MATERIAL SAFETY DATA SHEET

Product Name: Fentanyl Citrate Injection

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address
Hospira Inc.
275 North Field Drive
Lake Forest, Illinois USA
60045

Emergency Telephone
CHEMTREC: North America: 800-424-9300;
International 1-703-527-3887; Australia (02) 8014 4880

Hospira, Inc., Non-Emergency 224-212-2000

Product Name Fentanyl Citrate Injection

Synonyms N-(1-Phenethyl-4-piperidyl) propionanilide citrate (1:1)

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name Fentanyl Citrate

Chemical Formula C_{22}H_{28}N_2O \cdot C_6H_8O_7

Preparation Non-hazardous ingredients include Water for Injection. May contain sodium hydroxide and/or hydrochloric acid for pH adjustment.

<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>Fentanyl Citrate</td>
<td>0.005</td>
<td>990-73-8</td>
<td>UE5600000</td>
</tr>
</tbody>
</table>

3. HAZARD INFORMATION

Carcinogen List

<table>
<thead>
<tr>
<th>Substance</th>
<th>IARC</th>
<th>NTP</th>
<th>OSHA</th>
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</thead>
<tbody>
<tr>
<td>Fentanyl Citrate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Emergency Overview

Fentanyl Citrate Injection is a solution containing fentanyl citrate, a potent narcotic analgesic. Clinically, fentanyl citrate is indicated as an analgesic to supplement general or regional anesthesia. In the US, fentanyl citrate is a Schedule C-II narcotic and has the potential for abuse. Prolonged use may cause dependence. In the workplace, this material should be considered potentially irritating to the eyes and respiratory tract, a potent drug, and a potential occupational reproductive hazard. Based on clinical use, possible target organs include the eyes, nervous system, respiratory system, cardiovascular system and fetus.

Occupational Exposure Potential

Information on the absorption of this product via inhalation is not available. When applied dermally as an aqueous solution to the forearm of human volunteers, fentanyl citrate was absorbed through the skin in significant amounts (about 18 %). Avoid liquid aerosol generation and skin contact.

Signs and Symptoms

None known from occupational exposure. In clinical use, adverse effects may include respiratory depression, apnea, muscle rigidity, and bradycardia. Other adverse effects have included hypotension/hypertension, dizziness, blurred vision, nausea, emesis, laryngospasm and...
diaphoresis. Local reactions such as rash, erythema, and itching have been reported with transdermal use.

**Medical Conditions Aggravated by Exposure**

Pre-existing hypersensitivity to this material and/or similar materials; pre-existing nervous system, respiratory system or cardiovascular system ailments.

### 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. In the presence of hypoventilation or apnea, oxygen should be administered and respiration should be assisted or controlled as indicated. A patent airway must be maintained; an oropharyngeal airway or endotracheal tube might be indicated. If depressed respiration is associated with muscular rigidity, an intravenous neuromuscular blocking agent might be required to facilitate assisted or controlled respiration. The patient should be carefully observed for 24 hours; body warmth and adequate fluid intake should be maintained. If hypotension occurs and is severe or persists, the possibility of hypovolemia should be considered and managed with appropriate parenteral fluid therapy. A specific narcotic antagonist such as naloxone should be available for use as indicated to manage respiratory depression. This does not preclude the use of more immediate countermeasures. The duration of respiratory depression following overdosage of fentanyl may be longer than the duration of narcotic antagonist action. Consult the package insert of the individual narcotic antagonists for details about use.

### 5. FIRE FIGHTING MEASURES

#### Flammability

None anticipated for this aqueous product.

#### Fire & Explosion Hazard

None anticipated for this aqueous product.

#### Extinguishing media

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

#### Special Fire Fighting Procedures

No special provisions required beyond normal fire fighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus.

### 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 the liquid with suitable material and clean affected area with soap and water. Dispose of spill materials according to the applicable federal, state, or local regulations.
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7. HANDLING AND STORAGE

Handling
No special handling required under conditions of normal product use. In the US, fentanyl citrate is a Schedule C-II controlled substance. Appropriate training and procedures may be required during the routine handling of this product.

Storage
No special storage required for hazard control. For product protection, follow storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions
No special precautions required for hazard control.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

<table>
<thead>
<tr>
<th>Component</th>
<th>Type</th>
<th>Exposure limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl Citrate</td>
<td>Not Applicable</td>
<td>mg/m3 ppm µg/m3</td>
</tr>
<tr>
<td></td>
<td>N/A N/A N/A</td>
<td>None Established</td>
</tr>
</tbody>
</table>

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
If skin contact with the product formulation is likely, the use of latex or nitrile gloves is recommended.

