MATERIAL SAFETY DATA SHEET

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

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

1. PRODUCT IDENTIFICATION

TRADE NAME (AS LABELED): **CARDENE CAPSULES (20 & 30 MG)**
CARDENE P.R. CAPSULES (30, 45 & 60 MG)

CHEMICAL NAME: For Active Ingredient: 1,4-Dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid methyl 2- [methyl-phenylmethyl)amino]ethyl ester hydrochloride

COMMON NAME: For Active Ingredients: Nicardipine Hydrochloride

CHEMICAL FORMULA: For Active Ingredient: $C_{26}H_{29}N_3O_6$.• HCl

PRODUCT CODES: 40-2437-04; 40-2438-04; 40-2440-01; 40-2441-01; 40-2442-01

PRODUCT USE: Antianginal; antihypertensive

HOW SUPPLIED: White (20 mg), Light Blue/Blue (30 mg), Pink (30 mg), Blue (45 mg) and Light Blue/White (60 mg) Capsules

SUPPLIER/DISTRIBUTOR'S NAME: **Hoffmann-La Roche Inc.**

ADDRESS: 340 Kingsland Street
Nutley, NJ 07110-1199

EMERGENCY PHONE: 1-800-827-6243

INFORMATION NUMBER: 1-800-526-0189

2. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	%w/w	EXPOSURE LIMITS IN AIR					
			ACGIH-TLV		OSHA-PEL		NIOSH	OTHER
			TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	IDLH mg/m^3	mg/m^3
Magnesium Stearate (exposure limits are for Stearates)	557-04-0	<1	10	NE	NE	NE	NE	Carcinogen: TLV-A4
Methacrylic Acid	79-41-4	≈ 0-8	70	NE	NE	NE	NE	NIOSH RELs: TWA = 70 (Danger of Cutaneous absorption)
Starch and Starch Pregelatinized	9005-25-8	≈ 0-45	10	NE	15 (Total Dust) 5 (Respirable Fraction)	NE	NE	NIOSH REL: 10 (Total dust) 5 (Respirable fraction) Carcinogen: TLV-A4
Microcrystalline Cellulose	9004-34-6	≈ 0-14	10	NE	15 (Total dust) 5 (Respirable fraction)	NE	NE	NIOSH REL: 10 (Total dust) 5 (Respirable fraction)
Lactose monohydrate	64044-51-8	≈ 0-20	NE	NE	NE	NE	NE	NE
Starch Pregelatinized	51395-75-6	26-88	NE	NE	NE	NE	NE	NE
Nicardipine hydrochloride	54527-84-3	≈ 11-19	NE	NE	NE	NE	NE	Roche Group Internal Occupational Exposure Limit = 0.2

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

NOTE: ALL WHMIS required information is included in appropriate sections based on the ANSI Z400.1-1998 format. These products has been classified in accordance with the hazard criteria of the CPR and the MSDS contains all the information required by the CPR.

3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW: These products are supplied as white, light blue, blue, pink or light blue and white capsules. The chief health hazard in an occupational setting in event of exposure is the potential for mild irritation of contaminated skin or eyes. These products must be substantially pre-heated before ignition can occur. If these products are ignited, the decomposition products generated will include irritating vapors and toxic gases (e.g., carbon oxides, nitrogen oxides and hydrogen chloride). These products present no significant reactivity hazards. Emergency responders must wear personal protective equipment suitable for the situation to which they are responding.

SYMPTOMS OF OVEREXPOSURE BY ROUTE OF EXPOSURE: The extent of entry into the body by most routes has not been fully investigated. Occupational exposures to these products may cause acute health effects in humans, as described in the following paragraphs.

INHALATION: Inhalation of airborne dusts generated by these products may slightly irritate the nose, throat, and lungs. Symptoms are generally alleviated upon breathing fresh air.

CONTACT WITH SKIN or EYES: Contact with the skin may cause mild irritation, which is alleviated upon rinsing. Contact with the eyes of airborne dusts generated by these products may cause mild to moderate irritation, redness, and tearing.

SKIN ABSORPTION: The Methacrylic acid, a component of these products can be absorbed through intact skin, however due to form and method of administration of these products this is not a route of exposure for this component.

