Approval Date: August 24, 1995

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 140-338

B. Sponsor

The Upjohn Company
7000 Portage Road
Kalamazoo, MI 49001

C. Proprietary Name

NAXCEL® Sterile Powder

D. Established Name

ceftiofur sodium sterile powder

E. Dosage Form

NAXCEL® Sterile Powder is available in two package sizes: 1-gram and 4-gram vials.

Reconstituted product should be used within 12 hours if stored at controlled room temperature (15-30° C; 59-86° F) or within 7 days if stored in a refrigerator (2-8° C; 36-46° F).

1-gram vial
Reconstitute with 20 mL Sterile Water for Injection. Each mL of the resulting solution contains ceftiofur sodium equivalent to 50 mg ceftiofur.

4-gram vial
Reconstitute with 80 mL Sterile Water for Injection. Each mL of the resulting solution contains ceftiofur sodium equivalent to 50 mg ceftiofur.

F. Dosage Regimen

NAXCEL® Sterile Solution is to be administered to cattle at the dosage range of 0.5 to 1.0 mg ceftiofur per pound (lb) of body weight (BW); 1 to 2 mL reconstituted sterile solution per 100 lb BW. Treatment should be repeated every 24 hours for a total of three treatments. Additional treatments may be given on Days 4 and 5 to animals which do not show a satisfactory response (not recovered) after the first three treatments.

G. Route of Administration

NAXCEL® Sterile Powder (reconstituted as a sterile solution) should be administered by intramuscular injection to cattle.

H. Indication

NAXCEL® Sterile Powder is indicated for treatment of acute bovine interdigital necrobacillosis (foot rot, pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*.

I. Effect of Supplement

Provides for the use of ceftiofur sodium (NAXCEL® Sterile Powder) in cattle for a new indication.

II. EFFECTIVENESS

A. Pivotal Studies Summary (2):

Two separate clinical studies were conducted which demonstrate that ceftiofur sodium is effective as therapy for acute bovine interdigital necrobacillosis (foot rot, pododermatitis).

Ceftiofur sodium at the dosage range of 0.5 to 1.0 mg ceftiofur/lb BW administered intramuscularly at 24-h intervals for 3 to 5 days is approved for the treatment of bovine respiratory disease. The foot rot dose-finding study evaluated both the 0.5 and 1.0 mg ceftiofur/lb BW dosage regimes. Since both regimes were equally effective during the dose finding evaluation, the lower dosage regime (0.5 mg of ceftiofur/lb BW) was evaluated during the dose confirmation study. The lower ceftiofur dosage regime was effective therapy during the dose confirmation study (0.5 mg ceftiofur/lb BW); therefore, a dosage range of 0.5 to 1.0 mg ceftiofur/lb BW is indicated for therapy of acute bovine interdigital necrobacillosis (foot rot, pododermatitis).

Pivotal Dose Determination Study Summary:

Thirty-nine yearling beef cattle were evaluated during an induced acute foot rot dose determination model study. *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*, two bacteria associated with foot rot lesions, were used to induce foot rot in 3 feet of each study animal. Each animal was randomly assigned to one of 3 treatments: placebo (5 mL sterile water daily for 3 days), or 0.5 or 1.0 mg ceftiofur/lb BW for 3 days. All treatments were administered intramuscularly. Both ceftiofur treatments were more effective than placebo for treating foot rot ($P < 0.001$).

Based on these data, the treatment regime of 0.5 mg of ceftiofur per pound body weight administered intramuscularly at 24-h intervals for 3 consecutive days was evaluated for treatment of naturally occurring foot rot during a pivotal dose confirmation field study.

Pivotal Dose Confirmation Study Summary:

Eighty-eight cattle (47 beef, 41 lactating cows) from 11 different locations were used in a pivotal dose confirmation trial. Animals were randomly assigned to either placebo or 0.5 mg ceftiofur/lb BW for 3 days. Prior to the first treatment, foot rot lesions were sampled from 33 cattle at 5 locations (4 feedlots, 1 dairy). These samples were cultured and anaerobic bacteria isolated.

Twenty-eight *B. melaninogenicus* isolates and 21 *F. necrophorum* isolates were obtained from the lesions of 33 cattle. Both *B. melaninogenicus* and *F. necrophorum* were isolated from 61% (20/33) of the lesions.

These clinical data support the effectiveness of 0.5 mg of ceftiofur/lb BW administered intramuscularly once daily for 3 consecutive days for the treatment of bovine foot rot.

