

Approval Date: March 4, 2005

FREEDOM OF INFORMATION SUMMARY
SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION
NADA 038-233

RALGRO
(zeranol)

This supplement provides for deletion of the no residue designation and regulatory method and addition of a tolerance for zeranol of 20 ppb in edible tissues of sheep published in 21 CFR 556.760.

Sponsored by:

Schering-Plough Animal Health Corp.
1095 Morris Ave.
Union, NJ 07083

FREEDOM OF INFORMATION SUMMARY

RALGRO
Feedlot Lambs

1. GENERAL INFORMATION:

- a. File Number: NADA 038-233
- b. Sponsor: Schering-Plough Animal Health Corp.
1095 Morris Ave.
Union, NJ 07083
Drug Labeler Code: 000061
- c. Established Name: Zeranol
- d. Propriety Name: RALGRO
- e. Dosage Form: Implantation (ear implant) as per 21 CFR 522.2680
- f. How Supplied: Each carton contains ten 24-dose cartridges (12 mg dose).
- g. How Dispensed: OTC
- h. Amount of Active Ingredients: 12 mg zeranol.
- i. Route of Administration: Subcutaneous implantation on the posterior aspect of the middle one-third of the ear by means of an implant gun.
- j. Species/Class: Feedlot lambs.
- k. Recommended Dosage: One implant containing 12 mg zeranol.
- l. Pharmacological Category: Steroid hormone.
- m. Indications: For increased rate of weight gain and improved feed conversion of growing lambs.
- n. Effect of Supplement: This supplement provides for deletion of the no residue designation and regulatory method and addition of a tolerance for zeranol of 20 ppb in edible tissues of sheep published in 21 CFR 556.760.

2. DRUG EFFECTIVENESS:

No new effectiveness data are required for the approval of this supplement. The product's effectiveness in feedlot lambs has been established in the supplemental approval published in the Federal Register August 28, 1970 (pp. 13727-13728), for RALGRO (NADA 038233).

3. TARGET ANIMAL SAFETY:

No new target animal safety data are required for the approval of this supplement. The product's safety in feedlot lambs has been established in the supplemental approval published in the Federal Register August 28, 1970 (pp. 13727-13728), for RALGRO (NADA 038233).

4. HUMAN SAFETY:

The product's human food safety for feedlot lambs has been established in the supplemental approval published in the Federal Register August 28, 1970 (pp. 13727-13728), for RALGRO (NADA 038233).

A. Toxicology

Summaries of pivotal toxicology studies of zeranol can be found in earlier FOI Summaries for this NADA, particularly the FOI Summary dated January 1989 for the supplemental approval dated July 28, 1989, which describes the data supporting the deletion of the requirement for a withholding time for zeranol in cattle.

B. Residue Chemistry

The submission of residue data was not required for approval of this supplemental application. No changes have been made in the conditions of use, which were established relative to the regulatory method having a sensitivity of 20 ppb in the edible tissues of sheep. Although the description of the method is deleted from 21 CFR 556.760, that method is still available from FDA (Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855) and applicable to the new tolerance of 20 ppb for edible tissues of sheep.

5. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfies the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations providing for the deletion of 1) the no residue designation and regulatory method and 2) addition of a tolerance for zeranol of 20 ppb in edible tissues of sheep published in 21 CFR 556.760. As previously written, 21 CFR 556.760 evidenced an inconsistency between cattle and sheep. In particular, the 'no residue' designation originally applied to zeranol in both cattle and sheep. But in assessing a subsequent supplemental application proposing deletion of the 65-day withholding time for cattle treated with zeranol, FDA concluded that zeranol's toxicological properties are solely associated with its estrogenic activity (see January 1989

FOI Summary for approval dated July 28, 1989). FDA calculated an ADI and safe concentrations, and after a showing that the peak total residue concentrations in edible tissues of cattle were below the respective safe concentrations, concluded that a zero pre-slaughter withdrawal period was appropriate and that there was no need for a tolerance or regulatory method. Because the toxicology of a compound is determined independent of the target food animal, the sponsor asked that FDA make the changes noted above.

The Agency has concluded that the toxicological decisions made for cattle (subsequent to the original approvals for cattle and sheep) also apply to sheep. Moreover, since the original conditions of use were established with reference to the method's sensitivity of 20 ppb, the setting of a 20 ppb tolerance is a logical alternative. Approval of this supplemental application will have no impact on humans consuming tissues from sheep treated with zeranol.

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

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

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change. 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.

No patent information was submitted by the sponsor with this application.

6. ATTACHMENTS:

Facsimile Labeling is attached as indicated below:

RALGRO (feedlot lambs) 10 24-Dose Cartridge Carton Label (RALOGUN)
RALGRO (feedlot lambs) Package Insert (RALOGUN)