



A Subsidiary of Watson Pharmaceuticals, Inc.

# MATERIAL SAFETY DATA SHEET

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

## 1. PRODUCT IDENTIFICATION

**TRADE/MATERIAL NAME:** TRELSTAR 3.75 mg, TRELSTAR 11.25mg and TRELSTAR 22.5 mg

**Triptorelin Pamoate Lyophilized Powder 3.75 mg, 11.25 mg and 22.5 mg**

**DESCRIPTION:** Triptorelin Pamoate Powder

**OTHER DESIGNATIONS:** NDC#: 52544-0153-02, 52544-0154-02, 52544-0156-02

**CHEMICAL NAME:** 5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-tryptophyl-L-leucyl-L-arginyl-L-prolylglycine amide

**CHEMICAL FAMILY:** Hormone

**HOW SUPPLIED:** 3.75 mg, 11.25 mg and 22.5 mg lyophilized powder

**FORMULA:** C<sub>64</sub>H<sub>82</sub>N<sub>18</sub>O<sub>13</sub>•C<sub>23</sub>H<sub>16</sub>O<sub>6</sub>

<b>PRODUCT USE:</b>	Pharmaceutical for Human Use
<b>SUPPLIER/MANUFACTURER'S NAME:</b>	<b>WATSON LABORATORIES INC.</b>
<b>ADDRESS:</b>	311 Bonnie Circle Corona, CA 92880
<b>BUSINESS PHONE/GENERAL MSDS INFORMATION:</b>	1-800-272-5525
<b>EMERGENCY PHONE (U.S./NORTH AMERICA):</b>	CHEMTREC: 1-800-424-9300 (24 hours)
<b>EMERGENCY PHONE (OUTSIDE U.S.):</b>	CHEMTREC: +1-703-527-3887 (24 hours)

NOTE: ALL United States Occupational Safety and Health Administration Standard (29 CFR 1910.1200), U.S. State equivalent Standards, Canadian WHMIS [Controlled Products Regulations], and European Union [Regulation (EC) 1907/2006 Annex II] 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.

## 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.

### EMERGENCY OVERVIEW:

**Product Description:** This product is supplied as a white to off-white lyophilized powder.

**Health Hazards:** The chief health hazard associated with overexposures during normal use and handling is the potential for irritation of contaminated skin. Triptorelin Pamoate (the active component in this product) is a possible reproductive toxin. Individuals who have had allergic reactions to products containing Triptorelin Pamoate, any of the other ingredients in this product, other luteinizing hormone releasing hormone agonists, or luteinizing hormone releasing hormone may experience allergic reactions to this product. Anaphylactic reactions including shock and angioderma have been reported and can be life-threatening. Therapeutic use of this product can cause adverse symptoms of the cardiovascular system, urinary system, skin, gastrointestinal system, reproductive system, musculoskeletal system, and central nervous system.

**Flammability Hazards:** If heated to high temperatures for a prolonged period, the product may ignite. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon oxides, nitrogen oxides, and sodium oxides).

**Reactivity Hazards:** This product is not reactive.

**Environmental Hazards:** Large quantities released to the aquatic or terrestrial environment may have adverse effects.

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

## 3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	% w/v	EU CLASSIFICATION FOR COMPONENTS
Triptorelin Pamoate	57773-63-4	Unlisted	1-5	HAZARD CLASSIFICATION: Not applicable. RISK PHRASES: Not applicable.

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

### 3. COMPOSITION and INFORMATION ON INGREDIENTS (Continued)

CHEMICAL NAME	CAS #	EINECS #	% w/v	EU CLASSIFICATION FOR COMPONENTS
Polysorbate 80	9005-65-6	215-665-4	< 1	HAZARD CLASSIFICATION: Not applicable. RISK PHRASES: Not applicable.
Carboxymethylcellulose Sodium	9004-32-4	Unlisted	10-15	HAZARD CLASSIFICATION: Not applicable. RISK PHRASES: Not applicable.
Mannitol	69-65-8	200-711-8	25-35	HAZARD CLASSIFICATION: Not applicable. RISK PHRASES: Not applicable.
Poly(DL-lactide-co-glycolide)	26780-50-7	Unlisted	50-60	HAZARD CLASSIFICATION: Not applicable. RISK PHRASES: Not applicable.

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

### 4 FIRST-AID MEASURES

Persons developing hypersensitivity reactions should receive medical attention. If breathing is difficult, give oxygen. If not breathing, give artificial respiration. Take a copy of label and MSDS to physician or health professional with the contaminated individual.

**SKIN EXPOSURE:** Basic hygiene should prevent any problems. If the product contaminates 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 20 minutes. Victims must seek immediate medical attention, especially if an adverse reaction occurs.

**EYE EXPOSURE:** If airborne dusts generated by this product enter the eyes, open victim's eyes while under gently running water. Use sufficient force to open eyelids and then "roll" while flushing eyes. Minimum flushing is for 20 minutes if the exposure has resulted in an adverse effect. The contaminated individual must seek medical attention if any adverse effect continues after rinsing.

**INHALATION:** If airborne dusts generated by this product 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 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:** Pre-existing skin conditions may be aggravated by chronic overexposures to this product. The following pre-existing conditions may be aggravated by therapeutic doses of this product: menstrual bleeding problems, osteoporosis, pain or difficulty passing urine, spinal cord metastasis, and vaginal bleeding.

**RECOMMENDATIONS TO PHYSICIANS:** This product should only be given to patients by persons experienced in management of patients receiving the type of therapy intended for this product. Treat symptoms and eliminate exposure.