INGESTION: Ingestion is not anticipated to be a significant route of accidental exposure for these products. If these products are swallowed, it can cause effects as described in "Other Potential Health Effects".

INJECTION: Not a route of exposure due to form and method of administration of this product.

OTHER POTENTIAL HEALTH EFFECTS: Cardene is a pharmacological product used in the treatment of hypertension. Cardene may be used alone or in combination with other anti-hypertensive drugs indicated for the management of patients with chronic stable angina (effort-associated angina). The most common dose-dependent adverse effects associated with therapeutic treatments include flushing, headache, rash, vomiting, sore throat, vertigo, depression, confusion, anxiety, abnormal vision, blurred vision, increased urinary frequency, and hypotension.

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 Use and Handling Applications

See Section 16 for Definition of Ratings

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 these products are mild irritation of contaminated skin and eyes. In the event of exposures via ingestion of therapeutic doses of these products, effects described in "Other Potential Health Effects" may result.

CHRONIC: The Starch component of these products is an allergen; subsequent exposure to small amount may cause allergic reaction in susceptible individuals (by unspecified route of exposure). Chronic ingestion of this product may cause effects as described in "Other Potential Health Effects". Refer to Section 11 (Toxicological Information) for additional information on these products.

TARGET ORGANS: Skin, eyes (anticipated occupational exposures). Central nervous system, Cardiovascular system, gastrointestinal system (therapeutic doses).

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

4. FIRST-AID MEASURES

Victims of chemical exposure must be taken for medical attention. Rescuers should be taken for medical attention if necessary. Take a copy of label and MSDS to physician or health professional with victim.

SKIN EXPOSURE: Basic hygiene should prevent any problems. If these products contaminate the skin, immediately begin decontamination with running water. Remove exposed or contaminated clothing, taking care not to contaminate eyes. The minimum recommended flushing time is 15 minutes. Victims must seek immediate medical attention, especially if an adverse reaction occurs.

4. FIRST-AID MEASURES (Continued)

EYE EXPOSURE: If airborne dusts generated by these products enter the eyes, open victim's eyes while under gently running water. Use sufficient force to open eyelids. Have victim "roll" eyes. Minimum flushing is for 15 minutes. The contaminated individual must seek immediate medical attention after flushing if any adverse effect occurs.

INHALATION: If airborne dusts generated by these products are inhaled, remove victim to fresh air. If necessary, use artificial respiration to support vital functions. Seek medical attention if adverse effect continues after removal to fresh air.

INGESTION: If these products are swallowed, CALL PHYSICIAN OR POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. DO NOT INDUCE VOMITING, unless directed by medical personnel. If conscious, have victim rinse mouth with water. Never induce vomiting or give diluents (milk or water) to someone who is unconscious, having convulsions, or unable to swallow.

INJECTION: Not a route of exposure due to method of administration.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Pre-existing liver function conditions or reduced hepatic blood flow and other disorders involving the Target Organs of these products (see Section 3, Hazard Information) may be aggravated by exposures to these products (especially in doses approaching therapeutic levels for these products).

RECOMMENDATIONS TO PHYSICIANS: Treat symptoms and eliminate overexposure. Consult the Package Insert for additional information that can assist with treatment of overexposure.

5. FIRE-FIGHTING MEASURES

FLASH POINT: Not applicable.

AUTOIGNITION TEMPERATURE: Not applicable.

FLAMMABLE LIMITS (in air by volume, %):

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

FIRE EXTINGUISHING MATERIALS: In the event of a fire, use suppression methods for surrounding materials.

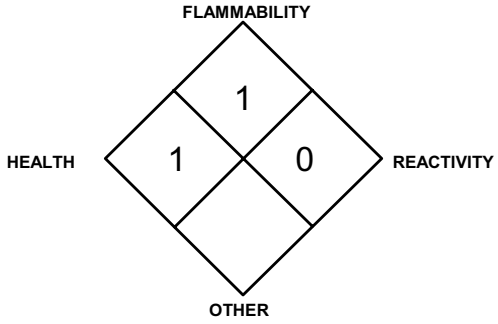
Water Spray: YES	Carbon Dioxide: YES
Dry Chemical: YES	Halon: YES
Foam: YES	Other: Any "ABC" Class.

