MATERIAL SAFETY DATA SHEET

Prepared to U.S. OSHA, CMA, ANSI, Canadian WHMIS, Australian WorkSafe, New Zealand Standards, European Union Standards, and the Mexican NOM018-STPS 2000 Standard

1. PRODUCT IDENTIFICATION

TRADE/MATERIAL NAME: Cosmegen® for Injection

DESCRIPTION: Dactinomycin for Injection
NDC DESIGNATIONS: NDC# 55292-811-55
CHEMICAL NAME: Dactinomycin; Actinomycin D; Meractinomycin
CHEMICAL FAMILY: Antibiotic- Actinomycins - Antineoplastic Agent
HOW SUPPLIED: 0.5 mg Dactinomycin with 20.0 mg Mannitol, for reconstitution with 1.1ml sterile WFI in a single use vial.
FORMULA: Dactinomycin: $C_{62}H_{86}N_{12}O_{16}$ + Mannitol: $C_6H_{14}O_6$

PRODUCT USE:	Pharmaceutical for Human Use
NDC Designation:	*55292-811-55*
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 (U.S., CANADA)
EMERGENCY PHONE (Outside U.S.)	CHEMTREC INTERNATIONAL: 1-703-527-3887
EMAIL ADDRESS:	info@recordatirarediseases.com
SUPPLIER/IMPORTER'S NAME (EUROPE):	**IDIS HOUSE**
PRODUCT DESIGNATIONS:	3400956434299 – FRANCE; 1209630 – GERMANY 0367386811348 – ITALY
ADDRESS:	Churchfield Road Weybridge, Surrey, KT13 8D8, United Kingdom
BUSINESS PHONE:	+ 44 1932 824000
SUPPLIER/IMPORTER'S NAME (AUSTRALIA):	***A.* MENARINI AUSTRAILIA PTY LTD.**
PRODUCT DESIGNATION:	9341677000094
ADDRESS:	Level 8, 67 Albert Avenue CHATSWOOD, NSW 2067 Australia
BUSINESS PHONE:	1-800-642-646
SUPPLIER/IMPORTER'S NAME (NEW ZEALAND):	**A. MENARINI AUSTRAILIA PTY LTD.**
PRODUCT DESIGNATION:	9341677000094
ADDRESS:	C/- Healthcare Logistics 58 Richard Pearse Drive Airport Oaks, Mangere, Auckland
BUSINESS PHONE:	0800-449-419

2. HAZARD IDENTIFICATION

EU/AUSTRALIAN LABELING/CLASSIFICATION: This product meets the definition of Carcinogenic Category 3, Category 3, Toxic and Irritant, as defined by the European Union Council Directives 67/548/EEC and 2001/59/EC and the Australian NOHSC. (See Section 15 for details on classification)

EU CLASSIFICATION: Carcinogenic Category 3; Toxic [T]; Irritant [Xi]
EU RISK PHRASES: [R: 25]; [R: 37]; [R: 40] SYMBOLS: *T; Xi*

EMERGENCY OVERVIEW:

Product Description: This product is supplied as an odorless, yellow to orange, lyophilized powder. The reconstituted product is a clear, gold-colored liquid.

Health Hazards: This material is a cytotoxic agent. This material must be assumed to be harmful by all routes of exposure. This material is moderately to severely irritating to contaminated tissue by all routes, or may cause burns especially in the presence of moisture. Therapeutic use can cause bone marrow suppression. The active ingredient is a suspect reproductive agent and carcinogenic agent.

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

Reactivity Hazards: This product is not reactive.

Environmental Hazards: Large quantities released to the aquatic and terrestrial environment may have an adverse effect.

Emergency Considerations: Emergency responders should wear appropriate protection for situation to which they respond.

3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	AICS INVENTORY STATUS	% w/v	EU CLASSIFICATION FOR COMPONENTS
Dactinomycin (active ingredient)	50-76-0	200-063-6	On Inventory	2.4%	HAZARD CLASSIFICATION: Carc. Cat. 3; T [Very Toxic]; C [Corrosive] RISK PHRASES: R: 28; R: 34; R: 36/37; R: 40
Mannitol	87-78-5	201-770-2	On Inventory	97.6%	HAZARD CLASSIFICATION: Not applicable. RISK PHRASES: Not applicable.

4. FIRST-AID MEASURES

Persons developing hypersensitivity reactions to preparations containing Dactinomycin 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: Wash contaminated area with soap and water and continue rinsing with copious amounts of running water until thoroughly decontaminated. Remove contaminated clothing, taking care not to contaminate eyes. If irritation continues after flushing, or burns or other adverse reaction occurs, seek medical attention.

EYE EXPOSURE: If product contacts the eyes, rinse eyes immediately and thoroughly with copious amounts of running water for at least 15 minutes. Open victim's eyes while under gently running water. Use sufficient force to open eyelids and then "roll" while flushing eyes. Seek medical attention.

INHALATION: In the event that inhalation occurs and adverse effect occurs, remove victim to fresh air. If necessary, use artificial respiration to support vital functions. Seek medical attention if adverse effect continues after removal to fresh air.

