MATERIAL SAFETY DATA SHEET

Product Name: Vincristine Sulfate Injection, USP

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

<table>
<thead>
<tr>
<th>Manufacturer Names And Addresses</th>
<th>Hospira, Inc.</th>
<th>Hospira Australia Pty Ltd</th>
</tr>
</thead>
<tbody>
<tr>
<td>275 North Field Drive</td>
<td>1 Lexia Place</td>
<td></td>
</tr>
<tr>
<td>Lake Forest, Illinois 60045</td>
<td>Mulgrave VIC 3170</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>AUSTRALIA</td>
<td></td>
</tr>
<tr>
<td>Emergency Telephone #'s</td>
<td>CHEMTREC: North America: 800-424-9300; International 1-703-527-3887; Australia (02) 8014 4880</td>
<td></td>
</tr>
<tr>
<td>Hospira, Inc., Non-Emergency</td>
<td>224 212-2055</td>
<td></td>
</tr>
<tr>
<td>Material Name</td>
<td>Vincristine Sulfate Injection, USP</td>
<td></td>
</tr>
<tr>
<td>Synonyms</td>
<td>Leurocristine sulfate; Oncovin®</td>
<td></td>
</tr>
</tbody>
</table>

2. HAZARD INFORMATION / CLASSIFICATION

Emergency Overview: Vincristine Sulfate Injection, USP contains vincristine sulfate, a salt of a vinca alkaloid that binds to microtubule proteins of the spindle, arresting cellular mitosis. Clinically, this product is used to treat some types of cancers. It is cytotoxic. In the workplace, this product should be considered very irritating to the skin, eyes, and respiratory tract, a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. Following an accidental over-exposure, possible target organs may include the bone marrow, gastrointestinal system, central nervous system, peripheral nervous system, kidneys, skin, gonads, and the fetus.

Occupational Exposure Potential: There are scientific studies that suggest that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity of these materials if workplace exposures are not properly controlled. The actual risk in the workplace is not known.

Signs and Symptoms: Vincristine sulfate is irritating to the skin and mucous membranes and extravasation may cause necrosis, cellulitis, and sloughing. This material should also be considered very irritating to the eyes and respiratory tract. In clinical use, adverse effects may include bone-marrow depression, anorexia, nausea and vomiting, and central and peripheral neurotoxicity. Other adverse effects include headache, malaise, dizziness, skin reactions, alopecia, dyspnea and bronchospasm, and infertility. Aspermia in men and amenorrhea in women have been reported following treatment.

Medical Conditions Aggravated by Exposure: Pre-existing hypersensitivity to vincristine sulfate or other vinca alkaloids. Pre-existing bone marrow, gastrointestinal, central nervous system, peripheral nervous system, neuromuscular, renal, gonadal, or skin ailments; or pregnancy.

Carcinogen Lists: IARC: Group 3 - not classifiable as to its carcinogenicity to humans. NTP: Not listed OSHA: Not listed

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Vincristine Sulfate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Formula</td>
<td>C_{46}H_{56}N_{4}O_{10}•H_{2}SO_{4}</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Component</th>
<th>Approximate Percent by Weight</th>
<th>CAS Number</th>
<th>RTECS Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vincristine Sulfate</td>
<td>0.1</td>
<td>2068-78-2</td>
<td>OH6340000</td>
</tr>
</tbody>
</table>

Non-hazardous ingredients include sterile water and 10% mannitol. Hazardous ingredients present at less than 1% include sodium hydroxide and/or sulfuric acid which are added to adjust the pH.
4. FIRST AID MEASURES

Eye Contact
Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Skin Contact
Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Inhalation
Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Ingestion
Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

5. FIRE FIGHTING MEASURES

Flammability
Non-flammable aqueous solution.

Fire & Explosion Hazard
None anticipated for this product.

Extinguishing Media
As with any fire, use extinguishing media appropriate for primary cause of fire.