1. Pivotal Dose Determination Study:

a. Type of Study: This dose determination study was conducted using an established model for inducing foot rot by interdigital inoculations with *F. necrophorum* and *B. melaninogenicus*.

b. Investigator: John N. Berg, DVM, PhD, Professor, Department of Veterinary Microbiology, College of Veterinary Medicine, University of Missouri, Columbia, MO 65211.

c. General Design:

1) Purpose of Study: The purpose of the study was to determine a ceftiofur dosage that was efficacious for the treatment of bovine foot rot.

2) Test Animals: Thirty-nine (39) yearling cattle were acclimated at least 30 days prior to challenge. Prior to administration of treatments, the animals were randomly assigned to treatments groups (1, 2, 3) as described in Table 1.

Table 1. Treatment groups evaluated. All treatments were administered intramuscularly at 24-h intervals for 3 days

Study Group	Control - 5 mL sterile water/ animal	Control - 5 mL sterile water/ animal	Treatment - 0.5 mg ceftiofur/ lb body weight	Treatment - 0.5 mg ceftiofur/ lb body weight	Treatment - 1.0 mg ceftiofur/ lb body weight	Treatment - 1.0 mg ceftiofur/ lb body weight
Sex (M*/F)	M*	F	M	F	M	F
No. of test animals	3	10	7	6	9	4

*Steers

3) Controls: A placebo (sterile water) contemporary control group was included in the study.

4) Diagnosis: To induce foot rot, the animals were challenged with an inoculum of *F. necrophorum* and *B. melaninogenicus* in the interdigital space of three feet. Animals were scored daily by the study veterinarian for clinical signs of lameness and extent of interdigital swelling and lesion size. The animals began to exhibit lameness 2 days post-challenge. Animals were randomly administered treatments by the drug administrator at the first sign of lameness.

5) Dosage Form: Ceftiofur sterile powder reconstituted to sterile solution by addition of sterile water for injection. Each mL of resulting solution contained ceftiofur sodium equivalent to 50 mg ceftiofur.

6) Route of Administration: Intramuscularly.

7) Doses: Five (5) mL sterile water (placebo); 0.5 and 1.0 mg ceftiofur/lb BW at 24-h intervals for 3 consecutive days.

8) Test Duration: Animals were monitored for 10 days after initial treatment by the study veterinarian.

9) Pertinent Parameters Measured: The study was conducted according to a blinded, parallel group design. The lesions were evaluated and scored by the study veterinarian on Day 2 postchallenge and on post-treatment Days 3, 7 and 10. Lesions were scored using a 0-5 scoring system (0 =no lesion to 5 =most severe). In addition, the animals were evaluated by the study veterinarian for lameness on post-treatment Days 0, 1, 2, 3, 5, 7 and 10. Lameness was scored using a 0-3 scoring system (0 =normal gait to 3 =severe lameness). The lesion and lameness scores were added together to obtain a numerical value for data analysis.

d. Post-treatment Microbiology: On Day 3 post-treatment, *F. necrophorum*, was isolated from all 12 lesions cultured from the placebo group, but in only 3 of 8 ceftiofur treated cattle. On post-treatment Day 7, *F. necrophorum* was isolated from 9 of 9 placebo cattle but only 1 of 4 treated cattle. This indicates that ceftiofur was eliminating the *F. necrophorum* in the majority of the cattle treated. *B. melaninogenicus* was isolated from all lesions cultured. This was not unexpected since *B. melaninogenicus* is commonly present in the feces and the lesions in the feet were constantly being recontaminated by the feces. Ceftiofur minimum inhibitory concentrations (MICs) data had previously determined that F. necrophorum is susceptible to ceftiofur (MIC range of 0.016 to 0.062 µg/mL).

e. Statistical Analysis: Within treatment group, the mean scores for lameness and lesions for all affected feet were added to obtain a numerical score. The statistical analysis was based on the changes in these combined lameness and lesion scores observed for each individual animal during the pre-treatment, treatment and observations periods.

The lameness, lesion and combined lameness and lesion scores were averaged for each day for each animal. The mean total scores and the mean foot scores for each treatment group were examined. Differences among treatments were tested using the GLM procedure of SAS and tested at alpha = 0.05.

f. Results: Combined mean lesion and lameness scores at post-treatment Days 0, 3, 7 and 10 are shown in Table 2.

Table 2. Combined lesion and lameness scores/days post-treatment.