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. Seek 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 anuria, impaired hepatic function, progressive liver disease, allergy, bronchial asthma, and systemic lupus erythematosus may be aggravated by clinical use of this product.

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 is mainly supportive.

5. FIRE-FIGHTING MEASURES

FLASH POINT: Not applicable.

AUTOIGNITION TEMPERATURE: Not applicable.

FLAMMABLE LIMITS (in air by volume, %):

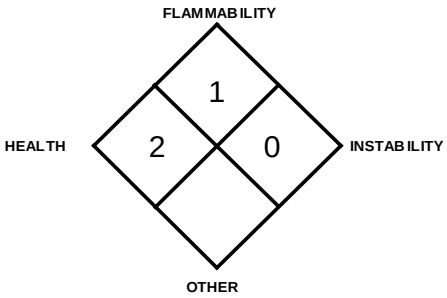
Lower (LEL): Not applicable. *Upper (UEL):* Not applicable.

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 corrosive and so presents a contact hazard to firefighters. This product must be substantially pre-heated before ignition can occur. When involved in a fire, the products of combustion or thermal decomposition can include irritating fumes and toxic gases (e.g., carbon oxides and nitrogen oxides).

NFPA RATING



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

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: This product is not sensitive to static discharge.

SPECIAL FIRE-FIGHTING PROCEDURES: No special procedures are necessary. Fire fighters should follow normal fire response procedures consistent with surrounding materials. All personal protective gear and contaminated fire-response equipment should be decontaminated with soapy water before being returned to service.

6. ACCIDENTAL RELEASE MEASURES

SPILL RESPONSE: Avoid producing airborne dusts of this product during cleanup. For small releases of this compound (1 vial), wear protective gown, double lightweight butyl or nitrile-type gloves, and safety glasses or goggles. Wipe up spilled material with damp sponge or polypad. Place in a cytotoxic compound bag and hold for waste disposal. The spill areas then should be cleaned (three times) using a detergent solution followed by a clean water rinse. In case of a large spill, clear the affected area and protect people. Trained personnel using pre-planned procedures should respond to large or uncontrolled releases. Proper protective equipment should be used, including light-weight glove underneath with heavy neoprene-type gloves as an over-glove, full body gown, and a Powered-Air Purifying Respirator (PAPR) equipped with a High Efficiency Particulate (HEPA) filter or Self-Contained Breathing Apparatus (SCBA). Eliminate all sources of ignition before clean-up operations begin. Use non-sparking tools. Clean-up or vacuum spilled solid (an explosion-proof HEPA vacuum should be used). Decontaminate the area of the spill thoroughly using a 5% trisodium phosphate (TSP) solution. A contact time with the TSP solution of 30 minutes is recommended. Place neutralized spill residue in an appropriate container and seal. Place all other spill residue in an appropriate cytotoxic compound container and seal. Dispose of in accordance with applicable U.S. Federal, State, and local procedures or appropriate standards of Canada, Australia, New Zealand, Mexico, or EU Member States (see Section 13, Disposal Considerations).

7. HANDLING and USE

NOTE: Consistent with the OSHA Bloodborne Pathogen regulation (29 CFR 1910.1030), ensure that safe work practices involving medical sharps are followed.

WORK PRACTICES AND HYGIENE PRACTICES: THIS MATERIAL IS A CYTOTOXIC AGENT; use careful work practices consistent with cytotoxic/antineoplastic agents. Post hazard and warning information in the work area about this compound. Communication of health and safety hazards of this compound must be given to employees prior to working with them. Follow SPECIFIC USE INSTRUCTIONS supplied with compound. Conduct all open manipulations in a Class II Biological Safety Cabinet and use adequate personal protective equipment to minimize all exposure to this material in powdered and reconstituted form. All work surfaces should be thoroughly washed with a 5% trisodium phosphate (TSP) solution 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 small spill. If airborne exposure to this material is possible during spill clean-up, wear appropriate respiratory protection (including PAPR or SCBA).

As with all chemicals, avoid getting this material ON YOU or IN YOU. Do not eat, drink, smoke, or apply cosmetics in work areas where this product is handled or stored. Personnel preparing drugs of this class should wear double chemical resistant, impervious gloves, safety goggles, outer garments and shoe covers. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces and inhalation of aerosols and dusts (see Section 8 for further details). Wash hands thoroughly after removing protective gloves that are worn for handling Cosmegen® or equipment and containers of this 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. Ensure vials are properly labeled. All equipment in used during the handling of this material that involves bulk amounts should be electrically grounded and intrinsically safe. All needles, syringes, vials, and other disposable items should be disposed of properly as chemotherapeutic medical sharps. Store this product away from incompatible materials (see Section 10, Stability and Reactivity). Store at controlled room temperature of 25°C (77°F) according Package Labeling instructions. Protect from light and humidity.

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

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear double latex or butyl-type rubber gloves, goggles, and lab coat. Wash equipment with a 5% trisodium phosphate (TSP) solution. Wipe equipment down with damp sponge or polypad. .