Eye protection
Eye protection is normally not required during intended product use. However, if eye contact is likely to occur, the use of chemical safety goggles (as a minimum) is recommended.

Engineering Controls
Engineering controls are normally not needed during the normal use of this product.

9. PHYSICAL/CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Appearance/Physical State</th>
<th>Liquid</th>
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<tbody>
<tr>
<td>Color</td>
<td>Clear, Colorless</td>
</tr>
<tr>
<td>Odor</td>
<td>NA</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>NA</td>
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<tr>
<td>pH</td>
<td>4.7 (4.0 to 7.5)</td>
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<tr>
<td>Melting point/Freezing point</td>
<td>NA</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point Range:</td>
<td>NA</td>
</tr>
<tr>
<td>Evaporation Rate</td>
<td>NA</td>
</tr>
<tr>
<td>Flammability (solid, gas):</td>
<td>NA</td>
</tr>
</tbody>
</table>
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Upper/Lower Flammability or Explosive Limits: NA
Vapor Pressure: NA
Vapor Density: NA
Specific Gravity: NA
Solubility: NA
Partition coefficient: n-octanol/water: NA
Auto-ignition temperature: NA
Decomposition temperature: NA

10. STABILITY AND REACTIVITY

Reactivity Not determined

Chemical Stability Stable under standard use and storage conditions

Hazardous Reactions Not determined

Conditions to avoid Not determined

Incompatibilities Not determined

Hazardous decomposition products Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx) and nitrogen oxides (NOx).

Hazardous Polymerization Not anticipated to occur with this product.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity
Not determined for the product formulation. Information for the ingredients is as follows:

<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>
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<tbody>
<tr>
<td>Fentanyl Citrate</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>18</td>
<td>mg/kg</td>
<td>Rat</td>
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<td></td>
<td></td>
<td>368</td>
<td>mg/kg</td>
<td>Mouse</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>mg/kg</td>
<td>Rat</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>10.1</td>
<td>mg/kg</td>
<td>Mouse</td>
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<td></td>
<td></td>
<td></td>
<td>14</td>
<td>mg/kg</td>
<td>Dog</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>0.03</td>
<td>mg/kg</td>
<td>Monkey</td>
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<tr>
<td>Fentanyl Citrate</td>
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<td>LD50</td>
<td>Intravenous</td>
<td>0.99, 3.0</td>
<td>mg/kg</td>
<td>Rat</td>
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<td></td>
<td>10.1</td>
<td>mg/kg</td>
<td>Mouse</td>
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<td>14</td>
<td>mg/kg</td>
<td>Dog</td>
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<td></td>
<td></td>
<td></td>
<td>0.03</td>
<td>mg/kg</td>
<td>Monkey</td>
</tr>
</tbody>
</table>

Aspiration Hazard None anticipated from normal handling of this product.

Dermal Irritation/Corrosion None anticipated from normal handling of this product.

Ocular Irritation/Corrosion None anticipated from normal handling of this product. However, inadvertent contact of this product with eyes may produce irritation with redness and tearing.

Dermal or Respiratory Sensitization None anticipated from normal handling of this product.
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Reproductive Effects

Fentanyl has been reported to impair fertility and to be embryocidal (an increase in resorptions in rats) when given at an intravenous dosage of 30 mcg/kg or at a subcutaneous dosage of 160 mcg/kg for 12 to 21 days. No teratogenic or other adverse fetal effects were noted in offspring when pregnant rats were treated throughout pregnancy with continuous infusions of 10 to 500 mcg/kg/day of fentanyl. Increased frequencies of death and developmental delays were noted in fetuses of pregnant mice given single injections of 14,500-16,000 mcg/kg of fentanyl.

The potential effects of fentanyl on male and female fertility were evaluated in rats. In a male fertility study, male rats were given fentanyl via continuous intravenous infusion at dosages of 0, 0.025, 0.1 or 0.4 mg/kg/day for 28 days prior to mating; female rats were not treated. In a female fertility study, male rats were given fentanyl via continuous intravenous infusion at dosages of 0, 0.025, 0.1 or 0.4 mg/kg/day for 14 days prior to mating until day 16 of pregnancy; male rats were not treated. Analysis of fertility parameters in both studies showed that intravenous dosages of fentanyl up to 0.4 mg/kg/day given to either the male or the female alone produced no effects on fertility. In a separate study, a single daily bolus dose of fentanyl was shown to impair fertility in rats when given in intravenous doses of 0.3 times the human dose for a period of 12 days.