Special Fire Fighting Procedures
Firefighters should wear self-contained breathing apparatus. Protective equipment and clothing should be worn to minimize contact with the respiratory tract, skin and eyes.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal
Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Absorb liquid with suitable material and clean affected area with soap and water. An undiluted solution of household bleach may be applied to the spill area for ten minutes to further inactivate this material. Absorb the liquid with an inert absorbent material (e.g. absorbent pad). Dispose of materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling
Vincristine sulfate is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastic agents to minimize potential exposures. Several guidelines on handling cytotoxic antineoplastic agents have been published. Consult your hygienist or safety professional for your site requirements.
7. HANDLING AND STORAGE: continued

Handling: continued Avoid ingestion, inhalation, skin contact, and eye contact. When handling, precautions may include the use of a containment cabinet. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials is required when working with this product.

Storage No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for antineoplastic agents. For product protection, follow USP controlled room temperature storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions Persons with known hypersensitivities to vincristine sulfate or other vinca alkaloids, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling this Product.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

<table>
<thead>
<tr>
<th>Component</th>
<th>OSHA-PEL</th>
<th>ACGIH-TLV</th>
<th>Hospira EEL</th>
<th>Other Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vincristine Sulfate</td>
<td>8-hr TWA: Not established</td>
<td>8-hr TWA: Not established</td>
<td>8-hr TWA: Not Established</td>
<td>NA</td>
</tr>
</tbody>
</table>

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
EEL: Employee Exposure Limit.
TWA: 8-hour Time Weighted Average.
STEL: 15-minute Short Term Exposure Limit.

Respiratory Protection Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N99 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA’s 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Skin Protection When handling this product, disposable gloves should be worn at all times. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability to this material. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.

Eye Protection As a minimum, the use of chemical safety goggles is recommended when handling this product.

Engineering Controls Good local exhaust ventilation is recommended to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is also recommended.
9. PHYSICAL/CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance/Physical State</td>
<td>Vincristine sulfate is a white to off-white powder. Vincristine Sulfate Injection, USP is a clear, colorless liquid in a vial.</td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless to faint vinegar-like odor</td>
</tr>
<tr>
<td>pH</td>
<td>4.0 to 5.0</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>NA</td>
</tr>
<tr>
<td>Flash Point:</td>
<td>NA</td>
</tr>
<tr>
<td>Flammability (solid, gas):</td>
<td>NA</td>
</tr>
<tr>
<td>Upper/Lower Flammability or Explosive Limits:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Pressure</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Density (Air =1)</td>
<td>NA</td>
</tr>
<tr>
<td>Evaporation Rate:</td>
<td>NA</td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>NA</td>
</tr>
<tr>
<td>Solubility</td>
<td>Soluble in methanol, freely soluble in water, but only slightly soluble in 95% ethanol.</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water:</td>
<td>NA</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>NA</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>NA</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>Not determined.</td>
</tr>
<tr>
<td>Chemical Stability</td>
<td>Stable under standard use and storage conditions.</td>
</tr>
<tr>
<td>Hazardous Reactions</td>
<td>Not determined</td>
</tr>
<tr>
<td>Conditions to avoid</td>
<td>Not determined</td>
</tr>
<tr>
<td>Incompatibilities</td>
<td>Sensitive to hydrolysis, oxidation and heat. Incompatible with strong oxidizing agents.</td>
</tr>
<tr>
<td>Hazardous Decomposition Products</td>
<td>Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx), nitrogen oxides (NOx), and sulfur oxides (SOx).</td>
</tr>
<tr>
<td>Hazardous Polymerization</td>
<td>Not anticipated to occur with this product.</td>
</tr>
</tbody>
</table>
## 11. TOXICOLOGICAL INFORMATION

### Acute Toxicity

<table>
<thead>
<tr>
<th>Ingredient(s)</th>
<th>Percent</th>
<th>Test Type</th>
<th>Route of Administration</th>
<th>Value</th>
<th>Units</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Vincristine Sulfate Injection</td>
<td>0.1</td>
<td>LD50</td>
<td>Oral</td>
<td>&gt; 1000</td>
<td>mg/kg</td>
<td>Rabbit</td>
</tr>
<tr>
<td>*Vincristine Sulfate Injection</td>
<td>0.1</td>
<td>LD50</td>
<td>Dermal</td>
<td>&gt; 1000</td>
<td>mg/kg</td>
<td>Rabbit</td>
</tr>
<tr>
<td>*Vincristine Sulfate</td>
<td>100</td>
<td>LC50(1hr)</td>
<td>Inhalation</td>
<td>&gt; 1200</td>
<td>mg/m3</td>
<td>Rat</td>
</tr>
<tr>
<td>Vincristine Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>1.9</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Vincristine Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>1.25</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Vincristine</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>1.3</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Vincristine Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>1.0</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Vincristine Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>1.7</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Vincristine</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>1.0</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Vincristine</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>3.0</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
</tbody>
</table>

LD50 is the dosage producing 50% mortality.