UNUSUAL FIRE AND EXPLOSION HAZARDS: These products must be substantially pre-heated before ignition can occur. When involved in a fire, these products may decompose and produce irritating fumes and toxic gases (including carbon oxides, nitrogen oxides and hydrogen chloride). The Starch component of these products is a potential sensitizer and so these products present a contact hazard to firefighters.

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

NFPA RATING



See Section 16 for Definition of Ratings

SPECIAL FIRE-FIGHTING PROCEDURES: Move containers from fire area if it can be done without risk to personnel. Incipient fire responders should wear eye protection. Structural firefighters must wear Self-Contained Breathing Apparatus and full protective equipment. Chemical resistant clothing may be necessary. Firefighters whose protective equipment becomes contaminated should thoroughly shower with warm, soapy water and should receive medical evaluation if any adverse effects occur. If possible, prevent runoff water from entering storm drains, bodies of water, or other environmentally sensitive areas.

6. ACCIDENTAL RELEASE MEASURES

SPILL AND LEAK RESPONSE: For small releases of these products (1 bottle), take basic hygiene precautions. Lightweight gloves, a lab coat, and eye protection should be worn. Sweep up spilled caplets. Wash contaminated area with soap and water, absorb with paper towels, and rinse with water. Trained personnel using pre-planned procedures should respond to large releases that are not immediately controlled. Proper protective equipment should be used. In case of a non-incidental spill, clear the affected area and protect people. Minimum Personal Protective Equipment should be **Level D: lab-gloves, chemical resistant apron, boots, and splash goggles. Respiratory protection should not be necessary.** Sweep up spilled caplets. Decontaminate the area thoroughly. Place all spill residue in a suitable container and seal. Dispose of in accordance with U.S. Federal, State, and local hazardous waste disposal regulations and those of Canada and its Provinces (see Section 13, Disposal Considerations).

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

7. HANDLING and STORAGE

WORK PRACTICES AND HYGIENE PRACTICES: As with all chemicals, avoid getting these products ON YOU or IN YOU. Wash hands thoroughly after handling these products or equipment and containers that contain these products. Avoid generating airborne dusts of these products. Do not eat or drink while administering or handling the product to patients. Follow SPECIFIC USE INSTRUCTIONS supplied with product. Particular care in working with these products must be practiced in pharmacies and other preparation areas and during manufacture of these products.

WORK PRACTICES AND HYGIENE PRACTICES (continued): Use of these products should meet the following provisions.

- Work should be performed in an appropriate, designated area;
- Contaminated waste must be properly handled; and,
- If necessary, work areas must be regularly decontaminated.

STORAGE AND HANDLING PRACTICES: All employees who handle this material should be trained to handle it safely. Contaminated waste must be properly handled. Work areas must be regularly decontaminated. Ensure containers of these products are properly labeled. Open containers slowly on a stable surface. Store bottles as directed in these products insert. Keep bottles tightly closed when not in use. Store away from incompatible materials. Store containers at room temperature, 15-30°C (59-86°F). Protect from light. Inspect bottles containing these products for leaks or damage. Read instructions provided with these products prior to use.

PRODUCT PREPARATION INSTRUCTIONS FOR MEDICAL PERSONNEL: Handle this material following standard medical practices and following the recommendations presented on the Package Insert.

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, follow practices indicated in Section 6 (Accidental Release Measures). Make certain that application equipment is locked and tagged-out safely as applicable. Collect all rinsates and dispose of according to applicable Federal, State, or local procedures.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

VENTILATION AND ENGINEERING CONTROLS: Use with adequate ventilation. Follow standard medical product handling procedures. Technicians should be aware of the risks associated with this drug via training and should use the same equipment recommended in Section 6 (Accidental Release Measures). Ensure eyewash/safety shower stations are available near areas where these products are used.

RESPIRATORY PROTECTION: Respiratory protection is not generally needed when using these products. When manufacturing or handling product in large quantities and dusts or particulates may be generated, maintain airborne contaminant concentrations below limits listed in Section 2 (Composition and Information on Ingredients). If respiratory protection is needed, use only protection authorized in the U.S. Federal OSHA Standard (29 CFR 1910.134), applicable U.S. State regulations, or the Canadian CSA Standard Z94.4-93 and applicable standards of Canadian Provinces. Oxygen levels below 19.5% are considered IDLH by OSHA. In such atmospheres, use of a full-facepiece pressure/demand SCBA or a full facepiece, supplied air respirator with auxiliary self-contained air supply is required under OSHA's Respiratory Protection Standard (1910.134-1998).

