Date of Approval: March 29, 2012

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-421

Ceftiofur for Injection
(ceftiofur sodium)

Sterile Powder

Cattle, swine, sheep, goats, horses, dogs, day-old turkey poults and day-old chicks

Indications:
For treatment of bovine respiratory disease; for treatment and control of swine bacterial respiratory disease; for treatment of sheep respiratory disease and caprine respiratory disease; for treatment of respiratory infections in horses associated with *S. zooepidemicus*; for treatment of canine urinary tract infections associated with *E. coli and P. mirabilis;* for control of early mortality, associated with *E. coli* organisms susceptible to ceftiofur, in day-old chicks and day-old turkey poults

Sponsored by:

Hospira, Inc.

TABLE OF CONTENTS

I. GENERAL INFORMATION:

A. File Number: ANADA 200-421

B. Sponsor: Hospira, Inc.
275 North Field Drive
Lake Forest, IL 60045

Drug Labeler Code: 000409

C. Proprietary Name: Ceftiofur for Injection

D. Established Name: ceftiofur sodium

E. Pharmacological Category: Antimicrobial

F. Dosage Form: Sterile powder

G. Amount of Active Ingredient: Each mL of the resulting solution contains ceftiofur sodium equivalent to 50 mg ceftiofur sodium

H. How Supplied: 1 gram vial; 4 gram vial

I. How Dispensed: Rx

J. Dosages: Cattle: 0.5 to 1.0 mg per pound (1.1 to 2.2 mg/kg) of body weight (1-2 mL reconstituted sterile solution per 100 lbs body weight). Treatment should be repeated at 24-hour intervals for a total of 3 consecutive days. Additional treatments may be given on days four and five for animals which do not show a satisfactory response (not recovered) after the initial three treatments.

Swine: 1.36 to 2.27 mg per pound (3.0 to 5.0 mg/kg) of body weight (1 mL of reconstituted sterile solution per 22 to 37 lbs body weight). Treatment should be repeated at 24-hour intervals for a total of 3 consecutive days.

Sheep: 0.5 to 1.0 mg per pound (1.1 to 2.2 mL reconstituted sterile solution per 100 lbs body weight). Treatment should be repeated at 24-hour intervals for a total of 3 consecutive days. Additional treatments may be given on days four and five for animals which do not show a satisfactory response (not recovered) after the

initial three treatments.

Goats: 0.5 to 1.0 mg per pound (1.1 to 2.2 mg/kg) of body weight (1-2 mL reconstituted sterile solution per 100 lbs body weight). Treatment should be repeated at 24-hour intervals for a total of 3 consecutive days. Additional treatments may be given on days four and five for animals which do not show a satisfactory response (not recovered) after the initial three treatments.

Horses: 1.0 to 2.0 mg per pound (2.2 to 4.4 mg/kg) of body weight (2-4 mL reconstituted sterile solution per 100 lb body weight). A maximum of 10 mL may be administered per injection site. Treatment should be repeated at 24-hour intervals, continued for 48 hours after clinical signs have disappeared and should not exceed 10 days.

Dogs: 1.0 mg per pound 2.2 mg/kg) of body weight (0.1 mL reconstituted sterile solution per 5 lbs body weight). Treatment should be repeated at 24 hour intervals for 5-14 days.

Day-Old Chicks: 0.08 to 0.20 mg/chick. One mL of the 50 mg/mL reconstituted solution will treat approximately 250 to 625 day-old chicks.

Day-Old Turkey Poults: 0.17 to 0.5 mg/poult. 1 ml of the 50 mg/mL reconstituted solution will treat approximately 100 to 294 day-old turkey poults.

K. Routes of Administration: For intramuscular and subcutaneous injection in cattle only. For intramuscular injection in swine, sheep, goats, and horses. For subcutaneous injection only in dogs, day-old chicks, and day-old turkey poults.

L. Species: Cattle, swine, sheep, goats, horses, dogs, day-old chicks, and day-old turkey poults

M. Indications: Cattle: Ceftiofur for Injection is indicated for treatment of bovine respiratory disease (shipping fever, pneumonia) associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni*. Ceftiofur for Injection is also for treatment of acute bovine

interdigital necrobacillosis (foot rot, pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus.*

Swine: Ceftiofur for Injection is indicated for treatment/control of swine bacterial respiratory disease (swine bacterial pneumonia) associated with *Actinobacillus (Haemophilus) pleuropneumoniae, Pasteurella multocida, Salmonella choleraesuis, and Streptococcus suis.*

Sheep: Ceftiofur for Injection is indicated for treatment of sheep respiratory disease (sheep pneumonia) associated with *Mannheimia haemolytica* and *Pasteurella multocida.*

Goats: Ceftiofur for Injection is indicated for treatment of caprine respiratory disease (goat pneumonia) associated with *Mannheimia haemolytica* and *Pasteurella multocida.*

Horses: Ceftiofur for Injection is indicated for treatment of respiratory infections in horses associated with *Streptococcus zooepidemicus.*

Dogs: Ceftiofur for Injection is indicated for the treatment of canine urinary tract infections associated with *Escherichia coli* and *Proteus mirabilis.*

Day-Old Chicks: Ceftiofur for Injection is for the control of early mortality, associated with *E. coli* organisms susceptible to ceftiofur, in day-old chicks.