Day	5 mL sterile water/ animal	0.5 mg ceftiofur/ lb body weight	1.0 mg ceftiofur/ lb body weight
0 (pre-treatment)	5.85	7.77	8.00
3	13.69	4.38	5.54
7	6.69	1.08	1.08
10	5.77	0.69	0.92

g. Decision Criteria: Ceftiofur at 0.5 or 1.0 mg/lb BW was effective for the therapy of acute bovine foot rot if the reduction in the summed lameness and lesion scores from Day 0 to Day 3 or 7 was significantly greater than the reduction seen for the placebo group.

   If both ceftiofur dosage regimens were determined to be significantly better than the placebo control group, the lower ceftiofur dosage regimen would be considered the effective regimen and evaluated further in a pivotal dose confirmation study with naturally occurring bovine foot rot.

h. Conclusions: Both 0.5 and 1.0 mg ceftiofur/lb BW administered intramuscularly at 24-h intervals for 3 consecutive days were more effective than placebo ($P < 0.0001$) in reducing the severity of lesions and lameness of bovine foot rot. The 0.5 and 1.0 mg of ceftiofur/lb BW regimens were not significantly different (alpha = 0.05) from each other.

i. Adverse Reactions: None.

2. Pivotal Multilocation Dose Confirmation Field Study:

a. Type of Study: Pivotal clinical field study to evaluate efficacy of ceftiofur as therapy for naturally occurring acute bovine foot rot.

b. Investigators:

   Dr. Jerald E. Swanson
   602 N. Oak
   Guymon, OK 73945

   Dr. Kelly Lechtenberg
   RR #2, Box 49
   Oakland, NE 68045

   Dr. Charles Sourk
   Route 2, Box 56
   Scott City, KS 67871

   Dr. Ernest Bliss
   2938 NW 161 Court
   Gainesville, FL 32609

   Dr. Jim Reynolds
   13589 River Road
   Walnut Grove, CA 95690

   Dr. Jan Shearer
   Shealy Dr./Ritchey Rd.
   Dairy Science Building
   University of Florida
   Gainesville, FL 32611

   Dr. R. A. Dubensky
   Milford Animal Hospital
   901 Chippey Cole Road

Milford, PA 18337

Dr. E. G. Johnson
24007 Highway 20/26
Parma, ID 83660

c. General Design:

1) Purpose of Study: The primary objective of the study was to evaluate the efficacy of 0.5 mg ceftiofur/lb BW administered intramuscularly at 24-h intervals for 3 consecutive days as therapy for naturally occurring acute bovine foot rot (under field conditions) compared to placebo controls.

2) Test Animals: Eighty-eight beef (feedlot cattle) and lactating dairy cows of various ages with acute foot rot located at 11 sites were distributed among the treatment groups as follows:

Table 3. Beef and lactating cows/treatment groups.

Type of Operation (No. of Sites)	**Ceftiofur Treatment (No. of Animals)**	**Sterile Water Treatment (No. of Animals)**
Beef (6)	23	24
Lactating Dairy Cows (5)	22	19
Total (11)	45	43

d. Results: The study veterinarians determined if the treatment regimes resulted in a "cure" or "failure" based on the lesion, swelling and lameness scores on Days 0, 4 and 7. The cure rates are illustrated in Table 4.

Table 4. Cure rates/treatment regime administered.

Type of Operation (No. of Sites)	**Ceftiofur Treatment % (n)**	**Sterile Water Treatment % (n)**
Beef (6)	69.6 (16/23)	16.7 (4/24)
Lactating Dairy Cows (5)	54.6 (12/22)	10.5 (2/19)
Combined Beef and Dairy (11)	62.2 (28/45)	14.0 (6/43)

A relapse was defined as a reoccurrence of foot rot in the same foot within 15 days after initial therapy. One ceftiofur treated beef animal relapsed on Day 14 after initiation of therapy and was not included as a cure.

Microbiology Results: Prior to administration of therapy, samples from foot rot lesions from cattle at 5 locations (4 feedlots, 1 dairy) were cultured and anaerobic bacteria isolated. Twenty-eight (28) *B. melaninogenicus* and 21 *F. necrophorum* were isolated from the lesions of 33 cattle. Both *B. melaninogenicus* and *F. necrophorum* were isolated from 61% (20/33) of the lesions.

e. Statistical Analysis: The primary parameter used to determine the effectiveness of ceftiofur sodium was the overall Day 4 and Day 7 clinical evaluation performed by a veterinarian. A cure was defined as a reduction in

lameness score by 2 points with none to moderate swelling and healed or healing lesions. Percent cure was calculated as number of animals evaluated as cured/total animals evaluated. Percent cure for each treatment group for each investigator was calculated, and transformed using the Freeman-Tukey double arcsine transformation (Freeman and Tukey, 1950) to satisfy the assumptions of the analysis of variance. The difference between the transformed cure rates was tested for significance at 0.05 (one-sided) using the GLM procedure of SAS (SAS Institute, Inc., 1989). The results are summarized in the following table:

Table 5. Analysis of variance table of Freeman-Tukey transformed cure rates for cattle given either ceftiofur (0.5 mg/lb BW) or sterile water.

