage to the developing embryo or fetus when MAK and BAT values are observed. **Group D:** Classification in one of the groups A-C is not yet possible because, although the data available may indicate a trend, they are not sufficient for final evaluation.

which are commonly used, include the following:

EXPOSURE LIMITS IN AIR (continued):

IDLH: Immediately Dangerous to Life and Health. This level represents a concentration from which one can escape within 30-minutes without suffering escape-preventing or permanent injury.

LOQ: Limit of Quantitation.

NE: Not Established. When no exposure guidelines are established, an entry of NE is made for reference.

NIC: Notice of Intended Change.

NIOSH CEILING: The exposure that shall not be exceeded during any part of the workday. If instantaneous monitoring is not feasible, the ceiling shall be assumed as a 15-minute TWA exposure (unless otherwise specified) that shall not be exceeded at any time during a workday.

NIOSH RELs: NIOSH's Recommended Exposure Limits.

PEL: OSHA's Permissible Exposure Limits. This exposure value means exactly the same as a TLV, except that it is enforceable by OSHA. The OSHA Permissible Exposure Limits are based in the 1989 PELs and the June, 1993 Air Contaminants Rule (Federal Register: 58: 35338-35351 and 58: 40191). Both the current PELs and the vacated PELs are indicated. The phrase, "Vacated 1989 PEL" is placed next to the PEL that was vacated by Court Order.

SKIN: Used when there is a danger of cutaneous absorption.

STEL: Short Term Exposure Limit, usually a 15-minute time-weighted average (TWA) exposure that should not be exceeded at any time during a workday, even if the 8-hr TWA is within the TLV-TWA, PEL-TWA or REL-TWA.

TLV: Threshold Limit Value. An airborne concentration of a substance that represents conditions under which it is generally believed that nearly all workers may be repeatedly exposed without adverse effect. The duration must be considered, including the 8-hour.

TWA: Time Weighted Average exposure concentration for a conventional 8-hr (TLV, PEL) or up to a 10-hr (REL) workday and a 40-hr workweek.

WEEL: Workplace Environmental Exposure Limits from the AIHA.

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS: This rating system was developed by the National Paint and Coating Association and has been adopted by industry to identify the degree of chemical hazards.

HEALTH HAZARD: 0 Minimal Hazard: No significant health risk, irritation of skin or eyes not anticipated. **Skin Irritation:** Essentially non-irritating. Mechanical irritation may occur. PII or Draize = 0. **Eye Irritation:** Essentially non-irritating, minimal effects clearing in < 24 hours. Mechanical irritation may occur. Draize = 0. **Oral Toxicity LD₅₀ Rat:** > 5000 mg/kg. **Dermal Toxicity LD₅₀ Rat or Rabbit:** > 2000 mg/kg. **Inhalation Toxicity 4-hrs LC₅₀ Rat:** > 20 mg/L.

DEFINITION OF TERMS (Continued)

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

HEALTH HAZARD (continued): 1 Slight Hazard: Minor reversible injury may occur; may irritate the stomach if swallowed; may defat the skin and exacerbate existing dermatitis. *Skin Irritation:* Slightly or mildly irritating. PII or Draize > 0 < 5. *Eye Irritation:* Slightly to mildly irritating, but reversible within 7 days. Draize > 0 < 25. *Oral Toxicity LD₅₀ Rat:* > 500–5000 mg/kg. *Dermal Toxicity LD₅₀ Rat or Rabbit:* > 1000–2000 mg/kg. *Inhalation Toxicity LC₅₀ 4-hrs Rat:* > 2–20 mg/L. **2 Moderate Hazard:** Temporary or transitory injury may occur; prolonged exposure may affect the CNS. *Skin Irritation:* Moderately irritating; primary irritant; sensitizer. PII or Draize ≥ 5, with no destruction of dermal tissue. *Eye Irritation:* Moderately to severely irritating; reversible corneal opacity; corneal involvement or irritation clearing in 8–21 days. Draize = 26–100, with reversible effects. *Oral Toxicity LD₅₀ Rat:* > 50–500 mg/kg. *Dermal Toxicity LD₅₀ Rat or Rabbit:* > 200–1000 mg/kg. *Inhalation Toxicity LC₅₀ 4-hrs Rat:* > 0.5–2 mg/L. **3 Serious Hazard:** Major injury likely unless prompt action is taken and medical treatment is given; high level of toxicity; corrosive. *Skin Irritation:* Severely irritating and/or corrosive; may cause destruction of dermal tissue, skin burns, and dermal necrosis. PII or Draize > 5–8, with destruction of tissue. *Eye Irritation:* Corrosive, irreversible destruction of ocular tissue; corneal involvement or irritation persisting for more than 21 days. Draize > 80 with effects irreversible in 21 days. *Oral Toxicity LD₅₀ Rat:* > 1–50 mg/kg. *Dermal Toxicity LD₅₀ Rat or Rabbit:* > 20–200 mg/kg. *Inhalation Toxicity LC₅₀ 4-hrs Rat:* > 0.05–0.5 mg/L. **4 Severe Hazard:** Life-threatening; major or permanent damage may result from single or repeated exposures; extremely toxic; irreversible injury may result from brief contact. *Skin Irritation:* Not appropriate. Do not rate as a 4, based on skin irritation alone. *Eye Irritation:* Not appropriate. Do not rate as a 4, based on eye irritation alone. *Oral Toxicity LD₅₀ Rat:* ≤ 1 mg/kg. *Dermal Toxicity LD₅₀ Rat or Rabbit:* ≤ 20 mg/kg. *Inhalation Toxicity LC₅₀ 4-hrs Rat:* ≤ 0.05 mg/L.