### 5. FIRE-FIGHTING MEASURES

**FLASH POINT:** Not established.

**AUTOIGNITION TEMPERATURE:** Not established.

**FIRE EXTINGUISHING MATERIALS:** Use extinguishing media appropriate for surrounding fire.

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

**FIRE EXTINGUISHING MATERIALS NOT TO BE USED:** None known.

**UNUSUAL FIRE AND EXPLOSION HAZARDS:** This product may ignite if highly heated for a prolonged period of time. When involved in a fire, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon oxides, nitrogen oxides, and sodium oxides).

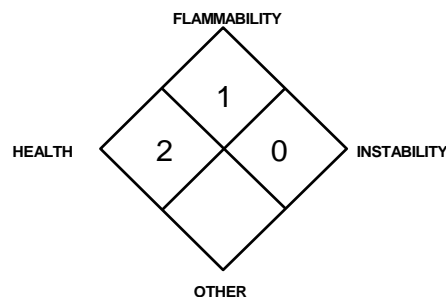
Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

**SPECIAL FIRE-FIGHTING PROCEDURES:** Incipient fire responders

should wear eye protection. Structural firefighters must wear Self-Contained Breathing Apparatus (SCBA) and full protective equipment. If protective equipment is contaminated by this product, it should be thoroughly washed with running water prior to removal of SCBA respiratory protection. Firefighters whose protective equipment becomes contaminated should thoroughly shower with warm, soapy water and should receive medical evaluation if they experience any adverse effects.

#### NFPA RATING



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

## 6. ACCIDENTAL RELEASE MEASURES

**SPILL RESPONSE:** For small releases of this compound (1 vial), take basic hygiene precautions. Lightweight gloves, a lab coat, and eye protection should be worn. Sweep up spilled powder, place in a bag, and hold for waste disposal. Avoid generating airborne dusts of this product during cleanup. In case of a large spill, clear the affected area and protect people. Large or uncontrolled releases (a case of vials) should be responded to by trained personnel using pre-planned procedures. Proper protective equipment should be used, including lab gloves, full body gown, boots, and splash goggles. Respiratory protection should not be necessary. Sweep up spilled powder. Decontaminate the area of the spill thoroughly using detergent and water. Place all spill residue in an appropriate container and seal. Dispose of in accordance with appropriate U.S. Federal, State, and local regulations or with regulations of the EU and its member states or Canada and its Provinces.

## 7. HANDLING and USE

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

**WORK PRACTICES AND HYGIENE PRACTICES:** As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke, or apply cosmetics while handling this product. Wash hands thoroughly after handling this product or equipment and containers that contain this product. Follow SPECIFIC USE INSTRUCTIONS supplied with this product. Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this compound, and during patient administration. Operations of high risk associated with the use of this product include:

- Manual manipulation (measuring, transferring, etc.) of reconstituted drug product; and
- Opening ampoules.

Use of this product should meet the provisions outlined as follows.

- 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:** Employees must be trained to properly use this product. Use of this product should be performed in a designated area for working with drugs. Ensure product is properly labeled. Store this product away from incompatible materials. Store this product in original container. Inspect bottles containing this product for leaks or damage.

**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, wear latex or butyl rubber gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. Wipe equipment down with damp sponge or polypad.

## 8. EXPOSURE CONTROLS - PERSONAL PROTECTION

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

**VENTILATION AND ENGINEERING CONTROLS:** Use with adequate ventilation. Follow standard medical product handling procedures. During decontamination of work surfaces, workers should wear the same equipment recommended in Section 6 (Accidental Release Measures) of this MSDS.

### EXPOSURE LIMITS/GUIDELINES:

CHEMICAL NAME	CAS #	EXPOSURE LIMITS IN AIR							
		ACGIH-TLVs		OSHA-PELs		NIOSH-RELS		NIOSH	OTHER
		TWA mg/m <sup>3</sup>	STEL mg/m <sup>3</sup>	TWA mg/m <sup>3</sup>	STEL mg/m <sup>3</sup>	TWA mg/m <sup>3</sup>	STEL mg/m <sup>3</sup>	IDLH mg/m <sup>3</sup>	mg/m <sup>3</sup>
Triptorelin Pamoate	57773-63-4	NE	NE	NE	NE	NE	NE	NE	NE
Polysorbate 80	9005-65-6	NE	NE	NE	NE	NE	NE	NE	NE
Carboxymethylcellulose Sodium	9004-32-4	NE	NE	NE	NE	NE	NE	NE	NE
Mannitol	69-65-8	NE	NE	NE	NE	NE	NE	NE	NE
Poly(DL-lactide-co-glycolide)	26780-50-7	NE	NE	NE	NE	NE	NE	NE	NE

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

**INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS:** Currently, there are no international exposure limits for components of this product.

*The following information on appropriate Personal Protective Equipment is provided to assist employers in complying with OSHA regulations found in 29 CFR Subpart I (beginning at 1910.132), equivalent standards of Canada (including CSA Standard Z94.4-02 and CSA Standard Z94.3-07), and standards of EU member states (including EN 529:2005 for respiratory PPE, CEN/TR 15419:2006 for hand/body protection, and CR 13464:1999 for face/eye protection). Please reference applicable regulations and standards for relevant details.*

## 8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

**RESPIRATORY PROTECTION:** A respirator is not required for routine conditions of use. If necessary, use only respiratory protection authorized in the U.S. Federal OSHA Respiratory Protection Standard (29 CFR 1910.134), equivalent U.S. State standards, Canadian CSA Standard Z94.4-02, European Standard EN 529:2005, or EU member state standards. 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:** For situations in which excessive splashes or sprays may be generated, wear chemical splash goggles or regular splash goggles. If necessary, refer to U.S. OSHA 29 CFR 1910.133, Canadian CSA Standard Z94.3-07, or European Standard CR 13464:1999.