Source	df	Mean Square	F	p-value
Type of Operation*	1	254.49	1.04	0.33327
Location (Type)	9	242.84	1.09	0.4488
Treatment	1	3986.42	17.48	0.0024
Type X Treatment	1	34.63	0.16	0.7023
Error	9	222.32		

* Dairy or Beef

The mean cure rate for animals treated with ceftiofur was significantly greater ($P < 0.003$) than for animals treated with sterile water. This difference was consistent for both beef and dairy cattle (i.e. there was no significant ($P = 0.07$) Type x Treatment interaction). Mean cure rates did not differ significantly ($P = 0.33$) between the two types of operations.

f. Conclusions: Cattle with acute interdigital necrobacillosis (foot rot, pododermatitis) administered 0.5 mg ceftiofur/lb BW intramuscularly at 24-h intervals for three consecutive days had a cure rate which was significantly greater ($P < 0.003$) than those cattle administered the sterile water treatment regime.

g. Adverse Reactions: None observed during the study.

J. Overall Conclusions:

Data from the pivotal dose determination and pivotal dose confirmation field study determined that both 0.5 mg and 1.0 mg ceftiofur/lb BW dosage regimes to be effective as therapy for acute bovine foot rot. Acute bovine foot lesions may vary in degree of severity from moderate to quite severe. Therefore, depending on the severity of the foot rot lesion, a ceftiofur dosage range identical to the dosage range approved for bovine respiratory disease (0.5 to 1.0 mg ceftiofur/lb BW) is indicated as follows:

INDICATIONS FOR USE: NAXCEL® Sterile Powder (ceftiofur as ceftiofur sodium) is indicated for treatment of acute bovine interdigital necrobacillosis (foot rot, pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*.

RECOMMENDED DOSAGE: NAXCEL® Sterile Solution (ceftiofur as ceftiofur sodium) is to be administered to cattle at the dosage range of 0.5 to 1.0 mg ceftiofur /lb BW (1 to 2 mL reconstituted sterile solution per 100 lb BW). Treatment should be repeated every 24 hours for a total of three treatments. Additional treatments may be given on Days 4 and 5 for animals which do not show a satisfactory response (not recovered) after the first three treatments.

K. Corroborative Studies (6):

Two laboratory studies (one *in vitro*, one *in vivo*) were conducted with ceftiofur for diseases caused by or associated with *F. necrophorum*.

One preliminary induced foot rot model study and three clinical efficacy studies were conducted. The data from these studies confirmed that ceftiofur administered intramuscularly once daily at 0.5 mg/lb BW for 3 consecutive days was effective therapy for acute bovine foot rot associated with *F. necrophorum* and *B. melaninogenicus*.

Laboratory Studies:

In vitro evaluation of ceftiofur sodium against *F. necrophorum*: Ceftiofur sodium was evaluated *in vitro* against *F. necrophorum* from bovine liver abscesses and foot rot and was highly active (MIC ¾ 0.25 µg/mL) against *F. necrophorum*. The results of the *in vitro* testing suggested that ceftiofur might be useful in treatment of certain anaerobic infections of domestic animals. In addition, the effectiveness of ceftiofur sodium was evaluated in a *F. necrophorum* mouse disease model. Ceftiofur was deemed effective *in vivo*, producing an ED50 value of 4.4±1.3 mg/kg.