FLAMMABILITY HAZARD: 0 Minimal Hazard: Materials that will not burn in air when exposure to a temperature of 815.5°C (1500°F) for a period of 5 minutes. **1 Slight Hazard:** Materials that must be pre-heated before ignition can occur. Material requires considerable pre-heating, under all ambient temperature conditions before ignition and combustion can occur. This usually includes the following: Materials that will burn in air when exposed to a temperature of 815.5°C (1500°F) for a period of 5 minutes or less; Liquids, solids and semisolids having a flash point at or above 93.3°C (200°F) (i.e. OSHA Class IIIB); and Most ordinary combustible materials (e.g. wood, paper, etc.). **2 Moderate Hazard:** Materials that must be moderately heated or exposed to relatively high ambient temperatures before ignition can occur. Materials in this degree would not, under normal conditions, form hazardous atmospheres in air, but under high ambient temperatures or moderate heating may release vapor in sufficient quantities to produce hazardous atmospheres with air. This usually includes the following: Liquids having a flash-point at or above 37.8°C (100°F); Solid materials in the form of course dusts that may burn rapidly but that generally do not form explosive atmospheres; Solid materials in a fibrous or shredded form that may burn rapidly and create flash fire hazards (e.g. cotton, sisal, hemp); and Solids and semisolids (e.g. viscous and slow flowing as asphalt) that readily give off flammable vapors. **3 Serious Hazard:** Liquids and solids that can be ignited under almost all ambient temperature conditions. Materials in this degree produce hazardous atmospheres with air under almost all ambient temperatures, or, unaffected by ambient temperature, are readily ignited under almost all conditions. This usually includes the following: Liquids having a flash point below 22.8°C (73°F) and having a boiling point at or above 38°C (100°F) and those liquids having a flash point at or above 22.8°C (73°F) and below 37.8°C (100°F) (i.e. OSHA Class IB and IC); Materials that on account of their physical form or environmental conditions can form explosive mixtures with air and are readily dispersed in air (e.g., dusts of combustible solids, mists or droplets of flammable liquids); and Materials that burn extremely rapidly, usually by reason of self-contained oxygen (e.g. dry nitrocellulose and many organic peroxides). **4 Severe Hazard:** Materials that will rapidly or completely vaporize at atmospheric pressure and normal ambient temperature or that are readily dispersed in air, and that will burn readily. This usually includes the following: Flammable gases; Flammable cryogenic materials; Any liquid or gaseous material that is liquid while under pressure and has a flash point below 22.8°C (73°F) and a boiling point below 37.8°C (100°F) (i.e. OSHA Class IA); and Materials that ignite spontaneously when exposed to air at a temperature of 54.4°C (130°F) or below (pyrophoric).

