SAFETY DATA SHEET

Prepared to U.S. OSHA, CMA, ANSI, Canadian WHMIS Standards, European Union CLP EC 1272/2008 and the Global Harmonization Standard

PART I *What is the material and what do I need to know in an emergency?*

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE

IDENTIFICATION of the SUBSTANCE or PREPARATION:

TRADE NAME: **BLEOMYCIN SULFATE API**

CHEMICAL NAME: N'-[3-(dimethylsul-phonio)propyl]bleomycin-amide (bleomycin A2) and N'-[4-(guaniodobutyl)]bleomycin-amide (bleomycin B2)

CHEMICAL CLASS: A complex of related glycopeptide antibiotics from *Streptomyces verticillus*

OTHER MEANS OF IDENTIFICATION/SYNONYMS: Bleomycin, sulfate (salt); Bleomycin, sulfate (salt) (9CI); 3-[[2-[2-[2-[[2-[[4-[[2-[[6-amino-2-[3-amino-1-[(2, 3-diamino-3-oxopropyl)amino]-3-oxopropyl]-5-methylpyrimidine-4-carbonyl] amino]-3-[3-[4-carbamoyloxy-3, 5-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-4, 5-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-3-(1H-imidazol-5-yl) propanoyl]amino]-3-hydroxy-2-methylpentanoyl]amino]-3-hydroxybutanoyl] amino]ethyl]-1,3-thiazol-4-yl]-1, 3-thiazole-4-carbonyl]amino]propyl-dimethylsulfanium; hydrogen sulfate

RELEVANT USE of the SUBSTANCE: Active Ingredient for Human Pharmaceutical

USES ADVISED AGAINST: Other than Relevant Use

COMPANY/UNDERTAKING ENTITY IDENTIFICATION:

U.S. SUPPLIER/MANUFACTURER'S NAME: **TEVA**

ADDRESS: 1090 Horsham Road
North Wales, PA 19454

BUSINESS PHONE: 215-591-3000 [08:00 AM --> 05:00 PM]

EUROPEAN CONTACT: **TEVA/TAPI**

ADDRESS: Sicor sri-Via Terrazzano
77-20017 Cho (MI), Italy

BUSINESS PHONE: +39 02 93197 306 [08:00 AM --> 05:00 PM]

EMERGENCY PHONE: United States/Canada/Puerto Rico: 1-800/424-9300 (Chemtrec) [24-hrs]
International: 01-703-527-3887 (Chemtrec) [24-hours]

EMAIL: TevaSDSRequest@tevapharm.com

DATE OF PREPARATION: May 1, 2013

DATE OF REVISION: New

ALL WHMIS required information is included in appropriate sections based on the ANSI Z400.1-2010 format. This material has been classified in accordance with the hazard criteria of the CPR and the SDS contains all the information required by the CPR. The material is also classified per all applicable EU Directives through EC 1907: 2006, the European Union CLP EC 1272/2008 and the Global Harmonization Standard.

2. HAZARD IDENTIFICATION

GLOBAL HARMONIZATION LABELING AND CLASSIFICATION: Classified in accordance with the Global Harmonization Standard. The following classification is self-classification for the pure material when not in a formulated human pharmaceutical product.

Classification: Carcinogenic Cat. 2, Germ Cell Mutagen Cat. 1B, Reproductive Toxicity Cat. 1B

Signal Word: Danger

Hazard Statement Codes: H351, H340, H360D

Precautionary Statement Codes: P201, P202, P280, P308 + P313, P405, P501

Hazard Symbol/Pictogram: GHS08

EU 67/548/EEC LABELING AND CLASSIFICATION: Classified in accordance with the European Community Council Directive 67/548/EEC or subsequent Directives. The material is not in finished pharmaceutical state. This is a self-classification.

Classification: Carcinogenic Cat. 3, Germ Cell Mutagen Cat. 2, Reproductive Toxicity Cat. 2

Risk Phrase Codes: R45, R46, R63

Safety Phrase Codes: S22, S36/37/39, S45, S53, S60

Hazard Symbol: T

EMERGENCY OVERVIEW: Material Description: This material is a white, crystalline, odorless solid. **Health Hazards:** THIS MATERIAL IS A CYTOTOXIC AGENT. EXPOSURE BY ALL ROUTES OF EXPOSURE MUST BE AVOIDED. In the workplace, exposure via inhalation or skin contact may cause irritation. Eye contact can cause mechanical irritation. May be harmful if swallowed or inhaled. When formulated in therapeutic use, this material may induce blood disorders and/or aggravate pre-existing blood disorders, hepatobiliary disorders, skin and subcutaneous tissue disorders or cause anaphylactoid reaction. Chronic exposure may cause adverse effects on liver, lungs, skin and blood. May cause harm to the fetus, based on animal information. Has been shown to be mutagenic both *in vitro* and *in vivo* studies. Suspect carcinogen. These effects may be possible as a result of workplace exposure. See Section 11 (Toxicological Information) for information on other potential health hazards known from therapeutic use. **Flammability Hazards:** If heated to high temperatures for a prolonged period, the material may ignite. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds, including carbon, sulfur and nitrogen oxides. **Reactivity Hazards:** This material 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 the situation to which they respond.

3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	% w/v	LABEL ELEMENTS EU Classification (67/548/EEC) GHS and EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements
Bleomycin Sulfate N'-[3-(dimethylsul-phonio)propyl]bleomycin-amide (bleomycin A2) and N'-[4-(guaniodobutyl)]bleomycin-amide (bleomycin B2)	9041-93-4	232-925-2	100%	SELF CLASSIFICATION EU 67/548 Classification: Carcinogenic Cat. 3, Germ Cell Mutagen Cat. 2, Reproductive Toxicity Cat. 2 Risk Phrase Codes: R45, R46, R63 Hazard Symbols: T GHS and EU 1272/2008 Classification: Carcinogenic Cat. 2, Germ Cell Mutagen Cat. 1B, Reproductive Toxicity Cat. 1B Hazard Codes: H351, H340, H360D Hazard Symbol/Pictogram: GHS08

See Section 16 for full classification information of this material.

PART II *What should I do if a hazardous situation occurs?*

4. FIRST-AID MEASURES

Upon contact of this product with skin, eyes, or mucous membranes, immediately decontaminate by flushing with water for at least 20 minutes. Remove contaminated clothing and shoes. Take a copy of this SDS to health professional with victim. Wash clothing and thoroughly clean shoes before reuse.

SKIN EXPOSURE: If skin contact with this material occurs, flush affected area with water. Minimum flushing is for 20 minutes. The contaminated individual must seek medical attention if any adverse effects occur after flushing.

EYE EXPOSURE: If this material enters the eyes, open contaminated individual's eyes while under gently running water. Use sufficient force to open eyelids. Have contaminated individual "roll" eyes. Minimum flushing is for 20 minutes. Contaminated individual must seek medical attention if adverse effect occurs or continues after flushing.

INHALATION: If dusts of this material lare inhaled, remove victim to fresh air. The contaminated individual must seek medical attention if any adverse effects occur.

