Approval Date: January 22, 1997

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 110-315

B. Sponsor

Ivy Laboratories, Inc.
8857 Bond Street
Overland Park, KS 66214

C. Proprietary Name

IMPLUS-C®

D. Established Name

progesterone and estradiol benzoate

E. Dosage Form

implantation

F. Dispensing Status

OTC

G. Dosage Regimen

One implant containing 100 mg progesterone and 10 mg estradiol benzoate

H. Route of Administration

Subcutaneous implantation on the posterior aspect of the middle one-third of the ear by means of an implant gun.

I. Indication

For increased rate of weight gain in suckling beef calves up to approximately 400 lbs body weight.

J. Effect of Supplement

This supplement provides for the deletion of the present labeling limitation against the use of Implus-C in heifer (suckling beef) calves intended for reproduction.

II. EFFECTIVENESS

This supplement providing for the deletion of the present labeling limitation against the use of Implus-C in heifer (suckling beef) calves intended for reproduction does not affect the effectiveness information contained in the current NADA.

III. TARGET ANIMAL SAFETY

A target animal safety study was conducted under a similar protocol by Dr. Larry Corah, Kansas State University, Manhattan, KS at the following locations: Finegan Ranch, Bingham, NE; Gates Ranch, Coldwater, KS; KSU/Hays Experiment Station, Hays, KS; KSU/ASI, Manhattan, KS; Bar S Ranch, Paradise, KS; and Thielen Ranch, Dorrance, KS. The purpose of the study was to evaluate the effect of Implus-C implants administered to suckling heifer calves on their subsequent reproductive performance. At all six locations, suckling heifer calves were stratified by body weight and randomly assigned to one of three treatment groups. Heifers were either implanted with a single dose of Implus-C at 45-120 days of age (Early Implant Group), implanted with a single dose of Implus-C at 6-8 months of age (Late Implant Group), or were not implanted (Control Group). At approximately 15 months of age, the heifers were bred by AI during a 60-day breeding season. Heifers that became pregnant were allowed to calve the following spring.

The following table shows the mean values for each of the parameters recorded during the study:

Table 1. Mean Values for Each of the Parameters Recorded

Items	Control Group	Early Group	Late Group
Initial No./Group	185	184	180
Age at Onset of Puberty (days)	382.8	383.7	383.4
% Cycling at Breeding	86.5	81.4	84.3
Pelvic Area (cm)	167.9	181.7	175.2
First Service Conception Rate (%)	56.5	58.2	55.1
Services/Conception - Pregnant Heifers	1.1	1.1	1.1
Pregnancy Rate (%)	83.2	83.6	84.3
Calving Rate (%)	78.9	79.8	80.9
Abortion Rate (%)	5.2	4.6	4.0
Age of Heifer at Calving (days)	725.9	725.2	724.0
Calving Ease Score	1.3	1.3	1.3
Heifer Initial Weight (lb)	235.2	232.3	236.6
Heifer Weaning Weight (lb)	551.7	565.4	553.4
Heifer Prebreeding Weight (lb)	748.9	763.1	756.6
Calf Birth Weight (lb)	72.1	73.1	74.0
Calf Weaning Weight (lb)	478.2	489.7	476.7
% Calves Weaned	94.5	95.9	93.0

No differences were observed between any of the treatment groups for the parameters measured in the study. All treatment groups had comparable values for each parameter measured. The data demonstrates that any difference in calving rate between the

treatment groups would be less than 10%. Accordingly, the data provides adequate evidence that IMPLUS-C had no adverse effect on subsequent reproduction when administered to heifer (suckling beef) calves after 45 days of age through 6-8 months of age.

IV. HUMAN FOOD SAFETY

This supplement providing for the deletion of the present labeling limitation against the use of Implus-C in heifer (suckling beef) calves intended for reproduction does not affect the human food safety information contained in the current NADA.

V. AGENCY CONCLUSIONS

Adequate data were provided to demonstrate that IMPLUS-C had no adverse effect on subsequent reproduction when administered to heifer (suckling beef) calves after 45 days of age.

Under the Center's supplement approval policy (21 CFR 514.106(b)(2)), this is a Category II change providing for the deletion of the labeling limitation against the use of IMPLUS-C in heifer (suckling beef) calves intended for reproduction. 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.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for food producing animals qualifies for THREE years of marketing exclusivity beginning on the date of approval because the supplemental application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) required for the approval of the application and conducted or sponsored by the applicant. The three years of marketing exclusivity applies only to the change in the labeling (deletion of the present labeling limitation against the use of Implus-C in heifer (suckling beef) calves intended for reproduction) for which the supplemental application was approved.

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.