1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

Material Name: Morphine Hydrochloride Oral Solution

- Trade Name: Morphine Mixture; RA-MORPH
- Chemical Family: Not determined
- Intended Use: Pharmaceutical active used as opioid analgesic

2. HAZARDS IDENTIFICATION

Appearance: Clear, colorless or pale yellow solution

Signal Word: WARNING

Statement of Hazard:
- May cause harm to the unborn child.
- May cause harm to breastfed babies.
- Possible mutagen

Additional Hazard Information:
- **Short Term:** May be harmful if swallowed. May cause eye irritation. (based on components).
- **Long Term:** Repeat-dose studies in animals have shown a potential to cause adverse effects on the developing fetus.

Known Clinical Effects:
- Ingestion of this material may cause effects similar to those seen in clinical use including dry mouth, drowsiness, headache, dizziness, nausea, vomiting, weakness, anxiety, blurred vision and dilated pupils. Cases of overdosage may also lead to respiratory depression, hypotension, coma, convulsions, cardiac arrhythmia, and tachycardia.

EU Indication of danger:
- Mutagenic Category 3
- Toxic to reproduction, Category 2

EU Hazard Symbols:

- ![X]

EU Risk Phrases:
- R61 - May cause harm to the unborn child.
- R64 - May cause harm to breastfed babies.
- R68 - Possible risk of irreversible effects.

Australian Hazard Classification (NOHSC):
Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Hazardous Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine hydrochloride</td>
<td>52-26-6</td>
<td>200-136-2</td>
<td>Mut.Cat.3, R68 Repr.Cat.2, R61 Xn; R22</td>
<td>0.1-5</td>
</tr>
<tr>
<td>Glycerol</td>
<td>56-81-5</td>
<td>200-289-5</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citric acid, anhydrous</td>
<td>77-92-9</td>
<td>201-069-1</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Sodium citrate</td>
<td>68-04-2</td>
<td>200-675-3</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Sodium Methyl p-Hydroxybenzoate</td>
<td>5026-62-0</td>
<td>225-714-1</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>(methylparaben sodium)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water for injection</td>
<td>7732-18-5</td>
<td>231-791-2</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

Additional Information: * Proprietary Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: Emits toxic fumes of carbon monoxide, carbon dioxide, nitrogen oxides, sulfur oxides and other sulfur-containing compounds.
MATERIAL SAFETY DATA SHEET

Material Name: Morphine Hydrochloride Oral Solution
Revision date: 08-Nov-2007

Fire Fighting Procedures: During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

Fire / Explosion Hazards: Not applicable

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Measures for Cleaning / Collecting: Contain the source of the spill if it is safe to do so. Absorb spills with non-combustible absorbent material and transfer into a labeled container for disposal.

Measures for Environmental Protections: Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

General Handling: Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8).

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Refer to available public information for specific member state Occupational Exposure Limits.

Glycerol

<table>
<thead>
<tr>
<th>Origin</th>
<th>Threshold Limit Value (TWA)</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH TWA</td>
<td>= 10 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>Australia TWA</td>
<td>= 10 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>Belgium OEL - TWA</td>
<td>= 10 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>Estonia OEL - TWA</td>
<td>= 10 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>Finland OEL - TWA</td>
<td>= 20 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>France OEL - TWA</td>
<td>= 10 mg/m³ VME</td>
<td></td>
</tr>
<tr>
<td>Greece OEL - TWA</td>
<td>= 10 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>Ireland OEL - TWAs</td>
<td>= 10 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>Netherlands OEL - TWA</td>
<td>= 10 mg/m³ MAC</td>
<td></td>
</tr>
<tr>
<td>OSHA - Final PELS - TWAs:</td>
<td>= 15 mg/m³ TWA total</td>
<td></td>
</tr>
<tr>
<td></td>
<td>= 5 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>Poland OEL - TWA</td>
<td>= 10 mg/m³ NDS</td>
<td></td>
</tr>
<tr>
<td>Portugal OEL - TWA</td>
<td>= 10 mg/m³ TWA</td>
<td></td>
</tr>
<tr>
<td>Spain OEL - TWA</td>
<td>= 10 mg/m³ VLA-ED</td>
<td></td>
</tr>
</tbody>
</table>

The purpose of the Occupational Exposure Band (OEB) classification system is to separate substances into different Hazard categories when the available data are sufficient to do so, but inadequate to establish an Occupational Exposure Limit (OEL). The OEB given is based upon an analysis of all currently available data; as such, this value may be subject to revision when new information becomes available.

Morphine hydrochloride

**Pfizer Occupational Exposure Band (OEB):** OEB3 (control exposure to the range of >10ug/m³ to < 100ug/m³)
Engineering Controls: Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Personal Protective Equipment:

Hands: Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.