INGESTION: If this material is swallowed, CALL PHYSICIAN OR POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. If professional advice is not available, seek immediate medical attention. If alert, victim should drink up to three glasses of water. 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 emergency medical attention.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: When formulated in therapeutic use, pre-existing hypersensitivity to Bleomycin Sulfate, hepatic and renal insufficiency, liver, pulmonary, skin or blood disorders may be aggravated by exposure. Workplace exposure may also aggravate these conditions.

INDICATION OF IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT IF NEEDED: Treat symptoms and eliminate exposure. No specific antidote is available. Persons developing hypersensitivity reactions should receive medical attention. Treatment of idiosyncratic reactions, similar to anaphylaxis is symptomatic including volume expansion, pressor agents, antihistamines, and corticosteroids.

5. FIRE-FIGHTING MEASURES

FLASH POINT: Not available.

AUTOIGNITION TEMPERATURE: Not available.

FLAMMABLE LIMITS (in air by volume, %): Not available.

FIRE EXTINGUISHING MEDIA: Unless incompatibilities exist for surrounding materials, carbon dioxide, water spray, 'ABC' type chemical extinguishers, foam, dry chemical and halon extinguishers can be used to fight fires involving this material.

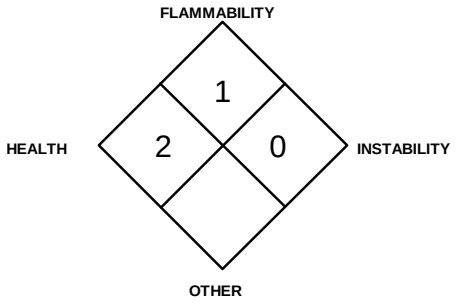
UNSUITABLE FIRE EXTINGUISHING MEDIA: None known.

SPECIAL HAZARDS ARISING FROM THE SUBSTANCE: This material must be substantially pre-heated before ignition can occur. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon, sulfur and nitrogen oxides).

Explosion Sensitivity to Mechanical Impact: Not applicable.

Explosion Sensitivity to Static Discharge: It is important to note that, as with all organic solids, large dust clouds of this material have the potential to ignite explosively.

NFPA RATING



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

SPECIAL PROTECTIVE ACTIONS FOR FIRE-FIGHTERS: Structural firefighters must wear Self-Contained Breathing Apparatus and full protective equipment. All personal protective gear and contaminated fire-response equipment should be decontaminated with soapy water and thoroughly rinsed before being returned to service. Move fire-exposed containers if it can be done without risk to firefighters. If possible, prevent runoff water from entering storm drains, bodies of water, or other environmentally sensitive areas.

6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS, PROTECTIVE EQUIPMENT AND EMERGENCY PROCEDURES: Spill kits, clearly labeled, should be kept in or near preparation and administrative areas. It is suggested that kits include a respirator, chemical splash goggles, two pairs of gloves, two sheets (12" x 12") of absorbent material, 250-mL and 1-liter spill control pillows, a small scoop to collect glass fragments (if applicable) and two large waste disposal bags. Absorbents should be able to be incinerated. Avoid generating airborne dusts of this material during spill response procedures as described below.

6. ACCIDENTAL RELEASE MEASURES (Continued)

PROTECTIVE EQUIPMENT:

Small Spills/Spills in Hoods: Personnel wearing nitrile or other appropriate gloves, labcoat or other protective clothing and eye protection should immediately clean incidental spills of less than 5 g.

Large Spills: Use proper protective equipment, including double nitrile or appropriate gloves, and protective clothing (i.e., disposable Tyvek coveralls). When there is any danger of airborne dusts being generated, use a full-face respirator equipped with a High Efficiency Particulate (HEPA) filter. Self-Contained Breathing Apparatus (SCBA) can be used instead of an air-purifying respirator.

METHODS FOR CLEAN-UP AND CONTAINMENT:

Cleanup of Small Spills: Solids should be gently covered with wet absorbent pads. Clean spill with pad and dispose of properly. Decontaminate the spill area (three times) using a bleach and detergent solution and then rinse with clean water.

Spills in Hoods: Decontamination of all interior hood surfaces may be required after the above procedures have been followed. If the HEPA filter of a hood is contaminated, label the unit "Do not use-contaminated" and have trained personnel wearing appropriate protective equipment change and dispose of the filter properly as soon as possible.

Large Spills: Restrict access to the spill areas. For spills of greater than 5 g, be sure not to generate dusts by gently covering with damp absorbent sheets, spill-control pads, pillows, cloths, or towels. The dispersion of particles into surrounding air and the possibility of inhalation is a serious matter and should be treated as such. Do not apply chemical in-activators as they may produce hazardous by-products. Thoroughly clean all contaminated surfaces three times using a bleach and detergent solution and then rinse with clean water.

All Spills: Use procedures described above and then place all spill residues in an appropriate, labeled container and seal. Move to a secure area. Dispose of in accordance with Federal, State, and local hazardous waste disposal regulations (see Section 13, Disposal Considerations). For spills on water, contain, minimize dispersion and collect. Dispose of recovered material and report spill per regulatory requirements.

ENVIRONMENTAL PRECAUTIONS: Prevent material from entering sewer or confined spaces, waterways, soil or public waters. Do not flush to sewer. For spills on water, contain, minimize dispersion and collect.

REFERENCE TO OTHER SECTIONS: Review Sections 2, 8, 11, & 12 before proceeding with cleanup. See Section 13, Disposal Considerations for more information.

PART III *How can I prevent hazardous situations from occurring?*

7. HANDLING and STORAGE

PRECAUTIONS FOR SAFE HANDLING: THIS IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL. All employees who handle this material should be thoroughly trained to handle it safely. As with all chemicals, avoid getting this material ON YOU or IN YOU. Do not eat or drink while handling this material. After handling this material, wash face and hands thoroughly prior to eating, drinking, smoking or applying cosmetics. Ensure this material is used with adequate ventilation. Appropriate personal protective equipment must be worn (see Section 8, Exposure Controls - Personal Protection). Open containers slowly on a stable surface in areas that have been designated for use of this material. Minimize all exposures to this material. Avoid generation of dusts. Areas in which this material is used should be wiped down, so that this material does not accumulate.

Eyewash fountains should be provided in areas where there is any possibility that workers could be exposed to the substance; this is irrespective of the recommendation involving the wearing of eye protection. Facilities for quickly drenching the body should be provided within the immediate work area for emergency use where there is a possibility of exposure. (Note: It is intended that these facilities provide a sufficient quantity or flow of water to quickly remove the substance from any body areas likely to be exposed. The actual determination of what constitutes an adequate quick drench facility depends on the specific circumstances. In certain instances, a deluge shower should be readily available, whereas in others, the availability of water from a sink or hose could be considered adequate.) Good hygiene practices must be in place for workers handling this material, including change facilities and a work place clothing program. Workers whose clothing may have become contaminated should change into uncontaminated clothing before leaving the work premises. Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Contaminated clothing is required to be disposed of properly or remain in the work place for cleaning.