PHYSICAL HAZARD: 0 Water Reactivity: Materials that do not react with water. *Organic Peroxides:* Materials that are normally stable, even under fire conditions and will not react with water. *Explosives:* Substances that are Non-Explosive. *Compressed Gases:* No Rating. *Pyrophorics:* No Rating. *Oxidizers:* No 0 rating. *Unstable Reactives:* Substances that will not polymerize, decompose, condense, or self-react. **1 Water Reactivity:** Materials that change or decompose upon exposure to moisture. *Organic Peroxides:* Materials that are normally stable, but can become unstable at high temperatures and pressures. These materials may react with water, but will not release energy violently. *Explosives:* Division 1.5 & 1.6 explosives. Substances that are very insensitive explosives or that do not have a mass explosion hazard. *Compressed Gases:* Pressure below OSHA definition. *Pyrophorics:* No Rating. *Oxidizers:* Packaging Group III oxidizers; Solids: any material that in either concentration tested, exhibits a mean burning time less than or equal to the mean burning time of a 3:7 potassium bromate/cellulose mixture and the criteria for Packing Group I and II are not met. Liquids: any material that exhibits a mean pressure rise time less than or equal to the pressure rise time of a 1:1 nitric acid (65%)/cellulose mixture and the criteria for Packing Group I and II are not met.

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

PHYSICAL HAZARD (continued): 1 (continued) Unstable Reactives: Substances that may decompose condense, or self-react, but only under conditions of high temperature and/or pressure and have little or no potential to cause significant heat generation or explosion hazard. Substances that readily undergo hazardous polymerization in the absence of inhibitors. **2 Water Reactivity:** Materials that may react violently with water. *Organic Peroxides:* Materials that, in themselves, are normally unstable and will readily undergo violent chemical change, but will not detonate. These materials may also react violently with water. *Explosives:* Division 1.4 explosives. Explosive substances where the explosive effects are largely confined to the package and no projection of fragments of appreciable size or range are expected. An external fire must not cause virtually instantaneous explosion of almost the entire contents of the package. *Compressed Gases:* Pressurized and meet OSHA definition but < 514.7 psi absolute at 21.1°C (70°F) [500 psig]. *Pyrophorics:* No Rating. *Oxidizers:* Packing Group II oxidizers. Solids: any material that, either in concentration tested, exhibits a mean burning time of less than or equal to the mean burning time of a 2:3 potassium bromate/cellulose mixture and the criteria for Packing Group I are not met. Liquids: any material that exhibits a mean pressure rise time less than or equal to the pressure rise of a 1:1 aqueous sodium chlorate solution (40%)/cellulose mixture and the criteria for Packing Group I are not met. *Reactives:* Substances that may polymerize, decompose, condense, or self-react at ambient temperature and/or pressure, but have a low potential (or low risk) for significant heat generation or explosion. Substances that readily form peroxides upon exposure to air or oxygen at room temperature. **3 Water Reactivity:** Materials that may form explosive reactions with water. *Organic Peroxides:* Materials that are capable of detonation or explosive reaction, but require a strong initiating source or must be heated under confinement before initiation; or materials that react explosively with water. *Explosives:* Division 1.3 explosives. Explosive substances that have a fire hazard and either a minor blast hazard or a minor projection hazard or both, but do not have a mass explosion hazard. *Compressed Gases:* Pressure ≥ 514.7 psi absolute at 21.1°C (70°F) [500 psig]. *Pyrophorics:* No Rating. *Oxidizers:* Packing Group I oxidizers. Solids: any material that, in either concentration tested, exhibits a mean burning time less than the mean burning time of a 3:2 potassium bromate/cellulose mixture. Liquids: any material that spontaneously ignites when mixed with cellulose in a 1:1 ratio, or which exhibits a mean pressure rise time less than the pressure rise time of a 1:1 perchloric acid (50%)/cellulose mixture. *Unstable Reactives:* Substances that may polymerize, decompose, condense, or self-react at ambient temperature and/or pressure and have a moderate potential (or moderate risk) to cause significant heat generation or explosion. **4 Water Reactivity:** Materials that react explosively with water without requiring heat or confinement. *Organic Peroxides:* Materials that are readily capable of detonation or explosive decomposition at normal temperature and pressures. *Explosives:* Division 1.1 & 1.2 explosives. Explosive substances that have a mass explosion hazard or have a projection hazard. A mass explosion is one that affects almost the entire load instantaneously. *Compressed Gases:* No Rating. *Pyrophorics:* Add to the definition of Flammability 4. *Oxidizers:* No 4 rating. *Unstable Reactives:* Substances that may polymerize, decompose, condense, or self-react at ambient temperature and/or pressure and have a high potential (or high risk) to cause significant heat generation or explosion.

