CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 65-010

Name: Neomycin Sulfate Oral Solution USP, 125 mg/5 mL [87.5 mg (base)/5 mL]

Sponsor: Pharma-Tek, Inc.

Approval Date: May 23, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-010

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-010

APPROVAL LETTER

ANDA 65-010

MAY 23 2002

Pharma-Tek, Inc.
Attention: Susan E. Badia
1000 Ft. Salonga Road, Suite #3
Northport, NY 11768

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated February 10, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Neo-Fradin Oral Solution (Neomycin Sulfate Oral Solution USP, 125 mg/5 mL [87.5 mg (base)/5 mL]). We note that this product is subject to the exception provisions of Section 125(d)(2) of Title I of the Food and Drug Administration Modernization Act of 1997.

Reference is also made to your amendment dated March 18, 2002.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Neo-Fradin Oral Solution, 125 mg/5 mL, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Mycifradin® Oral Solution, 125 mg/5 mL, of Pharmacia and Upjohn Co.).

Under section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print.

Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

Gary Buehler 5/23/02
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

cc: ANDA 65-010
Division File
FIELD COPY
HFD-610/RWest
HFD-92
~~HFD-210/B.Poole~~
HFD-330/
HFD-205/

Robert the last BBR is acceptable for drug product manufacturer. 5/23/2002

Endorsements:
HFD-643/M.Shih/4/30/02 5/2/02
HFD-643/R.Adams/5/1/02 R.C.Adams 5/6/02
HFD-617/M.Anderson/5/1/02 M Anderson 5/7/02
HFD-613/J.Council/5/1/02 J. Council 5/1/02
HFD-613/L.Golson/5/1/02 5/2/02

V:\firmsnz\pharma.tek\ltrs&rev\65010apd.doc
F/T by:

APPROVAL

CMC satisfactory 5/1/02

Issues regarding CGMP fin need to be resolved prior to AP action and updated 5/23/02

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-010

LABELING

Pharma-Tek

Neo-Fradin

Oral Solution

Neomycin Sulfate Oral Solution USP

℞ only

WARNING

SYSTEMIC ABSORPTION OF NEOMYCIN OCCURS FOLLOWING ORAL ADMINISTRATION AND TOXIC REACTIONS MAY OCCUR. Patients treated with neomycin should be under close clinical observation because of the potential toxicity associated with their use.

NEUROTOXICITY (INCUDING OTOTOXICITY) AND NEPHROTOXICITY FOLLOWING THE ORAL USE OF NEOMYCIN SULFATE HAVE BEEN REPORTED, EVEN WHEN USED IN RECOMMENDED DOSES. THE POTENTIAL FOR NEPHROTOXICITY, PERMANENT BILATERAL AUDITORY OTOTOXICITY AND SOMETIMES VESTIBULAR TOXICITY IS PRESENT IN PATIENTS WITH NORMAL RENAL FUNCTION WHEN TREATED WITH HIGHER DOSES OF NEOMYCIN AND/OR FOR LONGER PERIODS THAN RECOMMENDED. Serial, vestibular, and audiometric tests, as well as tests of renal function, should be performed (especially in high risk patients).

THE RISK OF NEPHROTOXICITY AND OTOTOXICITY IS GREATER IN PATIENTS WITH IMPAIRED RENAL FUNCTION. Ototoxicity is often delayed in onset and patients developing cochlear damage will not have symptoms during therapy to warn them of developing eighth nerve destruction and total or partial deafness may occur long after neomycin has been discontinued.

Neuromuscular blockage and respiratory paralysis have been reported following the oral use of neomycin. The possibility of the occurrence of neuro-muscular blockage and respiratory paralysis should be considered if neomycin is administered, especially to patients receiving anesthetics, neuro-muscular blocking agents such as tubocurarine, succinylcholine, decamethonium, or in patients receiving massive transfusions of citrate anticoagulated blood. If blockage occurs, calcium salts may reverse these phenomena but mechanical respiratory assistance may be necessary.

Concurrent and/or sequential systemic, oral, or topical use of other aminoglycosides including paromomycin and other potentially nephrotoxic and/or neurotoxic drugs such as bacitracin, cisplatin, vancomycin, amphotericin B, polymyxin B, colistin, and viomycin should be avoided because the toxicity may be additive.

Other factors which increase the risk of toxicity are advanced age and dehydration.

The concurrent use of neomycin with potent diuretics such as ethacrynic acid or furosemide should be avoided since certain diuretics by themselves may cause ototoxicity. In addition, when administered intravenously, diuretics may enhance neomycin toxicity by altering the antibiotic concentration in serum and tissue.

