1. **Product and Company Identification**

   **Manufactured/Supplied by**
   U.S. HUMAN HEALTH
   A Division of Merck & Co., Inc.
   P.O. Box 4
   West Point, PA  19486

   **Emergency Telephone Number**
   1-800-NSC-MERCK (1-800-672-6372)
   Merck National Service Center (MNSC)

   **Label Name**
   COSMEGEN®

   **Chemical Name**
   Not applicable.

   **Synonyms**
   Dactinomycin; Actinomycin-D; Meractinomycin

   **Material Product Number**
   3298; **NDC #** 0006-3298-22

   **Intended Use**
   Antineoplastic agent.

2. **Composition/Information on Ingredients**

<table>
<thead>
<tr>
<th>Component</th>
<th>Molecular Formula</th>
<th>Molecular weight</th>
<th>CAS Number</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DACTINOMYCIN</td>
<td>C62H86N12O16</td>
<td>1255.47</td>
<td>50-76-0</td>
<td>2.4</td>
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<tr>
<td>MANNITOL</td>
<td>C6H14O6</td>
<td>182.17</td>
<td>69-65-8</td>
<td>97.6</td>
</tr>
</tbody>
</table>

   **EC Label**
   Exempt from the EU Dangerous Substances Directive.

3. **Hazards Identification**

   **Appearance**
   Sterile, yellow to orange lyophilized powder. When reconstituted, COSMEGEN is a clear, gold-colored solution.

   **Emergency Overview**
   DANGER!
   FINISHED PHARMACEUTICAL PRODUCT
   CYTOTOXIC ANTINEOPLASTIC AGENT
   HIGHLY TOXIC IF SWALLOWED OR INHALED. CAUSES RESPIRATORY TRACT, MUCOUS MEMBRANE, EYE AND SKIN BURNS.
   CAUSES BONE MARROW SUPPRESSION.
   CAN CAUSE BIRTH DEFECTS.
   CAN CAUSE CANCER.

   Do not get on skin or clothing. Do not get in eyes, on skin or on clothing. Do not ingest. Avoid breathing dust. Keep container closed. Use only with adequate ventilation. Avoid exposure during pregnancy. Wash thoroughly after handling.

   **Potential Health Effects**
   See Section 11 for detailed information.

*** Continued on next page ***
4. **First Aid Measures**

**Eye Contact**
In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention immediately.

**Skin Contact**
In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Contaminated clothing should be destroyed. Thoroughly clean shoes before reuse. Get medical attention immediately.

**Inhalation**
If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

**Ingestion**
If swallowed, do not induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Get medical attention immediately.

**Notes to physician**
DACTINOMYCIN: No known antidote. Treat supportively and symptomatically.

5. **Fire Fighting Measures**

**Flash Point**
Not applicable.

**Flammable Limits (% in air)**
Not applicable.

**Autoignition Temperature**
Not applicable.

**Oxidizing Properties**
Not available

**Combustibility Information**
MANNITOL: May form combustible dust concentrations in air.

**Dust Explosivity Information**
Not available

**Shock Sensitivity**
Not available

**Fire/Explosion Hazards**
MANNITOL: May burn but does not ignite readily.
DACTINOMYCIN: Compound, if released in a fire, may pose a significant toxic risk to fire fighters.

**Special Fire Procedures**
Fire fighters should wear positive pressure self-contained breathing apparatus (SCBA) and full turnout gear.

**Extinguishing Media**
In case of fire, use water spray (fog), foam or dry chemicals.

**Hazardous Decomposition Products**
These products are carbon oxides, nitrogen oxides.

6. **Accidental Release Measures**

**Personal Precautions**
Immediately contact emergency personnel. Keep unnecessary personnel away. Use suitable protective equipment (Section 8). Follow all fire fighting procedures (Section 5).

*** Continued on next page ***
Methods for cleaning up

Entrainment of spilled dust must be minimized. To decontaminate spills, HEPA vacuum solid material and apply 4.4 milliliters of 5% trisodium phosphate (TSP) to the contaminated surface for every milligram of Dactinomycin spilled. A contact time with TSP for 30 minutes is recommended. Wipe with a rag. Place collected solid material in an appropriate container for disposal. Waste solution is not longer genotoxic and may be disposed of down the sink.

Soak equipment/utensils for 30 minutes with 4.4 milliliters of 5% trisodium phosphate for every (estimated) milligram of Dactinomycin to destroy all trace amounts of dactinomycin. This solution is no longer genotoxic and may be disposed of down the sink.