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS

HEALTH HAZARD: 0 Materials that, under emergency conditions, would offer no hazard beyond that of ordinary combustible materials. Gases and vapors with an LC₅₀ for acute inhalation toxicity greater than 10,000 ppm. Dusts and mists with an LC₅₀ for acute inhalation toxicity greater than 200 mg/L. Materials with an LD₅₀ for acute dermal toxicity greater than 2000 mg/kg. Materials with an LD₅₀ for acute oral toxicity greater than 2000 mg/kg. Materials essentially non-irritating to the respiratory tract, eyes, and skin. **1** Materials that, under emergency conditions, can cause significant irritation. Gases and vapors with an LC₅₀ for acute inhalation toxicity greater than 5,000 ppm but less than or equal to 10,000 ppm. Dusts and mists with an LC₅₀ for acute inhalation toxicity greater than 10 mg/L but less than or equal to 200 mg/L. Materials with an LD₅₀ for acute dermal toxicity greater than 1000 mg/kg but less than or equal to 2000 mg/kg. Materials that slightly to moderately irritate the respiratory tract, eyes and skin. Materials with an LD₅₀ for acute oral toxicity greater than 500 mg/kg but less than or equal to 2000 mg/kg. **2** Materials that, under emergency conditions, can cause temporary incapacitation or residual injury. Gases with an LC₅₀ for acute inhalation toxicity greater than 3,000 ppm but less than or equal to 5,000 ppm. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC₅₀ for acute inhalation toxicity, if its LC₅₀ is less than or equal to 5000 ppm and that does not meet the criteria for either degree of hazard 3 or degree of hazard 4. Dusts and mists with an LC₅₀ for acute inhalation toxicity greater than 2 mg/L but less than or equal to 10 mg/L. Materials with an LD₅₀ for acute dermal toxicity greater than 200 mg/kg but less than or equal to 1000 mg/kg. Compressed liquefied gases with boiling points between -30°C (-22°F) and -55°C (-66.5°F) that cause severe tissue damage, depending on duration of exposure. Materials that are respiratory irritants. Materials that cause severe, but reversible irritation to the eyes or are lachrymators. Materials that are primary skin irritants or sensitizers. Materials whose LD₅₀ for acute oral toxicity is greater than 50 mg/kg but less than or equal to 500 mg/kg. **3** Materials that, under emergency conditions, can cause serious or permanent injury. Gases with an LC₅₀ for acute inhalation toxicity greater than 1,000 ppm but less than or equal to 3,000 ppm.

DEFINITION OF TERMS (Continued)

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

HEALTH HAZARD (continued): 3 (continued) Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater its LC₅₀ for acute inhalation toxicity, if its LC₅₀ is less than or equal to 3000 ppm and that does not meet the criteria for degree of hazard 4. Dusts and mists with an LC₅₀ for acute inhalation toxicity greater than 0.5 mg/L but less than or equal to 2 mg/L. Materials with an LD₅₀ for acute dermal toxicity greater than 40 mg/kg but less than or equal to 200 mg/kg. Materials that are corrosive to the respiratory tract. Materials that are corrosive to the eyes or cause irreversible corneal opacity. Materials corrosive to the skin. Cryogenic gases that cause frostbite and irreversible tissue damage. Compressed liquefied gases with boiling points below -55°C (-66.5°F) that cause frostbite and irreversible tissue damage. Materials with an LD₅₀ for acute oral toxicity greater than 5 mg/kg but less than or equal to 50 mg/kg. **4** Materials that, under emergency conditions, can be lethal. Gases with an LC₅₀ for acute inhalation toxicity less than or equal to 1,000 ppm. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than ten times its LC₅₀ for acute inhalation toxicity, if its LC₅₀ is less than or equal to 1000 ppm. Dusts and mists whose LC₅₀ for acute inhalation toxicity is less than or equal to 0.5 mg/L. Materials whose LD₅₀ for acute dermal toxicity is less than or equal to 40 mg/kg. Materials whose LD₅₀ for acute oral toxicity is less than or equal to 5 mg/kg.