*Eli Lilly and Company MSDS

### Aspiration Hazard

None anticipated from normal handling of this product.

### Dermal Irritation/Corrosion

None anticipated from normal handling of this product. Moderate skin irritation was noted when applied to the skin of rabbits as a dilute (9%) aqueous solution for 24 hours. Based on clinical use, this product may be irritating to the skin.

### Ocular Irritation/Corrosion

Irritant. This product has produced severe eye irritation and pitting of the cornea followed by healing. Occupational exposure during manufacturing setting and in clinical settings has produced severe irritation, tearing, pain, and blurred vision.

### Dermal or Respiratory Sensitization

None anticipated from normal handling of this product. Rare instances of allergic reactions have occurred from clinical use of vincristine. No data on allergic sensitization potential from repeated skin contact were found.

### Reproductive Effects

Vincristine sulfate has been shown to impair fertility and to be embryocidal and teratogenic in mice, rats, hamsters, rabbits and monkeys at very low dosages (lowest LOAEL = 0.05 mg/kg). In monkeys, a single injection of vincristine at a dosage of 0.15-0.175 mg/kg on day 27 or 29 of gestation produced one fetus with encephalocele (skull defect) and one with syndactyly (webbing of fingers or toes). In rats, a single injection of vincristine at a dosage of 0.05-0.075 mg/kg on day 9 of gestation produced a high incidence of eye defects and some microcephaly and neural tube closure defects.

### Mutagenicity

Vincristine sulfate was not mutagenic Salmonella typhimurium with or without microsomal activation produced no chromosomal aberrations in CHO cells or in a Syrian hamster fibroblast cell line and failed to transform C3H/10T½ clone 8 cells. However, the drug did increase numerical and/or structural chromosomal aberrations in mouse bone-marrow cells and embryonic tissues. It also increased micronuclei formation in mouse bone-marrow cells and increased sister chromatid exchanges in a hamster cell line and human lymphocytes.

### Carcinogenicity

Vincristine sulfate was negative in one cancer study in rats and mice although the study was limited. Some patients who received chemotherapy with vincristine in combination with anti-cancer drugs known to be carcinogenic have developed second malignancies.

### Target Organ Effects

This product should be considered irritating to the skin, eyes and respiratory tract. Following an accidental over-exposure, possible target organs may include the bone marrow, gastrointestinal system, central nervous system, peripheral nervous system, kidneys, skin, gonads, and the fetus.
12. ECOLOGICAL INFORMATION

Aquatic Toxicity
Not determined.

Persistence/Biodegradability
Vincristine is not considered readily biodegradable; it degraded about 30% in a 28-day biodegradation assay.

Bioaccumulation
Not determined.

Mobility in Soil
Not determined.

General Notes
None

13. DISPOSAL CONSIDERATIONS

Waste Disposal
All waste materials must be properly characterized by the waste generator. Disposal should be performed in accordance with the federal, state or local regulatory requirements.

Container Handling and Disposal
Dispose of containers and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

DOT STATUS: Not Regulated
Proper Shipping Name: NA
Hazard Class: NA
UN Number: NA
Packing Group: NA
Reportable Quantity: NA

ICAO/IATA STATUS Not Regulated
Proper Shipping Name: NA
Hazard Class: NA
UN Number: NA
Packing Group: NA
Reportable Quantity: NA

IMDG STATUS Not Regulated
Proper Shipping Name: NA
Hazard Class: NA
UN Number: NA
Packing Group: NA
Reportable Quantity: NA

Notes: DOT – US Department of Transportation Regulations
15. REGULATORY INFORMATION

TSCA Status Exempt
CERCLA Status Not listed
SARA 302 Status Not listed
SARA 304 Status Not listed
SARA 313 Status Not listed
RCRA Status Not listed
PROP 65 (Calif.) This product is, or contains chemical(s) known to the State of California to cause developmental toxicity.


