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 AND OF THE COMPANY UNDERTAKING

IDENTIFICATION of the SUBSTANCE or PREPARATION:

TRADE NAME: **DOXORUBICIN HYDROCHLORIDE INJECTION USP**

CHEMICAL NAME: Active Ingredient: 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxylacetyl)-1-methoxy-, hydrochloride (8S-cis)-

CHEMICAL CLASS: Active Ingredient: Anthracycline Salt

THERAPEUTIC CLASS: Antineoplastic

HOW SUPPLIED: 10 mg/5 mL/Single Dose Vial; 50 mg/25 mL/Single Dose Vial; 200 mg/100 mL/Multiple Dose Vial

RELEVANT USE of the SUBSTANCE: Human Pharmaceutical

USES ADVISED AGAINST: Other than Relevant Use

COMPANY/UNDERTAKING 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. SUPPLIER/MANUFACTURER'S NAME: **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: bernadette.pogozelski@tevapharm.com

DATE OF PREPARATION: August 12, 2012

DATE OF REVISION: New

ALL WHMIS required information is included in appropriate sections based on the ANSI Z400.1-2010 format. This product has been classified in accordance with the hazard criteria of the CPR and the SDS contains all the information required by the CPR. The product 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 AND EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

EU LABELING/CLASSIFICATION: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

See Section 16 for full classification information of this product.

EMERGENCY OVERVIEW: Product Description: This product is a clear, orange-colored, odorless, aqueous solution. **Health Hazards:** WARNING! CONTAINS A CYTOTOXIC AGENT. There are scientific studies that suggest that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity of these materials if workplace exposures are not properly controlled. The actual risk in the workplace is not known. Exposure by all routes must be avoided. This product is harmful by ingestion. This product may be harmful by inhalation and may cause severe eye and skin irritation. May cause severe skin and respiratory allergic reactions. In therapeutic use, this product has caused adverse effects on the blood system, cardiotoxicity, muscles, bone marrow, digestive system, neurological and peripheral nervous systems and reproductive system. Ingestion, skin contact and inhalation may cause sensitization and allergic reaction in susceptible individuals. The active ingredient has been shown to be a reproductive toxin in animal tests, causing mutagenic and embryotoxic effects. The active ingredient is a suspect carcinogen, based on animal tests. See Section 11 (Toxicological Information) for more information on other possible therapeutic use effects. **Flammability Hazards:** This product is not flammable or combustible. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon and nitrogen oxides and hydrogen chloride). **Reactivity Hazards:** This product is not reactive. **Environmental Hazards:** This product may cause harm to animals and aquatic organisms if accidentally released to the environment. **Emergency Recommendations:** Emergency responders must wear personal protective equipment suitable for the situation to which they are responding.

3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	% w/v	EU Classification (67/548/EEC) GHS and EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements
ACTIVE INGREDIENT				
Doxorubicin HCl 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxylacetyl)-1-methoxy-, hydrochloride (8S-cis)-	25316-40-9	246-818-3	Proprietary	SELF CLASSIFICATION: EU 67/548 Classification: Reproductive Toxicity Cat. 2, Carcinogenicity Cat. 2, Mutagenic Cat. 2, Harmful, Irritant Risk Phrases: R45, R46, R25, R37/38, R41, R42/43, R48/20/22, R61, R62, R64 Symbols: T GHS and EU 1272/2008 Classification: Reproductive Cat. 1A, Germ Cell Mutagenicity Cat. 1B, Carcinogenicity Cat. 1B, Acute Oral Toxicity Cat. 4, Eye Damage/Corrosion Cat. 1, Skin Irritation Cat. 2, Skin Sensitization Cat. 1, Respiratory Sensitization Cat. 1, STOT Cat. 2, Effects on or Via Lactation Hazard Statement Codes: H360Df, H340, H350, H302, H315, H318, H317, H334, H371, H362 Hazard Symbols/Pictograms: GHS05, GHS07, GHS08
EXCIPIENTS				
Sodium Chloride	7647-14-5	231-598-3	Proprietary	EU 67/548 CLASSIFICATION: Not Applicable GHS AND EU 1272/2008 CLASSIFICATION: Not Applicable
Water	7732-18-5	231-791-2	Balance	EU 67/548 Hazard Classification: Not Applicable GHS and EU 1272/2008 HAZARD CLASSIFICATION: Not Applicable

NOTE: This product contains hydrochloric acid and/or sodium hydroxide for pH adjustment. No hazard from these chemicals remains in the final product and so this SDS does not address hazards for these chemicals. See Section 16 for full classification information of this product.

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

4. FIRST-AID MEASURES

DESCRIPTION OF FIRST AID MEASURES: **WARNING!** Persons experiencing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention. Contaminated individuals must be taken for medical attention if any adverse effects occur. Remove contaminated clothing and shoes. Wash clothing and thoroughly clean shoes before reuse. Take a copy of this SDS to health professional with victim.

SKIN EXPOSURE: If this product contaminates the skin, begin decontamination with running 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 product 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 continues after flushing.

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

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

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: In therapeutic use, pre-existing gastrointestinal respiratory, skin, gastrointestinal, blood forming and liver disorders, and cardioarrhythmia may be aggravated by exposure to the product. Persons in the workplace with these conditions may also have aggravation of symptoms.