DESCRIPTION

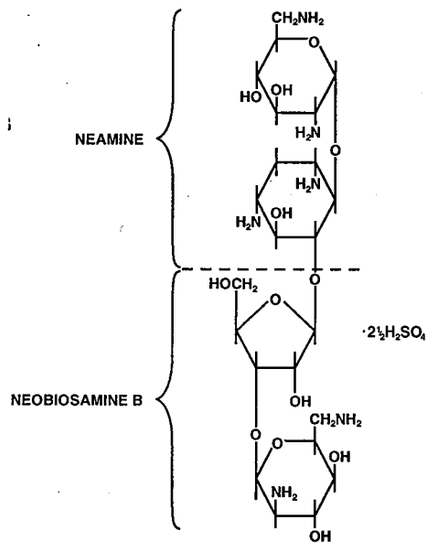
NEO-FRADIN Oral Solution for oral administration contains neomycin which is an antibiotic obtained from the metabolic products of the actinomycete *Streptomyces fradiae*. The pH range is 5.0 to 7.5. NEO-FRADIN Oral Solution is a clear orange solution with a cherry flavor. Each 5 mL of NEO-FRADIN Oral Solution contains 125 mg of neomycin sulfate (equivalent to 87.5 mg of neomycin). Inactive ingredients: benzoic acid, FD&C yellow no. 6, cherry flavor, glycerin, methylparaben, proplyparaben, sodium phosphate dibasic heptahydrate, sulfuric acid, diatomaceous earth, and purified water.

Sodium phosphate dibasic heptahydrate and sulfuric acid are used as pH adjusters.

The chemical name for Neomycin is: *0*-2, 6-diamino-2, 6-dideoxy-α-D-lucopyranosyl-(1→3) -*0*β-D-ribofuranosyl-(1→5)-0-[2, 6-diamino-2, 6-dideoxy-α-D-glucopyranosyl-(1→4)]-2-deoxy-D-streptamine. Neomycin B is identical except that the -α-D-glucopyranosyl residue in the neobiosamine moiety is β-L-idopyranosly.

The molecular weight of Neomycin is 614.67. The structural formula is represented below:

NEOMYCIN SULFATE USP



NEOMYCIN B SULFATE $C_{23}H_{46}N_6O_{13}\cdot 2\frac{1}{2}H_2SO_4$

CLINICAL PHARMACOLOGY

Neomycin sulfate is poorly absorbed from the gastrointestinal tract. The small absorbed fraction is rapidly distributed in the tissues and is excreted by the kidney in keeping with the degree of kidney function. The unabsorbed portion of the drug (approximately 97 percent) is eliminated unchanged in the feces.

Growth of most intestinal bacteria is rapidly suppressed following oral administration of neomycin sulfate, with the suppression persisting for 48-72 hours. Nonpathogenic yeasts and occasionally resistant strains of *Enterobacter aerogenes* (formerly *Aerobacter aerogenes*) replace the intestinal bacteria.

As with other aminoglycosides, the amount of systemically absorbed neomycin transferred to the tissues increases cumulatively with each repeated dose administered until a steady state is achieved. The kidney functions as the primary excretory path as well as the tissue binding site with the highest concentration found in renal cortex. With repeated dosings, progressive accumulation also occurs in the inner ear. Release of tissue bound neomycin occurs slowly over a period of several weeks after dosing has been discontinued.

Protein binding studies have shown that the degree of aminoglycoside protein binding is low and, depending upon the methods used for testing, this may be between 0 and 30 percent.

Microbiology

In vitro tests have demonstrated that neomycin is bactericidal and acts by inhibiting the synthesis of protein in susceptible bacterial cells. It is effective primarily against gram-negative bacilli but does have some activity against gram-positive organisms. Neomycin is active *in vitro* against *Escherichia coli* and the *Klebsiella-Enterobacter* group. Neomycin is not active against anaerobic bowel flora.

If susceptibility testing is needed, using a 30 mcg disc, organisms producing zones of 16 mm or greater are considered susceptible. Resistant organisms produce zones of 13 mm or less. Zones greater than 13 mm and less than 16 mm indicate intermediate susceptibility.

INDICATIONS AND USAGE

Hepatic coma (portal-systemic encephalopathy)

Neomycin sulfate has been shown to be effective adjunctive therapy in hepatic coma by reduction of the ammonia forming bacteria in the intestinal tract. The subsequent reduction in blood ammonia has resulted in neurologic improvement.