U.S. OSHA Classification Possibly Toxic by Ingestion
Irritant
Reproductive Toxin
Target Organ Toxin

GHS Classification* *Where medicinal products are not exempt, the recommended GHS workplace classification is as follows:

<table>
<thead>
<tr>
<th>Hazard Class</th>
<th>Acute Oral Toxicity</th>
<th>Eye Irritation</th>
<th>Toxic to Reproduction</th>
<th>Target Organ Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard Category</td>
<td>4</td>
<td>2B</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Symbol</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signal Word</td>
<td>Warning</td>
<td>Warning</td>
<td>Danger</td>
<td>Warning</td>
</tr>
<tr>
<td>Hazard Statement</td>
<td>Harmful if swallowed</td>
<td>Causes eye irritation</td>
<td>Suspected of damaging fertility or the unborn child</td>
<td>May cause damage to the include the bone marrow, gastrointestinal system, central nervous system, peripheral nervous system, kidneys, skin, and gonads through prolonged or repeated exposure.</td>
</tr>
</tbody>
</table>

GHS Precautionary Statements:

Prevention: Obtain special instructions before use.
Do not handle until all safety precautions have been read and understood.
Use personal protective equipment as required.
Avoid breathing aerosols or vapors.
In case of inadequate ventilation wear respiratory protection.
Wear protective gloves.
Contaminated work clothing should not be allowed out of the workplace.
Do not eat, drink or smoke when using this product.
Wash hands thoroughly after handling.

Response: IF SWALLOWED: Immediately call a POISON CENTER or doctor. Rinse mouth.
IF INHALED: If breathing is difficult, remove to fresh air and keep at rest in a position comfortable for breathing. If experiencing respiratory symptoms call a POISON CENTER or a doctor.
IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs, seek medical attention. Take off contaminated clothing and wash before reuse.
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention. If exposed or concerned, get medical attention.
15. REGULATORY INFORMATION: continued

EU Classification
*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance vincristine sulfate.

Classification(s):

<table>
<thead>
<tr>
<th>Harmful</th>
<th>Irritant</th>
<th>Toxic to Reproduction Category 2</th>
<th>Carcinogen Category 3</th>
</tr>
</thead>
</table>

Symbol:

Indication of Danger:

| Xn | Xi | T | Xn |

Risk Phrases:

- R22: Harmful if swallowed
- R36/37/38: Irritating to eyes, respiratory system, and skin
- R40: Limited evidence of a carcinogenic effect
- R41: Risk of serious damage to eyes
- R60: May impair fertility
- R61: May cause harm to the unborn child
- R64: May cause harm to breastfed babies

Safety Phrases:

- S23: Do not breathe vapor/spray
- S24: Avoid contact with the skin
- S25: Avoid contact with eyes
- S35: This material and its container must be disposed of in a safe way.
- S36/37/39: Wear suitable protective clothing, gloves and eye/face protection.

16. OTHER INFORMATION

Notes:

- ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value
- CAS: Chemical Abstracts Service Number
- CERCLA: US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
- DOT: US Department of Transportation Regulations
- EEL: Employee Exposure Limit
- IATA: International Air Transport Association
- LD₅₀: Dosage producing 50% mortality
- NA: Not applicable/Not available
- NE: Not established
- NIOSH: National Institute for Occupational Safety and Health
- OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
- Prop 65: California Proposition 65
- RCRA: US EPA, Resource Conservation and Recovery Act
- RTECS: Registry of Toxic Effects of Chemical Substances
- SARA: Superfund Amendments and Reauthorization Act
- STEL: 15-minute Short Term Exposure Limit
- TSCA: Toxic Substance Control Act
- TWA: 8-hour Time Weighted Average
16. OTHER INFORMATION: continued

MSDS Coordinator: Global Occupational Toxicology
Date Prepared: April 28, 2008
Revision Date: August 14, 2008
Revision Date: November 9, 2009

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