**HAND PROTECTION:** Double glove, using latex, nitrile, or rubber gloves (powderless) or other appropriate gloves. Check gloves for leaks. Wash hands before putting on gloves and after removing gloves. Gloves should cover the gown cuff. If necessary, refer to U.S. OSHA 29 CFR 1910.138, appropriate Standards of Canada, European Standard CEN/TR 15419:2006, or EU member states standards.

**BODY PROTECTION:** Use body protection appropriate for task, such as a lab coat. If necessary, refer to OSHA Technical Manual (Section VII: Personal Protective Equipment) or European Standard CEN/TR 15419:2006. 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 1910.136, Canadian CSA Standard Z195.1-02, *Guideline on Selection, Care, and Use of Protective Footwear*, or European Standard CEN ISO/TR 18690:2006.

## 9. PHYSICAL and CHEMICAL PROPERTIES

**BOILING POINT:** Not applicable for product.

**EVAPORATION RATE (nBuAc = 1):** Not established.

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

**ODOR THRESHOLD:** Not established.

**COEFFICIENT WATER/OIL DISTRIBUTION:** Not established.

**APPEARANCE, ODOR and COLOR:** This product is supplied as a white to off-white lyophilized powder.

**HOW TO DETECT THIS SUBSTANCE (warning properties):** The appearance of this product is a distinguishing characteristic.

**FREEZING/MELTING POINT:** Not established.

**SOLUBILITY IN WATER:** Soluble.

**SPECIFIC GRAVITY (water = 1):** Not applicable.

**pH:** Not established.

## 10. STABILITY and REACTIVITY

**STABILITY:** This product is stable.

**DECOMPOSITION PRODUCTS:** *Combustion:* If exposed to extremely high temperatures, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon oxides, nitrogen oxides, and sodium oxides). *Hydrolysis:* None known.

**MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE:** This product is generally compatible with other common materials in a medical facility. Acids, caustics, and other chemicals that could affect its performance should be avoided.

**HAZARDOUS POLYMERIZATION:** Will not occur.

**CONDITIONS TO AVOID:** Avoid heat and contact with incompatible chemicals.

## 11. TOXICOLOGICAL INFORMATION

**SYMPTOMS OF OVEREXPOSURE BY ROUTE OF EXPOSURE:** The health hazard information provided below is pertinent to medical employees using this product in an occupational setting. This product is designed for administration via intramuscular injections after it has been reconstituted. The following paragraphs describe the symptoms of exposure by route of exposure.

**INHALATION:** Inhalation of airborne dusts generated by this product may slightly irritate the nose, throat, and lungs. Symptoms of such overexposure may include sneezing, coughing, and nasal congestion. Symptoms are generally alleviated upon breathing fresh air. Anaphylactic reactions including shock and angioderma have been reported during therapeutic use; although these reactions have not been reported to occur from inhalation, inhalation of dusts or particulates should be avoided.

**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 this product may cause mild to moderate irritation, redness, and tearing.

**SKIN ABSORPTION:** The components of this product are not known to be absorbed through intact skin.

**INGESTION:** Ingestion is not a significant route of occupational overexposure. Acute ingestion of large quantities of this product or chronic ingestion caused by poor hygiene practices may cause nausea, vomiting, and diarrhea. Anaphylactic reactions including shock and angioderma have been reported and can be life-threatening.

**INJECTION:** Injection of this product is not anticipated to be a significant route of occupational overexposure. If injection does occur (through lacerations or abrasions of the skin, local reddening, tissue swelling, and discomfort may occur. Anaphylactic reactions including shock and angioderma have been reported and can be life-threatening. Symptoms may include those described for "Other Potential Health Effects".

## 11. TOXICOLOGICAL INFORMATION (Continued)

### OTHER POTENTIAL HEALTH EFFECTS-Therapeutic Doses:

Employees administering the product should not experience adverse effects if handled properly. Adverse effects from therapeutic doses have included (generally in less than 5% of patients):

- **Application Site Disorders:** Injection site pain.
- **Allergies:** Anaphylactic shock, angioderma.
- **Body as a Whole:** Edema, asthenia, back pain, fatigue, pain in legs or groin, rigors, chest pain, influenza-like symptoms hot flashes (sudden feelings of warmth or sweating), hair loss (alopecia), sudden weight loss or gain, numbness, tingling, weakness, paralysis.
- **Cardiovascular:** Palpitation, angina pectoris, heart disorder, transient increase in blood pressure (hypertension).
- **Endocrine:** Gynecomastia.
- **Gastrointestinal:** Constipation, diarrhea, vomiting, abdominal pain.
- **Hematological Disorders:** Thrombosis, anemia, lymphadenopathy, purpura, unusual bleeding or bruising.
- **Metabolic and Nutritional:** Cachexia, weight decrease, leg edema.
- **Musculoskeletal System:** Arthrosis, skeletal pain, arthralgia, muscle weakness, myalgia, decreased bone density in women, muscle, joint, or bone pains.
- **Neoplasms:** Tumor flare.
- **Nervous System:** Abnormal gait, paresthesia, headache, dizziness, spinal cord depression.
- **Psychiatric:** Confusion, anorexia, appetite increase, depression, nervousness, somnolence.
- **Reproductive System:** Decreased sexual desire or ability (impotence), other testis disorders, vaginal dryness, and abnormally heavy bleeding at menstruation, which may be associated with abnormally long periods, abnormal enlargement of breasts in men (gynaecomastia), genital swelling (edema).
- **Respiratory System:** Dyspnea, respiratory disorder, asthma, rhinitis.
- **Skin and Appendages:** Pruritus, skin disorders, sweating increase, swelling of the feet and legs.
- **Special Senses:** Tinnitus, abnormal vision, taste perversion.
- **Urinary System:** Urinary incontinence and retention, difficulty or pain on passing urine (dysuria), bladder pain, micturition frequency, urethral disorder, urinary tract infection, strangury, bloody or cloudy urine (hematuria).