Day-Old Turkey Poults: Ceftiofur for Injection is for the control of early mortality, associated with *E. coli* organisms susceptible to ceftiofur, in day-old turkey poults.

N. Reference listed new animal drug: NAXCEL Sterile Powder; ceftiofur sodium; NADA 140-338; Pharmacia & Upjohn Co, a Division of Pfizer, Inc.

II. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act of 1988, an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (reference listed new animal drug). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor is required to show that the generic product is bioequivalent to the RLNAD, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Hospira, Inc. (previously Orchid Healthcare, A Division of Orchid Chemicals & Pharmaceuticals, Ltd.), was granted a waiver from the requirement for an *in vivo* bioequivalence study for the generic product Ceftiofur for Injection (ceftiofur sodium) Sterile Powder. The generic product is administered as a sterile solution, contains the same active ingredient in the same concentration and dosage form as the RLNAD, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product NAXCEL Sterile Powder (ceftiofur sodium), the subject of Pharmacia & Upjohn Co., a Division of Pfizer, Inc. NADA 140-338, was approved on January 25, 1988.

III. EFFECTIVENESS:

CVM did not require effectiveness studies for this approval.

IV. TARGET ANIMAL SAFETY

CVM did not require target animal safety studies for this approval.

V. HUMAN FOOD SAFETY:

The following are assigned to this product for cattle, swine, sheep, goats, horses, dogs, and day-old turkey poults and chicks:

- **Tolerances for Residues:**
  The tolerances established for the pioneer product apply to the generic product. Tolerances for residues of desfuroylceftiofur in edible swine tissues are 0.25 parts per million (ppm) in kidney (target tissue), 3 ppm in liver and 2 ppm in muscle. Tolerances for residues of desfuroylceftiofur in edible cattle tissues are 0.4 ppm kidney (target tissue), 2 ppm in liver, 1ppm in muscle, and 0.1 ppm in milk under 21 CFR 556.113. The acceptable daily intake (ADI) for total residues of ceftiofur sodium is 30 micrograms per kilogram of body weight per day.

- **Withdrawal Times:**
  Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.

  A withdrawal period of 4 days has been established for ceftiofur sodium in cattle tissues and swine tissues. There is no milk discard time required for cattle's milk.

- **Regulatory Method for Residues:**
  The regulatory method for determination of DCA in swine kidney and muscle, and bovine kidney, muscle, and milk is the HPLC-DCA assay which successfully completed a sponsor-monitored multi-laboratory method trial. The method is on file with the Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855.

VI. USER SAFETY:

CVM did not require user safety studies for this approval.

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Ceftiofur for Injection Sterile Powder:

Warnings:

Not for human use. Keep out of reach of children. Restricted drug - Use Only as Directed (California).

Penicillins and cephalosporins can cause allergic reactions in sensitized individuals. Topical exposures to such antimicrobials, including ceftiofur, may elicit mild to severe allergic reactions in some individuals. Repeated or prolonged exposure may lead to sensitization. Avoid direct contact of the product with the skin, eyes, mouth, and clothing.

Persons with a known hypersensitivity to penicillin or cephalosporins should avoid exposure to this product. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, was with soap and water. Remove contaminated clothing. If allergic reaction occurs (e.g. skin rash, hives, difficult breathing), seek medical attention.

VII. AGENCY CONCLUSIONS:

This information submitted in support of this ANADA satisfies the requirements of section 512(n) of the Federal Food, Drug, and Cosmetic Act and demonstrates that Ceftiofur for Injection, when used according to the label, is safe and effective.

cc: Document Control Unit, for the administrative file of:
A-200421-E-0008-OT, T-0009, T-0010
Courtesy copy for the sponsor

SIGNATURE PAGE FOR THE
FREEDOM OF INFORMATION SUMMARY

ANADA: 200421
SUBMISSION NUMBER: E-0008
SPONSOR: Hospira, Inc.
NAME OF DRUG: Ceftiofur for Injection

	CONCURRENCE (DRAFT):		CONCURRENCE (FINAL):	
1.	Tami C. Cloyd	2/24/12		
	Primary Reviewer Tami C. Cloyd, HFV-171	Date	INITIAL	Date
2.	Katherine P. Weld	2/27/12		
	Team Leader Katherine P. Weld, HFV-171	Date	INITIAL	Date
3.	John K. Harshman	2/27/12		
	Director John K. Harshman, HFV-170	Date	INITIAL	Date
4.				
	Director Division of Human Food Safety, HFV-150	Date	INITIAL	Date
5.				
	Quality Assurance Team, HFV-107	Date	INITIAL	Date
6.	N/A			
	Director ONADE, HFV-100	Date	INITIAL	Date
7.	*If the approval does not require the Center Director's signature, insert NA on this line.*			
	N/A Director CVM, HFV-1	Date	INITIAL	Date