INDICATION OF IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT IF NEEDED: Treat symptoms and eliminate exposure. There is no specific antidote for this product. During therapy, after absorbing large amounts of this substance, early endoscopy should be used to assess mucous lesions in the esophagus and stomach. If necessary, suck away leftover substance. Effective countermeasures aimed at controlling hematologic side effects may include bone marrow transplantation and transfusions (platelets, blood) or the administration of hematologic growth factors. Supportive therapy should be fully used. It is not known whether this material or its metabolites can be removed by dialysis. No relevant experience is available. After accidental paravasation, necrosis has been observed in individual cases.

5. FIRE-FIGHTING MEASURES

FLASH POINT: Not applicable.

AUTOIGNITION TEMPERATURE: Not applicable.

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

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 product.

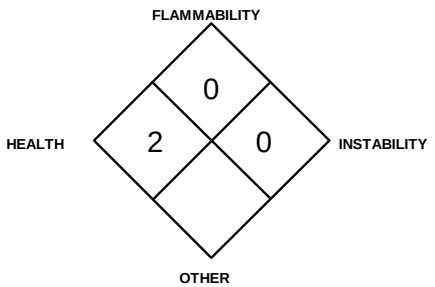
UNSUITABLE FIRE EXTINGUISHING MEDIA: None known.

SPECIAL HAZARDS ARISING FROM THE SUBSTANCE: This solution is not flammable or combustible. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon and nitrogen oxides and hydrogen chloride).

Explosion Sensitivity to Mechanical Impact: Not applicable.

Explosion Sensitivity to Static Discharge: Not applicable.

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.

5. FIRE-FIGHTING MEASURES (Continued)

SPECIAL PROTECTIVE ACTIONS FOR FIRE-FIGHTERS (continued): All personal protective gear and contaminated fire-response equipment should be decontaminated with soapy water 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 an appropriate respirator, chemical splash goggles, two pairs of gloves, two sheets (12 x 12) of absorbent material, 250-mL and 1-liter spill control pillows and a small scoop to collect glass fragments (if applicable). Absorbents should be incinerable. Finally, the kit should contain two large waste-disposal bags. Avoid aerosols of this product during spill response procedures.

PROTECTIVE EQUIPMENT:

Small Spills/Spills in Hoods: Personnel wearing gowns, double nitrile or other appropriate gloves and eye protection should immediately clean spills of less than 5 mL outside a hood.

Large Spills: Use proper protective equipment, including double nitrile or other appropriate gloves, full body gown, and full-face respirator equipped with an organic mist 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: Liquid spills should be gently covered with absorbent gauze pads. Remove the pads after absorption and dispose of properly. Clean 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: Review Sections 2, 8, 11 and 12 before proceeding with cleanup. For spills of amounts larger than 5 mL limit spread by gently covering with absorbent sheets or spill-control pads or pillows. Be sure not to generate aerosols. Restrict access to the spill areas. The dispersion of mists or sprays 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. All contaminated material should be labeled as cytotoxic waste. 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, and 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

NOTE: Consistent with the OSHA Bloodborne Pathogen regulation (29 CFR 1910.1030), observe Universal Precautions while using this product. Place used or product-contaminated hypodermic needles and syringes in a rigid “Sharps” container. Do not recap or clip used or product-contaminated hypodermic needles.

PRECAUTIONS FOR SAFE HANDLING: THIS PRODUCT CONTAINS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL. All employees who handle this product should be thoroughly trained to handle it safely. Special attention must be paid in avoiding releasing airborne particles of this product in areas in which this compound is handled or used. As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, smoke or drink while handling this product. Smokers who do not take simple protective measures such as gloving and hand washing may take in additional amounts of the drug orally through contaminated cigarettes, resulting in exposure. Appropriate personal protective equipment must be worn (see Section 8, Engineering Controls and Personal Protection). Avoid generation of aerosols. Areas in which this product is used should be wiped down, so that this product does not accumulate. Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Operations of high risk associated with the use of this product include:

- Withdrawal of needles from drug vials;
- Drug transfers using syringes and needles or filter straws;
- Opening ampoules; and
- Expulsion of air from drug-filled syringes.

DO NOT CLIP OR CRUSH NEEDLE WITH WHICH THIS PRODUCT WAS IN CONTACT. Use of this product should meet the following provisions:

- Work should be performed in a designated area for working with hazardous drugs;
- Containment devices, such as a Biological Safety Cabinet, should be used; contaminated waste must be properly handled; and
- Work areas must be regularly decontaminated.

CONDITIONS FOR SAFE STORAGE: Product should be stored in cabinet for cytotoxic materials in a cool, dry location, away from direct sunlight and sources of intense heat. Store away from incompatible materials (see Section 10, Stability and Reactivity).

7. HANDLING and STORAGE (Continued)

CONDITIONS FOR SAFE STORAGE (continued): Product should be stored in secondary containers. Inspect all incoming containers before storage, to ensure containers are properly labeled and not damaged. Store under refrigeration between 2° to 8°C (36° to 46°F). Protect from light.

SPECIFIC END USE(S): This product is a human pharmaceutical.