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

VENTILATION AND ENGINEERING CONTROLS: No open handling of powder or solutions of this product should occur. Admixtures or manipulations of this drug should be carried out in a cytotoxic drug safety cabinet or Class I or II Biological Safety Cabinet. The cabinet should be regularly cleaned following the manufacturer's recommendations and those of the NSF. HEPA filters in the safety cabinet should be changed per recommendations of the manufacturer or the NSF. The safety cabinet should be tested and certified as recommended by the National Sanitation Foundation in Standard Number 49. If appropriate, refer to Australian National Code of Practice for the Control of Workplace Hazardous Substances [NOHSC: 2007 (1994)] for further information.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

EXPOSURE LIMITS/GUIDELINES:

CHEMICAL NAME	CAS #	EXPOSURE LIMITS IN AIR									
		ACGIH-TLVs		OSHA-PELs		NIOSH-RELs		NIOSH	AIHA WEELs		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	TWA mg/m^3	STEL mg/m^3	mg/m^3
Dactinomycin (active ingredient)	50-76-0	DACTINOMYCIN IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL.									
Mannitol	87-78-5	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE

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

INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS: Currently, there are no additional international exposure limits available.

The following information on appropriate Personal Protective Equipment is provided to assist employers in complying with OSHA regulations found in 29 CFR Subpart I (beginning at 1910.132), equivalent standards of Canada (including CSA Standard Z94.4-02 and CSA Standard Z94.3-02), standards of EU member states (including EN 529:2005 for respiratory PPE, CEN/TR 15419:2006 for hand protection, and CR 13464:1999 for face/eye protection), or standards of Australia (including AS/NZS 1715:1994 for respiratory PPE, AS/NZS 4501.2:2006 for protective clothing, AS/NZS 2161.1:2000 for glove selection, and AS/NZS 1336:1997 for eye protection). Please reference applicable regulations and standards for relevant details.

RESPIRATORY PROTECTION: A respirator is not required for routine conditions of use with a Biological Safety Cabinet, or glove box. If respiratory protection is needed, such as in a spill or other situation where the material may be airborne, 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 Z94.4-93, the European Standard EN 529:2005 and Respiratory Protection Standards of EU member states, or the Australian Standard 1716-Respiratory Protective Devices and Australian Standard 1715-Selection, Use, and Maintenance of Respiratory Protective Devices. 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 (1910.134-1998) or the regulations of various U.S. States, Canada, Australia, New Zealand, Mexico, or EU Member States.

EYE PROTECTION: Prevent all eye contact with the use of safety glasses or chemical splash goggles. If necessary, refer to U.S. OSHA 29 CFR 1910.133, the Canadian CSA Standard Z94.3-M1982, *Industrial Eye and Face Protectors*, the European Standard CR 13464:1999, or the Australian Standard 1337-Eye Protection for Industrial Applications and Australian Standard 1336-Recommended Practices for Eye Protection in the Industrial Environment for further information.

HAND PROTECTION: Double glove, using butyl or nitrile-type rubber gloves 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, the Australian Standard 2161-Industrial Safety Gloves and Mittens and appropriate Standards Canada for further information.

BODY PROTECTION: During patient administration, use of lightweight cotton gown or other medical attire is recommended to prevent all skin contact. For operations involving open material, additional protective clothing such as sleeve covers, shoe covers and body suits may be necessary. Additional protective clothing would be necessary for spill clean-up or other operations involving open material, such as sleeve covers, shoe covers and body suits. If necessary, refer to the European Standard CEN/TR 15419:2006 or Australian Standard 3765-Clothing for Protection Against Hazardous Chemicals for further information.

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

9. PHYSICAL and CHEMICAL PROPERTIES

MOLECULAR WEIGHT (active ingredient): 1255.47

BOILING POINT: Not established.

FREEZING/MELTING POINT: Not established.

EVAPORATION RATE (nBuAc = 1): Not established.

SOLUBILITY IN WATER: Very soluble.

VAPOR PRESSURE (air = 1): Not applicable for product.

SPECIFIC GRAVITY (water = 1): Not established.

ODOR THRESHOLD: Not applicable.

pH: Not established.

COEFFICIENT WATER/OIL DISTRIBUTION: Dactinomycin: Log K_{OW} = 3.21; Mannitol: Log K_{OW} = -3.1

APPEARANCE, ODOR AND COLOR: Odorless, yellow to orange powder. When reconstituted the solution is a clear gold color.

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. Irritation and burning of eyes, mucous membranes or skin might be noticed in an exposure situation.

10. STABILITY and REACTIVITY

STABILITY: This product is stable when properly stored (see Section 7, Handling and Storage).

DECOMPOSITION PRODUCTS: If exposed to extremely high temperatures, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon oxides and nitrogen oxides).

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 following information describes the symptoms of exposure by route of exposure.

Acute Toxicity - Dermal: Not determined.