CONDITIONS FOR SAFE STORAGE: Containers of this material must be properly labeled. Store containers in a cool, dry location, away from direct sunlight and sources of intense heat. The sterile powder is stable under refrigeration 2°C (36°F) to 8°C (46°F). Store away from incompatible materials (see Section 10, Stability and Reactivity). Material should be stored in secondary containers. Keep containers tightly closed when not in use. Inspect all incoming containers before storage, to ensure containers are properly labeled and not damaged. Refer to NFPA 654, *Prevention of Fire and Dust Explosions from the Manufacturing, Processing and Handling of Combustible Particulate Solids* for additional information on storage. Have appropriate extinguishing equipment in the storage area (e.g., sprinkler system, portable fire extinguishers). Empty containers may contain residual material; therefore, empty containers should be handled with care and disposed of properly.

SPECIFIC END USE(S): This material is an active ingredient used in making human pharmaceuticals.

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear nitrile or other appropriate gloves (double gloving is recommended), goggles, and lab coat. Prevent dispersion of particulates by wetting or dampening surfaces prior to clean up of equipment. If applicable, wash equipment using a bleach and detergent solution and then rinse with clean water.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

EXPOSURE LIMITS/CONTROL PARAMETERS:

VENTILATION AND ENGINEERING CONTROLS: Use with adequate ventilation. Ensure eyewash stations and deluge showers are available and accessible in areas where this material is used. Wipe down work areas routinely to prevent accumulation of dusts.

Laboratory: Mixtures or manipulations of this material should be carried out in an approved chemical fume hood or biosafety cabinet appropriate for handling this material. The hood or cabinet should be regularly cleaned following the manufacturer's recommendations, but no less frequently than weekly. During decontamination, workers should wear the same equipment recommended in for a Large Spill in Section 6 (Accidental Release Measures) of this SDS. HEPA filters on the chemical fume hood or the biosafety cabinet should be changed minimally every six months, or more frequently as needed. The chemical fume hood or biosafety cabinet should be tested and certified annually as recommended by the National Sanitation Foundation in Standard Number 49.

Production Environment: Material should be handled using the proper engineering controls, prescribed work practices, and personal protective equipment as indicated in this SDS.

WORKPLACE EXPOSURE LIMITS/CONTROL PARAMETERS:

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
Bleomycin Sulfate N'-[3-(dimethylsul-phonio)propyl]bleomycin-amide (bleomycin A2) and N'-[4-(guaniodobutyl)]bleomycin-amide (bleomycin B2)	9041-93-4	NE	NE	NE	NE	NE	NE	NE	**Teva OEL Range $\mu g/m^3$ ≥ 0.1 - < 1** (established 20Mar2012 Carcinogen: IARC-2B

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

INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS: Currently there are no international exposure limits in place for this material.

PROTECTIVE EQUIPMENT: *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, including* U.S. Federal OSHA Respiratory Protection (29 CFR 1910.134), OSHA Eye Protection 29 CFR 1910.133, OSHA Hand Protection 29 CFR 1910.138, OSHA Foot Protection 29 CFR 1910.136 and OSHA Body Protection 29 CFR1910.132)*, equivalent standards of Canada (including CSA Respiratory Standard Z94.4-02,* Z94.3-M1982, *Industrial Eye and Face Protectors and* CSA Standard Z195-02, *Protective Footwear), or 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). Please reference applicable regulations and standards for relevant details.*

RESPIRATORY PROTECTION: Maintain airborne contaminant concentrations below exposure limits listed above. For materials without listed exposure limits, minimize respiratory exposure. If necessary, use only respiratory protection authorized under appropriate regulations. Oxygen levels below 19.5% are considered IDLH by U.S. 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. OSHA's Respiratory Protection Standard (1910.134-1998).

EYE PROTECTION: Wear splash goggles or safety glasses as appropriate for the task. Face shields are recommended if solutions are made. If necessary, refer to appropriate regulations.

HAND PROTECTION: Wash hands and wrists before putting on and after removing gloves. During manufacture or other similar operations, wear the appropriate hand protection for the process. Use double gloves for spill response, as stated in Section 6 (Accidental Release Measures) of this SDS. 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 torn or punctured. If necessary refer to appropriate regulations.

SKIN PROTECTION: Use appropriate protective clothing for the task (e.g., lab coat, etc.). If necessary, refer to the U.S. OSHA Technical Manual (Section VII: Personal Protective Equipment) or other appropriate regulations.

SPECIAL NOTE: Any contaminated protective clothing or gloves should be changed immediately and disposed of properly. Hands and wrists should be washed immediately after removing contaminated gloves.

9. PHYSICAL and CHEMICAL PROPERTIES

MOLECULAR WEIGHT: Bleomycin A2: 1414; Bleomycin B2: 1425

MOLECULAR FORMULA: Bleomycin A2: $C_{55}H_{84}N_{17}O_{21}S_3$; Bleomycin B2: $C_{55}H_{84}N_{20}O_{21}S_2$

FORM: Crystalline solid.

COLOR: White.

ODOR: Odorless.

ODOR THRESHOLD: Not applicable.

MELTING POINT: 71°C (159°F)

SPECIFIC GRAVITY: Not available.

BOILING POINT @ 760 mmHg: Not available.

FLASH POINT: Not available.

VAPOR PRESSURE @ 25°C: Not available.

pH: Not applicable to solid.

SOLUBILITY IN WATER: 2.82e-02 g/L

OTHER SOLUBILITIES: Not available.

COEFFICIENT OF OIL/WATER DISTRIBUTION (PARTITION COEFFICIENT): Not available.

HOW TO DETECT THIS SUBSTANCE (identification properties): The appearance of this material is a distinguishing characteristic.

10. STABILITY and REACTIVITY

CHEMICAL STABILITY: Normally stable.

DECOMPOSITION PRODUCTS: *Combustion:* Products of thermal decomposition may include carbon, sulfur and nitrogen oxides. *Hydrolysis:* None known.

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: Incompatible with oxidizing agents.

10. STABILITY and REACTIVITY (Continued)

POSSIBILITY OF HAZARDOUS REACTION/POLYMERIZATION: None known.
CONDITIONS TO AVOID: Exposure to or contact with extreme temperatures, incompatible chemicals.

PART IV *Is there any other useful information about this material?*

11. TOXICOLOGICAL INFORMATION

SYMPTOMS OF EXPOSURE BY ROUTE OF EXPOSURE: This material is a cytotoxic and anti-neoplastic agent that may cause significant health effects from workplace exposure. The main route of occupational exposure to this material is via inhalation of dusts and skin or eye contact. The anticipated symptoms of exposure, by route of exposure are described further in this section.

INHALATION: If dusts of this material are inhaled, irritation of the nose and upper respiratory system may occur. Symptoms of such exposure may include sneezing, coughing, and nasal congestion. Chronic inhalation exposure may result in hepatocellular damage. Symptoms can include lightheadedness, dizziness, nausea, and headache.