EYE PROTECTION: None needed under normal circumstances of drug administration. For operations in which airborne dusts of these products will be generated, wear splash goggles or safety glasses. If necessary, refer to U.S. OSHA 29 CFR 1910.133, or Canadian Standards.

HAND PROTECTION: Use latex or similar type of glove when handling this product. If necessary, refer to U.S. OSHA 29 CFR 1910.138 or appropriate Standards of Canada.

BODY PROTECTION: Use body protection appropriate for task, such as a lab coat. If a hazard of injury to the feet exists due to falling objects, rolling objects, where objects may pierce the soles of the feet or where employee's feet may be exposed to electrical hazards, use foot protection, as described in U.S. OSHA 29 CFR.

9. PHYSICAL and CHEMICAL PROPERTIES

RELATIVE VAPOR DENSITY (air = 1): Not established. EVAPORATION RATE (nBuAc = 1): Not applicable.
SPECIFIC GRAVITY (water = 1): Not established. FREEZING/MELTING POINT: Not established.
SOLUBILITY IN WATER: Soluble. BOILING POINT: Not established.
VAPOR PRESSURE, mm Hg @ 20°C: Not established. pH: Not available.
ODOR THRESHOLD: Not available.
LOG WATER/OIL DISTRIBUTION COEFFICIENT: Not available.
APPEARANCE AND COLOR: Yellow, pink, and white tablets.
HOW TO DETECT THIS SUBSTANCE: The appearance may act as a warning property associated with these products.

10. STABILITY and REACTIVITY

STABILITY: These products are stable, when stored at room temperature and protected from light.
DECOMPOSITION PRODUCTS: Thermal decomposition of these products may produce carbon oxides and nitrogen oxides.
MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: Strong oxidizers, strong acids.
HAZARDOUS POLYMERIZATION: Will not occur.
CONDITIONS TO AVOID: Freezing, extreme heat, and mixing these products with incompatible chemicals.

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

11. TOXICOLOGICAL INFORMATION

TOXICITY DATA: The following information is available for the components of these products present in greater that 1 percent concentration.

MICROCRYSTALLINE CELLULOSE:

TDLo (oral, rat) = 420 g/kg/4 weeks/continuous; Gastrointestinal: other changes; Nutritional and Gross Metabolic: weight loss or decreased weight gain

LC_{50} (inhalation, rat) > 5800 mg/m^3/4 hours

LD_{50} (oral, rat) > 5 g/kg

LD_{50} (intraperitoneal, rat) > 31600 mg/kg

LD_{50} (skin, rabbit) > 2 g/kg

MAGNESIUM STEARATE:

TDLo (oral, rat) = 1092 g/kg/13 weeks/continuous; Liver: changes in liver weight; Nutritional and Gross Metabolic: weight loss or decreased weight gain; Related to Chronic Data: death

NICARDIPINE HYDROCHLORIDE:

TDLo (Oral-Man) 26 mg/kg/30 days-intermittent: Kidney, Ureter, Bladder: urine volume decreased, other changes

TDLo (Oral-Woman) 1800 μg/kg/36 hours-intermittent: Kidney, Ureter, Bladder: urine volume decreased

LD_{50} (Oral-Rat) 184 mg/kg

LD_{50} (Oral-Mouse) 322 mg/kg: Behavioral: tremor, convulsions or effect on seizure threshold

LD_{50} (Intraperitoneal-Rat) 155 mg/kg: Behavioral: convulsions or effect on seizure threshold; Lungs, Thorax, or Respiration: respiratory depression; Liver: other changes

LD_{50} (Intraperitoneal-Mouse) 123 mg/kg: Behavioral: tremor, convulsions or effect on seizure threshold

LD_{50} (Subcutaneous-Rat) 606 mg/kg

LD_{50} (Subcutaneous-Mouse) 540 mg/kg: Behavioral: somnolence (general depressed activity); Lungs, Thorax, or Respiration: respiratory depression; Skin and Appendages: dermatitis, other (after systemic exposure)