Acute Toxicity - Inhalation: Not determined. Inhalation of airborne dusts can moderately to severely irritate the respiratory system, causing coughing, wheezing, and difficulty breathing. Burns to the respiratory system may occur if large amounts are inhaled. Inhalation may lead to systemic toxicity. See information on Other Potential Health Effects-Therapeutic Doses.

Corrosivity: Extremely corrosive to soft tissues, especially in the presence of moisture.

Dermal Irritation: Skin contact can moderately to severely irritate contaminated skin, causing redness, discomfort, and pain. In the presence of moisture, this product may cause burns. Prolonged or repeated skin contact may cause dermatitis.

Eye Irritation: Eye contact may be corrosive and may irritate or burn contaminated eyes, causing tearing, blurred vision, and pain.

Sensitization: Not determined for this product; other Actinomycin-type antibiotics can cause sensitization, and so this product should be viewed as having sensitization potential.

Skin Absorption: Not determined.

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

HEALTH HAZARD	(BLUE)	2
FLAMMABILITY HAZARD	(RED)	1
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

INGESTION: Ingestion is not expected to be a significant route of occupational overexposure. Ingestion of this product may result from poor hygiene practices. Significant ingestion may cause a burning sensation, nausea, vomiting, diarrhea, and symptoms described under “Other Potential Health Effects”. Persons who are hypersensitive to this product or to other actinomycins may have an allergic reaction to this drug.

INJECTION: If accidentally injected, irritation or burns at the injection site may occur. In event of accidental injection of a significant dose, symptoms can include nausea, vomiting, diarrhea, mucositis including stomatitis, gastrointestinal ulceration, skin disorders including exanthema, desquamation and epidermolysis, severe hematopoietic depression, veno-occlusive disease, acute renal failure and death. Persons who are hypersensitive to this product or to other actinomycins 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 carefully, consistent with antineoplastic drug procedures. Adverse effects from therapeutic doses have included the following:

- Miscellaneous: malaise, fatigue, lethargy, fever, myalgia, proctitis, hypocalcemia, growth retardation, infection.
- Oral: cheilitis, dysphagia, esophagitis, ulcerative stomatitis, pharyngitis.
- Lung: pneumonitis.
- Gastrointestinal: anorexia, nausea, vomiting, abdominal pain, diarrhea, gastrointestinal ulceration. Nausea and vomiting, which occur early during the first few hours after administration, may be alleviated by the administration of anti-emetics.
- Hepatic: liver toxicity including liver function test abnormalities, ascites, hepatomegaly, hepatitis, hepatic failure with reports of death, hepatic veno-occlusive disease which may be associated with intravascular clotting disorder and multi-organ failure.

11. TOXICOLOGICAL INFORMATION (Continued)

OTHER POTENTIAL HEALTH EFFECTS-Therapeutic Doses (continued):

- Hematologic: anemia, even to the point of aplastic anemia, agranulocytosis, leukopenia, thrombocytopenia, pancytopenia, reticulocytopenia. Platelet and white cell counts should be performed frequently to detect severe hematopoietic depression. If either count markedly decreases, the drug should be withheld to allow marrow recovery. This often takes up to three weeks.
- Dermatologic: alopecia, skin eruptions, acne, flare-up of erythema or increased pigmentation of previously irradiated skin.
- Soft tissues: Dactinomycin is extremely corrosive. If extravasation occurs during intravenous use, severe damage to soft tissues will occur. In at least one instance, this has led to contracture of the arms. Epidermolysis, erythema, and edema, at times severe, have been reported with regional limb perfusion.
- The active ingredient is a known reproductive toxin and carcinogen. See Section 11 (Toxicological Information) for additional information.

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 during occupational exposure to this product are moderate to severe irritation of contaminated tissues or symptoms described under "Ingestion" if swallowed. In presence of moisture, burns may occur. In the event of acute exposures to therapeutic doses of this product, effects described in "Other Potential Health Effects" may result.

CHRONIC: Prolonged or repeated skin contact may cause dermatitis. Persons who are hypersensitive to this product or to other actinomycins 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. This product is suspect reproductive toxin and carcinogenic agent. See Section 11 (Toxicological Information, for additional information).

TARGET ORGANS: ACUTE: Occupational Exposure: Skin, mucous membranes, respiratory system, eyes. Therapeutic Doses: Blood system, gastrointestinal system. CHRONIC: Occupational Exposure: Skin. Therapeutic Doses: Blood system, gastrointestinal system, skin, liver, reproductive system.

DEGREE OF EFFECT TO THE HEALTH OF THE POLLUTING AGENT OF ENVIRONMENT OF WORK (per Mexican NOM-010 STPS-1999): 2

GENERAL TOXICITY INFORMATION: Hematologic toxicity is one of the major and dose-limiting adverse effects of Dactinomycin and is manifested primarily by leukopenia and thrombocytopenia. Anemia, pancytopenia, reticulopenia, agranulocytosis, and aplastic anemia may also occur. Myelosuppression, which is often first manifested by a decrease in the platelet count, usually occurs 1–7 days after completion of a course of therapy with Dactinomycin. Leukocyte and platelet nadirs (peak depression) generally occur 14–21 days following completion of a course of therapy, and leukocyte and platelet counts usually return to normal levels within 21–25 days. The patient's hematologic status must be carefully monitored.