CONTACT WITH SKIN or EYES: It is anticipated that this material may irritate contaminated skin, especially if contact is prolonged. Symptoms of eye contact can cause redness, pain, and watering, as well as mechanical irritation.

SKIN ABSORPTION: No data is available on potential absorption of this material through intact skin in pure form. All possible contact must be avoided.

INGESTION: Ingestion of this material is not anticipated to be a significant route of occupational exposure. Ingestion of this material (i.e., through poor hygiene practices) may irritate the mouth, throat, and other tissues of the gastrointestinal system. No specific information is available on possible adverse effects from ingestion.

INJECTION: Accidental injection of this material, via laceration or puncture by a contaminated object may cause pain and irritation in addition to the wound and effects described under 'Other Potential Health Effects'.

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

OTHER POTENTIAL HEALTH EFFECTS: When formulated for therapeutic use, the most serious side effects are adverse pulmonary reactions, including pneumonitis occasionally progressing to pulmonary fibrosis. Bleomycin-induced pneumonitis produces nonspecific patchy opacities, usually of the lower lung fields. The most common changes in pulmonary function tests are a decrease in total lung volume and a decrease in vital capacity. However, these changes are not predictive of the development of pulmonary fibrosis. Bleomycin toxicity include capillary changes and subsequent fibrinous exudation (introduction of protein tissues through small vascular holes) into alveoli producing a change similar to hyaline membrane formation and progressing to a diffuse interstitial fibrosis resembling the Hamman-Rich syndrome. Bronchial carcinomas can also occur. These effects may be possible as a result of workplace exposure. The actual risk in the workplace is not known. Other adverse effects reported from therapeutic use described by body system are provided below.

- ***Cardiovascular:*** Vascular toxicities including myocardial infarction, cerebrovascular accident, thrombotic microangiopathy (HUS) or cerebral vasculitis (inflammation of small capillaries and blood vessels in the brain).
- ***Gastrointestinal System:*** Nausea and stomatitis.
- ***Skin and Mucous Membranes:*** Reddening of skin, rash, striae (skin bands, stripes, or lines), blistering, hyperpigmentation, tenderness of the skin, skin thickening, nail changes, hair loss, itching, have also been reported. Scleroderma-like skin changes have been reported.
- ***Idiosyncratic Reactions:*** An idiosyncratic reaction, similar to anaphylaxis clinically, has been reported. The reaction may be immediate or delayed for several hours, and usually occurs after the first or second dose. It consists of hypotension, mental confusion, fever, chills, and wheezing.
- ***Other:*** Fever, chills, vomiting and anaphylactoid reaction have been reported. Anorexia and weight loss have been reported and may persist long after termination of this medication.

HEALTH EFFECTS OR RISKS FROM EXPOSURE:

Acute: This material may cause irritation via inhalation or skin or eye contact. Ingestion and inhalation may be harmful.
Chronic: Repeated skin contact may cause dermatitis (dry, red skin). Chronic exposure may cause symptoms as described under 'Other Potential Health Effects'.

TARGET ORGANS: Acute: Occupational Exposure and Therapeutic Use: Skin, eyes, respiratory system. Chronic: Occupational Exposure: Skin, respiratory system. Therapeutic Use: See information under 'Other Health Effects'.

TOXICITY DATA: Currently, the following toxicological data are available for this material.

TDLo (Parenteral-Human-Woman) 20 µg/kg: Lungs, Thorax, or Respiration: cyanosis; Skin and Appendages: dermatitis, allergic (after systemic exposure
LDLo (Unreported-Human-Man) 0.286 units/kg/1 days-intermittent: Lungs, Thorax, or Respiration: fibrosis (interstitial), acute pulmonary edema
LD_{50} (Intravenous-Mouse) 210 mg/kg
LD_{50} (Intraperitoneal-Rat) 240 mg/kg
LD_{50} (Intraperitoneal-Mouse) 210 mg/kg
LD_{50} (Subcutaneous-Rat) 86 mg/kg: Gastrointestinal: hypermotility, diarrhea; Kidney/Ureter/Bladder: urine volume increased; Skin and Appendages: hair
LD_{50} (Subcutaneous-Mouse) 103 mg/kg: Sense Organs and Special Senses (Eye): ptosis; Gastrointestinal: hypermotility, diarrhea; Nutritional and Gross Metabolic: body temperature decrease
LDLo (Intramuscular-Rat) 59 mg/kg: Behavioral: ataxia
TDLo (Intraperitoneal-Rat) 8 mg/kg: female 6-9 day(s) after conception: Reproductive: Fertility: post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants); Reproductive: Effects on Embryo or Fetus: fetotoxicity (except death, e.g., stunted fetus); Reproductive: Specific Developmental Abnormalities: musculoskeletal system

TOXICITY DATA (continued):

