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

Material Name: Penicillin G procaine, Dihydrostreptomycin sulfate aqueous injection

Trade Name: Combiotic Injectable Suspension

Chemical Family: Mixture

Intended Use: Pharmaceutical product used as antibiotic agent

2. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS List</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G procaine</td>
<td>54-35-3</td>
<td>200-205-7</td>
<td>15-20</td>
</tr>
<tr>
<td>Lecithin</td>
<td>8002-43-5</td>
<td>232-307-2</td>
<td>*</td>
</tr>
<tr>
<td>Sodium formaldehyde sulfoxylate dihydrate</td>
<td>6035-47-8</td>
<td>Not listed</td>
<td>*</td>
</tr>
<tr>
<td>Sodium phosphite pentahydrate</td>
<td>13517-23-2</td>
<td>Not listed</td>
<td>*</td>
</tr>
<tr>
<td>Procaine hydrochloride</td>
<td>51-05-8</td>
<td>200-077-2</td>
<td>*</td>
</tr>
<tr>
<td>Dihydrostreptomycin sulfate</td>
<td>1425-61-2</td>
<td>215-843-1</td>
<td>25-30</td>
</tr>
<tr>
<td>Urea (45%)</td>
<td>57-13-6</td>
<td>200-315-5</td>
<td>*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS List</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium citrate, dihydrate</td>
<td>6132-04-3</td>
<td>Not listed</td>
<td>*</td>
</tr>
<tr>
<td>Water for injection</td>
<td>7732-18-5</td>
<td>231-791-2</td>
<td>*</td>
</tr>
<tr>
<td>Butylparaben</td>
<td>94-26-8</td>
<td>202-318-7</td>
<td>*</td>
</tr>
<tr>
<td>Povidone</td>
<td>9003-39-8</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.

3. HAZARDS IDENTIFICATION

Appearance: White to slightly yellow homogeneous suspension

Signal Word: WARNING

Statement of Hazard:

- May cause allergic reaction.
- May cause ototoxicity (harmful effects on the ear).
- May cause kidney effects
Short Term: May cause allergic reactions in susceptible individuals. Individuals who are allergic to penicillin antibiotics could have allergic reaction, possibly severe. If an allergic reaction occurs, the worker should be removed to the nearest emergency room and the appropriate therapy instituted.

Known Clinical Effects: Common adverse reactions associated with the clinical use of streptomycin include vestibular ototoxicity (nausea, vomiting, and vertigo); parasthesia of face; rash; fever; urticaria; angioneurotic edema; and eosinophilia. Streptomycin can cause fetal harm (ototoxicity) when administered to a pregnant woman. May cause effects similar to those generally seen in clinical use of antibiotics including gastrointestinal irritation, vomiting, transient diarrhea, nausea, and abdominal pain.

EU Indication of danger: Toxic to reproduction: Category 1
Irritant

EU Hazard Symbols: 

R43 - May cause sensitization by skin contact.
R61 - May cause harm to the unborn child.

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the product or its ingredients 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.

4. FIRST AID MEASURES

Eye Contact: Immediately flush eyes with water for at least 15 minutes. If irritation occurs or persists, get medical attention.

Skin Contact: Wash skin with soap and water. Remove contaminated clothing and shoes. This material may not be completely removed by conventional laundering. Consult professional laundry service. Do not home launder. If irritation occurs or persists, get medical attention.

Ingestion: Get medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. Get medical attention immediately.

5. FIRE FIGHTING MEASURES

Extinguishing Media: As for primary cause of fire.

Hazardous Combustion Products: Not known

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 spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

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: Use only in a well-ventilated area. Avoid contact with skin and clothing. Avoid breathing vapor or mist.

Storage Conditions: Store under refrigeration in closed container.

Storage Temperature: 2 - 8°C

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

No Occupational Exposure Limit (OEL) or Short Term Exposure Limit (STEL) has been identified.

Engineering Controls: Good general ventilation should be sufficient to control airborne levels. Engineering controls should be used as the primary means to control exposures. Local and general ventilation should be used as necessary, when handling this material in bulk.

Personal Protective Equipment:

- Hands: Rubber gloves
- Eyes: Wear safety glasses or goggles if eye contact is possible.
- Skin: None required with normal use of this material. Wear protective clothing with long sleeves when working with large quantities. Wash hands and arms thoroughly after handling this material. Clean up spills immediately.
- Respiratory protection: Whenever excessive air contamination (dust, mist, vapor) is generated, respiratory protection, with appropriate protection factors, should be used to minimize exposure.

9. PHYSICAL AND CHEMICAL PROPERTIES:

- Physical State: Homogenous Suspension
- Molecular Formula: Mixture
- Color: White to slightly yellow
- Molecular Weight: Mixture
- pH: 6.3 - 6.7
- Flash Point (Liquid) (°C): Non-flammable

10. STABILITY AND REACTIVITY

Stability: Stable
### 11. TOXICOLOGICAL INFORMATION

**General Information:**
There are no data for this formulation. The information included in this section describes the potential hazards of various forms of the active ingredients. The remaining information describes the potential hazards of the individual ingredients.