**HEALTH EFFECTS OR RISKS FROM EXPOSURE: An Explanation in Lay Terms.** Overexposure to this product may cause the following health effects:

**ACUTE:** The primary health effects that may be experienced by medical personnel exposed to this product is mild irritation of contaminated skin. Anaphylactic reactions including shock and angioderma have been reported and can be life-threatening. In the event of exposures to therapeutic doses of this product, effects described in "Other Potential Health Effects" may result.



**CHRONIC:** Repeated skin contact may cause dermatitis (dry, red skin). In the event of exposures to therapeutic doses of this product, effects described in "Other Potential Health Effects" may result. Triptorelin Pamoate (the active component in this product) is a possible reproductive toxin. Individuals who have had allergic reactions to products containing Triptorelin Pamoate, any of the other ingredients in this product, other luteinizing hormone releasing hormone agonists, or luteinizing hormone releasing hormone may experience allergic reactions to this product.

**TARGET ORGANS:** ACUTE: Industrial Exposure: Skin, eyes. Therapeutic Doses: Gastrointestinal system, central nervous system. CHRONIC: Industrial Exposure: Skin. Therapeutic Doses: Cardiovascular system, urinary system, skin, gastrointestinal system, reproductive system, musculoskeletal system, and central nervous system.

**GENERAL TOXICITY INFORMATION:** Individuals who have had allergic reactions to prescription as well as to over-the-counter products containing estrogens and/or progestins may experience allergic reactions to this product. In rats, doses of 120, 600, and 3000 µg/kg given every 28 days (approximately 0.3, 2.0, and 8 times the recommended human therapeutic dose based on body surface area) resulted in increased mortality with a drug treatment period of 13-19 months. Anaphylactic reactions including shock and angioderma have been reported and can be life-threatening. Symptoms described in patients given therapeutic doses of this substance include the following.

For Females Only: Decreased bone density, vaginal dryness, and abnormally heavy bleeding at menstruation, which may be associated with abnormally long periods.

For Males Only: Abnormal enlargement of breasts (gynaecomastia).

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM			
<b>HEALTH HAZARD</b>	(BLUE)	2*	
<b>FLAMMABILITY HAZARD</b>	(RED)	1	
<b>PHYSICAL HAZARD</b>	(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

## 11. TOXICOLOGICAL INFORMATION (Continued)

### GENERAL TOXICITY INFORMATION (continued):

*For Males And Females:* Nausea, bone pain, vomiting, diarrhea, constipation, abdominal pain, decreased sexual desire or ability (impotence), difficulty or pain on passing urine (dysuria), bladder pain, bloody or cloudy urine, decrease in urine volume or frequency of urination, dizziness or drowsiness, headache, hot flashes (sudden feelings of warmth or sweating), visual disturbances, muscle, joint, or bone pains, swelling of the feet and legs, hair loss (alopecia), weight gain, difficulty breathing, chest pain, pain in your legs or groin, pain at the injection site, numbness, tingling, weakness, paralysis, lower back or side pain, transient increase in blood pressure, and unusual bleeding or bruising. A reduction in serum testosterone and accessory sexual organ atrophy can occur with prolonged use. These symptoms usually resolve after cessation of therapy. Rarely, therapeutic use had lead to spinal cord compression or urethral obstruction.

**IRRITANCY OF PRODUCT:** This product may irritate contaminated tissue.

**SENSITIZATION OF PRODUCT:** Individuals who have had allergic reactions to products containing Triptorelin Pamoate, any of the other ingredients in this product, other luteinizing hormone releasing hormone agonists, or luteinizing hormone releasing hormone may experience allergic reactions to this product. Anaphylactic reactions including shock and angioderma have been reported and can be life-threatening.

**TOXICITY DATA:** Currently, the following toxicity data are available for the active component of this product. Additional data are available for the other components of this product, but are not presented in this MSDS. Contact Watson Pharmaceuticals for more information.

#### TRIPTORELIN:

TDLo (Subcutaneous-Rat) 2.5 mg/kg/5 days-intermittent: Endocrine: androgenic; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol)

TDLo (Subcutaneous-Rat) 31 mg/kg/62 days-intermittent: Endocrine: androgenic; Tumorigenic: active as anti-cancer agent; Related to Chronic Data: changes in testicular weight

**CARCINOGENIC POTENTIAL:** No oncogenic effect was observed in mice administered Triptorelin for 18 months at doses up to 6000 µg/kg every 28 days (approximately 100 times the recommended monthly dose for a 70 kg human). In rats, doses of 120, 600 and 3000 µg/kg given every 28 days for 23 months (corresponding to approximately 2 to 50 times the 70 kg human dose) resulted in an approximate twofold increase in the incidence of benign pituitary tumors (adenomas of the pars distalis) at each dose level, leading to premature death. In contrast, there was no evidence of pituitary neoplasms after 6 months of treatment in dogs (up to 3000 µg/kg/month) or in monkeys (up to 200 µg/kg/day). The relevancy of pituitary tumor development in rats to humans has not been established.

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.