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. Wash equipment with soap and water. Prevent dispersion of particulates by wetting or dampening surfaces prior to clean up of equipment.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

EXPOSURE LIMITS/CONTROL PARAMETERS:

VENTILATION AND ENGINEERING CONTROLS: Use with adequate ventilation. Follow standard medical product handling procedures. Mixtures or manipulations of this drug should be carried out in a cytotoxic drug safety cabinet. The cabinet should be regularly cleaned following the manufacturer's recommendations, but no less frequently than weekly. All surfaces should be cleaned (three times) using a bleach solution and detergent solution and then rinse with clean water. During decontamination, workers should wear the same equipment recommended in Section 6 (Accidental Release Measures) of this SDS for the clean up of a large spill. HEPA filters on the cytotoxic drug safety cabinet should be changed every six months. The safety cabinet should be tested and certified as recommended by the National Sanitation Foundation in Standard Number 49. Ensure eyewash stations are available and accessible in areas where this product is used. Wipe down work areas routinely to prevent accumulation of product.

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
Doxorubicin Hydrochloride 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxylacetyl)-1-methoxy-, hydrochloride (8S-cis)-	25316-40-9	THIS IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL.							
Sodium Chloride	7647-14-5	NE	NE	NE	NE	NE	NE	NE	NE

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

INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS: Currently, there are no exposure limits in force for components of this product. Exposure limits change or are added and should be checked periodically.

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 if applicable. 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. Face shields are recommended if solutions are made. If necessary, refer to appropriate regulations.

HAND PROTECTION: Check gloves for leaks. Wash hands before putting on gloves and after removing gloves. Gloves should cover the gown cuff. During manufacture or other similar industrial operations, wear the appropriate hand protection for the process. When used in medical administration of the product, double glove with nitrile or other appropriate gloves to avoid absorption of the compound. 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.

9. PHYSICAL and CHEMICAL PROPERTIES

The following information is for the drug product.

PHYSICAL FORM: Liquid.
COLOR: Orange.
ODOR: Practically odorless.
ODOR THRESHOLD: Not applicable.
MOLECULAR WEIGHT: Mixture.
MOLECULAR FORMULA: Mixture.
pH: Adjusted to 2.5-4.5

HOW TO DETECT THIS SUBSTANCE (identification/warning properties): There are no distinguishing characteristics of this product in event of accidental release.

The following information is for the active ingredient.

FORM: Lyophilized powder.
COLOR: Orange to red.
MOLECULAR FORMULA: $C_{27}H_{29}N0_{11}$•HCl
MOLECULAR WEIGHT: 579.99
ODOR: Odorless
ODOR THRESHOLD: Not applicable.
VAPOR PRESSURE @ 25°C: 9.64E-28 mmHg [predict.]
pH: 2.5-4.5 (formulated product for injection)
FLASH POINT: 443.8°C (830.8°F) [predict.]
EXPLOSION LIMITS IN AIR: Not available.
BOILING POINT @ 760 mmHg: 810.3°C (1490.5°F) [predict.]
AUTOIGNITION TEMPERATURE: Not available.

9. PHYSICAL and CHEMICAL PROPERTIES

Information for active ingredient (continued):

SOLUBILITY IN WATER: Soluble. MELTING/FREEZING POINT (decomposes): 216°C (420°F)

OTHER SOLUBILITIES: Soluble in aqueous alcohols, moderately soluble in anhydrous methanol, and insoluble in non-polar organic solvents

COEFFICIENT OF OIL/WATER DISTRIBUTION (PARTITION COEFFICIENT): Log P = 2.821 (est.)

10. STABILITY and REACTIVITY

CHEMICAL STABILITY: Normally stable.

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

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: Strong acids and bases. Avoid materials that are incompatible with water.

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 an anti-neoplastic agent which is a drug intended for administration under the supervision of physicians experienced in cancer chemotherapy. The main expected routes of occupational exposure to this compound are via inhalation of aerosols and skin contact. The anticipated symptoms of exposure, by route of exposure are as follows:

INHALATION: Inhalation of mists or sprays of this product may irritate the mucous membranes and upper respiratory tract. Symptoms of such exposure may include coughing, sneezing, and congestion. May cause allergic reaction.

CONTACT WITH SKIN or EYES: Skin contact may be highly irritating. Contact with the skin can cause adverse effects as described under 'Health Effects from Therapeutic Use' may occur from skin absorption. Eye contact may cause severe irritation. Prolonged eye contact may cause corrosive effect. May cause allergic reaction.

SKIN ABSORPTION: No data is available on potential absorption of this product through intact skin.

INGESTION: Ingestion of this product is not anticipated to be a significant route of occupational exposure. Ingestion may be harmful and cause adverse effects as described under 'Other Potential Health Effects'.

