MATERIAL SAFETY DATA SHEET

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

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

1. PRODUCT IDENTIFICATION

TRADE NAME:	**TREANDA**
CHEMICAL NAME/CLASS:	For Active Ingredient: 5-[Bis(2-chloroethyl)amino]-1-methyl-1H-benzimidazole-2-butanoic acid monohydrochloride / Nitrogen Mustard Compound of Benzimidazole
SYNONYMS:	For Active Ingredient: 5-[Bis(2-chloroethyl)amino)-1-methyl-1H-benzimidazol-2-yl]butanoic acid hydrochloride; 5-[Bis(2-chloroethyl)amino]-1-methyl-2-benzimidazolebutyric acid monohydrochloride; Bendamustin hydrochloride; Bendamustine hydrochloride; Cytostasan; IMET 3393; Ribomustin; SDX 105; ZIMET 33/93; CEP-18083
PRODUCT USE:	Pharmaceutical Use Only
U.S. SUPPLIER/MANUFACTURER'S NAME:	**CEPHALON, INC.**
ADDRESS:	145 Brandywine Parkway West Chester, PA 19380 USA
BUSINESS PHONE:	1-610-344-0200 [08:00 AM --> 05:00 PM]
EUROPEAN. SUPPLIER/MANUFACTURER'S NAME:	**CEPHALON FRANCE - Usine de Mitry-Mory**
ADDRESS:	ZI de Mitry-Compans - Rue Edouard Branly 77292 Mitry-Mory Cedex France
BUSINESS PHONE:	+33 (0)1 64 27 74 50 [08:00 AM --> 05:00 PM]
EMERGENCY PHONE:	United States/Canada/Puerto Rico: 1-800/424-9300 (Chemtrec) [24-hours] International: 01-703-527-3887 (Chemtrec) [24-hours]
EMAIL:	bpogozel@cephalon.com
DATE OF PREPARATION:	September 27, 2006
DATE OF REVISION:	April 6, 2010

NOTE: ALL United States Occupational Safety and Health Administration Standard (29 CFR 1910.1200), U.S. State equivalent Standards, Canadian WHMIS, and European Union required information is included in appropriate sections based on the U.S. ANSI Z400.1-2004 format. This product has been classified in accordance with the hazard criteria of the countries listed above and the MSDS contains all the information required by the Canadian WHMIS [Controlled Products Regulations] and European Union [Regulation (EC) 1907/2006 Annex II].

2. HAZARD IDENTIFICATION

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.

Hazard Classification: Not Applicable Risk Phrases: Not Applicable.

See Section 15 for full EU classification information of product and components.

EMERGENCY OVERVIEW: Product Description: This product is an odorless, white crystalline powder. **Health Hazards:** THE ACTIVE INGREDIENT OF THIS PRODUCT IS A POWERFUL CYTOTOXIC AGENT. EXPOSURE BY ALL ROUTES MUST BE AVOIDED. The main health hazards in a workplace setting are expected to be moderate to severe irritation of respiratory system from inhaled dusts and adverse effects from skin absorption. In therapeutic use, the active ingredient has caused adverse effects on the blood system, muscles, liver, bone marrow, digestive system 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 teratogenic effects. The active ingredient is a suspect carcinogen, based on animal tests. **Flammability Hazards:** This product is assumed to be combustible. The accumulation of dusts of this product can create a serious hazard of explosion. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon and nitrogen oxides). **Reactivity Hazards:** This product is not reactive. **Environmental Hazards:** Negligible. **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/w	EU CLASSIFICATION FOR COMPONENTS
BENDAMUSTINE HYDROCHLORIDE 5-[Bis(2-chloroethyl)amino]-1-methyl-1H-benzimidazole-2-butanoic acid monohydrochloride	3543-75-7	Unlisted	Proprietary	SELF-CLASSIFICATION: HAZARD CLASSIFICATION: T [Toxic] RISK PHRASES: R: 36; R: 45, R: 46, R: 48/23/24/25, R: 61
Excipients				
Mannitol	69-65-8	200-711-8	Proprietary	EU HAZARD CLASSIFICATION: Not applicable. EU RISK PHRASES: Not applicable.

See Section 15 for full EU classification information of product and components.

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

4. FIRST-AID MEASURES

Contaminated individuals must be taken for medical attention if any adverse effects occur. Take a copy of label and MSDS to health professional with victim.