LD_{50} (Intravenous-Dog) 5 mg/kg

NICARDIPINE HYDROCHLORIDE (continued):

LD (Oral-Dog) > 60 mg/kg

LD_{50} (Intravenous-Mouse) 19,900 μg/kg: Sense Organs and Special Senses (Eye): ptosis; Behavioral: ataxia; Lungs, Thorax, or Respiration:

TDLo (Unreported-Dog) 4550 mg/kg/26 weeks-intermittent: Behavioral: fluid intake; Cardiac: changes in heart weight; Liver: changes in liver weight

TDLo (Oral-Rat) 18,200 mg/kg/26 weeks-intermittent: Liver: fatty liver degeneration; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol); Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: transaminases

TDLo (Oral-Rat) 1050 mg/kg: female 14 day(s) pre-mating female 1-7 day(s) after conception: Reproductive: Fertility: litter size (e.g. # fetuses per litter; measured before birth)

TDLo (Oral-Rat) 2100 mg/kg: female 14 day(s) pre-mating female 1-7 day(s) after conception: Reproductive: Fertility: pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea)

TDLo (Oral-Rat) 2700 mg/kg: female 17-22 day(s) after conception lactating female 21 day(s) post-birth: Reproductive: Effects on Newborn: viability index (e.g., # alive at day 4 per # born alive)…

TDLo (Oral-Rat) 1350 mg/kg: female 17-22 day(s) after conception: lactating female 21 day(s) post-birth: Reproductive: Effects on Newborn: growth statistics (e.g.%, reduced weight gain)

TDLo (Oral-Rabbit) 1650 mg/kg: female 7-17 day(s) after conception: Reproductive: Fertility: post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants), litter size (e.g. # fetuses per litter; measured before birth); Effects on Embryo or Fetus: fetal death

NICARDIPINE HYDROCHLORIDE (continued):

TDLo (Oral-Dog) 1050 mg/kg/6 weeks-intermittent: Gastrointestinal: nausea or vomiting; Kidney, Ureter, Bladder: urine volume increased; Blood: normocytic anemia

TDLo (Intraperitoneal-Rat) 3360 mg/kg: male 9 week(s) pre-mating female 2 week(s) pre-mating-1 week(s) after conception: Reproductive: Fertility: pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea), post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants)

TDLo (Intravenous-Rat) 110 mg/kg: female 7-17 day(s) after conception: Reproductive: Fertility: litter size (e.g. # fetuses per litter; measured before birth); Effects on Embryo or Fetus: fetal death; Effects on Newborn: viability index (e.g., # alive at day 4 per # born alive)

TDLo (Intravenous-Rat) 55 mg/kg: female 7-17 day(s) after conception: Reproductive: Effects on Newborn: live birth index (measured after birth)

TDLo (Intravenous-Rat) 30 mg/kg: female 17-22 day(s) after conception: Reproductive: Effects on Newborn: stillbirth

TDLo (Intravenous-Rat) 60 mg/kg: female 17-22 day(s) after conception: Reproductive: Effects on Embryo or Fetus: fetotoxicity (except death, e.g., stunted fetus)

TDLo (Intravenous-Rabbit) 13 mg/kg: female 6-18 day(s) after conception: Reproductive: Fertility: pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea);Effects on Embryo or Fetus: fetal death