Clinical Effectiveness Studies:

1. Efficacy of ceftiofur sodium as therapy for experimentally induced bacterial foot rot:

The objective of this preliminary study was to evaluate the efficacy of 0.5 and 1.0 mg of ceftiofur sodium/lb BW administered IM once daily for 3 consecutive days for treatment of acute bacterial foot rot in cattle when compared to placebo controls. An established model that produces lesions virtually identical to naturally occurring acute foot rot was utilized for this study. The animals were challenged with an inoculum of *F. necrophorum* and *B. melaninogenicus* in the interdigital space of 3 feet to induce foot rot. The lesions were individually evaluated and scored on Day 3 post-challenge and on post-treatment Days 3, 7 and 14. Lesions were scored using a pre-established 0-5 scoring system (0 =no lesion to 5 =most severe). In addition, the animals were evaluated for lameness on post-treatment Days 1, 2, 3, 7 and 14. Lameness was scored using a pre-established 0-2 scoring system (0 =normal gait to 2 =severe lameness). The animals were evaluated by two veterinarians who worked independently and who were blinded to treatments. The lesion and lameness scores were added to obtain a combined score, which was used for data analysis and as the basis for evaluation of efficacy. Twenty-five (25) head of yearling cattle were acclimated for at least 21 days prior to challenge. Bacteriologic culturing for F. necrophorum and B. melaninogenicus was conducted on 18 selected lesions from 18 cattle prior to treatment to confirm the presence of the infectious agents. All lesions were

culturally positive for both *F. necrophorum* and *B. melaninogenicus*. All treatments were administered by intramuscular injection. The treatment groups were as follows:

Group A (8 cattle): Treated with ceftiofur as ceftiofur sodium at 0.5 mg/lb BW once daily for 3 days.

Group B (9 cattle): Treated with ceftiofur as ceftiofur sodium at 1.0 mg/lb BW once daily for 3 days.

Group A (8 cattle): Treated with placebo, 5 mL sterile water per animal, intramuscularly once daily for 3 days.

No statistically significant differences (alpha = 0.05) were detected among the 3 treatment groups. A trend for greater clinical improvement was observed for the 2 groups administered the ceftiofur treatment regimens. During this initial study, all animals were treated on Day 3 post-challenge resulting in some animals progressing to the advance stages of foot rot which did not respond well to treatment. Based on the information provided by these preliminary data, it was recommended that future protocols using this model be designed so the treatments are administered as animals exhibit signs of lameness in even one foot. This is consistent with the treatment of foot rot by the practicing veterinarian.

Ceftiofur MIC were determined for the *F. necrophorum* isolate used in this study and for 37 other isolates of cattle origin. MIC for all isolates were 0.016 to 0.062 µg/mL. These data indicate that *F. necrophorum* is quite susceptible to ceftiofur.

2. Efficacy of ceftiofur sodium for the treatment of acute foot rot in cattle:

The objective of the study was to evaluate ceftiofur sodium administered intramuscularly at 1.0 mg ceftiofur/kg BW (0.5 mg ceftiofur/lb) for 3 consecutive days as treatment for acute naturally acquired bovine foot rot. The study was conducted in Cheshire, United Kingdom. Forty-three lactating dairy cows ranging in weight from 350 to 798 kg with acute bovine foot rot were treated intramuscularly with 1.0 mg ceftiofur/kg BW (0.5 mg ceftiofur/lb) at 24 hour intervals for 3 consecutive days. Local treatments, paring and bandaging were not administered to animals in this study. The study veterinarian evaluated the cows 1 and 4 days after the last treatment. Clinical efficacy was defined as the number of animals treated that were free of lameness on Day 7. Cows not improved by Day 4, and all animals that were not completely free of lameness on Day 7 were treatment failures. No untreated control groups or positive control groups were included in this study. One animal was excluded from the study. The observed cure rate was 31 of 42 cases or 73.8 %. Under the conditions of this study, ceftiofur sodium at a dose of 1 mg ceftiofur/kg BW (0.5 mg ceftiofur/lb) administered intramuscularly at 24-hour intervals for 3 consecutive days is an effective treatment for acute bovine foot rot (interdigital necrobacillosis).

3. Efficacy of ceftiofur sodium as therapy of foot rot in lactating dairy cows:

The objective of this field experience report study was to determine if ceftiofur sodium was efficacious as therapy for acute foot rot in lactating dairy cows. Thirty-eight lactating dairy cows from eight farms in three regions of Chile with moderate to severe foot rot, were utilized in this study. Each animal was treated with ceftiofur sodium by intramuscular injection at a dose of 1 mg ceftiofur/kg BW (0.5 mg ceftiofur/lb) daily for 3 consecutive days. Treatment effects were scored at 3 and 7 days after the last injection. The results demonstrated that 35/38 animals (92 %) recovered completely within 10 days of the last treatment. It was concluded that ceftiofur is highly effective for the treatment of bovine foot rot.