The potential effects of fentanyl on embryo-fetal development were evaluated in rats, mice, and rabbits. Intravenous administration of fentanyl at dosages of 0, 0.01, or 0.03 mg/kg to female rats from gestation days 6 to 18 suggested evidence of embryotoxicity, and a slight increase in mean delivery time in the 0.03 mg/kg/day group. There was no clear evidence of teratogenicity noted.

Pregnant female New Zealand White rabbits were treated with fentanyl at dosages of 0, 0.025, 0.1, 0.4 mg/kg via intravenous infusion from days 6 to day 18 of pregnancy. Fentanyl produced a slight decrease in the body weight of the live fetuses at the high dose, an effect attributed to maternal toxicity. There was no evidence for fentanyl induced adverse effects on embryo-fetal development at doses up to 0.4 mg/kg in this study.

The potential effects of fentanyl on prenatal and postnatal development were examined in rats. Female Wistar rats were treated with dosages of 0, 0.025, 0.1, or 0.4 mg/kg/day fentanyl via intravenous infusion from day 6 of pregnancy through 3 weeks of lactation. At the high dose, fentanyl treatment significantly decreased body weight in male and female pups and also decreased survival in pups at day 4. Both the mid-dose and high-dose of fentanyl animals demonstrated alterations in development (delayed incisor eruption and eye opening) and transient behavioral development. * DURAGESIC® Package Insert 2009

Mutagenicity

There was no evidence of mutagenicity in the Ames Salmonella mutagenicity assay, the primary rat hepatocyte unscheduled DNA synthesis assay, the BALB/c 3T3 transformation test, and the human lymphocyte and CHO chromosomal aberration in-vitro assays. * DURAGESIC® Package Insert 2009

Carcinogenicity

In a two-year carcinogenicity study conducted in rats, fentanyl was not associated with an increased incidence of tumors at subcutaneous doses up to 33 mcg/kg/day in males or 100 mcg/kg/day in females (0.16 and 0.39 times the human daily exposure obtained via the 100 mcg/hour patch based on AUC0–24h comparison). * DURAGESIC® Package Insert 2009

Target Organ Effects

Based on clinical use, possible target organs include the eyes, nervous system,
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respiratory system, cardiovascular system and fetus.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity  Not determined for product
Persistence/Biodegradability  Not determined for product
Bioaccumulation  Not determined for product
Mobility in Soil  Not determined for product

13. DISPOSAL CONSIDERATIONS

Waste Disposal  All waste materials must be properly characterized. Further, disposal should be performed in accordance with the federal, state or local regulatory requirements.
Container Handling and Disposal  Dispose of container and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

ADR/ADG/DOT STATUS:  Not regulated
IMDG STATUS:  Not regulated
ICAO/IATA STATUS:  Not regulated
Transport Comments:  None

15. REGULATORY INFORMATION

USA Regulations

<table>
<thead>
<tr>
<th>Substance</th>
<th>TSCA Status</th>
<th>CERCLA Status</th>
<th>SARA 302 Status</th>
<th>SARA 313 Status</th>
<th>PROP 65 Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl Citrate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

RCRA Status  Not Listed
U.S. OSHA Classification  Target Organ Toxin
Possible Reproductive Toxin
Possible Irritant

GHS Classification  *In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user:

Hazard Class  Not Applicable
Hazard Category  Not Applicable
Product Name: Fentanyl Citrate Injection

Signal Word: Not Applicable
Symbol: Not Applicable


Hazard Statement: Not Applicable

Response: 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. Wash hands after handling.

Get medical attention if you feel unwell.

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

Classification(s): Not Applicable
Symbol: Not Applicable
Indication of Danger: Not Applicable
Risk Phrases: Not Applicable
Safety Phrases:
S23 - Do not breathe vapor.
S24 - Avoid contact with skin.
S25 - Avoid contact with eyes.
S37/39 - Wear suitable 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

MSDS Coordinator: Hospira GEHS
Date Prepared: 09/21/2011
Obsolete Date: 10/21/2008
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