11. TOXICOLOGICAL INFORMATION (Continued)

SUSPECTED CANCER AGENT: Rats treated with Nicardipine Hydrochloride in the diet (at concentrations calculated to provide daily dosage levels of 5, 15 or 45 mg/kg/day) for 2 years showed a dose-dependent increase in thyroid hyperplasia and neoplasia (follicular adenoma/carcinoma). One- and 3-month studies in the rat have suggested that these results are linked to a Nicardipine-induced reduction in plasma thyroxine (T_4) levels with a consequent increase in plasma levels of thyroid stimulating hormone (TSH). Chronic elevation of TSH is known to cause hyperstimulation of the thyroid. In rats on an iodine deficient diet, Nicardipine administration for 1 month was associated with thyroid hyperplasia that was prevented by T_4 supplementation. Mice treated with Nicardipine in the diet (at concentrations calculated to provide daily dosage levels of up to 100 mg/kg/day) for up to 18 months showed no evidence of neoplasia of any tissue and no evidence of thyroid changes. There was no evidence of thyroid pathology in dogs treated with up to 25 mg Nicardipine/kg/day for 1 year and no evidence of effects of Nicardipine on thyroid function (plasma T_4 and TSH) in man. The ACGIH has concluded that Starch is Not Classifiable as a Human Carcinogen. The remaining components of these products are not found on the following lists: FEDERAL OSHA Z LIST, NTP, CAL/OSHA, and therefore are neither considered to be nor suspected to be cancer causing agents by these agencies.

IRRITANCY OF PRODUCT: Contact with the skin or eyes may cause mild irritation, which is alleviated upon rinsing.

SENSITIZATION TO THESE PRODUCTS: Individuals who have had allergic reactions to prescription as well as to over-the-counter products containing Nicardipine may experience allergic reactions to this product. The Starch component of these products is an allergen; subsequent exposure to small amount may cause allergic reaction in susceptible individuals (by unspecified route of exposure).

REPRODUCTIVE TOXICITY INFORMATION: The Nicardipine Hydrochloride component of these products is rated as Pregnancy Category C. Listed below is information concerning the effects of these products' active component on animal or human reproductive systems.

Mutagenicity: There was no evidence of a mutagenic potential of these products in a battery of genotoxicity tests conducted on microbial indicator organisms, in micronucleus tests in mice and hamsters, or in a sister chromatid exchange study in hamsters.

Embryotoxicity: The components of these products are not reported to cause human embryotoxic effects.

Teratogenicity: In pregnant rats administered Nicardipine orally at up to 100 mg/kg/day (50 times the maximum recommended human dose) there was no evidence of embryo-lethality or teratogenicity. However, dystocia, reduced birth weights, reduced neonatal survival and reduced neonatal weight gain were noted. There are no adequate and well-controlled studies in pregnant women. Cardene should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Reproductive Toxicity: No impairment of fertility was seen in male or female rats administered these products at oral doses as high as 100 mg/kg/day (50 times the maximum recommended daily dose in man, assuming a patient weight of 60 kg).

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

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

12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

ENVIRONMENTAL STABILITY: The components of these products will degrade in the environment into organic and inorganic constituents, especially upon exposure to light.

EFFECT OF MATERIAL ON PLANTS or ANIMALS: Due to the small product size, no unusual effects on plants are expected if these products are released into the environment.

EFFECT OF CHEMICAL ON AQUATIC LIFE: No information is currently available on the effect of the components of these products on aquatic plants or animals in the environment.

13. DISPOSAL CONSIDERATIONS

PREPARING WASTES FOR DISPOSAL: Waste disposal must be in accordance with appropriate U.S. Federal, State, and local regulations and those of Canada and its Provinces. These products, if unaltered by use, may be disposed of by treatment at a permitted facility or as advised by your local hazardous waste regulatory authority. All 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. Reusable equipment should be cleaned with soap and water. Incineration is recommended.

U.S. EPA WASTE NUMBER: Not applicable.

14. TRANSPORTATION INFORMATION

THESE PRODUCTS ARE NOT HAZARDOUS AS DEFINED BY 49 CFR 172.101 BY THE U.S. DEPARTMENT OF TRANSPORTATION

PROPER SHIPPING NAME: Not Regulated
HAZARD CLASS NUMBER and DESCRIPTION: Not Applicable
UN IDENTIFICATION NUMBER: Not Applicable
PACKING GROUP: Not Applicable
DOT LABEL(S) REQUIRED: Not Applicable
EMERGENCY RESPONSE GUIDEBOOK NUMBER (2000): Not Applicable
MARINE POLLUTANT: Not applicable (49 CFR 172.101, Appendix B).

TRANSPORT CANADA, TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: These products are not considered as dangerous goods, per regulations of Transport Canada.

15. REGULATORY INFORMATION

ADDITIONAL U.S. REGULATIONS:

U.S. SARA REPORTING REQUIREMENTS: The components of these products are not subject to Sections 302, 304, and 313 reporting requirements under the Superfund Amendment and Reauthorization Act.