Eyes: Wear safety glasses or goggles if eye contact is possible.

Skin: Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

Respiratory protection: If airborne exposures are within or exceed the Occupational Exposure Band (OEB) range, wear an appropriate respirator with a protection factor sufficient to control exposures to the bottom of the OEB range.

9. PHYSICAL AND CHEMICAL PROPERTIES:

<table>
<thead>
<tr>
<th>Physical State:</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color:</td>
<td>Clear, colorless or Pale yellow</td>
</tr>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
</tr>
<tr>
<td>Molecular Weight:</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

Stability: Stable under normal conditions of use.

Conditions to Avoid: None known

Incompatible Materials: As a precautionary measure, keep away from strong oxidizers

11. TOXICOLOGICAL INFORMATION

General Information: The information included in this section describes the potential hazards of various forms of the active ingredient. The remaining information describes the potential hazards of the individual ingredients.

Acute Toxicity: (Species, Route, End Point, Dose)

**Citric acid, anhydrous**

Rat Oral LD50 3000 mg/kg

**Morphine Sulfate**

Rat Oral LD50 461 mg/kg
Rat Intravenous LD50 70 mg/kg
Rat Intraperitoneal LD50 235 mg/kg
Mouse Oral LD50 600 mg/kg
Mouse Intravenous LD50 156 mg/kg

**Morphine hydrochloride**

Rat Oral LD50 335 mg/kg
Mouse Oral LD50 745 mg/kg
Rat Subcutaneous LD50 480 mg/kg
Glycerol
Rat  Oral  LD 50  12600 mg/kg

**Irritation / Sensitization: (Study Type, Species, Severity)**

**Citric acid, anhydrous**
Eye Irritation  Rabbit  Severe
Skin Irritation  Rabbit  Mild

**Glycerol**
Skin Irritation  Rabbit  Mild
Eye Irritation  Rabbit  Mild

**Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)**

**Morphine Sulfate**
- 18 Week(s)  Rat  Oral  60 g/kg  LOAEL  Lungs
- 15 Day(s)  Rat  Subcutaneous  3144 mg/kg  LOAEL  Kidney, Ureter, Bladder
- 9 Week(s)  Rat  Subcutaneous  3150 mg/kg  LOAEL

**Glycerol**
- 28 Day(s)  Rat  Oral  16800 mg/kg  LOAEL  Endocrine system

**Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))**

**Morphine Sulfate**
- Embryo / Fetal Development  Mouse  Subcutaneous  0.15 mg/kg  LOAEL  Teratogenic
- Embryo / Fetal Development  Hamster  Subcutaneous  35 mg/kg  LOAEL  Teratogenic
- Embryo / Fetal Development  Mouse  Oral  200 mg/kg  LOAEL  Teratogenic
- Embryo / Fetal Development  Rat  Subcutaneous  35 mg/kg  LOAEL  Fetotoxicity

**Glycerol**
- Reproductive & Fertility-Males  Rat  Oral  100 mg/kg  LOEL  Fertility

**Genetic Toxicity: (Study Type, Cell Type/Organism, Result)**

**Morphine Sulfate**
- *In Vivo* Micronucleus  Mouse  Positive
- *In Vivo* Chromosome Aberration  Mouse Lymphocytes  Positive
- *In Vitro* Direct DNA Damage  Human Lymphocytes  Positive
- *In Vitro* Chromosome Aberration  Mouse  Negative

**Dominant Lethal Assay**  Drosophila  Negative

**Carcinogen Status:** None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

### 12. ECOLOGICAL INFORMATION

**Environmental Overview:** Environmental properties of the formulation have not been thoroughly investigated. Releases to the environment should be avoided.
13. DISPOSAL CONSIDERATIONS

Disposal Procedures: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered.

14. TRANSPORT INFORMATION

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

EU Symbol: Xn
EU Indication of danger: Mutagenic Category 3
Toxic to reproduction, Category 2

EU Risk Phrases: R61 - May cause harm to the unborn child.
R64 - May cause harm to breastfed babies.
R68 - Possible risk of irreversible effects.

EU Safety Phrases: S23 - Do not breathe fumes/vapour/spray.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label: WARNING
May cause harm to the unborn child.
May cause harm to breastfed babies.
Possible mutagen

Canada - WHMIS: Classifications

WHMIS hazard class: D1b toxic materials
D2a very toxic materials

Morphine hydrochloride

PZ00694
16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.
R61 - May cause harm to the unborn child.
R64 - May cause harm to breastfed babies.
R68 - Possible risks of irreversible effects.

Data Sources: Publicly available toxicity information. Pfizer proprietary drug development information. Safety data sheets for individual ingredients.

Prepared by: Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety

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End of Safety Data Sheet