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

OTHER HEALTH EFFECTS FROM THERAPEUTIC USE: In therapeutic use, the most common signs of acute toxicity are nausea and vomiting. Therapeutic use can include adverse effects on the cardiovascular system, the blood forming system (including bone marrow), digestive system, reproductive system, and liver. Symptoms can include changes in blood count, fatigue, hair loss, weakness, cardioarrhythmia, mylosupression, muscle pain, nausea and vomiting. Damage to the fetus can occur (based on animal data). Exposure by inhalation, skin contact and ingestion can cause sensitization and allergic reaction in susceptible individuals. Symptoms are described under routes of exposure above. Once sensitized, exposure to very small concentration can cause allergic reaction. Other adverse symptoms have included, infections, fever, neutropenia, thrombocytopenia, blood and lymphatic system disorders, anemia, stomatitis/mucositis, gastrointestinal disorders, including diarrhea, nausea and vomiting, pronounced alopecia, skin related toxicities (e.g. rash, dry skin), fatigue/malaise/asthenia, dizziness, injection site toxicity. Doxorubicin injures neurons in the PNS, specifically those of the dorsal root ganglia and autonomic ganglia. Other less common effects can include shortness of breath and swollen ankles because of heart failure, irregular heart beat, low, potassium level in the blood (which may be noticed as weakness and cramps), breathing difficulties, cough, chest pains and fainting, coughing blood, swelling and reddening and blistering of the skin around the injection site, stomach pains from an open sore on the lining of the stomach, also called gastric ulcer and pain and swelling of the food pipe, fever and chills (covers pneumonitis, plus breathing difficulties and cough), muscle weakness and aches, yellowing of the skin and/or eyes, also called jaundice, change in frequency of urination, painful urination and blood in the urine**,** constipation, feeling thirsty and loss of appetite, skin problems including itchiness of the skin, tender, swollen areas around hair roots and nail disorders, abnormal manner of walking, speech difficulties, back pain, nose bleeds, agitation, sleepiness or drowsiness but sometimes insomnia.

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

HEALTH HAZARD	(BLUE)	2*
FLAMMABILITY HAZARD	(RED)	0
PHYSICAL HAZARD	(YELLOW)	0

PROTECTIVE EQUIPMENT

EYES	RESPIRATORY	HANDS	BODY
	See Section 8		See Section 8

For Routine Industrial Use and Handling Applications

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

HEALTH EFFECTS OR RISKS FROM EXPOSURE:

Acute: This product may be harmful by ingestion and inhalation. Eye contact may cause severe irritation.

11. TOXICOLOGICAL INFORMATION (Continued)

HEALTH EFFECTS OR RISKS FROM EXPOSURE (continued):

Chronic: Dermatitis (inflammation and redness of the skin) may occur after chronic, low-level skin contact. May cause harm to fetus or adverse effects on fertility for both genders. May cause mutagenic or carcinogenic effects. Can cause skin and/or respiratory sensitization and serious allergic reactions. Chronic therapeutic use has caused other adverse effects as described under 'Other Potential Health Effects'.

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

TOXICITY DATA: The following toxicity data are currently available for active ingredient of this product. Data are available for the excipient ingredient, but are not presented in this SDS. Contact Teva for more information.

DOXORUBICIN HYDROCHLORIDE:

LDLo (Intravenous-Man) 2571 µg/kg/3 weeks-intermittent: Kidney/Ureter/Bladder: changes in tubules (including acute renal failure, acute tubular necrosis)

TDLo (Intravenous-Man) 12 mg/kg/26 weeks-intermittent: Cardiac: cardiomyopathy including infarction; Lungs, Thorax, or Respiration: acute pulmonary edema

TDLo (Intravenous-Human) 0.5 mg/kg: Immunological Including Allergic: anaphylaxis

TDLo (Intravenous-Human) 1 mg/kg/29 days-intermittent: Gastrointestinal: hypermotility, diarrhea, nausea or vomiting; Blood: normocytic anemia

TDLo (Intravenous-Human) 1 mg/kg/29 days-intermittent: Blood: leukopenia, thrombocytopenia; Skin and Appendages: hair

LD_{50} (Oral-Mouse) 698 mg/kg: Sense Organs and Special Senses (Eye): lacrymation; Behavioral: muscle weakness; Gastrointestinal: hypermotility, diarrhea

LD_{50} (Oral-Mouse) 570 mg/kg: Blood: other changes

LD_{50} (Intraperitoneal-Rat) 16,030 µg/kg: Gastrointestinal: hypermotility, diarrhea; Skin and Appendages: dermatitis, allergic (after topical exposure); Nutritional and Gross Metabolic: weight loss or decreased weight gain

LD_{50} (Intraperitoneal-Mouse) 11,160 µg/kg

LD_{50} (Intraperitoneal-Mouse) 4.6 mg/kg: Blood: other changes

LD_{50} (Subcutaneous-Rat) 21,840 µg/kg: Gastrointestinal: hypermotility, diarrhea; Skin and Appendages: dermatitis, allergic (after topical exposure); Nutritional and Gross Metabolic: weight loss or decreased weight gain

LD_{50} (Subcutaneous-Mouse) 7678 µg/kg

LD_{50} (Subcutaneous-Mouse) 13.5 mg/kg: Blood: other changes

LD_{50} (Intravenous-Rat) 12,510 µg/kg: Gastrointestinal: hypermotility, diarrhea; Skin and Appendages: dermatitis, allergic (after topical exposure); Nutritional and Gross Metabolic: weight loss or decreased weight gain

LD_{50} (Intravenous-Mouse) 1245 µg/kg

LD_{50} (Intravenous-Mouse) 12.5 mg/kg: Blood: other changes

LD_{50} (Intravenous-Rabbit) 5980 µg/kg: Behavioral: food intake (animal), muscle weakness

LD_{50} (Intramuscular-Rat) 16 mg/kg

LD_{50} (Intramuscular-Mouse) 13,700 µg/kg

LDLo (Intravenous-Cat) 20 mg/kg: Vascular: BP lowering not characterized in autonomic section; Lungs, Thorax, or Respiration: respiratory obstruction

LDLo (Intravenous-Cat) 2 mg/kg: Vascular: BP lowering not characterized in autonomic section; Lungs, Thorax, or Respiration: dyspnea