For additional assistance in the U.S., CHEMTREC provides a toll-free Hotline for chemical emergencies regarding spills, leaks, exposure or accidents: 1-800-424-9300.
For emergency calls from outside the U.S.: 1-703-527-3887

7. Handling and Storage

Handling

Do not get in eyes, on skin or on clothing. Do not ingest. Do not breathe dust. Keep container closed. Use only with adequate ventilation. Avoid exposure during pregnancy. Wash thoroughly after handling.

Due to the drug’s toxic and mutagenic properties, open handling is not recommended for the preparation of COSMEGEN. The National Institute of Health presently recommends that the preparation of injectable antineoplastic drugs should be performed in a Class II biological safety cabinet (BSC) and that personnel preparing drugs of this class should wear appropriate personal protective equipment (Section 8).

Storage

Keep container tightly closed. Keep container in a cool, well-ventilated area. Store at room temperature 25°C (77°F) or lower. Protect from light. Protect from moisture.

8. Exposure Controls/Personal Protection

Exposure Guidelines

<table>
<thead>
<tr>
<th>Component</th>
<th>OSHA Permissible Exposure Limit (PEL)</th>
<th>ACGIH Threshold Limit Value (TLV)</th>
<th>Merck Exposure Control Limit (ECL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DACTINOMYCIN</td>
<td>Not established</td>
<td>Not established</td>
<td>PB-ECL Category 4*</td>
</tr>
<tr>
<td>MANNITOL</td>
<td>Not established</td>
<td>Not established</td>
<td>Not established</td>
</tr>
</tbody>
</table>

ADI = 0.1 ug/day
Wipe Test Criteria = 0.1 ug/100 cm²

*PB-ECL Category 4. A containment-oriented approach should be used to maintain potential exposure levels as low as possible, and preferably non-detectable, below 0.01 ug/m³. PB-ECL category is an internal Merck control band.
Analytical methods should be sensitive enough to detect the compound at or below these values.

Engineering Controls

*** Continued on next page ***
**Ventilation**

Ventilation is not necessary for sealed vials. Vials should be reconstituted in a Class II biological safety cabinet (BSC).

**Personal Protective Equipment**

**Eye/Face Protection**

Safety glasses should be worn when reconstituting compound. Splash goggles, face shield, or other full-face protection are recommended when potential exists for direct exposure.

**Hand/Arm Protection**

Use surgical (or chemo) latex or PVC gloves when handling or reconstituting vials. Double gloving is recommended. Additional body garments should be used based upon the task being performed (e.g. sleeveless, apron, gauntlets, disposable suits).

**Respiratory Protection**

No respiratory protection required when handling sealed vials. As an adjunct to engineering controls, use an approved, properly fitted, powered-air purifying respirator, or respirator of equivalent or greater protection, as an adjunct to engineering controls, if the potential exists for exposure to airborne aerosols.

**Additional Protective Equipment**

None required when handling sealed vials. Disposable work uniform, preferably made of Tyvek or a closed front surgical-type gown with knit cuffs, is recommended for protection against aerosols.

### 9. Physical and Chemical Properties

**Appearance**

Sterile, yellow to orange lyophilized powder. When reconstituted, COSMEGEN is a clear, gold-colored solution.

**Odor/Threshold Limit**

DACTINOMYCIN: Odorless.

**pH**

Not available.

**Boiling Point**

MANNITOL: 166°C (330.8°F)

DACTINOMYCIN: 245 to 248°C (473 to 478.4°F)

**Melting Point**

MANNITOL: 460°C (860°F)

**Flash point**

Not applicable.

**Flammable Limits (% in air)**

Not applicable.

**Autoignition Temperature**

MANNITOL: 460°C (860°F)

**Solubility**

Very soluble

**Partition Coefficient**

MANNITOL: Log Kow: -3.1

DACTINOMYCIN: Log Kow: 3.21

**Specific Gravity**

MANNITOL: 1.52 (Water = 1)

**Vapor Density**

Not applicable.

**Vapor Pressure**

Not applicable.

**Vapor Density**

0% (w/w)
10. Stability and Reactivity

Stability

MANNITOL: The product is stable.

Conditions to Avoid

DACTINOMYCIN: Compound is both air and light sensitive and is somewhat hygroscopic.

Incompatibility

MANNITOL: Avoid contact with strong oxidizers.

DACTINOMYCIN: Strong oxidizing agents, strong acids, and strong bases.

Hazardous Polymerization

Will not occur.

Hazardous Decomposition Products

These products are carbon oxides, nitrogen oxides.

