1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

COMMON NAME: NAXCEL® Sterile Powder
CHEMICAL FAMILY: Cephalosporin antibiotic
SYNONYMS: EXCENEL®
USE: Veterinary product for the treatment of bovine respiratory disease. Not for human use.
MANUFACTURER/SUPPLIER:
PHARMACIA & UPJOHN
7171 PORTAGE RD
KALAMAZOO, MI 49001-0199
TELEPHONE NUMBERS:
(616) 833-5122 - (24 Hours, Emergency)
(616) 833-7555 - (8:00 AM - 4:30 PM, EST Emergency)
(800) 253-8600 - (8:00 AM - 4:30 PM, EST)

2. COMPOSITION/INFORMATION ON INGREDIENTS

INGREDIENT 1
COMMON NAME: Ceftiofur Sodium.
CHEMICAL NAME: 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-3-[[(2-furanylcarbonyl)thio]methyl]-8-oxo-,monosodium salt, [6*R*-[6 ,-7 (*Z*)]]-
% BY WEIGHT: 98% to 100%
CAS NUMBER: 104010-37-9
EXPOSURE LIMIT(S): PHARMACIA & UPJOHN EXPOSURE LIMIT-TWA: 0.2 mg/m^3

INGREDIENT 2
COMMON NAME: Sodium Hydroxide.
% BY WEIGHT: <1% (May be added to adjust pH when necessary.)
CAS NUMBER: 1310-73-2
EXPOSURE LIMIT(S): OSHA PEL-CEILING: 2 mg/m^3 ACGIH TLV-CEILING: 2 mg/m^3

INGREDIENT 3
COMMON NAME: Potassium Phosphate Monobasic.
% BY WEIGHT: <1% (Added as a buffer).
CAS NUMBER: 7778-77-0
EXPOSURE LIMIT(S): Not established.

EXPOSURE LIMIT(S) FOR THE MATERIAL: Not established.

3. HAZARDS IDENTIFICATION

PRIMARY ROUTE(S) OF EXPOSURE: Skin contact, eye contact, inhalation, and ingestion.
EFFECTS OF OVEREXPOSURE: The primary concern with inhalation or skin exposure to this agent would be the capability to elicit very mild to severe allergic reaction in some individuals. Repeated exposure may lead to sensitization. Manifestations of an allergic response may include skin rash, fever, bronchospasm, angioedema (swelling of lips, tongue and face accompanied by asthmatic breathing and hives) and anaphylaxis. Drug solutions of ceftiofur sodium have the potential for mild delayed-type dermal sensitization following repeated topical contact. May also cause diarrhea, nausea, vomiting and anemia. Target organs, therefore, include the skin, respiratory tract, immune system, gastrointestinal tract and blood.
MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Hypersensitivity to ceftiofur sodium or to the cephalosporin group of antibiotics. Persons with known sensitivity to other beta-lactam antibiotics such as penicillin may be at increased risk of developing hypersensitivity to ceftiofur sodium.

4. FIRST AID MEASURES

EYES: Flush with water for 15 minutes. Hold eyelids open to assure complete contact with water.
SKIN: Wash with soap and water. Remove contaminated clothing.
INHALATION: Remove from exposure.
INGESTION: Contact a physician or poison control center.
NOTES TO PHYSICIAN: Serious, acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management, as clinically indicated.

5. FIRE FIGHTING MEASURES

FLASH POINT: Not applicable (solid).
LOWER EXPLOSION LIMIT (LEL): Not applicable.
UPPER EXPLOSION LIMIT (UEL): Not applicable.
EXTINGUISHING MEDIA: Water, carbon dioxide or dry chemical.
FIRE FIGHTING PROCEDURES: Wear self-contained breathing apparatus and full-body protective equipment.
UNUSUAL FIRE OR EXPLOSION HAZARDS: As with all finely divided organic powders, it is advisable to eliminate explosion hazards by methods such as grounding mechanical equipment in contact with the material to prevent the buildup of static electricity, inerting the atmosphere or controlling dust levels.
HAZARDOUS COMBUSTION PRODUCTS: Carbon monoxide. Carbon dioxide. Nitrogen oxides. Sulfur oxides.

6. ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED: Remove ignition sources; control the generation of dust/vapors; provide ventilation and respiratory, skin and eye protection to prevent

overexposure. Keep out of drains; prevent entry to surface water, groundwater and soil. Vacuum (with HEPA-filtered and explosion-proof equipment) or scoop spilled material and place in container.

7. HANDLING AND STORAGE

PRECAUTIONS FOR HANDLING AND STORING: Avoid generating dust/vapors and contact with skin, eyes and clothing. Use with adequate ventilation. Wash thoroughly after handling. Launder contaminated clothing before reuse. Store at room temperature. Do not get in eyes, on skin or clothing. Avoid breathing dust or mist. Use adequate dust/vapor control. Keep out of reach of children.

8. EXPOSURE CONTROLS/ PERSONAL PROTECTION

RESPIRATORY PROTECTION: Approved respirator if there is the opportunity for dust generation, especially with large quantities.
VENTILATION: Local-exhaust.
PROTECTIVE GLOVES: Rubber.
EYE PROTECTION: Safety glasses with side shields.
OTHER PROTECTIVE EQUIPMENT: Protective covering for exposed areas of skin.

9. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE/PHYSICAL STATE: Off-white to tan powder.
BOILING POINT: Decomposes.
FREEZING POINT: Not applicable.
MELTING POINT: Decomposes above 190°C without melting.
MOLECULAR WEIGHT: Mixture.
PARTITION COEFFICIENT (n-OCTANOL/WATER): 0.3 (at pH5)
SOLUBILITY IN SOLVENTS: Methanol: <5 mg/mL; propylene glycol: 226 mg/mL; 2-pyrrolidone: 302 mg/mL; THF: <5 mg/mL.
SOLUBILITY IN WATER: >400 mg/mL initially. Gels with time. No gelling or precipitation at 70 mg/mL.
VAPOR DENSITY (AIR = 1): Negligible.
VAPOR PRESSURE: Negligible.
VOLATILITY: Negligible.