LDLo (Intramuscular-Mouse) 74 mg/kg: Behavioral: ataxia
TDLo (Intravenous-Rabbit) 15600 µg/kg: female 6-18 day(s) after conception: Reproductive: Fertility: abortion
TDLo (Intraperitoneal-Rat) 20400 µg/kg: female 14 day(s) pre-mating 1-20 day(s) after conception: Reproductive: Effects on Newborn: viability index (e.g., # alive at day 4 per # born alive), weaning or lactation index (e.g., # alive at weaning per # alive at day 4
TDLo (Intraperitoneal-Rat) 8700 µg/kg: female 15-22 day(s) after conception lactating female 21 day(s) post-birth: Reproductive: Effects on Newborn: growth statistics (e.g.%, reduced weight gain)
TDLo (Intraperitoneal-Rat) 17400 µg/kg: female 15-22 day(s) after conception lactating female 21 day(s) post-birth: Reproductive: Effects on Newborn: live birth index (measured after birth)
TDLo (Intratracheal-Rat) 32 mg/kg: Lungs, Thorax, or Respiration: fibrosis (interstitial)
TDLo (Intratracheal-Mouse) 4 units/kg: Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation
TDLo (Intratracheal-Mouse) 8 units/kg: Lungs, Thorax, or Respiration: fibrosing alveolitis; Immunological Including Allergic: increased immune response; Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation
TDLo (Subcutaneous-Rat) 14 mg/kg/68 weeks-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Kidney/Ureter/Bladder: Kidney tumors; Tumorigenic: tumors at site of application
TDLo (Parenteral-Rat) 18 mg/kg/52 weeks-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Kidney/Ureter/Bladder: Kidney tumors; Tumorigenic: tumors at site of application
TDLo (Parenteral-Rat) 36 mg/kg/52 weeks-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Kidney/Ureter/Bladder: Kidney tumors; Tumorigenic: tumors at site of application
Cytogenetic Analysis (Human Cells-Not Otherwise Specified) 35 mg/L/4 hours
Cytogenetic Analysis (Human Cells-Not Otherwise Specified) 20 mg/L/2 hours
Cytogenetic Analysis (Human Lymphocyte) 2.5 mg/L/24 hours
DNA Damage (Human Leukocyte) 350 nmol/L
DNA Damage (Human Lymphocyte) 1.25 mg/L/48 hours
Micronucleus Test (Human Lymphocyte) 5 mg/L
Micronucleus Test (Human Cells-Not Otherwise Specified) 1.17 mg/L/24 hours
Micronucleus Test (Human Cells-Not Otherwise Specified) 5 mg/L/3 hours
Micronucleus Test (Human Lymphocyte) 50 µmol/L/3 hours
Micronucleus Test (Human Lymphocyte) 2.5 mg/L/24 hours
Micronucleus Test (Human Lymphocyte) 0.5 mg/L/3 hours
Micronucleus Test (Human Lymphocyte) 31.3 mg/L/20 hours
Dominant lethal test (Oral-Insect-Not Otherwise Specified) 100 ppm
Specific Locus Test (Oral-Mouse) 12.5 mg/kg/5D (intermittent)
Specific Locus Test (Oral-Insect-Drosophila Melanogaster) 13 ppm
Specific Locus Test (Oral- Insect-Drosophila Melanogaster) 0.05 mmol/L/2 hours-continuous
Micronucleus Test (Rat Lymphocyte) 5 mg/L
Micronucleus Test (Mouse Cells-Not Otherwise Specified) 1 mg/L/3 hours
Micronucleus Test (Mouse Cells-Not Otherwise Specified) 0.1 mg/L/24 hours
Micronucleus Test (Mouse Fibroblast) 0.1 mg/L/4 hours
Micronucleus Test (Mouse Embryo) 20 mg/L/12 hours
Micronucleus Test (Mouse Fibroblast) 20 mg/L/12 hours
Micronucleus Test (Mouse Lymphocyte) 1 mg/L
Micronucleus Test (Mouse Mammary Gland) 1 mg/L/24 hours
Micronucleus Test (Hamster Ovary) 0.11 mg/L/24 hours
Micronucleus Test (Hamster Ovary) 0.88 mg/L/3 hours
Micronucleus Test (Hamster Lung) 1 mg/L
Micronucleus Test (Hamster Embryo) 0.05 mg/L/4 hours
Micronucleus Test (Hamster Ovary) 0.86 µmol/L/24 hours
Micronucleus Test Micronucleus Test (Hamster Fibroblast) 0.25 mg/L/3 hours
Micronucleus Test (Hamster Fibroblast) 0.125 mg/L/24 hours
Micronucleus Test (Hamster Lung) 20 mg/L/24 hours
Micronucleus Test (Multiple Routes- Non-mammalian Species) 30 nmol/L
IC_{50} (In vitro-Hamster-Lung Fibroblast) 26 mg/L/72 hour: In Vitro Toxicity Studies: cell protein synthesis
Cytogenetic Analysis (Mouse Lymphocyte) 1 mg/L
Cytogenetic Analysis (Hamster Ovary) 10 mg/L
Cytogenetic Analysis (Hamster Ovary) 1 mg/L/30 minutes
DNA Damage (Rat Liver) 2 µmol/L
DNA Damage (Rat Liver) 0.25 µmol/L/3 hours
DNA Damage (Hamster Ovary) 10 mg/L
DNA Damage (Bacteria-Salmonella Typhimurium) 250 units/L/120 minutes
DNA Damage (Mammal-Cattle Cells-Not Otherwise Specified) 25 µmol/L/1 hour
DNA Repair (Bacteria-*Escherichia Coli*) 250 ng/plate
Gene Conversion and Mitotic Recombination (Yeast-Saccharomyces Cerevisiae) 100 mg/L
Host-Mediated Assay (Mouse Bacteria-Escherichia Coli) 10 mg/kg
Morphological Transformation (Intravenous Rat) 25 units/kg
Mutation in Mammalian Somatic Cells (Mouse Lymphocyte) 1 mg/L
Mutation in Mammalian Somatic Cells (Hamster Ovary) 50 mg/L
Mutation in Mammalian Somatic Cells (Bacteria-Salmonella Typhimurium) 10 µg/plate
Mutation in Microorganisms (Bacteria-Salmonella Typhimurium) 0.05 µg/plate/72 hours
Mutation in Microorganisms (Yeast-Saccharomyces cerevisiae) 0.39 mg/L/16 hours
Mutation in Microorganisms (Yeast-Saccharomyces Cerevisiae) 50 mg/L/18 hours
Mutation Test Systems-Not Otherwise Specified (Bacteria-Escherichia Coli) 100 µg/L
Mutation test systems - not otherwise specified (Mouse Cells-Not Otherwise Specified) 1 mg/L/4 hours
Mutation Test Systems-Not Otherwise Specified (Mouse Fibroblast) 1 mg/L/4 hours
Phage Inhibition Capacity (Bacteria-Escherichia Coli) 6250 pg/well
Sex Chromosome Loss and Non-Disjunction (Parenteral-Insect-Drosophila Melanogaster) 100 mg/L
Specific Locus Test (Intraperitoneal-Mouse) 10 mg/kg
Specific Locus Test (Mouse Embryo) 20 mg/L/3 hours
Specific Locus Test (Mouse Fibroblast) 20 mg/L/3 hours
Unscheduled DNA synthesis (Parenteral-Mouse) 1 gm/kg/10 days-continuous
TDLo (Intravenous-Rabbit) 15600 µg/kg: female 6-18 day(s) after conception: Reproductive: Fertility: abortion
TDLo (Intraperitoneal-Rat) 20400 µg/kg: female 14 day(s) pre-mating 1-20 day(s) after conception: Reproductive: Effects on Newborn: viability index (e.g., # alive at day 4 per # born alive), weaning or lactation index (e.g., # alive at weaning per # alive at day 4
TDLo (Intraperitoneal-Rat) 8 mg/kg: female 6-9 day(s) after conception: Reproductive: Fertility: post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants); Reproductive: Effects on Embryo or Fetus: fetotoxicity (except death, e.g., stunted fetus); Reproductive: Specific Developmental Abnormalities: musculoskeletal system
TDLo (Intraperitoneal-Rat) 8700 µg/kg: female 15-22 day(s) after conception lactating female 21 day(s) post-birth: Reproductive: Effects on Newborn: growth statistics (e.g.%, reduced weight gain)
TDLo (Intraperitoneal-Rat) 17400 µg/kg: female 15-22 day(s) after conception lactating female 21 day(s) post-birth: Reproductive: Effects on Newborn: live birth index (measured after birth)
TDLo (Intratracheal-Rat) 32 mg/kg: Lungs, Thorax, or Respiration: fibrosis (interstitial)
TDLo (Intratracheal-Mouse) 4 units/kg: Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation
TDLo (Intratracheal-Mouse) 8 units/kg: Lungs, Thorax, or Respiration: fibrosing alveolitis; Immunological Including Allergic: increased immune response; Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation
TDLo (Subcutaneous-Rat) 14 mg/kg/68 weeks-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Kidney/Ureter/Bladder: Kidney tumors; Tumorigenic: tumors at site of application
TDLo (Parenteral-Rat) 18 mg/kg/52 weeks-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Kidney/Ureter/Bladder: Kidney tumors; Tumorigenic: tumors at site of application
TDLo (Parenteral-Rat) 36 mg/kg/52 weeks-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Kidney/Ureter/Bladder: Kidney tumors; Tumorigenic: tumors at site of application
Cytogenetic Analysis (Human Cells-Not Otherwise Specified) 35 mg/L/4 hours
Cytogenetic Analysis (Human Cells-Not Otherwise Specified) 20 mg/L/2 hours
Cytogenetic Analysis (Human Lymphocyte) 2.5 mg/L/24 hours
DNA Damage (Human Leukocyte) 350 nmol/L
DNA Damage (Human Lymphocyte) 1.25 mg/L/48 hours
Micronucleus Test (Human Lymphocyte) 5 mg/L
Micronucleus Test (Human Cells-Not Otherwise Specified) 1.17 mg/L/24 hours
Micronucleus Test (Human Cells-Not Otherwise Specified) 5 mg/L/3 hours
Micronucleus Test (Human Lymphocyte) 50 µmol/L/3 hours
Micronucleus Test (Human Lymphocyte) 2.5 mg/L/24 hours
Micronucleus Test (Human Lymphocyte) 0.5 mg/L/3 hours
Micronucleus Test (Human Lymphocyte) 31.3 mg/L/20 hours
Dominant lethal test (Oral-Insect-Not Otherwise Specified) 100 ppm
Specific Locus Test (Oral-Mouse) 12.5 mg/kg/5D (intermittent)
Specific Locus Test (Oral-Insect-Drosophila Melanogaster) 13 ppm
Specific Locus Test (Oral- Insect-Drosophila Melanogaster) 0.05 mmol/L/2 hours-continuous
Micronucleus Test (Rat Lymphocyte) 5 mg/L
Micronucleus Test (Mouse Cells-Not Otherwise Specified) 1 mg/L/3 hours
Micronucleus Test (Mouse Cells-Not Otherwise Specified) 0.1 mg/L/24 hours
Micronucleus Test (Mouse Fibroblast) 0.1 mg/L/4 hours
Micronucleus Test (Mouse Embryo) 20 mg/L/12 hours
Micronucleus Test (Mouse Fibroblast) 20 mg/L/12 hours
Micronucleus Test (Mouse Lymphocyte) 1 mg/L
Micronucleus Test (Mouse Mammary Gland) 1 mg/L/24 hours
Micronucleus Test (Hamster Ovary) 0.11 mg/L/24 hours
Micronucleus Test (Hamster Ovary) 0.88 mg/L/3 hours
Micronucleus Test (Hamster Lung) 1 mg/L
Micronucleus Test (Hamster Embryo) 0.05 mg/L/4 hours
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Micronucleus Test (Hamster Lung) 20 mg/L/24 hours
Micronucleus Test (Multiple Routes- Non-mammalian Species) 30 nmol/L
IC_{50} (In vitro-Hamster-Lung Fibroblast) 26 mg/L/72 hour: In Vitro Toxicity Studies: cell protein synthesis
Cytogenetic Analysis (Mouse Lymphocyte) 1 mg/L
Cytogenetic Analysis (Hamster Ovary) 10 mg/L
Cytogenetic Analysis (Hamster Ovary) 1 mg/L/30 minutes
DNA Damage (Rat Liver) 2 µmol/L
DNA Damage (Rat Liver) 0.25 µmol/L/3 hours
DNA Damage (Hamster Ovary) 10 mg/L
DNA Damage (Bacteria-Salmonella Typhimurium) 250 units/L/120 minutes
DNA Damage (Mammal-Cattle Cells-Not Otherwise Specified) 25 µmol/L/1 hour
DNA Repair (Bacteria-*Escherichia Coli*) 250 ng/plate
Gene Conversion and Mitotic Recombination (Yeast-Saccharomyces Cerevisiae) 100 mg/L
Host-Mediated Assay (Mouse Bacteria-Escherichia Coli) 10 mg/kg
Morphological Transformation (Intravenous Rat) 25 units/kg
Mutation in Mammalian Somatic Cells (Mouse Lymphocyte) 1 mg/L
Mutation in Mammalian Somatic Cells (Hamster Ovary) 50 mg/L
Mutation in Mammalian Somatic Cells (Bacteria-Salmonella Typhimurium) 10 µg/plate
Mutation in Microorganisms (Bacteria-Salmonella Typhimurium) 0.05 µg/plate/72 hours
Mutation in Microorganisms (Yeast-Saccharomyces cerevisiae) 0.39 mg/L/16 hours
Mutation in Microorganisms (Yeast-Saccharomyces Cerevisiae) 50 mg/L/18 hours
Mutation Test Systems-Not Otherwise Specified (Bacteria-Escherichia Coli) 100 µg/L
Mutation test systems - not otherwise specified (Mouse Cells-Not Otherwise Specified) 1 mg/L/4 hours
Mutation Test Systems-Not Otherwise Specified (Mouse Fibroblast) 1 mg/L/4 hours
Phage Inhibition Capacity (Bacteria-Escherichia Coli) 6250 pg/well
Sex Chromosome Loss and Non-Disjunction (Parenteral-Insect-Drosophila Melanogaster) 100 mg/L
Specific Locus Test (Intraperitoneal-Mouse) 10 mg/kg
Specific Locus Test (Mouse Embryo) 20 mg/L/3 hours
Specific Locus Test (Mouse Fibroblast) 20 mg/L/3 hours
Unscheduled DNA synthesis (Parenteral-Mouse) 1 gm/kg/10 days-continuous