11. Toxicological Information

Routes of Entry

Ingestion: Yes
Inhalation: Yes
Skin Contact: Yes

Toxicity Data

<table>
<thead>
<tr>
<th>Component</th>
<th>Test</th>
<th>Species</th>
<th>Route</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>DACTINOMYCIN</td>
<td>LD50</td>
<td>Rat</td>
<td>Oral</td>
<td>7.2 mg/kg</td>
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<tr>
<td></td>
<td>LD50</td>
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<td>7.8 to 13 mg/kg</td>
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<tr>
<td></td>
<td>LD50</td>
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<td>Dermal</td>
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<tr>
<td></td>
<td>LD50</td>
<td>Dog</td>
<td>Dermal</td>
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<tr>
<td>MANNITOL</td>
<td>LD50</td>
<td>Rat</td>
<td>Oral</td>
<td>13500 mg/kg</td>
</tr>
</tbody>
</table>

Effects of Acute Exposure

Eye contact

No data are available on the formulated product. Dactinomycin, the active ingredient, has been shown to be corrosive to the eyes in animal studies.

Skin contact

No data are available on the formulated product. Dactinomycin, the active ingredient, is corrosive to the skin. The reconstituted drug is irritating to the skin.

Inhalation

There are no data on the effects of COSMEGEN by this route. However, the compound may be severely irritating or corrosive to the respiratory tract.

Ingestion

Not a normal route of administration; therefore there are no data available by this route in humans. Acute animal data indicate that the active ingredient, dactinomycin, is very toxic by ingestion and may be irritating to the upper GI tract.

**Effects of Chronic Exposure**

DACTINOMYCIN: Dactinomycin is a potent cytotoxic anticancer agent that presents a serious risk of birth defects, systemic toxicity and cancer. In short-term studies in animals, weight loss, hemorrhaging and ulceration of the digestive tract, testicular, blood and lymphoid effects were seen at doses as low as 0.01 mg/kg/day. The compound is mutagenic and caused local tumors in rats and mice that received injections of doses as low as 0.01 mg/kg/day. When injected in rats and mice, it was embryotoxic and teratogenic.

*** Continued on next page ***
In clinical use, serious toxic effects usually appear 10 to 14 days after therapy is initiated. These include ulcers of the digestive tract, liver injury, bone marrow suppression and death.

Carcinogen Designation
Not listed as a carcinogen by OSHA, NTP or IARC.

Medical Conditions Aggravated by Overexposure:
**DACTINOMYCIN**: Pre-existing bone marrow, blood, GI, kidney, liver, skin or testicular disorders, chicken pox, herpes zoster and pregnancy.

12. Ecological Information

Environmental Effects
Not available

Ecotoxicity Data

<table>
<thead>
<tr>
<th>Component</th>
<th>Species</th>
<th>Period</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>DACTINOMYCIN</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>MANNITOL</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
</tr>
</tbody>
</table>

Environmental Fate
Not available

13. Disposal Considerations

Waste Disposal Information
Avoid contact of spilled material and runoff with soil and surface waterways. Dispose of or treat all spill residues including contaminated soils following all applicable regulations.

Any residual COSMEGEN or contaminated materials should be incinerated or chemically deactivated and then sewer. Do not sewer COSMEGEN directly.

14. Transport Information

Shipping Description

<table>
<thead>
<tr>
<th>U.S. DOT</th>
<th>UN2811 Toxic solid, organic, n.o.s. (Cosmegen), 6.1, III</th>
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<tbody>
<tr>
<td>IATA/ICAO</td>
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<tr>
<td>IMO</td>
<td>UN 2811 TOXIC SOLID, ORGANIC, N.O.S. (Cosmegen), 6.1, III</td>
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<td>ADR/RID</td>
<td>UN 2811 Toxic solid, organic, n.o.s. (Cosmegen), 6.1, III</td>
</tr>
</tbody>
</table>

15. Regulatory Information

U.S. Federal Regulations

State Regulations
Not available

International Regulations
Exempt from the EU Dangerous Substances Directive.

*** Continued on next page ***
16. Other Information

Revisions: Merck PB-ECL
Date of Preparation: October 1990
Date of Previous Issue: 1-Jan-2007
Validation Date: 4/12/2007.
MSDS Coordinator: 1-908-423-7903
Merck & Co., Inc.
Two Merck Drive
P.O. Box 200, WS2W-13
Whitehouse Station, NJ 08889-0200
U.S.A.

Disclaimer:
While this information and recommendations set forth are believed to be accurate as of the date hereof, MERCK & CO, INC. makes no warranty with respect hereto and disclaims all liability from reliance thereon.