SKIN EXPOSURE: Wash skin with soap and water. Remove contaminated clothing and shoes. Wash clothing and thoroughly clean shoes before reuse. If irritation occurs or persists, get medical attention.

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

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.

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: Respiratory, skin, gastrointestinal, blood forming and liver disorders, and cardioarrhythmia may be aggravated by exposure to this product. In addition, existing disorders to the target organs, described in Section 11, may also be aggravated by exposure to this product.

RECOMMENDATIONS TO PHYSICIANS: Treat symptoms and eliminate overexposure. There is no specific antidote for this material.

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 determined.

AUTOIGNITION TEMPERATURE: Not determined.

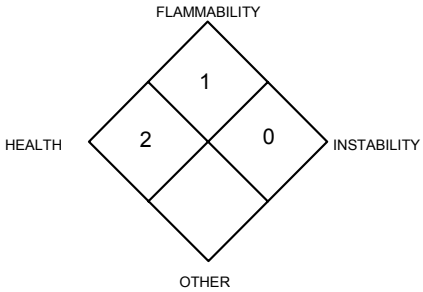
FLAMMABLE LIMITS (in air by volume, %): Not determined.

FIRE EXTINGUISHERS TO USE: 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.

FIRE EXTINGUISHERS NOT TO BE USED: None known.

GENERAL FIRE HAZARDS: Contact with this product may cause allergic reaction and so poses a contact hazard to fire-fighters. This product is assumed to be combustible. When involved in a fire, this product may decompose and produce irritating vapors and toxic compounds (including carbon and nitrogen oxides and hydrogen chloride). Large dust clouds of this product have the potential to ignite explosively.

NFPA RATING



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

Explosion Sensitivity to Mechanical Impact: Not applicable.

Explosion Sensitivity to Static Discharge: Accumulation of dusts from this product has the potential to be ignited by static discharge and create an air/dust explosion hazard.

SPECIAL FIRE-FIGHTING PROCEDURES: 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 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

OCCUPATIONAL SPILL: 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 and a small scoop to collect glass fragments (if applicable). Absorbents should be incinerable. Finally, the kit should contain two large cytotoxic compound waste-disposal bags. Avoid generating airborne dusts of this product during spill response procedures. Decontaminate the area of the spill thoroughly by using a 0.05M Boric acid solution adjusted to pH 9 with 10 N sodium hydroxide solution followed by a detergent wash and clean water rinse or triple wash using a ;bleach solution followed by a detergent solution wash and clean water rinse. The proper personal equipment for incidental releases should include gloves, safety glasses, and a lab coat.

Cleanup of Small Spills: Spills of less than 5 mL or 500 mg outside a hood should be cleaned immediately by personnel wearing gowns, double surgical latex gloves and eye protection. Liquids should be wiped with absorbent gauze pads; solids should be wiped with wet absorbent gauze. All contaminated surfaces should be cleaned using 0.05M Boric acid solution adjusted to pH 9 with 10 N sodium hydroxide followed by a detergent wash and then clean water rinse. Spill areas can also be cleaned (three times) using a bleach solution and a detergent solution followed by clean water.

6. ACCIDENTAL RELEASE MEASURES (Continued)

OCCUPATIONAL SPILL (continued):

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, the unit must be labeled "Do not use--contaminated," and the filter must be changed and disposed of properly as soon as possible by trained personnel wearing appropriate protective equipment.

Large Spill: Review Sections 8, 11 & 12 before proceeding with clean up. For spills of amounts larger than 5 mL or 500 mg, spread should be limited by gently covering with absorbent sheets or spill-control pads or pillows or, if a powder is involved, with damp cloths or towels. Be sure not to generate aerosols. Access to the spill areas should be restricted. The dispersion of particles into surrounding air and the possibility of inhalation is a serious matter and should be treated as such. Chemical in-activators may produce hazardous by-products and should not be applied to the absorbed material. Proper protective equipment should be used, including double latex or nitrile gloves, full body gown, and 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.