U.S. SARA THRESHOLD PLANNING QUANTITY: There are no specific Threshold Planning Quantities for the components of these products. 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: These products are regulated by the Food and Drug Administration; it is exempt from the requirements of TSCA.

OTHER U.S. FEDERAL REGULATIONS: Not applicable.

U.S. STATE REGULATORY INFORMATION: Components of these products that are listed in Section 2 (Composition and Information on Ingredients) are covered under specific State regulations, as denoted below:

Alaska - Designated Toxic and Hazardous Substances: Starch, Methacrylic Acid.
California - Permissible Exposure Limits for Chemical Contaminants: Starch, Methacrylic Acid.
Florida - Substance List: , Methacrylic Acid.
Illinois - Toxic Substance List: Starch, Methacrylic Acid.
Kansas - Section 302/313 List: No.
Massachusetts - Substance List: Methacrylic Acid.
Michigan - Critical Materials Register: No.
Minnesota - List of Hazardous Substances: Starch, Methacrylic Acid.
Missouri - Employer Information/Toxic Substance List: Starch, Methacrylic Acid.
New Jersey - Right to Know Hazardous Substance List: , Methacrylic Acid.
North Dakota - List of Hazardous Chemicals, Reportable Quantities: No.
Pennsylvania - Hazardous Substance List: No.
Rhode Island - Hazardous Substance List: Starch, Methacrylic Acid.
Texas - Hazardous Substance List: No.
West Virginia - Hazardous Substance List: No.
Wisconsin - Toxic and Hazardous Substances: No.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT (PROPOSITION 65): No components of these products are on the California Proposition 65 lists.

ANSI LABELING (Z129.1; Provided to Summarize Occupational Hazard Information): **CAUTION!** MAY CAUSE RESPIRATORY TRACT, SKIN, AND EYE IRRITATION. MAY BE HARMFUL IF INGESTED IN LARGE QUANTITIES. MAY CAUSE ALLERGIC RESPIRATORY OR SKIN REACTION. Do not taste or swallow. Do not get on skin, in eyes, or on clothes. Avoid breathing dusts or particulates. Keep container closed. Use only with adequate ventilation. Wash thoroughly after handling. Wear gloves and goggles. FIRST-AID: In case of contact, immediately flush skin or eyes with plenty of water. If inhaled, remove to fresh air. If ingested, do not induce vomiting. Get medical attention if necessary. IN CASE OF FIRE: Use water fog, dry chemical, CO_2, or "alcohol" foam. IN CASE OF SPILL: Sweep up spill and place in suitable container. Consult Material Safety Data Sheet for additional information.

CANADIAN REGULATIONS:

CANADIAN DSL/NDSL INVENTORY STATUS: These products are regulated by the Therapeutic Products Programme (TPP) of Health Canada and so it excepted from requirements of the DSL/NDSL Inventory.

OTHER CANADIAN REGULATIONS: Requirements under the Therapeutic Products Programme (TPP) of Health Canada.

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

CANADIAN CLASSIFICATION AND WHMIS SYMBOLS: **D2B:** Materials Causing Other Toxic Effects/Toxic Material (sensitization).

16. OTHER INFORMATION

PREPARED BY:

CHEMICAL SAFETY ASSOCIATES, Inc.
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(619) 670-0609

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 component.

EXPOSURE LIMITS IN AIR:

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

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.);

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

HEALTH HAZARD (continued):

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]).

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

PHYSICAL HAZARD:

0 (*Water Reactivity*: Materials that do not react with water. *Organic Peroxides*: Materials that are normally stable, even under fire conditions and will not react with water. *Explosives*: Substances