TDLo (Intravenous-Rat) 2 mg/kg: Reproductive: Paternal Effects: testes, epididymis, sperm duct; Nutritional and Gross Metabolic: weight loss or decreased weight gain

TDLo (Intravenous-Rat) 6 mg/kg: Blood: changes in erythrocyte (RBC) count; Reproductive: Paternal Effects: testes, epididymis, sperm duct; Nutritional and Gross Metabolic: weight loss or decreased weight gain

TDLo (Intravenous-Rat) 7.5 mg/kg: Liver: other changes; Kidney/Ureter/Bladder: other changes; Biochemical: Metabolism (Intermediary): lipids including transport

TDLo (Intravenous-Rat) 7.5 mg/kg: Cardiac: cardiomyopathy including infarction; Kidney/Ureter/Bladder: other changes; Biochemical: Metabolism (Intermediary): effect on inflammation or mediation of inflammation

TDLo (Intravenous-Rat) 12,480 µg/kg/13 weeks-intermittent: Cardiac: changes in heart weight; Blood: leukopenia; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: phosphatases

TDLo (Intravenous-Rat) 15 mg/kg/5 weeks-intermittent: Cardiac: other changes; Nutritional and Gross Metabolic: weight loss or decreased weight gain

TDLo (Intravenous-Rat) 22,400 µg/kg/4 weeks-intermittent: Kidney/Ureter/Bladder: proteinuria; Blood: normocytic anemia, changes in leukocyte (WBC) count

TDLo (Intravenous-Rat) 9 mg/kg/3 weeks-intermittent: Cardiac: EKG changes not diagnostic of specified effects; Nutritional and Gross Metabolic: weight loss or decreased weight gain; Related to Chronic Data: death

DOXORUBICIN HYDROCHLORIDE (continued):

TDLo (Intravenous-Rat) 12 mg/kg/6 weeks-intermittent: Cardiac: other changes; Related to Chronic Data: death

TDLo (Intravenous-Rat) 20 mg/kg/4 days-intermittent: Related to Chronic Data: death

TDLo (Intravenous-Rat) 18.75 mg/kg/5 days-intermittent: Related to Chronic Data: death

TDLo (Intravenous-Rat) 18.75 mg/kg/5 days-intermittent: Kidney/Ureter/Bladder: changes in tubules (including acute renal failure, acute tubular necrosis); Blood: leukopenia, thrombocytopenia

TDLo (Intravenous-Rat) 6.25 mg/kg/5 days-intermittent: Nutritional and Gross Metabolic: weight loss or decreased weight gain

TDLo (Intravenous-Rat) 7.5 mg/kg/3 days-intermittent: Endocrine: changes in spleen weight, changes in thymus weight; Blood: changes in cell count (unspecified)

TDLo (Intravenous-Rat) 2 mg/kg/2 weeks-intermittent: Reproductive: Paternal Effects: spermatogenesis (incl. genetic material, sperm morphology, motility, and count)

TDLo (Intravenous-Rat) 4 mg/kg/4 weeks-intermittent: Reproductive: Paternal Effects: spermatogenesis (incl. genetic material, sperm morphology, motility, and count); Nutritional and Gross Metabolic: weight loss or decreased weight gain; Related to Chronic Data: changes in testicular weight

TDLo (Intravenous-Mouse) 40 mg/kg/7 weeks-intermittent: Cardiac: other changes; Nutritional and Gross Metabolic: weight loss or decreased weight gain

TDLo (Intravenous-Mouse) 600 µg/kg: female 30 day(s) pre-mating: Reproductive: Maternal Effects: ovaries, fallopian tubes

TDLo (Intravenous-Mouse) 16 mg/kg/2 weeks-intermittent: Endocrine: tumors; Tumorigenic: protects against induction of experimental tumors

TDLo (Intravenous-Rabbit) 18 mg/kg/30 days-continuous: Endocrine: changes in thymus weight; Blood: normocytic anemia; Related to Chronic Data: death

TDLo (Intravenous-Rabbit) 18 mg/kg: male 30 day(s) pre-mating: Reproductive: Paternal Effects: testes, epididymis, sperm duct

TDLo (Intravenous-Dog) 15,600 µg/kg/13 weeks-intermittent: Blood: normocytic anemia, leukopenia; Biochemical: Metabolism (Intermediary): other proteins

TDLo (Intravenous-Dog) 5 mg/kg/10 days-intermittent: Cardiac: arrhythmias (including changes in conduction); Blood: changes in bone marrow (not otherwise specified); Related to Chronic Data: death

TDLo (Intravenous-Dog) 6.25 mg/kg/25 days-intermittent: Cardiac: arrhythmias (including changes in conduction); Blood: changes in bone marrow (not otherwise specified); Skin and Appendages: hair

TDLo (Intravenous-Dog) 1.875 mg/kg/15 days-intermittent: Cardiac: EKG changes not diagnostic of specified effects; Skin and Appendages: hair

TDLo (Intravenous-Monkey) 27 mg/kg/2 years-intermittent: Tumorigenic: equivocal tumorigenic agent by RTECS criteria; Blood: leukemia

TDLo (Intraperitoneal-Rat) 60 mg/kg/30 days-continuous: Liver: changes in liver weight; Endocrine: changes in spleen weight; Blood: normocytic anemia

TDLo (Intraperitoneal-Rat) 18,900 µg/kg/21 days-intermittent: Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: transaminases