Contain the source of the spill. Scoop spilled material into a labeled container for recovery or disposal. Clean spill area thoroughly. All contaminated surfaces should be cleaned using 0.05M Boric acid solution adjusted to pH 9 with 10 N sodium hydroxide followed by a detergent wash and then clean water rinse; this solution results in the degradation of this product into less hazardous materials instantaneously. Spill areas can also be cleaned (three times) using a bleach solution and a detergent solution followed by clean water. Bleach solution may expedite degradation of this product into less hazardous materials. All contaminated absorbents and clean up materials should be disposed of in the designated cytotoxic compound waste bag(s) in covered receptacles. Place all spill residue in an appropriate, labeled container and seal. Move to a secure area. Dispose of in accordance with U.S. Federal, State, and local hazardous waste disposal regulations, those of Canada and its Provinces or those of the EU Member States (see Section 13, Disposal Considerations). For spills on water, contain, minimize dispersion and collect. Dispose of recovered material and report spill per regulatory requirements.

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

7. HANDLING and STORAGE

WORK PRACTICES AND HYGIENE PRACTICES: **THIS PRODUCT CONTAINS IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST POSSIBLE LEVEL.** As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, smoke or drink while handling this product. Wash thoroughly after handling this product or equipment or containers that contain this product. Smokers who do not take simple protective measures such as gloving and hand washing may ingest additional amounts of the drug through contaminated cigarettes, resulting in exposure. 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 vials; and
- Expulsion of air from drug-filled syringes.

DO NOT RECAP, BEND, CUT, CLIP, CRUSH, OR OTHERWISE REMOVE NEEDLES THAT WERE IN CONTACT WITH THIS PRODUCT. DISPOSE OF NEEDLES IN AN APPROVED “SHARPS” CONTAINER. 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.

STORAGE and HANDLING PRACTICES: Employees must be trained to properly use this product. Special attention must be paid in avoiding releasing airborne particles of Treanda in areas in which this compound is handled or used. Ensure vials are properly labeled. Store this product away from incompatible materials (see Section 10, Stability and Reactivity). Protect from light. Dispose of Treanda contaminated wastes in covered receptacles.

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

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear latex or nitrile gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. Dispose of all needles, syringes, vials, and other contaminated disposable items properly. Prevent dispersion of particulates by wetting or dampening surfaces prior to clean up of equipment.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

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 using 0.05M Boric acid solution adjusted to pH 9 with 10 N sodium hydroxide followed by a detergent wash and then clean water rinse; this solution results in the degradation of this product into less hazardous materials instantaneously. During decontamination, workers should wear the same equipment recommended in for a Large Spill in Section 6 (Accidental Release Measures) of this MSDS. HEPA filters on the cytotoxic drug safety cabinet should be changed every six months.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

VENTILATION AND ENGINEERING CONTROLS (continued): 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 dusts.

EXPOSURE LIMITS/GUIDELINES:

CHEMICAL NAME	CAS #	EXPOSURE LIMITS IN AIR							
		ACGIH-TLVs		OSHA-PELs		NIOSH-RELs		NIOSH	OTHER
		TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	IDLH mg/m^3	ug/m^3
Bendamustine Hydrochloride 1H-Benzimidazole-2-butanoic acid, 5-[bis(2-chloroethyl)amino]-1-methyl-, monohydrochloride (9CI)	3543-75-7	THIS IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL.							Cephalon OEL: TWA = 3 $\mu g/m^3$
Mannitol	69-65-8	NE	NE	NE	NE	NE	NE	NE	NE

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

NOTE: (1) This material has no regulatory established exposure limit; Cephalon has established an exposure limit for this material as shown above.

INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS: Currently, there are no regulatory exposure limits for components of this product; Cephalon has established a Cephalon OEL of 3 $\mu g/m^3$ as an 8 hour TWA.

RESPIRATORY PROTECTION: A respirator is not required for routine conditions of use with adequate engineering controls. A full-face Air-Purifying Respirator with high-efficiency particulate filter or a Supplied-Air Respirator must be worn during operations where engineering controls are not sufficient, large spill cleanup, or when processing generates airborne dust. If necessary, use only respiratory protection authorized in the U.S. Federal OSHA Respiratory Protection Standard (29 CFR 1910.134) or equivalent U.S. State standards, Canadian CSA Standard Z94.4-93, or the European Standard EN 529:2005, and EU member state standards. Oxygen levels below 19.5% are considered IDLH by OSHA. In such atmospheres, use of a full-face piece pressure/demand SCBA or a full face piece, supplied air respirator with auxiliary self-contained air supply is required under OSHA's Respiratory Protection Standard (1910.134-1998).