11. TOXICOLOGICAL INFORMATION (Continued)

CARCINOGENIC POTENTIAL OF MATERIAL: The carcinogenic potential of Bleomycin Sulfate in humans is unknown. A study in F344type male rats demonstrated an increased incidence of nodular hyperplasia after induced lung carcinogenesis by nitrosamines, followed by treatment with bleomycin. In another study where the drug was administered to rats by subcutaneous injection at 0.35 mg/kg weekly (3.82 units/m² weekly or about 30% at the recommended human dose), necropsy findings included dose-related injection site fibrosarcomas as well as various renal tumors.

In addition, Bleomycins are rated by agencies tracking the carcinogenic potential of chemical compounds, as follows: IARC-2B (Possibly Carcinogenic to Humans)

This material is not found on the following lists: U.S. EPA, U.S. NTP, U.S. OSHA, U.S. NIOSH, GERMAN MAK, or ACGIH.

IRRITANCY OF MATERIAL: This material may cause mechanical eye irritation and may be irritating to the respiratory system. Prolonged skin contact may be irritating.

SENSITIZATION TO THE MATERIAL: A severe idiosyncratic reaction (similar to anaphylaxis) consisting of hypotension, mental confusion, fever, chills, and wheezing has been reported in approximately 1% of lymphoma patients treated with Bleomycin Sulfate. Bleomycin causes sensitization of lung tissue to oxygen with repeated therapeutic use, which can lead to rapid pulmonary deterioration. It is unknown if these sensitization effects can occur by normal routes of workplace exposure.