TDLo (Intraperitoneal-Rat) 6 mg/kg: male 2 week(s) pre-mating: Reproductive: Paternal Effects: spermatogenesis (incl. genetic material, sperm morphology, motility, and count), testes, epididymis, sperm duct, prostate, seminal vesicle, Cowper's gland, accessory glands

TDLo (Intraperitoneal-Rat) 6300 µg/kg/3 days-intermittent: Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: transaminases

TDLo (Intraperitoneal-Rat) 38 mg/kg/14 weeks-intermittent: Cardiac: EKG changes not diagnostic of specified effects; Kidney/Ureter/Bladder: other changes in urine composition; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol)

TDLo (Intraperitoneal-Mouse) 18 mg/kg/5 weeks-intermittent: Tumorigenic: protects against induction of experimental tumors

DOXORUBICIN HYDROCHLORIDE (continued):

TDLo (Intraperitoneal-Mouse) 1 mg/kg: male 5 week(s) pre-mating: Reproductive: Paternal Effects: spermatogenesis (incl. genetic material, sperm morphology, motility, and count), testes, epididymis, sperm duct

TDLo (Intraperitoneal-Mouse) 7 mg/kg: male 5 week(s) pre-mating: Reproductive: Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated), pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea)

TDLo (Intraperitoneal-Rabbit) 30 mg/kg: male 30 day(s) pre-mating: Reproductive: Paternal Effects: testes, epididymis, sperm duct

TDLo (Intraperitoneal-Rabbit) 60 mg/kg: female 30 day(s) pre-mating: Reproductive: Maternal Effects: ovaries, fallopian tubes

TDLo (Subcutaneous-Rat) 1500 µg/kg: male 5 week(s) pre-mating: Reproductive: Paternal Effects: prostate, seminal vesicle, Cowper's gland, accessory glands

TDLo (Subcutaneous-Mouse) 4500 µg/kg: male 5 week(s) pre-mating: Reproductive: Paternal Effects: spermatogenesis (incl. genetic material, sperm morphology, motility, and count), testes, epididymis, sperm duct

DNA Damage (Human Cells-Not Otherwise Specified) 1 µmol/L

DNA Inhibition (Human Cells-Not Otherwise Specified) 400 nmol/L

Mutation Test Systems-Not Otherwise Specified (Human Cells-Not Otherwise Specified) 300 nmol/L

Mutation Test Systems-Not Otherwise Specified (Human Cells-Not Otherwise Specified) 300 nmol/L

Body Fluid Assay (Human Bacteria-*Salmonella typhimurium*) 714 µg/kg

Body Fluid Assay (Human Bacteria-*Salmonella typhimurium*) 714 µg/kg

Sister Chromatid Exchange (Human-Lymphocyte) 100 nmol/L

Mutation in Mammalian Somatic Cells (Human Cells-Not Otherwise Specified) 0.045 mg/L/4 hours

Cytogenetic Analysis (Human Cells-Not Otherwise Specified) 0.045 mg/L/4 hours

Cytogenetic Analysis (Human-Lymphocyte) 0.2 µmol/L/20 hours

DNA Damage (Human-Sperm) 0.8 µmol/L/1 hour

DNA Damage (Human Lymphocyte) 0.2 µmol/L/20 hours

Micronucleus Test (Human-Lymphocyte) 0.010 mmol/L/72 hours

Mutation in Microorganisms (Bacteria-*Salmonella typhimurium*) 700 ng/plate

Mutation in Microorganisms (Bacteria-*Escherichia coli*) 40 µg/plate

DNA Repair (Bacteria-*Escherichia coli*) 1250 ng/plate

Phage Inhibition Capacity (Bacteria-*Escherichia coli*) 350 µg/L

Mutation Test Systems-Not Otherwise Specified (Microorganism-Not Otherwise Specified) 1 gm/L

Specific Locus Test (*Drosophila melanogaster*) 1 mg/L

Specific Locus Test (*Drosophila melanogaster*) 500 ppm

Micronucleus Test (Non-Mammalian Species Testis) 2 µmol/L

Cytogenetic Analysis (Non-mammalian species-Testis) 2 µmol/L

Cytogenetic Analysis (Non-Mammalian Species Cells-Not Otherwise Specified) 200 nmol/L

Cytogenetic Analysis (Hamster-Lung) 5 µg/L

Cytogenetic Analysis (Hamster-Ovary) 1 µmol/L

Cytogenetic Analysis (Intraperitoneal-Mouse) 12 mg/kg

Sex Chromosome Loss and Non-Disjunction (Non-Mammalian Species-Testis) 2 µmol/L

Sex Chromosome Loss and Non-Disjunction (Non-Mammalian Species Cells-Not Otherwise Specified) 200 nmol/L

DNA Damage (Rat-Liver) 300 nmol/L

DNA Damage (Mouse-Leukocyte) 1 µmol/L

DNA Damage (Rat-Liver) 5.0 µmol/L/3 hours

DNA Damage (Hamster-Lung) 1500 µg/L

DNA Inhibition (Mouse-Leukocyte) 1500 nmol/L

DNA Inhibition (Intraperitoneal-Mouse) 15 mg/kg

11. TOXICOLOGICAL INFORMATION (Continued)

TOXICITY DATA (continued):