EYE PROTECTION: Wear safety glasses for routine handling. If dusts are generated during handling, use dust goggles. If necessary, refer to U.S. OSHA 29 CFR 1910.133, the European Standard CR 13464:1999 and the Canadian CSA Standard Z94.3-M1982, *Industrial Eye and Face Protectors*.

HAND PROTECTION: Double glove, using latex, nitrile, or rubber gloves (powderless), or other appropriate glove, as described in OSHA 29 CFR 1910.138, the European Standard CEN/TR 15419:2006, or appropriate Standards of Canada. Check gloves for leaks. Wash hands before putting on gloves and after removing gloves. Gloves should cover the gown cuff. Because all gloves are to some extent permeable and their permeability increases with time, they should be changed regularly (hourly is preferable) or immediately if they are torn or punctured. Use triple gloves for spill response, as stated in Section 6 (Accidental Release Measures) of this MSDS.

SKIN PROTECTION: A protective disposable gown made of lint-free low permeability fabric with a closed front, long sleeves, and elastic or knit-closed cuffs must be worn, with the cuffs tucked under the gloves. The gown should be made of Tyvek(TM), PE-Coated Tyvek(TM), or SARANEX(TM). Gowns and gloves in use should not be worn outside the preparation area. If necessary, refer to the OSHA Technical Manual (Section VII: Personal Protective Equipment) or appropriate Standards of Canada, or the European Standard CEN/TR 15419:2006.

9. PHYSICAL and CHEMICAL PROPERTIES

The following information is for the active ingredient:

PHYSICAL FORM: Crystalline powder
COLOR: White to off white
MOLECULAR WEIGHT: 394.72
ODOR: Odorless
VAPOR PRESSURE: Not applicable
MOLECULAR FORMULA: $C_{16}H_{21}Cl_2N_3O_2 \bullet HCl$
MELTING/FREEZING POINT: 167-170°C
pH: 2.7 for 1% (w/v) solution
SOLUBILITY IN WATER: pH 1.9: 7.5 mg/mL; pH 3.3: 3.3 mg/mL; pH 4.1: 1.1 mg/mL; all with degradation @ 20°C
SOLUBILITY IN SOLVENTS @ 20°C: methanol: 220; ethanol: 45; acetone: 0.4; acetonitrile: 1.5
COEFFICIENT OF OIL/WATER DISTRIBUTION (PARTITION COEFFICIENT): Log D (n-octanol/water) at pH 7.4: 0.68

The following information is for the product:

APPEARANCE, ODOR and COLOR: This product is an odorless, white crystalline powder.
HOW TO DETECT THIS SUBSTANCE (warning properties): The appearance may be a distinguishing characteristic of this product in the event of an accidental release. Visible white powder spill; irritation of contaminated skin and eyes, respiratory irritation, or effects of therapeutic use.

10. STABILITY and REACTIVITY

STABILITY: Stable under normal conditions. This material decomposes above 240°C (464°F).
DECOMPOSITION PRODUCTS: *Combustion:* Products of thermal decomposition may include carbon monoxide, carbon dioxide, nitrogen oxides and hydrogen chloride. *Hydrolysis:* None known.
MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: Strong oxidizing agents, strong bases.
HAZARDOUS POLYMERIZATION: Will not occur.
OXIDIZING PROPERTIES: No data available.
EXPLOSIVE PROPERTIES: Accumulation of large amounts of dust from this product can present an air/dust explosion hazard.

10. STABILITY and REACTIVITY (Continued)

CONDITIONS TO AVOID: Exposure to or contact with extreme temperatures, incompatible chemicals, exposure to excessive light.

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

11. TOXICOLOGICAL INFORMATION

SYMPTOMS OF OVEREXPOSURE BY ROUTE OF EXPOSURE: This product is a powerful cytotoxic and anti-neoplastic agent which is an experimental drug intended for administration under the supervision of physicians experienced in cancer chemotherapy. The main expected routes of occupational overexposure to this product are via inhalation of dusts and skin contact. The anticipated symptoms of overexposure, by route of exposure are as follows:

INHALATION: If dusts of this product are inhaled, moderate to severe irritation of the nose and upper respiratory system may occur. Symptoms of such exposure may include sneezing, coughing, and nasal congestion. Inhalation of dusts from this material may cause allergic reaction in susceptible individuals. Symptoms can include difficulty breathing, wheezing and coughing. Chronic exposure may cause symptoms as described under 'Health Effects from Therapeutic Use'.