4. Efficacy of ceftiofur sodium as therapy for acute foot rot in French lactating dairy cattle:

The purpose of this field experience study was to evaluate ceftiofur sodium for the treatment of acute bovine foot rot in the Bretagne region of France. Lactating dairy cattle with acute foot rot of not more than 3 days duration were enrolled in the study. On Day 1, the degree of lameness, amount of edema and extent of necrotic lesions, were scored by the veterinarians. If inclusion criteria were met, animals were treated by intramuscular injection of ceftiofur sodium at a dose of 1 mg ceftiofur/kg BW (0.5 mg ceftiofur/lb) given at 24-hour intervals for 3 days. No additional local or general treatment was administered. The response to therapy was evaluated Day 4 (the day after the last treatment). Lameness, edema and necrotic lesions were scored again on Day 4 as on Day 1, and the treatment was judged to be very efficacious, efficacious or ineffective. A total of 27 cows met the inclusion criteria for the study. The ceftiofur treatment regime was found to be very efficacious in 13/27 (48 %), efficacious in 9/27 (33.5 %) and ineffective in 5/27 (18.5 %) of the animals. No relapses were reported. Under the conditions of this study, ceftiofur sodium at a dose of 1 mg ceftiofur/kg (0.5 mg ceftiofur/lb) administered intramuscularly once daily for 3 consecutive days was effective for the treatment of bovine foot rot.

III. TARGET ANIMAL SAFETY

Target animal safety is addressed in the FOI summary dated January 25, 1988.

IV. HUMAN FOOD SAFETY

A. Toxicity Tests

Toxicity studies are addressed in the FOI summary dated January 25, 1988. These include mutagenicity, oral feeding and hypersensitivity potential studies.

The lowest no-observed-effect-level from the oral feeding studies was 30 mg ceftiofur per kg body weight.

B. Safe Concentrations of Total Residues

The safe concentrations for total residues of ceftiofur in tissues were addressed in the FOI summaries dated January 25, 1988, and March 21, 1991.

C. Total Residue and Metabolism Studies

These data are addressed in the FOI summary dated March 21, 1991.

D. Comparative Metabolism Study Results

These data are addressed in the FOI summary dated March 21, 1991.

E. Tolerance for the Marker Residue

These data are addressed in FOI summary dated March 21, 1991.

F. Study Establishing Withdrawal Period

No milk discard time or preslaughter holding period is required because observed total residues of ceftiofur are well below the calculated safe concentrations. These data are addressed in FOI summaries dated January 25, 1988, and March 21, 1991.

G. Regulatory Method

A regulatory method is not required.

V. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA comply with the requirements of Section 512 of the Food, Drug, and Cosmetic Act and 21 CFR 514.11 of the implementing regulations. The data demonstrate that NAXCEL® Sterile Powder (ceftiofur sodium), when used under labeled conditions of use is safe and effective for the treatment of acute bovine interdigital necrobacillosis (foot rot, pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus*.

According to the Center's supplemental approval policy, 21 CFR 514.106(b)(2)(v), this is a Category II change. This supplement provides for the use of ceftiofur sodium in cattle for a new indication. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

Both clinical efficacy and *in vitro* bacterial susceptibility data were utilized to support the effectiveness of ceftiofur sodium at the dosage range of 0.5 to 1.0 mg ceftiofur/lb body weight administered intramuscularly once every 24 hours for 3 to 5 days for the treatment of bovine foot rot. The recommended dosage range (0.5 to 1.0 mg/lb) gives the practitioner greater flexibility of using the drug based on his/her clinical judgment.

The product remains a prescription drug for safe and effective use by a veterinarian in the treatment of properly diagnosed foot rot in cattle.

The agency has carefully considered the potential environmental effects of this action and has concluded that the action will not have a significant impact on the human environment. The agency's finding of no significant impact (FONSI) and the evidence supporting that finding are contained in an environmental assessment, which may be seen in the Dockets Management Branch (HFA-305), Park Building (Room 1-23), 12420 Parklawn Dr., Rockville, Maryland 20855.

Under Section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of approval because the application contains reports of new clinical or field investigations

(other than bioequivalence or residue studies) and, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) essential to the approval of the application and conducted or sponsored by the applicant.

VI. LABELING

Since addition of this new indication requires no revisions to the approved NAXCEL® Sterile Powder bottle, packer and shipper labeling, these labeling pieces are not being included in this supplemental application.

1. Naxcel® Sterile Powder draft package insert

Copies of this label may be obtained by writing to the:

Freedom of Information Office
Center for Veterinary Medicine, FDA
7500 Standish Place
Rockville, MD 20855

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.