FLAMMABILITY HAZARD: 0 Materials that will not burn under typical fire conditions, including intrinsically noncombustible materials such as concrete, stone, and sand. Materials that will not burn in air when exposed to a temperature of 816°C (1500°F) for a period of 5 minutes in according with Annex D of NFPA 704. **1** Materials that must be preheated before ignition can occur. Materials in this degree require considerable preheating, under all ambient temperature conditions, before ignition and combustion can occur: Materials that will burn in air when exposed to a temperature of 816°C (1500°F) for a period of 5 minutes in according with Annex D of NFPA 704. Liquids, solids, and semisolids having a flash point at or above 93.4°C (200°F) (i.e. Class IIIB liquids). Liquids with a flash point greater than 35°C (95°F) that do not sustain combustion when tested using the *Method of Testing for Sustained Combustibility*, per 49 CFR 173, Appendix H or the *UN Recommendations on the Transport of Dangerous Goods, Model Regulations* (current edition) and the related *Manual of Tests and Criteria* (current edition). Liquids with a flash point greater than 35°C (95°F) in a water-miscible solution or dispersion with a water non-combustible liquid/solid content of more than 85% by weight. Liquids that have no fire point when tested by ASTM D 92, *Standard Test Method for Flash and Fire Points by Cleveland Open Cup*, up to the boiling point of the liquid or up to a temperature at which the sample being tested shows an obvious physical change. Combustible pellets with a representative diameter of greater than 2 mm (10 mesh). Most ordinary combustible materials. Solids containing greater than 0.5% by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent. **2** Materials that must be moderately heated or exposed to relatively high ambient temperatures before ignition can occur. Materials in this degree would not under normal conditions form hazardous atmospheres with air, but under high ambient temperatures or under moderate heating could release vapor in sufficient quantities to produce hazardous atmospheres with air. Liquids having a flash point at or above 37.8°C (100°F) and below 93.4°C (200°F) (i.e. Class II and Class IIIA liquids.) Solid materials in the form of powders or coarse dusts of representative diameter between 420 microns (40 mesh) and 2 mm (10 mesh) that burn rapidly but that generally do not form explosive mixtures with air. Solid materials in fibrous or shredded form that burn rapidly and create flash fire hazards, such as cotton, sisal, and hemp. Solids and semisolids that readily give off flammable vapors. Solids containing greater than 0.5% by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent. **3** Liquids and solids that can be ignited under almost all ambient temperature conditions. Materials in this degree produce hazardous atmospheres with air under almost all ambient temperatures or, though unaffected by ambient temperatures, are readily ignited under almost all conditions. Liquids having a flash point below 22.8°C (73°F) and having a boiling point at or above 37.8°C (100°F) and those liquids having a flash point at or above 22.8°C (73°F) and below 37.8°C (100°F) (i.e. Class IB and IC liquids). Materials that on account of their physical form or environmental conditions can form explosive mixtures with air and are readily dispersed in air. Flammable or combustible dusts with representative diameter less than 420 microns (40 mesh). Materials that burn with extreme rapidity, usually by reason of self-contained oxygen (e.g. dry nitrocellulose and many organic peroxides). Solids containing greater than 0.5% by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent. **4** Materials that will rapidly or completely vaporize at atmospheric pressure and normal ambient temperature or that are readily dispersed in air and will burn readily. Flammable gases. Flammable cryogenic materials. Any liquid or gaseous materials that is liquid while under pressure and has a flash point below 22.8°C (73°F) and a boiling point below 37.8°C (100°F) (i.e. Class IA liquids). Materials that ignite when exposed to air, Solids containing greater than 0.5% by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent.

INSTABILITY HAZARD: 0 Materials that in themselves are normally stable, even under fire conditions. Materials that have an instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) below 0.01 W/mL.

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

INSTABILITY HAZARD: 0 (continued) Materials that do not exhibit an exotherm at temperatures less than or equal to 500°C (932°F) when tested by differential scanning calorimetry. **1** Materials that in themselves are normally stable, but that can become unstable at elevated temperatures and pressures. Materials that have an instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) at or above 0.01 W/mL and below 10 W/mL. **2** Materials that readily undergo violent chemical change at elevated temperatures and pressures. Materials that have an instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) at or above 10 W/mL and below 100W/mL. **3** Materials that in themselves are capable of detonation or explosive decomposition or explosive reaction, but that require a strong initiating source or that must be heated under confinement before initiation. Materials that have an estimated instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) at or above 100 W/mL and below 1000 W/mL. Materials that are sensitive to thermal or mechanical shock at elevated temperatures and pressures. **4** Materials that in themselves are readily capable of detonation or explosive decomposition or explosive reaction at normal temperatures and pressures. Materials that are sensitive to localized thermal or mechanical shock at normal temperatures and pressures. Materials that have an estimated instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) of 1000 W/mL or greater.