CONTACT WITH SKIN or EYES: Contact with the skin can cause allergic reaction in susceptible individuals. Symptoms can include rash, itching, welts and dry, red skin. Eye irritation due to dust is expected to be mechanical in nature and may cause redness and watering of the eyes.

SKIN ABSORPTION: This product may cause sensitization and allergic reaction by skin absorption. Adverse effects as described under 'Health Effects from Therapeutic Use' may occur from skin absorption.

INGESTION: Ingestion of this product is not anticipated to be a significant route of occupational overexposure. Ingestion of this product (i.e. through poor hygiene) may have adverse effects on the digestive system and result in symptoms as described under 'Health Effects from Therapeutic Use'. Certain individuals may experience allergic reaction after ingestion. Symptoms may include those described under inhalation.

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

ACCIDENTAL INJECTION: Accidental injection can cause confusion, daze and irregular cardiac activity.

HEALTH EFFECTS FROM THERAPEUTIC USE: Therapeutic use can affect 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 a very small amount can cause allergic reaction.

HEALTH EFFECTS OR RISKS FROM EXPOSURE (An explanation in **lay terms**).

ACUTE: The primary health effects that may be experienced by medical personnel exposed to this product are irritation of contaminated skin and eyes, or pain, redness and local swelling after accidental injection. Acute overexposure may also result in effects seen after therapeutic doses (see above). All workplace exposures to this material must be minimized.

CHRONIC: Chronic exposure to this product may cause damage to the blood forming system, digestive system, and liver. This material can cause sensitization and allergic reaction by inhalation, ingestion and skin contact. Some evidence in animal testing suggests that adverse effects on the liver may occur with chronic use of this compound. This material is a suspect reproductive toxin and suspect carcinogen.

TARGET ORGANS: ACUTE: Respiratory system, digestive system, skin, and eyes. CHRONIC: Skin, respiratory system, reproductive system, blood forming system, and liver.

TOXICITY DATA: The calculated LD50 (Oral-Rat) for this formulated product is 967.7 mg/kg. The following toxicity data are currently available for the active ingredient of this product. Data are available for the excipient component, but are not presented in this MSDS. Contact Cephalon for more information.

BENDAMUSTIN HYDROCHLORIDE:

LD_{50} (Oral-Rat) 200 mg/kg: Blood: changes in spleen

LD_{50} (Oral-Mouse) 250 mg/kg

LD_{50} (Intravenous-Rat) 40 mg/kg: Blood: changes in spleen

LD_{50} (Intravenous-Mouse) 80 mg/kg: Blood: changes in spleen

BENDAMUSTIN HYDROCHLORIDE (continued):

LD_{50} (Intraperitoneal-Mouse) 1 mg/kg

TDLo (Oral-Mouse) 250 mg/kg/4 days-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Lungs, Thorax, or Respiration: tumors; Skin and Appendages: tumors

TDLo (Intraperitoneal-Mouse) 50 mg/kg/4 days-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Lungs, Thorax, or Respiration: tumors

BENDAMUSTIN HYDROCHLORIDE (continued):

TDLo (Intraperitoneal-Mouse) 70 mg/kg: female 11 day(s) after conception: Reproductive: Fertility: post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants); Specific Developmental Abnormalities: musculoskeletal system; other developmental abnormalities

11. TOXICOLOGICAL INFORMATION (Continued)

CARCINOGENIC POTENTIAL OF COMPONENTS: In animal tests involving the active ingredient, lung tumors and mammary carcinomas were detected in mice. The components of this product are not found on the following lists: U.S. EPA, U.S. NTP, U.S. OSHA, U.S. NIOSH, GERMAN MAK, IARC, or ACGIH and therefore are neither considered to be nor suspected to be cancer-causing agents by these agencies.

IRRITANCY OF PRODUCT: Inhalation of dusts from this product may be irritating to the respiratory system. Irritative effects are expected to diminish upon removal to fresh air. Dusts will also be irritating to the eyes.

SENSITIZATION TO THE PRODUCT: The active ingredient of this product 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.

REPRODUCTIVE TOXICITY INFORMATION: The toxicological properties of the active ingredient have not been fully investigated. It is currently not known if this product and its components produce reproductive effects in humans.