REPRODUCTIVE TOXICITY INFORMATION: There are no adequate and well-controlled studies of Bleomycin Sulfate in pregnant women. In the workplace, the risk to the fetus should be communicated and the appropriate action should be taken to prevent exposure in accordance with company policy and regulatory requirements. In formulated products, Bleomycin Sulfate is rated by the FDA for therapeutic risk as Pregnancy Risk Category D (refer to Definition of Terms for full category definitions).

Mutagenicity: Bleomycin has been shown to be mutagenic both in vitro and in vivo.

Embryotoxicity/Teratogenicity: Bleomycin Sulfate can cause fetal harm when administered to a pregnant woman. It has been shown to be teratogenic in rats. Administration of intraperitoneal doses of 1.5 mg/kg/day to rats (about 1.6 times the recommended human dose on a unit/m² basis) on days 6 to 15 of gestation caused skeletal malformations, shortened innominate artery and hydroureter. Bleomycin Sulfate is abortifacient but not teratogenic in rabbits at intravenous doses of 1.2 mg/kg/day (about 2.4 times the recommended human dose on a unit/m² basis) given on gestation days 6 to 18.

Reproductive Toxicity: The effects of Bleomycin on fertility have not been studied. It is not known whether Bleomycin is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, nursing mothers should be advised of these effects and the appropriate action should be taken to prevent exposure.

BIOLOGICAL EXPOSURE INDICES: Currently, there are no Biological Exposure Indices (BEIs) determined for this material.

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.

BIO-ACCUMULATION POTENTIAL: This material has not been tested for bioaccumulation potential.

ECOTOXICITY: This material may be harmful to contaminated plant and animal life, especially in large quantities. All releases to terrestrial, atmospheric and aquatic environments should be avoided. No toxicological data are available for this material.

RESULTS OF PBT AND vPvB ASSESSMENT: No Data Available. PBT and vPvB assessments are part of the chemical safety report required for some substances in European Union Regulation (EC) 1907/2006, Article 14.

OTHER ADVERSE EFFECTS: This material is not listed as having 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

WASTE TREATMENT/DISPOSAL METHODS: 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. All protective clothing, gloves, and disposable materials used in the preparation or handling of this drug should be disposed of in accordance with established hazardous waste disposal procedures. 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. Incineration is recommended for the product and disposable equipment. Shipment of wastes must be done with appropriately permitted and registered transporters. Reusable equipment should be cleaned with soap and water and thoroughly rinsed.

DISPOSAL OF CONTAMINATED PROTECTIVE EQUIPMENT: Employees should be trained in proper methods to remove contaminated gloves and gowns. After use, gloves and gowns should be disposed of in accordance with American Society of Health System Pharmacist (ASHP) or Hospital Pharmacy Europe recommendations.

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.

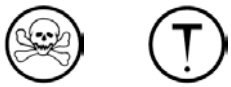
EUROPEAN EWC WASTE CODE: Wastes from natal care, diagnosis, treatment, or prevention of disease in humans: cytotoxic and cytostatic medicines, 18-01-08

14. TRANSPORTATION INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION: This material is NOT classified as dangerous goods, per U.S. DOT regulations, under 49 CFR 172.101.
TRANSPORT CANADA TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: This material does not meet the criteria of classification of Dangerous Goods, per regulations of Transport Canada.
INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA): This material does not meet the criteria as Dangerous Goods, per rules of IATA.
INTERNATIONAL MARITIME ORGANIZATION (IMO) DESIGNATION: This material is NOT classified as Dangerous Goods by the International Maritime Organization.
EUROPEAN AGREEMENT CONCERNING THE INTERNATIONAL CARRIAGE OF DANGEROUS GOODS BY ROAD (ADR): This material does not meet the criteria as Dangerous Goods of the United Nations Economic Commission for Europe.
TRANSPORT IN BULK ACCORDING TO THE IBC CODE: Not applicable.
ENVIRONMENTAL HAZARDS: This material does not meet the criteria of environmentally hazardous according to the criteria of the UN Model Regulations (as reflected in the IMDG Code, ADR, RID, and ADN) and is not specifically listed in Annex III under MARPOL 73/78.

15. REGULATORY INFORMATION

ADDITIONAL U.S. REGULATIONS:
U.S. SARA REPORTING REQUIREMENTS: This material is 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 this material. The default Federal SDS submission and inventory requirement filing threshold of 10,000 lb (4,540 kg) may apply, per 40 CFR 370.20.
U.S. SARA HAZARD CATEGORIES (SECTION 311/312, 40 CFR 370-21): ACUTE: Yes; CHRONIC: Yes; FIRE: No; REACTIVE: No; SUDDEN RELEASE: No
U.S. CERCLA REPORTABLE QUANTITY (RQ): Not applicable.
U.S. TSCA INVENTORY STATUS: This material is regulated under Food and Drug Administration (FDA) standards; this material is not subject to requirements under TSCA.
OTHER U.S. FEDERAL REGULATIONS: Under the Hazard Communication Standard (HCS), Section (b)(5)(ii) drugs are subject to labeling requirements by the FDA under the Federal Food, Drug and Cosmetic Act and are exempt from labeling provisions of the HCS; this section of the HCS exempts only labeling requirements and not requirements for a Safety Data Sheet for drugs.
CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT (PROPOSITION 65): This material is not listed on the California Proposition 65 Lists by itself. A listing exists, but only in combination with another drug compound, Etoposide.
ADDITIONAL CANADIAN REGULATIONS:
CANADIAN DSL/NDSL STATUS: This material is regulated by the Therapeutic Products Programme (TPP) of Health Canada; it is exempt from the requirements of CEPA.
CANADIAN ENVIRONMENTAL PROTECTION ACT (CEPA) PRIORITY SUBSTANCES LISTS: This material is not on the CEPA substances lists.
OTHER CANADIAN REGULATIONS: Requirements under the Canadian Heath Canada, Laboratory Biosafety Guidelines may be applicable.
CANADIAN WHMIS CLASSIFICATION and SYMBOLS: If used in the preparation of pharmaceutical products, the WHMIS Requirements of the Hazardous Products Act does not apply in respect of the advertising, sale or importation of any cosmetic, device, drug or food within the meaning of the Food and Drugs Act. If this compound is used for other purposes, the following classification and symbols are applicable. **Classes D2A, D2B:** Materials Causing Other Toxic Effects- Acute Toxicity, Irritation



ADDITIONAL EUROPEAN REGULATIONS:
SAFETY, HEALTH, AND ENVIRONMENTAL REGULATIONS/LEGISLATION SPECIFIC FOR THE MATERIAL: When formulated in a finished medicinal product for human use, this material is subject to Directive 2001/83/EC and subsequent amendments to the directive.
CHEMICAL SAFETY ASSESSMENT: No Data Available. The chemical safety assessment is required for some substances according to European Union Regulation (EC) 1907/2006, Article 14.