DOXORUBICIN HYDROCHLORIDE (continued):
DNA Inhibition (Chicken-Embryo) 900 nmol/L
DNA Adduct (Intraperitoneal-Rat) 4 mg/kg

DOXORUBICIN HYDROCHLORIDE (continued):
Mutation Test Systems-Not Otherwise Specified (Intraperitoneal-Mouse) 15 mg/kg

DOXORUBICIN HYDROCHLORIDE (continued):
Mutation Test Systems-Not Otherwise Specified (Mouse-Leukocyte) 580 nmol/L

CARCINOGENIC POTENTIAL OF COMPONENTS: Carcinogenicity studies have not been conducted with Doxorubicin. Secondary acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) have been reported in patients treated with Doxorubicin-containing combination chemotherapy regimens. Pediatric patients treated with Doxorubicin or other topoisomerase II inhibitors are at risk for developing acute myelogenous leukemia and other neoplasms. Doxorubicin HCl has been shown to have carcinogenic properties when tested in experimental models.

Doxorubicin Hydrochloride is classified as follows by agencies tracking the carcinogenic potential of chemical compounds as follows.

DOXORUBICIN HYDROCHLORIDE: NTP-R (Reasonably Anticipated to be a Human Carcinogen)

The anhydrous form, Doxorubicin, is listed as follows:

DOXORUBICIN: IARC-2A (Probably Carcinogenic to Humans)

IRRITANCY OF PRODUCT: This product may irritate the respiratory system, mucous membranes, and eyes. Eye irritation may be more severe.

SENSITIZATION TO THE PRODUCT: This material may cause sensitization by inhalation, ingestion and skin contact in susceptible individuals. Exposure by these routes of exposure may result in allergic reaction; once sensitized subsequent exposure to very small amounts may cause allergic reaction. Respiratory reactions can be severe and possibly life-threatening.

REPRODUCTIVE TOXICITY INFORMATION: This product is rated 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). There are no adequate, well-controlled studies of this compound in pregnant women.

Mutagenicity: Doxorubicin is mutagenic as it induced DNA damage in rabbit spermatozoa and dominant lethal mutations in mice. Therefore, Doxorubicin may potentially induce chromosomal damage in human spermatozoa. Oligospermia or azoospermia were evidenced in men treated with doxorubicin, mainly in combination therapies. Doxorubicin was mutagenic in the in vitro Ames assay, and clastogenic in multiple in vitro assays (CHO cell, V79 hamster cell, human lymphoblast, and SCE assays) and the in vivo mouse micronucleus assay.

Embryotoxicity/Teratogenicity: Doxorubicin can cause fetal harm when administered to a pregnant woman. Doxorubicin was teratogenic and embryotoxic at doses of 0.8 mg/kg/day (about 1/13 the recommended human dose on a body surface area basis) when administered during the period of organogenesis in rats. Teratogenicity and embryotoxicity were also seen using discrete periods of treatment. The most susceptible was the 6 to 9 day gestation period at doses of 1.25 mg/kg/day and greater. Characteristic malformations included esophageal and intestinal atresia, tracheo-esophageal fistula, hypoplasia of the urinary bladder and cardiovascular anomalies. Doxorubicin was embryotoxic (increase in embryofetal deaths) and abortifacient at 0.4 mg/kg/day (about 1/14 the recommended human dose on a body surface area basis) in rabbits when administered during the period of organogenesis.

Reproductive Toxicity: Doxorubicin decreased fertility in female rats at the doses of 0.05 and 0.2 mg/kg/day (about 1/200 and 1/50 the recommended human dose on a body surface area basis) when administered from 14 days before mating through late gestation period. A single IV dose of doxorubicin at 0.1 mg/kg (about 1/100 the recommended human dose on a body surface area basis) was toxic to male reproductive organs, producing testicular atrophy and oligospermia in rats. In men, Doxorubicin treatment is associated with reversible testicular toxicity. There are no data with which to evaluate whether the pregnancies conceived after male Doxorubicin therapy have an increased incidence of abnormal outcome. Doxorubicin demonstrates dose and age dependent testicular toxicity in rats and testicular toxicity in mice. Genetic abnormalities & dominant lethal mutations have been reported in pregnancies fathered by treated male rodents.

BIOLOGICAL EXPOSURE INDICES: Currently, there are no Biological Exposure Indices (BEIs) determined for the components of this product.

12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

MOBILITY: No information is available on mobility of this product.

PERSISTENCE AND BIODEGRADABILITY: No information on persistence or biodegradability is available for this product.

BIO-ACCUMULATION POTENTIAL: No information available.

ECOTOXICITY: This product 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 data are currently available for this product.

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: The components of this product are 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.

13. DISPOSAL CONSIDERATIONS (Continued)

WASTE TREATMENT/DISPOSAL METHODS (continued): All gowns, 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. Incineration is recommended. Reusable equipment should be cleaned with soap and water. 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. Incineration is recommended for the product and disposable equipment. 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.

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 product 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 product does not meet the criteria as Dangerous Goods, per rules of IATA.

INTERNATIONAL MARITIME ORGANIZATION (IMO) DESIGNATION: This product is NOT classified as Dangerous Goods by the International Maritime Organization.

EUROPEAN AGREEMENT CONCERNING THE INTERNATIONAL CARRIAGE OF DANGEROUS GOODS BY ROAD (ADR): This product 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 product 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 product 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 product is regulated under Food and Drug Administration (FDA) standards; this product is not subject to requirements under TSCA.