Mutagenicity: The active ingredient induces chromosome aberrations and exhibits mutagenic activity in cell culture and animal models.

Embryotoxicity: There are currently no human embryotoxicity data available for this product or its components. Studies involving the active ingredient have been conducted with this product on reproduction and embryonic development of Wistar rats. Single doses from 20 through 100 mg/kg body weight were given intraperitoneally on the 4th, 7th, 9th, 11th or 13th day post coitum. All test animals were sacrificed on the 20th day of pregnancy. The following parameters served as a base for evaluation: the means of implantation rates, resorption rates, fetal body weights and the number of dead and living fetuses. Malformations were detected by outer inspection for gross anomalies, by means of the razor blade technique for malformations of organs and by alizarin preparations for detecting anomalies of the osseuos skeleton. All results were compared with those of an untreated control group and evaluated by statistical means. Notwithstanding the fact of giving high doses (1/2 LD_{50}) there is no loss of blastocysts before implantation: the number of implantation sites equals that of the control group. The resorption rate increases at all examined days of development after application of 40 mg/kg, but 20 mg/kg exert effects only on days 4, 7, and 11 p. c. There is no action on the number of living fetuses after injection of 20 mg of the active ingredient/kg body weight. After application of 40 mg/kg the number of living fetuses decreases especially on the 7th, 9th, and 13th day p. c. There is a dose-dependent stunting: the fetal body weight is not reduced after a dosage of 20 mg/kg, but 40 mg/kg cause a considerable loss of weight during embryogenesis (days 9, 11, 13). It is impossible to induce stunting during blastogenesis (days 4 and 7). The observed patterns of malformation are relatively uniform: kinked tails, omphaloceles, hydronephroses, hydrocephali. Skeletal defects are absent. The results received are comparable with other findings on aklylating anti-tumor drugs.

Teratogenicity: There are currently no human teratogenicity data available for this product or its components. The active ingredient was teratogenic in pregnant mice.

Reproductive Toxicity: There are currently no human reproductive toxicity data available for this product or its components.

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.

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: This product has not been tested for mobility in soil. It is expected to be somewhat mobile in soil.

PERSISTEANCE AND BIODEGRADABILITY: This product has not been tested for persistence or biodegradability. It is expected that some biodegradation will occur to this product; however, no specific information is known.

BIO-ACCUMULATION POTENTIAL: This product has not been tested for bio-accumulation potential. No component has high bio-accumulation potential.

EFFECT OF MATERIAL ON PLANTS or ANIMALS: This product may be harmful or fatal to contaminated plant and animal-life (especially if large quantities are released).

EFFECT OF CHEMICAL ON AQUATIC LIFE: This product has not been tested for aquatic toxicity. This product may be harmful or fatal to contaminated aquatic plant and animal life. This product is practically insoluble in water.

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

PREPARING WASTES FOR DISPOSAL: Cytotoxic waste (routine accumulation, used containers, syringes, discarded gloves, gowns, etc.) should be disposed of in sealable plastic or wire tie bags of 4-mil thick polyethylene or 2-mil polypropylene, labeled with a cytotoxic hazard label and colored differently from other hospital/facility trash bags. All related wastes should be put into these bags, and nothing else. Reusable equipment should be decontaminated using 0.05M Boric acid solution adjusted to pH 9 with 10 N sodium hydroxide followed by a detergent wash and then clean water rinse or by using a bleach solution (triple wash) and a detergent solution followed by clean water rinse.

DISPOSAL METHODS: It is the responsibility of the generator to determine at the time of disposal whether the product meets the criteria of a hazardous waste per regulations of the area in which the waste is generated and/or disposed of. Incineration is recommended for the product and disposable equipment. Waste disposal must be in accordance with appropriate Federal, State, and local regulations. Shipment of wastes must be done with appropriately permitted and registered transporters.

13. DISPOSAL CONSIDERATIONS (Continued)

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

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

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

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. This classification is based on a calculated LD_{50} oral-rat of the product of 967.7 mg/kg.

TRANSPORT CANADA TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: This material does NOT meet the criteria as Dangerous Goods, per regulations of Transport Canada. This classification is based on a calculated LD_{50} oral-rat of the product of 967.7 mg/kg.

INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA): This product does NOT meet the criteria as Dangerous Goods, per rules of IATA. This classification is based on a calculated LD_{50} oral-rat of the product of 967.7 mg/kg.

