Approval Date: January 29, 1993

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 065-505

B. Sponsor

Anthony Products Co.
5600 Peck Road
Arcadia, CA 91006

C. Proprietary Name

Microcillin-AG®

D. Established Name

Penicillin G Procaine Suspension

E. Amount of Active Ingredient

300,000 units of penicillin G procaine per milliliter

F. How Supplied

Microcillin-AG ® is available in 100 mL and 250 mL multidose vials

G. Dispensing Status

OTC

H. Dosage Regimen

The dosage for cattle, sheep, swine, and horses is 3000 units per pound of body weight or 1.0 mL for each 100 lbs. of body weight once daily. Continue treatment at least 48 hours after temperature has returned to normal and other signs of infection have subsided. Treatment should not exceed seven (7) consecutive days in non-lactating dairy cattle, beef cattle, sheep, and swine or 5 days in lactating cattle. If improvement is not noticed within forty-eight hours after treatment, a veterinarian should be consulted.

Not for use in horses intended for food.

Milk taken from animals during treatment and for forty-eight (48) hours (4 milkings) after the last treatment must not be used for food.

The drug should be discontinued for the following time periods before treated animals are slaughtered for food:

- Calves: 7 days
- Cattle: 4 days
- Sheep: 8 days

- Swine: 6 days

I. Route of Administration

Microcillin-AG® is administered intramuscularly

J. Indication

Microcillin-AG ® in aqueous suspension is intended for use in the treatment of the following diseases when due to penicillin susceptible organisms in cattle, sheep, swine, and horses.

Cattle and Sheep: Microcillin-AG® is indicated for the treatment of bacterial pneumonia (shipping fever) caused by *Pasteurella multocida*.

Swine: Microcillin-AG® is indicated for the treatment of erysipelas caused by *Erysipelothrix insidiosa*.

Horses: Microcillin-AG® is indicated for the treatment of strangles caused by *Streptococcus equi*.

II. EFFECTIVENESS

Procaine penicillin G in aqueous suspension was the subject of a final rule, and was published in the FEDERAL REGISTER of August 25, 1970 (35 FR 13544 - 13545). The final rule amended the animal drug regulations (1) to indicate those portions which reflect the National Academy of Science-National Research Council, Drug Efficacy Study Group (/NAS/NRC) evaluation of the product and (2) to specify the conditions of use for which approval of similar products need not include certain types of efficacy data, but may require submission of bioequivalence or similar data.

The Anthony Product has been shown to be bioequivalent to the pioneer product, Crysticillin ® (NADA 65-174) made by E.R. Squibb and Sons, which was approved April 6, 1979 as safe and effective. The name and address of the investigator is:

Diane Fagerberg
Colorado Animal Research Enterprises, Inc.
6200 East County Road 56
Fort Collins, Colorado 80524

A. Bioequivalence study

The bioequivalence study was designed as a 20-animal crossover trial in steer beef cattle. The 20 test animals were randomized to the two treatment groups after stratification for body weight. Single, equivalent doses (300,000 IU/100 lbs. body weight) of either the test or the reference product were administered intramuscularly to individuals in 10-animal groups at each of two periods that were separated by a 14-day washout period. No adverse reactions were observed during the study.

Blood samples were collected from each animal during each of the two periods prior to drug administration and 13 times post-dosing: at 20 min.; 40 min.; 60 min.; 80 min.; 100 min.; 120 min.; 4 hr; 6 hr; 12 hr; 18 hr; 24 hr; 48 hr; and 72 hr. Serum was analyzed for penicillin G concentration by a cylinder-plate microbiological method using Micrococcus luteus (ATCC 9341 a), with a limit of detection < "/ml.<p"

0.025 IU> The method used is based on the method described in the publication: "Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods, Reports and Protocols," National Center for Antibiotic and Insulin Analysis, Food and Drug Administration, Department of Human Health Service, Washington 20204.

