Approval Date: January 19, 2006

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-040

CELERIN

Microencapsulated Estradiol Benzoate Suspension Implant (Estradiol Benzoate)

For increased rate of weight gain in suckling beef calves and for increased rate of weight gain and improved feed efficiency in steers and heifers fed in confinement for slaughter.

This supplement provides for the addition of the suckling beef calf indication "For increased rate of weight gain," originally approved under NADA 141-041 as CELERIN C to CELERIN. In addition it updates the dosage administration for suckling beef calves to 0.5 mL (10 mg). This supplement also provides for a change in the indication and dosage to allow use for increased rate of weight gain in steers fed in confinement for slaughter, previously at 10 mg (0.5 mL) to 20 mg (1.0 mL). In addition, this supplement also provides for a new 10 mL vial size.

Sponsored by:

PR Pharmaceuticals, Inc.
1716 Heath Pkwy.
Fort Collins, CO 80524

1. **GENERAL INFORMATION**

2. **EFFECTIVENESS**

3. **TARGET ANIMAL SAFETY**

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FREEDOM OF INFORMATION SUMMARY

CELERIN (estradiol benzoate)
Microencapsulated Estradiol Benzoate
Suspension Implant

1. GENERAL INFORMATION:

a. File Number:	NADA 141-040
b. Sponsor:	PR Pharmaceuticals, Inc. 1716 Heath Pkwy. Fort Collins, CO 80524 Drug Labeler Code: 067210
c. Established Name:	Estradiol benzoate
d. Proprietary Name:	CELERIN
e. Dosage Form:	Suspension implant
f. How Supplied:	50 mL: Each package contains one vial of 1000 mg estradiol benzoate in THERAPHASE microspheres and one 50 mL vial of sterile diluent for suspension. The entire package constitutes 100 x 10 mg doses, or 50 x 20 mg doses of estradiol benzoate. 10 mL: Each package contains one vial of 200 mg estradiol benzoate in THERAPHASE microspheres and one 10 mL vial of sterile diluent for suspension. The entire package constitutes 20 x 10 mg doses, or 10 x 20 mg doses of estradiol benzoate.
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	One mL dose contains 20 mg estradiol benzoate.
i. Route of Administration:	Subcutaneous injection in the ear only. A 16 to 20 gauge needle with 45° bevel is recommended.

j. Species/Class:	Suckling beef calves and steers and heifers fed in confinement for slaughter. Do not use in veal calves, calves intended for reproduction, or calves less than 30 days old.
k. Recommended Dosage:	For increased rate of weight gain in suckling beef calves administer 0.5 mL (10 mg). For improved feed efficiency and increased rate of weight gain in steers and heifers, administer 1 mL (20 mg).
l. Pharmacological Category:	Steroid hormone
m. Indications:	For increased rate of weight gain in suckling beef calves and for increased rate of weight gain and improved feed efficiency in steers and heifers fed in confinement for slaughter.
n. Effect of Supplement	This supplement provides for the addition of the suckling beef calf indication "For increased rate of weight gain," originally approved under NADA 141-041 as CELERIN C to CELERIN. In addition it updates the dosage administration for suckling beef calves to 0.5 mL (10 mg). This supplement also provides for a change in the indication and dosage to allow use for increased rate of weight gain in steers fed in confinement for slaughter, previously at 10 mg (0.5 mL) to 20 mg (1.0 mL). In addition, this supplement also provides for a new 10 mL vial size.

2. EFFECTIVENESS:

No new effectiveness data are required for the approval of this supplement. The product's effectiveness in suckling beef calves has been established in the Freedom of Information (FOI) Summary for the parent new animal drug application for CELERIN C (NADA 141-041) dated June 25, 2003. The product's effectiveness in steers and heifers fed in confinement for slaughter has been established in the Freedom of Information (FOI) Summary for the parent new animal drug application for CELERIN (NADA 141-040) dated June 25, 2003. In the June 25, 2003, approval, increased rate of weight gain in steers fed in

confinement for slaughter was approved at the 10 mg estradiol benzoate dose. Since 20 mg was equally effective as 10 mg for increased rate of weight gain in steers, the current supplement also provides for a change in the indication and dosage to allow use for increased rate of weight gain in steers fed in confinement for slaughter at the dose of 20 mg. Since the 10 and 20 mg doses were not statistically different for increased rate of weight gain in steers fed in confinement for slaughter, the CELERIN label carries the following statement: *"Note: In a clinical study evaluating 0, 2.5, 5, 10, and 20 mg of CELERIN in heifers and steers fed in confinement for slaughter, the 20 mg dose was not different from the 10 mg dose for increased rate of weight gain in steers."*

Improved feed efficiency in steers fed in confinement for slaughter, originally approved at the 20 mg dose, remains in effect.

3. TARGET ANIMAL SAFETY:

No new target animal safety data are required for the approval of this supplement. The product's target animal safety in steers and heifers fed in confinement for slaughter has been established in the Freedom of Information (FOI) Summary for the parent new animal drug application for CELERIN (NADA 141-040) dated June 25, 2003. The product's target animal safety in suckling beef calves has been established in the Freedom of Information (FOI) Summary for the parent new animal drug application for CELERIN C (NADA 141-041) dated June 25, 2003.

4. HUMAN SAFETY:

No new human food safety data are required for the approval of this supplement. The product's human food safety in steers and heifers fed in confinement for slaughter has been established in the Freedom of Information (FOI) Summary for the parent new animal drug application for CELERIN (NADA 141-040) dated June 25, 2003. The product's human food safety in suckling beef calves has been established in the Freedom of Information (FOI) Summary for the parent new animal drug application for CELERIN C (NADA 141-041) dated June 25, 2003.

5. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that estradiol benzoate when administered at 20 mg/mL is safe and effective for the claims indicated in section 1 of this FOI Summary.

This approval does not qualify for marketing exclusivity under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act.

Pursuant to 21 CFR 514.106 (b)(2)(i), this supplemental NADA approval is regarded as a Category II supplemental change which did not require a reevaluation of safety and efficacy data in the parent NADA.

The Center for Veterinary Medicine has concluded that, for this product, adequate directions of use by the layperson have been provided and the product will have over-the-counter (OTC) status. Label directions provide detailed instruction in plain language. The drug product is not a controlled substance. Thus, the drug product is assigned OTC status, and the labeling is adequate for the intended use.

Estradiol benzoate is under the following U.S. patent numbers:

U.S. Patent Number	Date of Expiration
5,288,496	February 22, 2011
5,401,507	March 28, 2012
5,427,796	February 22, 2011

***6. ATTACHMENTS**:*

Facsimile Labeling is attached as indicated below:

Inner Carton Label (1 x 50 mL)
Vial Label (1000 mg estradiol benzoate)
Vial Label (50 mL sterile diluent)
Case Shipper Label (10 x 50 mL)
Package Insert (1 x 50 mL)
Inner Carton Label (1 x 10 mL)
Vial Label (200 mg estradiol benzoate)
Vial Label (10 mL sterile diluent)
Case Shipper Label (10 x 10 mL)
Package Insert (1 x 10 mL)