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. This classification is based on a calculated LD_{50} oral-rat of the product of 967.7 mg/kg.

15. REGULATORY INFORMATION

ADDITIONAL U.S. REGULATIONS:

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

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

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

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

OTHER U.S. FEDERAL REGULATIONS: This product is a “drug” as defined by the Federal Food, Drug and Cosmetic Act (21 USC 321 et. Seq.); requirements under the FDA apply. Requirements under FDA regulations may apply to this compound. In addition, when used as an injectable drug, the requirements of the OSHA Bloodborne Pathogen Standard (29 CFR 1910.1030) are applicable. Employers should refer to OSHA Technical Instructions, TED 1.15, when employees are working with hazardous drugs.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT (PROPOSITION 65): The components of this product are not on the California Proposition 65 lists.

ANSI LABELING (Z129.1) [Precautionary Statements]: **CAUTION!** CONTAINS A CYTOTOXIC AGENT. ALL EXPOSURE MUST BE MINIMIZED. ACCIDENTAL INJECTION CAN BE FATAL. MAY BE HARMFUL IF SWALLOWED. MAY CAUSE RESPIRATORY SYSTEM, EYE, AND SKIN IRRITATION. THERAPEUTIC USE MAY CAUSE REPRODUCTIVE EFFECTS AND CAN CAUSE HARM DURING PREGNANCY. 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 spray, ABC, dry chemical or CO_2, HALON, or alcohol foam. **IN CASE OF SPILL:** Wipe up spilled product with polypad or other suitable absorbent material. Dampen polypad if spilled material is solid. Decontaminate area with soapy water. Place waste in a suitable container and dispose properly. Refer to MSDS for additional information.

In addition to standard pharmacy labeling practices, all syringes and IV bags containing this product should be labeled as follows:

SPECIAL HANDLING AND DISPOSAL REQUIRED

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.

OTHER CANADIAN REGULATIONS: Requirements under the Canadian Heath Canada, Laboratory Biosafety Guidelines may be applicable.

15. REGULATORY INFORMATION (Continued)

ADDITIONAL CANADIAN REGULATIONS (continued):

CANADIAN ENVIRONMENTAL PROTECTION ACT (CEPA) PRIORITY SUBSTANCES LISTS: This material is not on the CEPA Priority Substances Lists.

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 COMMUNITY REGULATIONS:

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.

Hazard Classification: Not Applicable Risk Phrases: Not Applicable
Safety Phrases: Not Applicable Symbol: Not Applicable.

EU LABELING AND CLASSIFICATION FOR COMPONENTS:

BENDAMUSTINE HYDROCHLORIDE:

EU CLASSIFICATION: No hazard classification has been published under European Union Council Directive 67/548/EEC and subsequent directives. The following is a self-classification:

EU RISK PHRASES: [R: 25]: Toxic if swallowed. [R: 36]: Irritating to eyes. [R: 42/43]: May cause sensitisation by inhalation and skin contact. [R: 46]: May cause heritable genetic damage. [R: 48/20/21/22]: Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed. [R: 61]: May cause harm to the unborn child.

EU SAFETY PHRASES: [S: 1/2]: Keep locked up and out of reach of children. [S: 13]: Keep away from food, drink and animal feedingstuffs. [S: 20]: When using, do not eat or drink. S: 22]: Do not breathe dust. [S: 24]: Avoid contact with skin. [S: 25]: Avoid contact with eyes. [S: 26]: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. [S: 35]: This material and its container must be disposed of in a safe way. [S: 36]: Wear suitable protective equipment. [S: 45]: In case of accident, or if you feel unwell, seek medical advice immediately (show label where possible.) [S: 46]: If swallowed, seek medical advice immediately and show this container and label.

MANNITOL:

EU CLASSIFICATION: No hazard classification has been published under European Union Council Directive 67/548/EEC and subsequent directives.

EU RISK PHRASES: Not applicable.

EU SAFETY PHRASES: Not applicable.

16. OTHER INFORMATION

PREPARED BY: CHEMICAL SAFETY ASSOCIATES, Inc.
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DEFINITIONS OF TERMS

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

CAS #: This is the Chemical Abstract Service Number that uniquely identifies each constituent.

EXPOSURE LIMITS IN AIR:

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

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.