10. STABILITY AND REACTIVITY

STABILITY: Stable.
PHYSICAL CONDITIONS TO AVOID: Slowly degrades on exposure to UV or fluorescent light, water exposure or increases in temperatures.
INCOMPATIBILITY WITH OTHER MATERIALS: Alkaline pH, oxidizing agents, and heavy metal ions.
HAZARDOUS DECOMPOSITION PRODUCTS: None.
HAZARDOUS POLYMERIZATION: Does not occur.

11. TOXICOLOGICAL INFORMATION

ACUTE STUDIES: Not acutely toxic. The following data applies to ceftiofur sodium, the active ingredient in NAXCEL.
EYE IRRITATION (RABBIT): Minimally irritating, but absorption via the ocular route may occur.
SKIN IRRITATION (RABBIT): Practically non-irritating to intact skin.
SENSITIZATION: May cause hypersensitivity reactions.
INHALATION: >8.3 mg/L
ORAL TOXICITY (DOG): The no observable effect level (NOEL) of 30 mg/kg/day was established in the dog as a result of a 90-day oral toxicity study.
ORAL LD50 (RAT): >7,760 mg/kg
INTRAPERITONEAL LD50 (RAT): 927 mg/kg
OTHER STUDIES:
GENOTOXICITY: Ceftiofur was negative in the Ames assay, micronucleus test, V79 mammalian cell mutation assay, and unscheduled DNA synthesis assay. In the in vitro chromosome aberration assay using CHO cells (in the absence of S9 metabolic activation), lengthy treatment with high doses of ceftiofur sodium resulted in increased frequency of aberrations. Aberrations were in the categories of chromatid breaks and gaps and isochromatid gaps. No evidence of the formation of rearrangements could be seen in these cells.
REPRODUCTION/FERTILITY: The reproduction NOEL in the rat is 1,000 mg/kg/day orally. Oral administration at this level did not cause adverse effects upon fertility or reproductive performance of F0 and F1 generation animals. Likewise, no adverse effects were observed in the growth and viability of the F2 litter through to the weaning period.
TERATOGENICITY: Not teratogenic in rats at oral doses up to 3,200 mg/kg/day.
CARCINOGENICITY: Negative genetox tests would suggest that ceftiofur sodium is not carcinogenic. Ingredient(s) are not listed as carcinogenic by IARC, NTP or OSHA.

12. ECOLOGICAL INFORMATION

ENVIRONMENTAL FATE:
MOBILITY: Ceftiofur sodium is very soluble in water, therefore, it is expected to be relatively mobile and migrate toward the aquatic compartment. Since ceftiofur sodium

decomposes above 190°C without melting and has no measurable vapor pressure, it is not expected to enter the air.

PERSISTENCE/DEGRADABILITY: In the aqueous environment, ceftiofur or its metabolites are subject to degradation by hydrolysis. At pH 7 and 22°C, ceftiofur is 50% destroyed in 8 days and is completely destroyed in 80 days or less. Increases in temperature or pH, accelerate the rate of hydrolysis and destruction of antibacterial activity of ceftiofur and its metabolites. Degradation rate is also accelerated upon exposure to light or oxidizers. Ceftiofur sodium and its metabolites rapidly degrade in manure to 0 PPM bioactivity within 72 hours at ambient temperatures. Furthermore, a study of aerobic biodegradation in several soils showed that ceftiofur had no inhibitory effects on the soil organisms and readily biodegrades to carbon dioxide. It can be concluded that ceftiofur will not reach concentrations in soil at which adverse effects would occur.

BIOACCUMULATIVE POTENTIAL: Ceftiofur sodium has an octanol/water partition coefficient of 0.3 at pH 5. Based on this value, it would be expected to migrate to the aqueous environment but it should not bioaccumulate in aquatic organisms. The biological concentration factor (BCF) is 0.235. Since all the metabolites are more polar and water soluble than ceftiofur, these compounds should also remain in the aqueous environment with no bioaccumulation.

ABIOTIC POTENTIAL: Based on its anticipated use and fate in the environment, and its decomposition rate in water, manure and soils, the concentration of ceftiofur and related metabolites in soil is expected to be below the minimal inhibitory concentration of most bacteria and soil fungi. Therefore, no detrimental effects to these classes of organisms are expected. Small amounts released to sanitary sewerage should not adversely effect the biotic flora of sewerage treatment facilities.

ECOTOXICITY: No information found.

13. DISPOSAL CONSIDERATIONS

WASTE DISPOSAL METHOD: Dispose of by incineration in accordance with applicable international, national, state and/or local waste disposal regulations.

14. SHIPPING REGULATIONS

Not regulated for transportation by the United States Department of Transportation (DOT), International Maritime Organization (IMO), or International Air Transport Association (IATA). May be subject to state and/or local transportation requirements.

15. OTHER INFORMATION

PREPARED BY: Environment & Safety.

DISCLAIMER: The MSDS information is believed to be correct but should only be used as a guide. Pharmacia & Upjohn disclaims any express or implied warranty as to the accuracy of the MSDS information and shall not be held liable for any direct, incidental or consequential damages resulting from reliance on the information.

16. LABELING

This drug is subject to FDA labeling requirements; therefore, it is exempt from the labeling requirements of the OSHA Hazard Communication Standard.

NDC 0009-3362-03
NDC 0009-3362-04

July 28, 1997