The other major and dose-limiting adverse effects of Dactinomycin are GI and oral mucosal toxicities. Nausea and vomiting usually occur within a few hours after administration of the drug and can last up to 24 hours. Antiemetics may be effective in preventing or treating nausea and vomiting. Anorexia, abdominal pain, diarrhea, proctitis, and GI ulceration may also occur. Stomatitis, cheilitis, glossitis, dysphagia, and oral ulceration occur often in patients receiving Dactinomycin; esophagitis and pharyngitis may also occur. If stomatitis or diarrhea develops in patients who receive Dactinomycin with other antineoplastic agents, the manufacturer recommends that therapy be discontinued until these symptoms have subsided.

Dactinomycin inhibits rapidly proliferating cells of normal and neoplastic origin and, on a molar basis, is among the most potent anti-tumor agents known.

IRRITANCY OF PRODUCT: This product is corrosive and can irritate and burn contaminated tissue.

SENSITIZATION POTENTIAL OF PRODUCT: Persons who are hypersensitive to this product or to other actinomycins may have an allergic reaction to this drug.

TOXICITY DATA: The calculated LD_{50} (oral, rat) for this product is 300 mg/kg. The following are toxicity data for the active component of this product. The data given are Human, LD_{50} (oral-rat), and LD_{50} (oral-mouse) data. Other data are available but are not presented in this MSDS. Contact Recordati Rare Diseases Inc. for additional information.

DACTINOMYCIN:

TDLo (Intravenous-Human) 40 µg/kg:/4 days-intermittent: Skin and Appendages: dermatitis, other (after systemic exposure)

LD_{50} (Oral-Rat) 7200 µg/kg: Gastrointestinal: hypermotility, diarrhea; Blood: other changes

LD_{50} (Oral-Mouse) 13 mg/kg: Gastrointestinal: hypermotility, diarrhea; Blood: other changes

LD_{50} (Oral-Mouse) 20 mg/kg: Lungs, Thorax, or Respiration: dyspnea; Liver: liver function tests impaired; Kidney/Ureter/Bladder: renal function tests depressed

DACTINOMYCIN (continued):

DNA Damage (Human-HeLa cell) 400 µg/L/15 minutes

DNA Damage (Human Cells-Not Otherwise Specified) 10 µg/L

Mutation Test Systems-Not Otherwise Specified (Human Cells-Not Otherwise Specified) 40 µg/L

Mutation Test Systems-Not Otherwise Specified (Human HeLa cell) 250 µg/L

DNA Inhibition (Human-HeLa cell) 700 nmol/L

DNA Inhibition (Human Cells-Not Otherwise Specified) 300 pmol/L

DNA Inhibition (Human Cells-Not Otherwise Specified) 10 µg/L/2 hours-continuous

11. TOXICOLOGICAL INFORMATION (Continued)

TOXICITY DATA (continued):

DACTINOMYCIN (continued):
DNA Inhibition (Human Cells-Not Otherwise Specified) 40 mg/L
Cytogenetic Analysis (Human-Lymphocyte) 200 µg/L/2 hours
Cytogenetic Analysis (Human-Leukocyte) 200 µg/L/24 hours

DACTINOMYCIN (continued):
Cytogenetic Analysis (Human-HeLa cell) 250 µg/L/1 hour
Sister Chromatid Exchange (Human-Lymphocyte) 1 nmol/L
Mutation in Mammalian Somatic Cells (Human-Fibroblast) 1 mg/L

CARCINOGEN POTENTIAL OF COMPONENTS: The International Agency on Research on Cancer has judged that Dactinomycin is a positive carcinogen in animals. Local sarcomas were produced in mice and rats after repeated subcutaneous or intraperitoneal injection. Mesenchymal tumors occurred in male F344 rats given intraperitoneal injections of 50 mcg/kg, 2 to 5 times per week for 18 weeks. The first tumor appeared at 23 weeks.

The remaining components of this product are not found on the following lists: FEDERAL OSHA Z LIST, NTP, IARC, and CAL/OSHA 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. When 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: Dactinomycin has been shown to be mutagenic in a number of test systems *in vitro* and *in vivo* including human fibroblasts and leukocytes, and HeLa cells. DNA damage and cytogenetic effects have been demonstrated in the mouse and the rat.

Embryotoxicity: Dactinomycin has been shown to cause embryotoxicity in rat, rabbit, and hamster when given in doses of 50-100 µg/kg (approximately 0.5–2 times the maximum recommended daily human dose on a body surface area basis).

Teratogenicity: Dactinomycin may cause fetal harm when administered to a pregnant woman. Dactinomycin has been shown to cause malformations in rat, rabbit, and hamster when given in doses of 50-100 µg/kg (approximately 0.5–2 times the maximum recommended daily human dose on a body surface area basis).