EXPOSURE LIMITS IN AIR (continued):

DFG MAK Germ Cell Mutagen Categories (continued): 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.

DEFINITIONS OF TERMS (Continued)

EXPOSURE LIMITS IN AIR (continued):

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.); **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.);

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

PHYSICAL HAZARD (continued): 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 whose LC_{50} for acute inhalation toxicity is greater than 10,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is greater than 200 mg/L. Materials whose LD_{50} for acute dermal toxicity is greater than 2000 mg/kg. Materials whose LD_{50} for acute oral toxicity is greater than 2000 mg/kg. Materials that are essentially non-irritating to the respiratory tract, eyes and skin. **1** (materials that, under emergency conditions, can cause significant irritation): Gases and vapors whose LC_{50} for acute inhalation toxicity is greater than 5,000 ppm but less than or equal to 10,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is greater than 10 mg/L but less than or equal to 200 mg/L. Materials whose LD_{50} for acute dermal toxicity is greater than 1000 mg/kg but less than or equal to 2000 mg/kg. Materials whose LD_{50} for acute oral toxicity is greater than 500 mg/kg but less than or equal to 2000 mg/kg. Materials that cause slight to moderate irritation to the respiratory tract, eyes and skin. **2** (materials that, under emergency conditions, can cause temporary incapacitation or residual injury): Gases and vapors whose LC_{50} for acute inhalation toxicity is greater than 3,000 ppm but less than or equal to 5,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is greater than 2 mg/L but less than or equal to 10 mg/L. Materials whose LD_{50} for acute dermal toxicity is greater than 200 mg/kg but less than or equal to 1000 mg/kg. Materials whose LD_{50} for acute oral toxicity is greater than 50 mg/kg but less than or equal to 500 mg/kg. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC_{50} for acute inhalation toxicity, if its LC_{50} is less than or equal to 5000 ppm and that does not meet the criteria for either degree of hazard 3 or degree of hazard 4. Compressed liquefied gases with boiling points between -30°C (-22°F) and -55°C (-66.5°F) that cause severe tissue damage, depending on duration of exposure. Materials that are respiratory irritants. Materials that cause severe, but reversible irritation to the eyes or are lachrymators. Materials that are primary skin irritants or sensitizers. **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.

DEFINITIONS OF TERMS (Continued)

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

HEALTH HAZARD (continued): **3 (continued):** 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 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 & liquids) which kills 50% of the exposed animals; **LC_{50}** - Lethal Concentration (gases) which kills 50% of the exposed animals; **ppm** concentration expressed in parts of material per million parts of air or water; **mg/m^3** concentration expressed in weight of substance per volume of air; **mg/kg** quantity of material, by weight, administered to a test subject, based on their body weight in kg. Other measures of toxicity include **TDLo**, the lowest dose to cause a symptom and **TCLo** the lowest concentration to cause a symptom; **TDo**, **LDLo**, and **LDo**, or **TC**, **TCo**, **LCLo**, and **LCo**, the lowest dose (or concentration) to cause lethal or toxic effects. **Cancer Information:** The sources are: **IARC** - the International Agency for Research on Cancer; **NTP** - the National Toxicology Program, **RTECS** - the Registry of Toxic Effects of Chemical Substances, **OSHA** and **CAL/OSHA**. IARC and NTP rate chemicals on a scale of decreasing potential to cause human cancer with rankings from 1 to 4. Subrankings (2A, 2B, etc.) are also used. **Other Information: BEI** - ACGIH Biological Exposure Indices, represent the levels of determinants which are most likely to be observed in specimens collected from a healthy worker who has been exposed to chemicals to the same extent as a worker with inhalation exposure to the TLV.

ECOLOGICAL INFORMATION:

EC is the effect concentration in water. **BCF =** Bioconcentration Factor, which is used to determine if a substance will concentrate in lifeforms which consume contaminated plant or animal matter. **TL_m** = median threshold limit; Coefficient of Oil/Water Distribution is represented by **log K_{ow}** or **log K_{oc}** and is used to assess a substance's behavior in the environment.

REGULATORY INFORMATION:

U.S. and CANADA:

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

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

EUROPEAN and INTERNATIONAL:

The DFG: This is the Federal Republic of Germany's Occupation Health Agency, similar to the U.S. OSHA. **EU** is the European 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. **MITI** is the Japanese Minister of International Trade and Industry.