Date of Approval: October 1, 2010

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-473

PHARMASIN Soluble
(tylosin tartrate)

Chickens, Turkeys, Swine, and Honey Bees

Indications: As an aid in the treatment of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin in broiler and replacement chickens. For the control of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin at time of vaccination or other stress in chickens. For the control of chronic respiratory disease (CRD) associated with *Mycoplasma synoviae* sensitive to tylosin in broiler chickens

For maintaining weight gain and feed efficiency in the presence of infectious sinusitis associated with *Mycoplasma gallisepticum* sensitive to tylosin in turkeys

For the treatment and control of swine dysentery caused by *Brachyspira hyodysenteriae* in swine

For the control of American Foulbrood (*Paenibaccillus larvae)* in honey bees

Sponsored by:

Huvepharma AD

1. GENERAL INFORMATION:

A. File Number: ANADA 200-473

B. Sponsor:

Huvepharma AD
33 James Boucher Blvd.
Sofia 1407
Bulgaria

Drug Labeler Code: 016592

U.S. Agent:
Kelly W. Beers, Ph.D
Huvepharma Inc.
525 Westpark Drive, Suite 230
Peachtree City, GA 30269

C. Proprietary Name(s): PHARMASIN Soluble

D. Established Name(s): Tylosin tartrate

E. Pharmacological Category: Antimicrobial

F. Dosage Form(s): Granules, for solution

G. Amount of Active Ingredient(s): 100 g tylosin tartrate per pouch and per jar

H. How Supplied: 100 g pouch, 100 g jar

I. How Dispensed: OTC

J. Dosage(s):

Chickens and Turkeys: To assure thorough dissolution, place the PHARMASIN (contents of the jar or pouch) in a mixing container and add one gallon of water (3790 mL) to the material. Mix this concentrated solution with water to make 50 gallons of treated drinking water.

Swine: To assure thorough dissolution, place the PHARMASIN (contents of the jar or pouch) in a mixing container and add one gallon of water (3790 mL) to the material. Mix this concentration solution with water to make 400 gallons of treated drinking water resulting in 250 mg/gallon.

Honey Bees: Mix 200 mg tylosin in 20 g

	confectioners/powdered sugar. Use immediately.
K. Route(s) of Administration:	Oral in water
L. Species/Class(es):	Chickens, turkeys, swine, and honey bees
M. Indication(s):	Chickens: As an aid in the treatment of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin in broiler and replacement chickens. For the control of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin at time of vaccination or other stress in chickens. For the control of chronic respiratory disease (CRD) associated with *Mycoplasma synoviae* sensitive to tylosin in broiler chickens. Turkeys: For maintaining weight gain and feed efficiency in the presence of infectious sinusitis associated with *Mycoplasma gallisepticum* sensitive to tylosin. Swine: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae.* Honey Bees: For the control of American Foulbrood (*Paenibaccillus larvae*).
N. Reference listed new animal drug (RLNAD):	TYLAN Soluble; tylosin tartrate; NADA 013-076; Elanco Animal Health, A Division of Eli Lilly & Co.

2. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor is required to show that the generic product is bioequivalent to the RLNAD, which has been shown to be safe and effective. If the product is intended for use in food producing animals and bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2000).

Based on the formulation characteristics of the generic product, Huvepharma AD was granted a waiver from the requirement for an *in vivo* bioequivalence study for the generic product PHARMASIN Soluble. The generic product is administered orally in water, contains the same active ingredient in the same concentration and dosage form as the RLNAD product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The reference listed new animal drug (RLNAD) is TYLAN Soluble (tylosin tartrate), the subject of Elanco Animal Health, A Division of Eli Lilly & Co., NADA 013-076, was approved on November 8, 1996.

3. HUMAN SAFETY:

Human Warnings are provided on the product label as follows: Not for use in humans. Keep out of reach of children.

- **Tolerances for Residues**:
  The tolerance established for the pioneer product applies to the generic product. A tolerance of 0.2 part per million (ppm) (negligible residue) is established for tylosin residues in the uncooked edible tissues in uncooked fat, muscle, liver and kidney of chickens, turkeys and swine under 21 CFR 556.740.
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- **Withdrawal Times:**
  Under the CVM Bioequivalence Guidelines, when a generic product is granted a waiver of *in vivo* bioequivalence testing, the withdrawal period established for the RLNAD is also assigned to the generic product.

  For this reason, the following withdrawal periods have been established for the indicated species: 24 hours for chickens, 5 days for turkeys, 48 hours in swine and 4 weeks before main honey flow in honey bees. (21 CFR 520.2640).
- **Regulatory Method for Residues:**

The analytical method for the determination of tylosin in honey is a microbiological assay using an oxytetracycline-resistant strain of *Paenibacillus larvae* in tissues (the causative agent of American foulbrood disease of honey bees). A copy of the method is on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

The analytical method for the determination of tylosin residues in tissues uses a microbiological assay procedure. This method is found in the Food Additives Analytical Manual on file at the Center for Veterinary Medicine, FDA, 7500 Standish Place, Rockville, MD 20855.

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that PHARMASIN Soluble, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. **ATTACHMENTS:**

Facsimile generic labeling and currently approved RLNAD labeling are attached as indicated below:

Generic Labeling for ANADA 200-473:
100 g jar labels with outsert, 100 g pouches, and shipping labels for the 100 g jar and pouch

RLNAD Labeling for NADA 013-076:
100 g jar container label