Reproductive Toxicity: Adequate fertility studies have not been reported, although, reports suggest an increased incidence of infertility following treatment with other antineoplastic agents.

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. It is expected that it will slowly degrade in the environment and form a variety of organic and inorganic materials; however, no specific information is known.

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.

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 Federal, State, 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.

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.

13. DISPOSAL CONSIDERATIONS (Continued)

EUROPEAN WASTE CODES: Wastes from Human or Animal Health Care or Related Research: 18 01 01: Sharps; 18 01 08: Cytotoxic and Cytostatic Medicines

14. TRANSPORTATION INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION REGULATIONS: This product is NOT classified as a hazardous material, per U.S. DOT regulations, under 49 CFR 172.101.

TRANSPORT CANADA, TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: This product is NOT classified as dangerous goods, per regulations of Transport Canada.

INTERNATIONAL AIR TRANSPORT ASSOCIATION SHIPPING INFORMATION (IATA): This product is NOT classified as dangerous goods.

INTERNATIONAL MARITIME ORGANIZATION SHIPPING INFORMATION (IMO): This product is NOT classified as dangerous goods.

EUROPEAN AGREEMENT CONCERNING THE INTERNATIONAL CARRIAGE OF DANGEROUS GOODS BY ROAD (ADR): This product is NOT classified by the United Nations Economic Commission for Europe to be dangerous goods.

AUSTRALIAN FEDERAL OFFICE OF ROAD SAFETY CODE FOR THE TRANSPORTATION OF DANGEROUS GOODS BY ROAD OR RAIL: This product is NOT classified as dangerous goods, per regulations of the Australian Federal Office of Road Safety.

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 Dactinomycin 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/NDSL INVENTORY STATUS: The components of this product are listed on the DSL Inventory or a exempt.

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 Effect Toxic Material (Based on calculated LD_{50}); **Class D2B:** Materials Causing Other Toxic Effects-Skin and Eye Irritation

EUROPEAN UNION INFORMATION:

EU LABELING/CLASSIFICATION: This material meets the definition of EU hazard class Carcinogen Category 3, T (Toxic), and Xi (Irritant).

EU CLASSIFICATION: Carcinogenic Category 3; Toxic [T]; Irritant [Xi]

EU RISK PHRASES: [R: 25:] Toxic if swallowed. [R: 37] Irritating to respiratory system. [R: 40] Limited evidence of a carcinogenic effect.

EU SAFETY PHRASES: [S:(2–)*] Keep 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: 23] Do not breathe vapour or spray. [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: 60] This material and its container must be disposed of as hazardous waste.

15. REGULATORY INFORMATION (Continued)

EUROPEAN UNION INFORMATION (continued):

EUROPEAN UNION ANNEX II HAZARD SYMBOLS: T; Xi

AUSTRALIAN INFORMATION:

AUSTRALIAN INVENTORY OF CHEMICAL SUBSTANCES (AICS) STATUS: The components of this product are listed on the AICS or are exempt.

HAZARDOUS SUBSTANCES INFORMATION SYSTEM (HSIS): The components of this product are not listed in the HSIS.

STANDARD FOR THE UNIFORM SCHEDULING OF DRUGS AND POISONS: Not applicable.

LABELING AND CLASSIFICATION: The following hazard classification data have been selected, based a review of the regulation [NOHSC: 10005 (1994)]:

CLASSIFICATION: Carcinogenic Category 3; Toxic [T]; Irritant [Xi].

RISK PHRASES: [R: 25]: Toxic if swallowed. [R: 37]: Irritating to respiratory system. [R: 40]: Limited evidence of a carcinogenic effect.

SAFETY PHRASES: [S:(2–)*]: Keep 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: 23]: Do not breathe vapour or spray. [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: 60]: This material and its container must be disposed of as hazardous waste.

HAZARD SYMBOL:

NEW ZEALAND INFORMATION:

HAZARDOUS SUBSTANCES AND NEW ORGANISMS ACT (1996): The Dactinomycin component of this product is registered as a hazardous substance with the Environmental Risk Management Authority. There may be specific national controls assigned to this compound to manage its environmental effects and risks.

NEW ZEALAND MEDICINE AND MEDICAL DEVICES SAFETY AUTHORITY: The Dactinomycin component of this product is classified as a prescription medicine.

16. OTHER INFORMATION

PREPARED BY: CHEMICAL SAFETY ASSOCIATES, Inc.
PO Box 3519, La Mesa, CA 91944-3519
800/441-3365 / 619/670-0609

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DEFINITION OF TERMS

A large number of abbreviations and acronyms appear on a MSDS. Some of these, which are commonly used, include the following:

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 which have been shown to increase the mutant frequency in the progeny of exposed humans. **2:** Germ cell mutagens which have been shown to increase the mutant frequency in the progeny of exposed mammals. **3A:** Substances which 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 which 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 which 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.

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-Permissible Exposure Limit: 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 a there is a danger of cutaneous absorption.

STEL-Short Term Exposure Limit: 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: 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.