**REPRODUCTIVE TOXICITY INFORMATION:** Listed below is information concerning the effects of this product and its components on the human reproductive system. Triptorelin Pamoate is rated as a Pregnancy Category X (CONTRAINDICATED IN PREGNANCY, Fetal risk after drug administration outweighs any health benefit to patient). The reproductive effects described are related to therapeutic use of this product and are not reported to occur from industrial handling and exposure.

**Mutagenicity:** Mutagenicity studies performed with Triptorelin using bacterial and mammalian systems (in vitro Ames test and chromosomal aberration test in CHO cells and an *in vivo* mouse micronucleus test) provided no evidence of mutagenic potential.

**Embryotoxicity:** Studies in pregnant rats administered Triptorelin at doses of 2, 10, and 100 µg/kg/day (approximately equivalent to 0.2, 0.8, and 8 times the recommended human therapeutic dose based on body surface area) during the period of organogenesis displayed maternal toxicity and embryotoxicity.

**Teratogenicity:** Studies in pregnant rats administered Triptorelin at doses of 2, 10, and 100 µg/kg/day (approximately equivalent to 0.2, 0.8, and 8 times the recommended human therapeutic dose based on body surface area) during the period of organogenesis displayed no fetotoxicity or teratogenicity. Similarly, no teratogenic effects were observed when mice were administered doses of 2, 20, and 200 µg/kg/day (approximately equivalent to 0.1, 0.7, and 7 times the recommended human therapeutic dose based on body surface area).

**Reproductive Toxicity:** After 60 days of treatment followed by a minimum of four estrus cycles prior to mating, Triptorelin, at doses of 2, 20, and 200 µg/kg/day in saline (approximately 0.2, 2.0, and 16 times the recommended human therapeutic dose based on body surface area) or 20 µg/kg/day in slow release micro spheres, had no effect on the fertility or general reproductive performance of female rats. After 6 months treatment of Triptorelin as doses up to approximately 50 times recommended 70 kg human dose, macro- and microscopic changes in the reproductive organs of male monkeys and rats occurred. This is considered to be a reflection of suppressed gonadal function caused by the pharmacologic action of the drug. These effects mostly reversed upon cessation of treatment during a 2-4 month recovery period. Testicular changes have also been reported after prolonged administration of Triptorelin in patients with prostrate cancer.

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

**ACGIH BIOLOGICAL EXPOSURE INDICES (BEIs):** Currently, ACGIH Biological Exposure Indices (BEIs) have not been determined for the components of this product.

## 12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

**MOBILITY:** This product has not been tested for mobility in soil.

**PERSISTENCE AND BIODEGRADABILITY:** This product has not been tested for persistence or biodegradability. It is expected that the components will slowly degrade in the environment and form a variety of organic and inorganic materials; however, no specific information is known.

**BIO-ACCUMULATION POTENTIAL:** This product has not been tested for bio-accumulation potential.

**ECOTOXICITY:** All releases to terrestrial, atmospheric and aquatic environments should be avoided. No specific data is available for this product.

**OTHER ADVERSE EFFECTS:** This product does not contain any component with known ozone depletion potential.

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

## 13. DISPOSAL CONSIDERATIONS

**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. All gowns, gloves, and disposable materials used in the preparation or handling of this drug should be disposed of in accordance with established waste disposal procedures. Handle as if capable of transmitting infectious agents. Incineration is recommended. Reusable equipment should be cleaned with soap and water. Waste disposal must be in accordance with appropriate International, national, state, and local regulations. This product, if unaltered by use, may be disposed of by treatment at a permitted facility or as advised by your local waste regulatory authority. Shipment of wastes must be done with appropriately permitted and registered transporters.

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

**U.S. EPA WASTE NUMBER:** Not applicable.

**EWC WASTE CODE:** Wastes from natal care, diagnosis, treatment, or prevention of disease in humans: chemicals consisting of or containing dangerous substances, 18-01-06

## 14. TRANSPORTATION INFORMATION

**U.S. DEPARTMENT OF TRANSPORTATION REGULATIONS:** This product is NOT classified as dangerous goods, per U.S. DOT regulations, under 49 CFR 172.101.

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

**INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA):** This product is NOT classified as Dangerous Goods, by rules of IATA:

**INTERNATIONAL MARITIME ORGANIZATION (IMO):** This product is NOT classified as Dangerous Goods, per rules of IMO.

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

## 15. REGULATORY INFORMATION

### **ADDITIONAL UNITED STATES REGULATIONS:**

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

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

**U.S. CERCLA REPORTABLE QUANTITIES (RQ):** Not applicable.

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

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

**OTHER U.S. FEDERAL REGULATIONS:** Manufacturers, packers, and distributors of drug and drug products for human use are responsible for complying with the labeling, certification, and usage requirements as prescribed by the Federal Food, Drug, and Cosmetic Act, as amended (sections 201–902, 52 Stat. 1040 et seq., as amended; 21 U.S.C. 321–392). Based on this product's use, the requirements of the OSHA Bloodborne Pathogen Standard (29 CFR 1910.1030) are applicable.