OTHER U.S. FEDERAL REGULATIONS: This product is regulated under FDA regulations.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT (PROPOSITION 65): The Doxorubicin Hydrochloride is on the California Proposition 65 lists. WARNING! This product contains a compound is known to the State of California to cause cancer and reproductive harm.

ADDITIONAL CANADIAN REGULATIONS:

CANADIAN DSL/NDSL STATUS: This product 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: Components are 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: 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.

ADDITIONAL EUROPEAN REGULATIONS:

SAFETY, HEALTH, AND ENVIRONMENTAL REGULATIONS/LEGISLATION SPECIFIC FOR THE PRODUCT: Formulated, finished medicinal products for human use, are subject to Directive 2001/83/EC and subsequent amendments to the directive.

15. REGULATORY INFORMATION (Continued)

ADDITIONAL EUROPEAN REGULATIONS (continued):

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!** CONTAINS CYTOTOXIC AGENT. ALL EXPOSURE MUST BE MINIMIZED. ACCIDENTAL INJECTION CAN BE FATAL. MAY BE HARMFUL IF SWALLOWED. MAY CAUSE SERIOUS EYE IRRITATION. MAY CAUSE REPRODUCTIVE EFFECTS IN BOTH GENDERS AND CAN CAUSE HARM DURING PREGNANCY. MAY CAUSE CARCINOGENIC AND MUTAGENIC EFFECT. CAN CAUSE ADVERSE EFFECTS ON DIGESTIVE SYSTEM, BLOOD FORMING SYSTEM, LIVER. MAY CAUSE ALLERGIC REACTION VIA INHALATION, SKIN CONTACT AND INGESTION. This product should be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents. Avoid accidental injection. Avoid accidental ingestion. Avoid contact with skin, eyes, and clothing. Keep container closed. Use gloves, safety glasses, and appropriate respiratory and body protection. FIRST-AID: If swallowed, do not induce vomiting. 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. Seek medical attention. IN CASE OF FIRE: Use water fog, dry chemical or CO_2, or alcohol foam. IN CASE OF SPILL: Sweep up or vacuum spilled product or absorb spilled liquid on appropriate sorbent materials. Decontaminate area with soapy water and triple rinse area. Place in a suitable container. Refer to SDS for additional information.

GLOBAL HARMONIZATION AND EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

67/548/EEC EU LABELING/CLASSIFICATION: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

CLASSIFICATION FOR COMPONENTS:

FULL TEXT GLOBAL HARMONIZATION AND EU CLP REGULATION (EC) 1272/2008:

DOXORUBICIN HYDROCHLORIDE: This is a self-classification.

Classification: Reproductive Category 1A, Germ Cell Mutagenicity Category 1B, Carcinogenicity Category 1B, Acute Oral Toxicity Category 4, Eye Damage/Corrosion Category 1, Skin Irritation Category 2, Skin Sensitization Category 1, Respiratory Sensitization Category 1, Specific Target Organ Toxicity Category 2, Effects on or Via Lactation

Hazard Statements: H360Df: May damage the unborn child. Suspected of damaging fertility. H340: May cause genetic effects. H350: May cause cancer. H302: Harmful if swallowed. H315: Causes skin irritation. H318: Causes serious eye damage. H317: May cause an allergic skin reaction. H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled. H371: May cause damage to blood forming system and liver. H362: May cause harm to breast-fed children.

ALL OTHER COMPONENTS:

An official classification for these substances has not been published in the CLP 1272: 2008 and is not applicable for self-classification.

FULL TEXT EU 67/548/EEC:

DOXORUBICIN HYDROCHLORIDE: This is a self-classification.

Classification: Reproductive Toxicity Category 2, Carcinogenicity Category 2, Mutagenic Category 2, Harmful, Irritant

Risk Phrases: R45: May cause cancer. R46: May cause heritable genetic damage. R22: Harmful if swallowed. R37/38: Irritating to respiratory system and skin. R41: Risk of serious damage to eyes. R42/43: May cause sensitisation by inhalation and skin contact. R48/20/22: Harmful: danger of serious damage to health by prolonged exposure through inhalation and if swallowed. R61: May cause harm to the unborn child. R62: Possible risk of impaired fertility. R64: May cause harm to breast-fed babies.

ALL OTHER COMPONENTS:

An official classification for these substances has not been published in Commission Directives 93/72/EEC, 94/69 EC, 96/54/EC or subsequent directives and is not applicable for self-classification.

REVISION DETAILS: New

REFERENCES AND DATA SOURCES: Contact the supplier for information.

METHODS OF EVALUATING INFORMATION FOR THE PURPOSE OF CLASSIFICATION: Bridging principles were used to classify this product.

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

DATE OF PRINTING: August 24, 2012

REVISION HISTORY: New

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:

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.

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

Ceiling Level (C). Skin absorption effects must also be considered.

EXPOSURE LIMITS IN AIR (continued):

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.

DEFINITIONS OF TERMS (Continued)

EXPOSURE LIMITS IN AIR (continued):

DFG MAK Germ Cell Mutagen Categories (continued): 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: 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.);

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

FLAMMABILITY HAZARD (continued): 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 and 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 and 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. **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.

DEFINITIONS OF TERMS (Continued)

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

HEALTH HAZARD (continued): **2 (continued):** 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.

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

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 and 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.

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.