16. OTHER INFORMATION

ANSI LABELING (Z129.1, Provided to Summarize Occupational Hazard Information): **DANGER!** CYTOTOXIC AGENT. ALL EXPOSURE MUST BE MINIMIZED. MAY BE HARMFUL IF SWALLOWED OR INHALED. MAY CAUSE RESPIRATORY SYSTEM, EYE, AND SKIN IRRITATION. MAY CAUSE REPRODUCTIVE EFFECTS AND CAN CAUSE HARM DURING PREGNANCY. MAY CAUSE MUTAGENIC EFFECTS, BASED ON *IN VITRO* AND *IN VIVO* TEST RESULTS. SUSPECTED OF LIMITED CARCINOGENIC EFFECT. MAY CAUSE ADVERSE EFFECTS ON SKIN, RESPIRATORY AND BLOOD FORMING SYSTEMS, LIVER. COMBUSTIBLE IF EXPOSED TO HIGH TEMPERATURES.

16. OTHER INFORMATION (Continued)

ANSI LABELING (continued): Do not taste or swallow. Avoid contact with skin, eyes, and clothing. Keep container closed. Use gloves, safety glasses, and appropriate respiratory and body protection. **FIRST-AID:** If exposed, seek immediate medical attention. If swallowed, do not induce vomiting. If alert, give victim up to three glasses of water. Never give anything by mouth to an unconscious person. In case of contact, immediately flush skin with copious amounts of warm water for 20 minutes. Remove contaminated clothing and shoes. If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. **IN CASE OF FIRE:** Use water fog, dry chemical or CO_2, or alcohol foam. **IN CASE OF SPILL:** Refer to Safety Data Sheet for complete spill response procedures. Spill response should be performed by persons properly trained to do so. Decontaminate area with bleach and detergent solution and triple rinse area. Place spill debris in a suitable container. Refer to SDS for additional information.

SPECIAL HANDLING AND DISPOSAL REQUIRED

GLOBAL HARMONIZATION AND EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: Classified in accordance with CLP Regulation (EC) 1272/2008. The following classification is self-classification for the pure material when not in a formulated human pharmaceutical product.

Classification: Germ Cell Mutagen Category 1B, Carcinogenic Category 2, Reproductive Toxicity Category 1B

Signal Word: Danger

Hazard Statement Codes: H340: May cause genetic effects. H351: Suspected of causing cancer. H360D: May damage the unborn child.

Precautionary Statements:

Prevention: P201: Obtain special instructions before use. P202: Do not handle until all safety precautions have been read and understood. P280: Wear protective gloves/protective clothing/eye protection/face protection.

Response: P308 + P313: IF exposed or concerned: Get medical advice/attention.

Storage: P405: Store locked up.

Disposal: P501: Dispose of contents/containers in accordance with all local, regional, national and international regulations.

Hazard Symbol/Pictograms: GHS08

67/548/EEC EU LABELING/CLASSIFICATION: Classified in accordance with the European Community Council Directive 67/548/EEC or subsequent Directives. The following classification is self-classification for the pure material when not in a formulated human pharmaceutical product.

Classification: Carcinogenic Cat. 3, Germ Cell Mutagen Cat. 2, Reproductive Toxicity Cat. 2

Risk Phrases: R45: Limited evidence of a carcinogenic effect. R46: May cause heritable genetic damage. R63: Possible risk of harm to the unborn child.

Safety Phrases: S22: Do not breathe dust. S36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S45: In case of accident or if you feel unwell seek medical advice immediately (show the label where possible). S53: Avoid exposure - obtain special instructions before use. S60: This material and its container must be disposed of as hazardous waste.

Hazard Symbols: T

REFERENCES AND DATA SOURCES: Contact the supplier for information.

METHODS OF EVALUATING INFORMATION FOR THE PURPOSE OF CLASSIFICATION: The criteria of CLP 1272: 2008/2011 and 67/548/EEC were used to classify this material.

PREPARED BY: CHEMICAL SAFETY ASSOCIATES, Inc. • PO Box 1961, Hilo, HI 96721-1961 • (800) 441-3365

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DEFINITIONS OF TERMS

For information on medical terms used in this SDS consult an on-line database such as Medline Plus: http://www.nlm.nih.gov/medlineplus/druginformation.html.
A large number of abbreviations and acronyms appear on a SDS. Some of these, which are commonly used, include the following:

EXPOSURE LIMITS IN AIR:

CAS #: This is the Chemical Abstract Service Number that uniquely identifies each constituent.
CEILING LEVEL: The concentration that shall not be exceeded during any part of the working exposure.
ACGIH - American Conference of Governmental Industrial Hygienists, a professional association which establishes exposure limits. **TLV -** Threshold Limit Value - an airborne concentration of a substance which 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 Time Weighted Average **(TWA)**, the 15-minute Short Term Exposure Limit, and the instantaneous Ceiling Level **(C)**. Skin absorption effects must also be considered.
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.
MAK: Federal Republic of Germany Maximum Concentration Values in the workplace.
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); **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:

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

FLAMMABILITY HAZARD (continued): 1 (continued): 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.); **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.); **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. *Unstable 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 with an LC_{50} for acute inhalation toxicity greater than 10,000 ppm. Dusts and mists with an LC_{50} for acute inhalation toxicity greater than 200 mg/L. Materials with an LD_{50} for acute dermal toxicity greater than 2000 mg/kg. Materials with an LD_{50} 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 LC_{50} for acute inhalation toxicity greater than 5,000 ppm but less than or equal to 10,000 ppm. Dusts and mists with an LC_{50} for acute inhalation toxicity greater than 10 mg/L but less than or equal to 200 mg/L. Materials with an LD_{50} 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 LD_{50} for acute oral toxicity greater than 500 mg/kg but less than or equal to 2000 mg/kg.

DEFINITIONS OF TERMS (Continued)

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

HEALTH HAZARD (continued): **2** Materials that, under emergency conditions, can cause temporary incapacitation or residual injury. Gases with an LC_{50} 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 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. Dusts and mists with an LC_{50} for acute inhalation toxicity greater than 2 mg/L but less than or equal to 10 mg/L. Materials with an LD_{50} 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 LD_{50} for acute oral toxicity is greater than 50 mg/kg but less than or equal to 500 mg/kg. Dusts and mists with an LC_{50} for acute inhalation toxicity greater than 10 mg/L but less than or equal to 200 mg/L. Materials with an LD_{50} 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 LD_{50} for acute oral toxicity greater than 500 mg/kg but less than or equal to 2000 mg/kg. **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. **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.

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

INSTABILITY HAZARD (continued): **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.

REPRODUCTIVE TOXICITY INFORMATION:

A mutagen is a chemical which causes permanent changes to genetic material (DNA) such that the changes will propagate through generational lines. An embryotoxin is a chemical which 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 which causes damage to a developing fetus, but the damage does not propagate across generational lines. A reproductive toxin is any substance which interferes in any way with the reproductive process.

United States FDA Pharmaceutical Pregnancy Categories: Pregnancy Category A: Adequate and well-controlled human studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters). **Pregnancy Category B:** Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester. **Pregnancy Category C:** Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. **Pregnancy Category D:** There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. **Pregnancy Category X:** Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits. **Pregnancy Category N:** FDA has not classified this drug.

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 Community (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.