## 15. REGULATORY INFORMATION (Continued)

### ADDITIONAL UNITED STATES REGULATIONS (continued):

**ANSI LABELING (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): CAUTION!** POSSIBLE BIRTH DEFECT HAZARD. CONTAINS MATERIAL THAT MAY CAUSE BIRTH DEFECTS BASED ON ANIMAL DATA. MAY CAUSE SKIN AND EYE IRRITATION. MAY CAUSE ALLERGIC REACTION AND CAN CAUSE ANAPHYLACTIC REACTIONS THAT ARE LIFE-THREATENING. Do not breathe dusts or particulates. Avoid contact with skin, eyes, and clothing. Wash thoroughly after handling. Wear gloves, goggles, and appropriate body protection during handling or administration. **FIRST-AID:** In case of contact, flush skin or eyes with plenty of water. If adverse respiratory reaction occurs from allergic reaction, give oxygen and seek immediate medical attention. If ingested, DO NOT induce vomiting—seek immediate medical attention. **IN CASE OF FIRE:** Use water fog, dry chemical, CO<sub>2</sub>, or “alcohol” foam. **IN CASE OF SPILL:** Pick up or sweep up spilled product. Place residual in appropriate container and seal. Dispose of according to applicable regulations. Consult Material Safety Data Sheet for additional information.

### ADDITIONAL CANADIAN REGULATIONS:

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

**CANADIAN ENVIRONMENTAL PROTECTION ACT (CEPA) PRIORITIES SUBSTANCES LISTS:** The components of this product are not on the CEPA Priorities Substances Lists.

**OTHER CANADIAN REGULATIONS:** Not applicable.

**CANADIAN WHMIS CLASSIFICATION AND SYMBOL:** 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 UNION REGULATIONS:

**EU LABELING AND 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.

### **INFORMATION FOR COMPONENTS:**

#### **ALL COMPONENTS:**

**Classification:** An official classification for this substance has not been published in Commission Directives.

## 16. OTHER INFORMATION

This Material Safety Data Sheet is offered pursuant to OSHA's Hazard Communication Standard, 29 CFR, 1910.1200. Other government regulations must be reviewed for applicability to this product. To the best of Watson Laboratories, Inc. knowledge, the information contained herein is reliable and accurate as of this date; however, accuracy, suitability or completeness are not guaranteed and no warranties of any type, either express or implied, are provided. The information contained herein relates only to this specific product. If this product is combined with other materials, all component properties must be considered. Data may be changed from time to time. Be sure to consult the latest edition.

#### **PREPARED BY:**

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#### **DATE OF PRINTING:**

March 29, 2010

### **DEFINITION OF TERMS**

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

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

#### **EXPOSURE LIMITS IN AIR:**

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

**DFG MAKs:** Federal Republic of Germany Maximum Concentration Values in the workplace. Exposure limits are given as TWA (Time-Weighted Average) or PEAK (short-term exposure) values.

**DFG MAK Germ Cell Mutagen Categories:** **1:** Germ cell mutagens that have been shown to increase the mutant frequency in the progeny of exposed humans. **2:** Germ cell mutagens that have been shown to increase the mutant frequency in the progeny of exposed mammals. **3A:** Substances that 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 that 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 that 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.

# DEFINITION OF TERMS

## EXPOSURE LIMITS IN AIR (continued):

**DFG MAK Pregnancy Risk Group Classification (continued): Group C:** There is no reason to fear a risk of damage to the developing embryo or fetus when MAK and BAT values are observed. **Group D:** Classification in one of the groups A–C is not yet possible because, although the data available may indicate a trend, they are not sufficient for final evaluation.

**IDLH:** Immediately Dangerous to Life and Health. This level represents a concentration from which one can escape within 30-minutes without suffering escape-preventing or permanent injury.

**LOQ:** Limit of Quantitation.

**NE:** Not Established. When no exposure guidelines are established, an entry of NE is made for reference.

**NIC:** Notice of Intended Change.

**NIOSH CEILING:** The exposure that shall not be exceeded during any part of the workday. If instantaneous monitoring is not feasible, the ceiling shall be assumed as a 15-minute TWA exposure (unless otherwise specified) that shall not be exceeded at any time during a workday.

**NIOSH RELS:** NIOSH's Recommended Exposure Limits.

**PEL:** 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 there is a danger of cutaneous absorption.

**STEL:** 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 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. Mechanical irritation may occur. PII or Draize = 0. *Eye Irritation:* Essentially non-irritating, minimal effects clearing in < 24 hours. Mechanical irritation may occur. Draize = 0. *Oral Toxicity LD<sub>50</sub> Rat:* > 5000 mg/kg. *Dermal Toxicity LD<sub>50</sub> Rat or Rabbit:* > 2000 mg/kg. *Inhalation Toxicity 4-hrs LC<sub>50</sub> Rat:* > 20 mg/L. Minor reversible injury may occur; may irritate the stomach if swallowed; may defat the skin and exacerbate existing dermatitis. **1 Slight Hazard:** *Skin Irritation:* Slightly or mildly irritating. PII or Draize > 0 < 5. *Eye Irritation:* Slightly to mildly irritating, but reversible within 7 days. Draize > 0 ≤ 25. *Oral Toxicity LD<sub>50</sub> Rat:* > 500–5000 mg/kg. *Dermal Toxicity LD<sub>50</sub> Rat or Rabbit:* > 1000–2000 mg/kg. *Inhalation Toxicity LC<sub>50</sub> 4-hrs Rat:* > 2–20 mg/L. **2 Moderate Hazard:** Temporary or transitory injury may occur; prolonged exposure may affect the CNS. *Skin Irritation:* Moderately irritating; primary irritant; sensitizer. PII or Draize ≥ 5, with no destruction of dermal tissue. *Eye Irritation:* Moderately to severely irritating; reversible corneal opacity; corneal involvement or irritation clearing in 8–21 days. Draize = 26–100, with reversible effects. *Oral Toxicity LD<sub>50</sub> Rat:* > 50–500 mg/kg. *Dermal Toxicity LD<sub>50</sub> Rat or Rabbit:* > 200–1000 mg/kg. *Inhalation Toxicity LC<sub>50</sub> 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 cause destruction of dermal tissue, skin burns, and 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<sub>50</sub> Rat:* > 1–50 mg/kg. *Dermal Toxicity LD<sub>50</sub> Rat or Rabbit:* > 20–200 mg/kg. *Inhalation Toxicity LC<sub>50</sub> 4-hrs Rat:* > 0.05–0.5 mg/L. **4 Severe Hazard:** Life-threatening; major or permanent damage may result from single or repeated exposures; extremely toxic; irreversible injury may result from brief contact. *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<sub>50</sub> Rat:* ≤ 1 mg/kg. *Dermal Toxicity LD<sub>50</sub> Rat or Rabbit:* ≤ 20 mg/kg. *Inhalation Toxicity LC<sub>50</sub> 4-hrs Rat:* ≤ 0.05 mg/L.