This method was validated using penicillin-free serum samples which were spiked with penicillin to determine recoverability of penicillin from test animal sera. Spiked concentrations were prepared using standard USP Penicillin G, Potassium and the average percentage of penicillin recovery from the spiked samples was determined and compared closely with actual test animal sample recovery. In addition, as further validation, Precision and Accuracy controls were run with each day's samples with good correlation. Bovine serum penicillin levels in response to both products during both periods of the trial were statistically analyzed.

No statistically significant differences were noted between the two drugs. Values for serum levels over time, Ka, Tmax, Cmax, Ke, T1/2, Tp and AUC were very similar between the two products. Therefore, it is concluded that Crysticillin ® and Anthony's product, Microcillin-AG ®, are bioequivalent and will be similarly effective when used in cattle, sheep, swine, and horses.

III. TARGET ANIMAL SAFETY

The pioneer product, Squibb's Crysticillin, NADA 65-174, was approved as safe and effective for use as labeled on April 6, 1979 (**44 Fed. Reg. 20673**). The demonstration of bioequivalence to that product established that no additional target animal safety studies were required for Microcillin-AG®.

IV. HUMAN FOOD SAFETY

The bioequivalence study in cattle as previously described, demonstrates that the Anthony Products penicillin G procaine preparation is bioequivalent to the Squibb pioneer product (NAS/NRC approved and codified 4/6/79), as determined by CVM's current bioequivalency guidelines. Residue depletion data with other equivalent, approved products have demonstrated that pre-slaughter withdrawal periods of 4 days for cattle, 7 days for non ruminating cattle (calves) 8 days for sheep, 6 days for swine, and a milk discard period of 48 hours (4 milkings) for lactating cattle are adequate to ensure that penicillin residues do not exceed 0.05 ppm in edible tissues of cattle or zero in the edible tissues of sheep and swine or in milk of treated animals. The Anthony generic penicillin G procaine product will have these same pre slaughter withdrawal periods on the label. Therefore in this instance, the data from the bioequivalence study in cattle are also sufficient to support approval of this product for cattle, sheep, and swine.

V. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Act and demonstrate that Anthony's product, Microcillin-AG®, when used under its proposed conditions of use is safe and effective in cattle, sheep,swine, and horses.

The sponsor submitted bioequivalency data for cattle which demonstrated biological equivalence to the approved pioneer product. This bioequivalency blood level study was accepted in lieu of tissue depletion. Therefore, for human food safety considerations, when bioequivalence is demonstrated through blood level studies, the DESI "Me-Too" product is assigned the same withdrawal period as the reference product. The withdrawal period for cattle is 4 days, for non ruminating cattle (calves) is 7 days, for

sheep is 8 days, for swine is 6 days, and a milk discard period of 48 hours (4 milkings) for lactating cattle. The tolerance for penicillin is established at 0.05 parts per million (negligible residue) in the uncooked edible tissue of cattle and zero in the uncooked edible tissue of sheep and swine or in milk (21 CFR 556.510).

Penicillin G Procaine in Aqueous Suspension is an injectable over-the-counter product. Over-the-counter injectable procaine penicillin products are currently on the market for use in food animals. Adequate directions for use have been written for the layman, and the conditions for use prescribed on labeling are likely to be followed in practice. Therefore, the Center for Veterinary Medicine (CVM) has concluded that this productbe granted over-the- counter marketing status.

This approval does not qualify for an exclusivity period under any of the provisions of section 512 (c)(2)(F)(ii) of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act of 1988.

VI. ATTACHMENTS

1. 100 mL label
2. 250 mL label

Copies of applicable labels may be obtained by writing to the:

Food and Drug Administration
Freedom of Information Staff (HFI-35)
5600 Fishers Lane
Rockville, MD 20857

Or requests may be sent via fax to: (301) 443-1726. If there are problems sending a fax, call (301) 443-2414.

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.