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. PII or Draize = "0". *Eye Irritation*: Essentially non-irritating, or minimal effects which clear in < 24 hours [e.g. mechanical irritation]. Draize = "0". *Oral Toxicity LD_{50} Rat*: < 5000 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: < 2000 mg/kg. *Inhalation Toxicity 4-hrs LC_{50} Rat*: < 20 mg/L.); **1** (Slight Hazard: Minor reversible Injury may occur; slightly or mildly irritating. *Skin Irritation*: Slightly or mildly irritating. *Eye Irritation*: Slightly or mildly irritating. *Oral Toxicity LD_{50} Rat*: > 500-5000 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: > 1000-2000 mg/kg. *Inhalation Toxicity LC_{50}* 4-hrs *Rat*: > 2-20 mg/L);

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

HEALTH HAZARD (continued):

2 (Moderate Hazard: Temporary or transitory injury may occur. *Skin Irritation*: Moderately irritating; primary irritant; sensitizer. PII or Draize > 0, < 5. *Eye Irritation*: Moderately to severely irritating and/or corrosive; reversible corneal opacity; corneal involvement or irritation clearing in 8-21 days. Draize > 0, ≤ 25. *Oral Toxicity LD_{50} Rat*: > 50-500 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: > 200-1000 mg/kg. *Inhalation Toxicity LC_{50} 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 destroy dermal tissue, cause skin burns, 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 LD_{50} Rat*: > 1-50 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: > 20-200 mg/kg. *Inhalation Toxicity LC_{50} 4-hrs Rat*: > 0.05-0.5 mg/L.); **4** (Severe Hazard: Life-threatening; major or permanent damage may result from single or repeated exposure. *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 LD_{50} Rat*: ≤ 1 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: ≤ 20 mg/kg. *Inhalation Toxicity LC_{50} 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 require considerable pre-heating, under all ambient temperature conditions before ignition and combustion can occur, Including: 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] (e.g. OSHA Class IIIB, or; 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 in air, Including: 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; Solids and semisolids that readily give off flammable vapors.); 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; Solids and semisolids 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, including: Liquids having a flash point below 22.8°C [73°F] and having a boiling point at or above 38°C [100°F] and below 37.8°C [100°F] [e.g. 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]; 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 which will burn readily, including: 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] [e.g. OSHA Class IA; Material that ignite spontaneously when exposed to air at a temperature of 54.4°C [130°F] or below [e.g. 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. Unstable *Compressed Gases*: No Rating. *Pyrophorics*: No Rating. *Oxidizers*: No "0" rating allowed. *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. *Explosives*: Division 1.5 & 1.6 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; 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. *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 explosive hazard. Substances that readily undergo hazardous polymerization in the absence of inhibitors.);

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

PHYSICAL HAZARD (continued):

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 – Explosive substances where the explosive effect 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 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 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 1.2 – 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 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 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-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 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 whose LC_{50} for acute inhalation toxicity is greater than 10,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is greater than 200 mg/L. Materials whose LD_{50} for acute dermal toxicity is greater than 2000 mg/kg. Materials whose LD_{50} for acute oral toxicity is greater than 2000 mg/kg. Materials that are essentially non-irritating to the respiratory tract, eyes and skin. **1** (materials that, under emergency conditions, can cause significant irritation): Gases and vapors whose LC_{50} for acute inhalation toxicity is greater than 5,000 ppm but less than or equal to 10,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is greater than 10 mg/L but less than or equal to 200 mg/L. Materials whose LD_{50} for acute dermal toxicity is greater than 1000 mg/kg but less than or equal to 2000 mg/kg. Materials whose LD_{50} for acute oral toxicity is greater than 500 mg/kg but less than or equal to 2000 mg/kg. Materials that cause slight to moderate irritation to the respiratory tract, eyes and skin. **2** (materials that, under emergency conditions, can cause temporary incapacitation or residual injury): Gases and vapors whose LC_{50} for acute inhalation toxicity is greater than 3,000 ppm but less than or equal to 5,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is greater than 2 mg/L but less than or equal to 10 mg/L. Materials whose LD_{50} for acute dermal toxicity is greater than 200 mg/kg but less than or equal to 1000 mg/kg. Materials whose LD_{50} for acute oral toxicity is greater than 50 mg/kg but less than or equal to 500 mg/kg. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC_{50} for acute inhalation toxicity, if its LC_{50} 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. 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.