FLAMMABILITY LIMITS IN AIR:

Much of the information related to fire and explosion is derived from the National Fire Protection Association (NFPA). **Flash Point:** Minimum temperature at which a liquid gives off sufficient vapor to form an ignitable mixture with air near the surface of the liquid or within the test vessel used. **Autoignition Temperature:** Minimum temperature of a solid, liquid, or gas required to initiate or cause self-sustained combustion in air with no other source of ignition. **LEL:** Lowest concentration of a flammable vapor or gas/air mixture that will ignite and burn with a flame. **UEL:** Highest concentration of a flammable vapor or gas/air mixture that will ignite and burn with a flame.

TOXICOLOGICAL INFORMATION:

Human and Animal Toxicology: Possible health hazards as derived from human data, animal studies, or from the results of studies with similar compounds are presented. **LD₅₀:** Lethal Dose (solids & liquids) that kills 50% of the exposed animals. **LC₅₀:** Lethal Concentration (gases) that kills 50% of the exposed animals. **ppm:** Concentration expressed in parts of material per million parts of air or water. **mg/m³:** Concentration expressed in weight of substance per volume of air. **mg/kg:** Quantity of material, by weight, administered to a test subject, based on their body weight in kg. **TDLo:** Lowest dose to cause a symptom. **TCLo:** Lowest concentration to cause a symptom. **TD₀, LDLo, and LD₀, or TC, TC₀, LCLo, and LCo:** Lowest dose (or concentration) to cause lethal or toxic effects. **Cancer Information:** **IARC:** International Agency for Research on Cancer. **NTP:** National Toxicology Program. **RTECS:** Registry of Toxic Effects of Chemical Substances. IARC and NTP rate chemicals on a scale of decreasing potential to cause human cancer with rankings from 1 to 4. Subrankings (2A, 2B, etc.) are also used. **Other Information:** **BEI:** ACGIH Biological Exposure Indices, represent the levels of determinants which are most likely to be observed in specimens collected from a healthy worker who has been exposed to chemicals to the same extent as a worker with inhalation exposure to the TLV.

ECOLOGICAL INFORMATION:

EC: Effect concentration in water. **BCF:** Bioconcentration Factor, which is used to determine if a substance will concentrate in life forms that consume contaminated plant or animal matter. **TLM:** Median threshold limit. **log K_{OW}** or **log K_{OC}:** Coefficient of Oil/Water Distribution is used to assess a substance's behavior in the environment.

REGULATORY INFORMATION: This section explains the impact of various laws and regulations on the material.

U.S.:

EPA: U.S. Environmental Protection Agency. **ACGIH:** American Conference of Governmental Industrial Hygienists, a professional association that establishes exposure limits. **OSHA:** U.S. Occupational Safety and Health Administration. **NIOSH:** National Institute of Occupational Safety and Health, which is the research arm of OSHA. **DOT:** U.S. Department of Transportation. **IC:** Transport Canada. **SARA:** Superfund Amendments and Reauthorization Act. **TSCA:** U.S. Toxic Substance Control Act. **CERCLA:** Comprehensive Environmental Response, Compensation, and Liability Act. Marine Pollutant status according to the DOT; CERCLA or Superfund; and various state regulations. This section also includes information on the precautionary warnings that appear on the material's package label.

CANADA:

WHMIS: Canadian Workplace Hazardous Materials Information System. **IC:** Transport Canada. **DSL/NDL:** Canadian Domestic/Non-Domestic Substances List.

EUROPE:

EU: European Union (formerly known as the EEC, European Economic Community). **INECS:** European Inventory of Now-Existing Chemical Substances. **ARD:** European Agreement Concerning the International Carriage of Dangerous Goods by Road. **RID:** International Regulations Concerning the Carriage of Dangerous Goods by Rail.