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

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Species</th>
<th>Route</th>
<th>End Point</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dihydrostreptomycin sulfate</td>
<td>Mouse</td>
<td>Oral</td>
<td>LD50</td>
<td>&gt; 600 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Rat</td>
<td>SC</td>
<td>LD50</td>
<td>1100 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Mouse</td>
<td>IP</td>
<td>LD50</td>
<td>1380 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Rat</td>
<td>IV</td>
<td>LD50</td>
<td>137 mg/kg</td>
</tr>
<tr>
<td>Lecithin</td>
<td>Rat</td>
<td>Oral</td>
<td>LD50</td>
<td>&gt; 8 ml/kg</td>
</tr>
<tr>
<td>Penicillin G procaine</td>
<td>Mouse</td>
<td>Oral</td>
<td>LD50</td>
<td>&gt; 2000 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Rat</td>
<td>Oral</td>
<td>LD50</td>
<td>&gt; 2000 mg/kg</td>
</tr>
<tr>
<td>Povidone</td>
<td>Rat</td>
<td>Oral</td>
<td>LD50</td>
<td>100 g/kg</td>
</tr>
<tr>
<td>Procaine hydrochloride</td>
<td>Rat</td>
<td>IP</td>
<td>LD50</td>
<td>160 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Rat</td>
<td>IV</td>
<td>LD50</td>
<td>38 mg/kg</td>
</tr>
<tr>
<td>Urea (45%)</td>
<td>Rat</td>
<td>Oral</td>
<td>LD50</td>
<td>8471 mg/kg</td>
</tr>
</tbody>
</table>

**Acute Toxicity Comments:**
A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

**Inhalation Acute Toxicity**
Allergic reactions might occur based on effects of the individual components.

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

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Study Type</th>
<th>Species</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (45%)</td>
<td>Skin</td>
<td>Human</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Eye</td>
<td>Rabbit</td>
<td>Moderate</td>
</tr>
<tr>
<td>Eye Irritation / Sensitization</td>
<td>No data available</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Irritation / Sensitization</td>
<td>Streptomycin and penicillins are known to cause contact dermatitis and allergic reactions in sensitive individuals. Hypersensitivity reactions can occur in individuals sensitive to penicillin, streptomycin, and/or other aminoglycosides.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Duration</th>
<th>Species</th>
<th>Route</th>
<th>Dose</th>
<th>End Point</th>
<th>Target Organ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dihydrostreptomycin sulfate</td>
<td>75 Day(s)</td>
<td>Monkey</td>
<td>Intramuscular</td>
<td>9375 mg/kg/day</td>
<td>LOEL</td>
<td>None identified</td>
</tr>
<tr>
<td>Subchronic Effects</td>
<td>In subchronic oral studies in mice and rats, doses up to 3000 mg/kg of penicillin V potassium resulted in lesions of the glandular stomach and/or forestomach.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Chronic Effects/Carcinogenicity
No evidence of carcinogenicity was seen in long-term animal studies conducted by the US National Toxicology Program (NTP) with penicillin V potassium. Low incidences of non-cancerous lesions in the nasal mucosa, lung and stomach were noted.

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

Dihydrostreptomycin sulfate
Reproductive & Fertility Rat Intramuscular 7500 mg/kg/day LOEL Developmental toxicity
Reproductive Effects Reproductive studies with penicillins in mice, rats, and rabbits revealed no evidence of fertility impairment.
Teratogenicity Streptomycin can cause fetal harm (ototoxicity) when administered to pregnant women. Teratogenicity studies in mice, rats, rabbits, and guinea pigs have not shown adverse effects due to streptomycin administration during pregnancy, with the possible exception of ototoxicity.
Mutagenicity There are negative results reported for bacterial assays and mixed results for mammalian cell assays conducted with penicillins. Penicillins are not generally regarded as mutagenic.
Carcinogen Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.
Povidone
IARC: Group 3
At increase risk from exposure: Allergy to penicillins, streptomycins, and/or other aminoglycosides Individuals with impaired kidney function.

12. ECOLOGICAL INFORMATION

Environmental Overview: The environmental characteristics of this mixture have not been fully evaluated. Releases to the environment should be avoided.

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Urea (45%)
Daphnia Magna EC-50 24 Hours > 10,000 mg/L
Aquatic Toxicity Comments: A greater than symbol (>) indicates that aquatic toxicity was not observed at the maximum dose tested.

13. DISPOSAL CONSIDERATIONS

Disposal Procedures: Dispose of waste in accordance with all applicable laws and regulations.

14. TRANSPORT INFORMATION

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

**EU Symbol:**
T

**EU Indication of danger:**
Toxic to reproduction: Category 1
Irritant

**EU Risk Phrases:**
R43 - May cause sensitization by skin contact.
R61 - May cause harm to the unborn child.

**EU Safety Phrases:**
S24 - Avoid contact with skin.
S36 - Wear suitable protective clothing.
S53 - Avoid exposure - obtain special instructions before use.

**OSHA Label:**
WARNING
May cause allergic reaction.
May cause ototoxicity (harmful effects on the ear).
May cause kidney effects

**Canada - WHMIS: Classifications**

**WHMIS hazard class:**
Class D, Division 2, Subdivision A

**Penicillin G procaine**
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
- EU EINECS List: 200-205-7

**Lecithin**
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present

**Sodium citrate, dihydrate**
- Australia (AICS): Present

**Water for injection**
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS List: 231-791-2

**Butylparaben**
- Inventory - United States TSCA - Sect. 8(b): Present
16. OTHER INFORMATION

Reasons for Revision: Updated Section 3 - Hazard Identification. Updated Section 5 - Fire Fighting Measures. Updated Section 6 - Accidental Release Measures. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 11 - Toxicology Information. Updated Section 12 - Ecological Information. Updated Section 13 - Disposal Considerations. Updated Section 15 - Regulatory Information.

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

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without a warranty of any kind, expressed or implied.

End of Safety Data Sheet