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued)

HEALTH HAZARD (continued): **3** (materials that, under emergency conditions, can cause serious or permanent injury): Gases and vapors whose LC_{50} for acute inhalation toxicity is greater than 1,000 ppm but less than or equal to 3,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is greater than 0.5 mg/L but less than or equal to 2 mg/L. Materials whose LD_{50} for acute dermal toxicity is greater than 40 mg/kg but less than or equal to 200 mg/kg. Materials whose LD_{50} for acute oral toxicity is greater than 5 mg/kg but less than or equal to 50 mg/kg. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC_{50} for acute inhalation toxicity, if its LC_{50} is less than or equal to 3000 ppm and that does not meet the criteria for degree of hazard 4. Compressed liquefied gases with boiling points between -30°C (-22°F) and -55°C (-66.5°F) that cause frostbite and irreversible tissue damage. Materials that are respiratory irritants. Cryogenic gases that cause frostbite and irreversible tissue damage. Materials that are corrosive to the respiratory tract. Materials that are corrosive to the eyes or cause irreversible corneal opacity. Materials that are corrosive to the skin. **4** (materials that, under emergency conditions, can be lethal): Gases and vapors whose LC_{50} for acute inhalation toxicity less than or equal to 1,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is less than or equal to 0.5 mg/L. Materials whose LD_{50} for acute dermal toxicity is less than or equal to 40 mg/kg. Materials whose LD_{50} for acute oral toxicity is less than or equal to 5 mg/kg. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC_{50} for acute inhalation toxicity, if its LC_{50} is less than or equal to 1000 ppm.

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. **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 accordance with Annex D. 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 *Recommendation 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 percent 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 a 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). Solids containing greater than 0.5 percent by weight of a flammable or combustible solvent are rated by the closed up flash point of the solvent. Most ordinary combustible materials. **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 in 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 percent 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 (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 a 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 percent by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent.

DEFINITION OF TERMS (Continued)

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

FLAMMABILITY HAZARD (continued): **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 percent 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 estimated instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) below 0.01 W/mL. 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 estimated 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 estimated 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 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. Materials that are sensitive to localized thermal or mechanical shock at normal temperatures and pressures.

FLAMMABILITY LIMITS IN AIR:

Much of the information related to fire and explosion is derived from the **N**ational **F**ire **P**rotection **A**ssociation (**NFPA**). Flash Point - Minimum temperature at which a liquid gives off sufficient vapors to form an ignitable mixture with air. Autoignition Temperature: The minimum temperature required to initiate combustion in air with no other source of ignition. LEL - the lowest percent of vapor in air, by volume, that will explode or ignite in the presence of an ignition source. UEL - the highest percent of vapor in air, by volume, that will explode or ignite in the presence of an ignition source.

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. Definitions of some terms used in this section are: **LD_{50}** - Lethal Dose (solids & liquids) which kills 50% of the exposed animals; **LC_{50}** - Lethal Concentration (gases) which kills 50% of the exposed animals; **ppm** concentration expressed in parts of material per million parts of air or water; **mg/m^3** 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. Other measures of toxicity include **TDLo**, the lowest dose to cause a symptom and **TCLo** the lowest concentration to cause a symptom; **TDo**, **LDLo**, and **LDo**, or **TC**, **TCo**, **LCLo**, and **LCo**, the lowest dose (or concentration) to cause lethal or toxic effects. **Cancer Information:** The sources are: **IARC** - the International Agency for Research on Cancer; **NTP** - the National Toxicology Program, **RTECS** - the Registry of Toxic Effects of Chemical Substances, **OSHA** and **CAL/OSHA**. 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 is the effect concentration in water. **BCF** = Bioconcentration Factor, which is used to determine if a substance will concentrate in lifeforms which consume contaminated plant or animal matter. **TL_m** = median threshold limit; Coefficient of Oil/Water Distribution is represented by **log K_{ow}** or **log K_{oc}** and is used to assess a substance's behavior in the environment.

REGULATORY INFORMATION:

U.S. and CANADA:

ACGIH: American Conference of Governmental Industrial Hygienists, a professional association which establishes exposure limits.

This section explains the impact of various laws and regulations on the material. **EPA** is the U.S. Environmental Protection Agency. **NIOSH** is the National Institute of Occupational Safety and Health, which is the research arm of the U.S. **O**ccupational **S**afety and **H**ealth **A**dministration (**OSHA**). **WHMIS** is the Canadian Workplace Hazardous Materials Information System. **DOT** and **TC** are the U.S. Department of Transportation and the Transport Canada, respectively. Superfund Amendments and Reauthorization Act **(SARA)**; the Canadian Domestic/Non-Domestic Substances List **(DSL/NDSL)**; the U.S. Toxic Substance Control Act **(TSCA)**; Marine Pollutant status according to the **DOT**; the Comprehensive Environmental Response, Compensation, and Liability Act **(CERCLA or Superfund)**; and various state regulations. This section also includes information on the precautionary warnings which appear on the material's package label. **OSHA** - U.S. Occupational Safety and Health Administration.

EUROPEAN and INTERNATIONAL:

The DFG: This is the Federal Republic of Germany's Occupation Health Agency, similar to the U.S. OSHA. **EU** is the European Union (formerly known as the **EEC,** European Economic Community). **EINECS:** This is the European Inventory of Now-Existing Chemical Substances. The **ARD** is the European Agreement Concerning the International Carriage of Dangerous Goods by Road and the **RID** are the International Regulations Concerning the Carriage of Dangerous Goods by Rail. **AICS** is the Australian Inventory of Chemical Substances. **MITI** is the Japanese Minister of International Trade and Industry