that are Non-Explosive. Unstable *Compressed Gases*: No Rating. *Pyrophorics*: No Rating. *Oxidizers*: No "0" rating allowed. *Unstable Reactives*: Substances that will not polymerize, decompose, condense or self-react.);**1** *Water Reactivity*: Materials that change or decompose upon exposure to moisture. *Organic Peroxides*: Materials that are normally stable, but can become unstable at high temperatures and pressures. These materials may react with water, but will not release energy. *Explosives*: Division 1.5 & 1.6 substances that are very insensitive explosives or that do not have a mass explosion hazard. *Compressed Gases*: Pressure below OSHA definition. *Pyrophorics*: No Rating. *Oxidizers*: Packaging Group III; Solids: any material that in either concentration tested, exhibits a mean burning time less than or equal to the mean burning time of a 3:7 potassium bromate/cellulose mixture and the criteria for Packing Group I and II are not met. Liquids: any material that exhibits a mean pressure rise time less than or equal to the pressure rise time of a 1:1 nitric acid (65%)/cellulose mixture and the criteria for Packing Group I and II are not met. *Unstable Reactives*: Substances that may decompose, condense or self-react, but only under conditions of high temperature and/or pressure and have little or no potential to cause significant heat generation or explosive hazard. Substances that readily undergo hazardous polymerization in the absence of inhibitors.); **2** (*Water Reactivity*: Materials that may react violently with water. *Organic Peroxides*: Materials that, in themselves, are normally unstable and will readily undergo violent chemical change, but will not detonate. These materials may also react violently with water. *Explosives*: Division 1.4 – Explosive substances where the explosive effect are largely confined to the package and no projection of fragments of appreciable size or range are expected. An external fire must not cause virtually instantaneous explosion of almost the entire contents of the package. *Compressed Gases*: Pressurized and meet OSHA definition but < 514.7 psi absolute at 21.1°C (70°F) [500 psig]. *Pyrophorics*: No Rating. *Oxidizers*: Packing Group II Solids: any material that, either in concentration tested, exhibits a mean burning time of less than or equal to the mean burning time of a 2:3 potassium bromate/cellulose mixture and the criteria for Packing Group I are not met. **)** Liquids: any material that exhibits a mean pressure rise time less than or equal to the pressure rise of a 1:1 aqueous sodium chlorate solution (40%)/cellulose mixture and the criteria for Packing Group I are not met. *Unstable Reactives*: Substances that may polymerize, decompose, condense, or self-react at ambient temperature and/or pressure, but have a low potential for significant heat generation or explosion. Substances that readily form peroxides upon exposure to air or oxygen at room temperature); **3** (*Water Reactivity*: Materials that may form explosive reactions with water. *Organic Peroxides*: Materials that are capable of detonation or explosive reaction, but require a strong initiating source, or must be heated under confinement before initiation; or materials that react explosively with water. *Explosives*: Division 1.2 – Explosive substances that have a fire hazard and either a minor blast hazard or a minor projection hazard or both, but do not have a mass explosion hazard. *Compressed Gases*: Pressure ≥ 514.7 psi absolute at 21.1°C (70°F) [500 psig]. *Pyrophorics*: No Rating. *Oxidizers*: Packing Group I Solids: any material that, in either concentration tested, exhibits a mean burning time less than the mean burning time of a 3.:2 potassium bromate/cellulose mixture. Liquids: Any material that spontaneously ignites when mixed with cellulose in a 1:1 ratio, or which exhibits a mean pressure rise time less than the pressure rise time of a 1:1 perchloric acid (50%)/cellulose mixture. *Unstable Reactives*: Substances that may polymerize, decompose, condense or self-react at ambient temperature and/or pressure and have a moderate potential to cause significant heat generation or explosion.);

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

PHYSICAL HAZARD:

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** (material that on exposure under fire conditions would offer no hazard beyond that of ordinary combustible materials); **1** (materials that on exposure under fire conditions could cause irritation or minor residual injury); **2** (materials that on intense or continued exposure under fire conditions could cause temporary incapacitation or possible residual injury); **3** (materials that can on short exposure could cause serious temporary or residual injury); **4** (materials that under very short exposure could cause death or major residual injury).

FLAMMABILITY HAZARD: **0** Materials that will not burn under typical fire conditions, including intrinsically noncombustible materials such as concrete, stone, and sand. **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 **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. **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. **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.

INSTABILITY HAZARD: **0** Materials that in themselves are normally stable, even under fire conditions. **1** Materials that in themselves are normally stable, but that can become unstable at elevated temperatures and pressures. **2** Materials that readily undergo violent chemical change at elevated temperatures and pressures. **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. **4** Materials that in themselves are readily capable of detonation or explosive decomposition or explosive reaction 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.

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.

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.

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.