**FLAMMABILITY HAZARD: 0 Minimal Hazard:** Materials that will not burn in air when exposed 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 requires considerable pre-heating, under all ambient temperature conditions before ignition and combustion can occur. This usually includes the following: 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) (i.e. OSHA Class IIIB); and 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 with air. This usually includes the following: Liquids having a flash-point at or above 37.8°C (100°F); Solid materials in the form of coarse 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); and Solids and semisolids (e.g. viscous and slow flowing as asphalt) that readily give off flammable vapors.

## HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD

### RATINGS (continued):

**FLAMMABILITY HAZARD (continued): 3 Serious Hazard:** Liquids and solids that can be ignited under almost all ambient temperature conditions. Materials in this degree produce hazardous atmospheres with air under almost all ambient temperatures, or, unaffected by ambient temperature, are readily ignited under almost all conditions. This usually includes the following: Liquids having a flash point below 22.8°C (73°F) and having a boiling point at or above 38°C (100°F) and those liquids having a flash point at or above 22.8°C (73°F) and below 37.8°C (100°F) (i.e. 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); and 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 that will burn readily. This usually includes the following: 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) (i.e. OSHA Class IA); and Materials that ignite spontaneously when exposed to air at a temperature of 54.4°C (130°F) or below (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. *Compressed Gases:* No Rating. *Pyrophorics:* No Rating. *Oxidizers:* No 0 rating. *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 violently. *Explosives:* Division 1.5 & 1.6 explosives. 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 oxidizers; 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 explosion 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 explosives. Explosive substances where the explosive effects 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 oxidizers. Solids: any material that, either in concentration tested, exhibits a mean burning time of less than or equal to the mean burning time of a 2:3 potassium bromate/cellulose mixture and the criteria for Packing Group I are not met. Liquids: any material that exhibits a mean pressure rise time less than or equal to the pressure rise of a 1:1 aqueous sodium chlorate solution (40%)/cellulose mixture and the criteria for Packing Group I are not met. *Reactives:* Substances that may polymerize, decompose, condense, or self-react at ambient temperature and/or pressure, but have a low potential (or low risk) 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 1.3 explosives. 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 oxidizers. 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 (or moderate risk) 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 explosives. 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 (or high risk) to cause significant heat generation or explosion.

## DEFINITION OF TERMS (Continued)

### NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS:

**HEALTH HAZARD: 0** Materials that, under emergency conditions, would offer no hazard beyond that of ordinary combustible materials. Gases and vapors with an LC<sub>50</sub> for acute inhalation toxicity greater than 10,000 ppm. Dusts and mists with an LC<sub>50</sub> for acute inhalation toxicity greater than 200 mg/L. Materials with an LD<sub>50</sub> for acute dermal toxicity greater than 2000 mg/kg. Materials with an LD<sub>50</sub> for acute oral toxicity greater than 2000 mg/kg. Materials essentially non-irritating to the respiratory tract, eyes, and skin. **1** Materials that, under emergency conditions, can cause significant irritation. Gases and vapors with an LC<sub>50</sub> for acute inhalation toxicity greater than 5,000 ppm but less than or equal to 10,000 ppm. Dusts and mists with an LC<sub>50</sub> for acute inhalation toxicity greater than 10 mg/L but less than or equal to 200 mg/L. Materials with an LD<sub>50</sub> for acute dermal toxicity greater than 1000 mg/kg but less than or equal to 2000 mg/kg. Materials that slightly to moderately irritate the respiratory tract, eyes and skin. Materials with an LD<sub>50</sub> for acute oral toxicity greater than 500 mg/kg but less than or equal to 2000 mg/kg. **2** Materials that, under emergency conditions, can cause temporary incapacitation or residual injury. Gases with an LC<sub>50</sub> for acute inhalation toxicity greater than 3,000 ppm but less than or equal to 5,000 ppm. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC<sub>50</sub> for acute inhalation toxicity, if its LC<sub>50</sub> is less than or equal to 5000 ppm and that does not meet the criteria for either degree of hazard 3 or degree of hazard 4. Dusts and mists with an LC<sub>50</sub> for acute inhalation toxicity greater than 2 mg/L but less than or equal to 10 mg/L. Materials with an LD<sub>50</sub> for acute dermal toxicity greater than 200 mg/kg but less than or equal to 1000 mg/kg. Compressed liquefied gases with boiling points between -30°C (-22°F) and -55°C (-66.5°F) that cause severe tissue damage, depending on duration of exposure. Materials that are respiratory irritants. Materials that cause severe, but reversible irritation to the eyes or are lachrymators. Materials that are primary skin irritants or sensitizers. Materials whose LD<sub>50</sub> for acute oral toxicity is greater than 50 mg/kg but less than or equal to 500 mg/kg. **3** Materials that, under emergency conditions, can cause serious or permanent injury. Gases with an LC<sub>50</sub> for acute inhalation toxicity greater than 1,000 ppm but less than or equal to 3,000 ppm. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than 3000 ppm and that does not meet the criteria for degree of hazard 4. Dusts and mists with an LC<sub>50</sub> for acute inhalation toxicity greater than 0.5 mg/L but less than or equal to 2 mg/L. Materials with an LD<sub>50</sub> for acute dermal toxicity greater than 40 mg/kg but less than or equal to 200 mg/kg. Materials that are corrosive to the respiratory tract. Materials that are corrosive to the eyes or cause irreversible corneal opacity. Materials corrosive to the skin. Cryogenic gases that cause frostbite and irreversible tissue damage. Compressed liquefied gases with boiling points below -55°C (-66.5°F) that cause frostbite and irreversible tissue damage. Materials with an LD<sub>50</sub> for acute oral toxicity greater than 5 mg/kg but less than or equal to 50 mg/kg. **4** Materials that, under emergency conditions, can be lethal. Gases with an LC<sub>50</sub> for acute inhalation toxicity less than or equal to 1,000 ppm. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than ten times its LC<sub>50</sub> for acute inhalation toxicity, if its LC<sub>50</sub> is less than or equal to 1000 ppm. Dusts and mists whose LC<sub>50</sub> for acute inhalation toxicity is less than or equal to 0.5 mg/L. Materials whose LD<sub>50</sub> for acute dermal toxicity is less than or equal to 40 mg/kg. Materials whose LD<sub>50</sub> for acute oral toxicity is less than or equal to 5 mg/kg.

**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 of NFPA 704. **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 according with Annex D of NFPA 704. Liquids, solids, and semisolids having a flash point at or above 93.4°C (200°F) (i.e. Class IIB 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 Recommendations on the Transport of Dangerous Goods, Model Regulations* (current edition) and the related *Manual of Tests and Criteria* (current edition). Liquids with a flash point greater than 35°C (95°F) in a water-miscible solution or dispersion with a water non-combustible liquid/solid content of more than 85% 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 the 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). Most ordinary combustible materials. Solids containing greater than 0.5% by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent. **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 with 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% 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 (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.

### NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

**FLAMMABILITY HAZARD (continued): 3 (continued):** Flammable or combustible dusts with 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% 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% by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent.

**INSTABILITY HAZARD: 0** Materials that in themselves are normally stable, even under fire conditions. Materials that have an 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 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 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 are sensitive to localized thermal or mechanical shock 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.

### FLAMMABILITY LIMITS IN AIR:

Much of the information related to fire and explosion is derived from the National Fire Protection Association (NFPA). **Flash Point:** Minimum temperature at which a liquid gives off sufficient vapor to form an ignitable mixture with air near the surface of the liquid or within the test vessel used. **Autoignition Temperature:** Minimum temperature of a solid, liquid, or gas required to initiate or cause self-sustained combustion in air with no other source of ignition. **LEL:** Lowest concentration of a flammable vapor or gas/air mixture that will ignite and burn with a flame. **UEL:** Highest concentration of a flammable vapor or gas/air mixture that will ignite and burn with a flame.

### 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. **LD<sub>50</sub>:** Lethal Dose (solids & liquids) that kills 50% of the exposed animals. **LC<sub>50</sub>:** Lethal Concentration (gases) that kills 50% of the exposed animals. **ppm:** Concentration expressed in parts of material per million parts of air or water. **mg/m<sup>3</sup>:** 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. **TDLo:** Lowest dose to cause a symptom. **TCLo:** Lowest concentration to cause a symptom. **TD<sub>0</sub>, LDLo, and LD<sub>0</sub>:** or **TC, TC<sub>0</sub>, LCLo, and LCo:** Lowest dose (or concentration) to cause lethal or toxic effects. **Cancer Information: IARC:** International Agency for Research on Cancer. **NTP:** National Toxicology Program. **RTECS:** Registry of Toxic Effects of Chemical Substances. 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:** Effect concentration in water. **BCF:** Bioconcentration Factor, which is used to determine if a substance will concentrate in life forms that consume contaminated plant or animal matter. **TLm:** Median threshold limit. **log K<sub>ow</sub>** or **log K<sub>oc</sub>:** Coefficient of Oil/Water Distribution is used to assess a substance's behavior in the environment.

### REGULATORY INFORMATION:

#### U.S. and CANADA:

This section explains the impact of various laws and regulations on the material. **EPA:** U.S. Environmental Protection Agency. **ACGIH:** American Conference of Governmental Industrial Hygienists, a professional association that establishes exposure limits. **OSHA:** U.S. Occupational Safety and Health Administration. **NIOSH:** National Institute of Occupational Safety and Health, which is the research arm of OSHA. **WHMIS:** Canadian Workplace Hazardous Materials Information System. **DOT:** U.S. Department of Transportation. **TC:** Transport Canada. **SARA:** Superfund Amendments and Reauthorization Act. **DSL/NDL:** Canadian Domestic/Non-Domestic Substances List. **TSCA:** U.S. Toxic Substance Control Act. **CERCLA:** Comprehensive Environmental Response, Compensation, and Liability Act. Marine Pollutant status according to the DOT; CERCLA or Superfund; and various state regulations. This section also includes information on the precautionary warnings that appear on the material's package label.

#### EUROPE:

**EU:** European Union (formerly known as the EEC, European Economic Community). **EINECS:** European Inventory of Now-Existing Chemical Substances. **ARD:** European Agreement Concerning the International Carriage of Dangerous Goods by Road. **RID:** International Regulations Concerning the Carriage of Dangerous Goods by Rail.