CONTRAINDICATIONS

Neomycin sulfate oral preparations are contraindicated in the presence of intestinal obstruction and in individuals with a history of hypersensitivity to the drug.

Patients with a history of hypersensitivity or serious toxic reaction to other aminoglycosides

may have a cross-sensativity to neomycin.

Neomycin sulfate oral solution is contraindicated in patients with inflammatory or ulcerative gastrointestinal disease because of the potential for enhanced gastrointestinal absorption of neomycin.

WARNINGS

(see boxed WARNINGS)

Additional manifestations of neurotoxicity may include numbness, skin tingling, muscle twitching, and convulsions.

The risk of hearing loss continues after drug withdrawal.

Aminoglycosides can cause fetal harm when administered to a pregnant woman. Aminoglycoside antibiotics cross the placenta and there have been several reports of total irreversible bilateral congenital deafness in children whose mothers received streptomycin during pregnancy. Although serious side effects to fetus or newborn have not been reported in the treatment of pregnant women with other aminoglycosides, the potential for harm exists. Animal reproduction studies of neomycin have not been conducted. If neomycin is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

PRECAUTIONS

General

As with other antibiotics, use of oral neomycin may result in overgrowth of non-susceptible organisms, particularly fungi. If this occurs, appropriate therapy should be instituted.

Neomycin is quickly and almost totally absorbed from body surfaces (except the urinary bladder) after local irrigation and when applied topically in association with surgical procedures. Delayed-onset, irreversible deafness, renal failure, and death due to neuromuscular blockade (regardless of the status of renal function) have been reported following irrigation of both small and large surgical fields with minute quantities of neomycin.

Cross-allergenicity among aminoglycosides has been demonstrated.

Aminoglycosides should be used with caution in patients with muscular disorders such as myasthenia gravis or parkinsonism since these drugs may aggravate muscle weakness because of their potential curare-like effect on the neuromuscular junction.

Small amounts of orally administered neomycin are absorbed through intact intestinal mucosa.

There have been many reports in the literature of nephrotoxicity and/or ototoxicity with the oral use of neomycin. If renal insufficiency develops during oral therapy, consideration should be given to reducing the drug dosage or discontinuing therapy.

An oral neomycin dose of 12 grams per day produces a malabsorption syndrome for a variety of substances including fat, nitrogen, cholesterol, carotene, glucose, xylose, lactose, sodium, calcium, cyanocobalamin and iron.

Oral administered neomycin increases fecal bile acid excretion and reduces intestinal lactase activity.

Information for the patient

Before administering the drug, patients or members of their families should be informed of possible toxic effects on the eighth nerve. The possibility of acute toxicity increases in premature infants and neonates.

Laboratory tests

Patients with renal insufficiency may develop toxic neomycin blood levels unless doses are properly regulated. If renal insufficiency develops during treatment, the dosage should be reduced or the antibiotic discontinued. To avoid nephrotoxicity and eighth nerve damage associated with high doses and prolonged treatment, the following should be performed prior to and periodically during therapy: urinalysis for increased excretion of protein, decreased specific gravity, casts and cells; renal function tests such as serum creatinine, BUN or creatinine clearance; tests of the vestibulocochlearis nerve (eighth cranial nerve) function.

Serial, vestibular and audiometric tests should be performed (especially in high risk patients). Since elderly patients may have reduced renal function which may not be evident in the results of routine screening tests such as BUN or serum creatinine, a creatinine clearance determination may be more useful.

Drug Interactions

Caution should be taken in concurrent or serial use of other neurotoxic and/or nephrotoxic drugs because of possible enhancement of the nephrotoxicity and/or ototoxicity of neomycin (see boxed WARNINGS).

Caution should also be taken in concurrent or serial use of other aminoglycosides and polymyxins because they may enhance neomycin's nephrotoxicity and/or ototoxicity and potentiate neomycin's neuromuscular blocking effects.

Oral neomycin inhibits the gastrointestinal absorption of penicillin V, oral vitamin B-12, methotrexate and 5-fluorouracil. The gastrointestinal absorption of digoxin also appears to be inhibited. Therefore, digoxin serum levels should be monitored.

Oral neomycin may enhance the effect of courmarin in anticoagulants by decreasing vitamin K availability.

Carcinogenesis, mutagenesis, impairment of fertility

No long-term animal studies have been performed with neomycin to evaluate carcinogenic or mutagenic potential or impairment of fertility.

Pregnancy Category D (see WARNINGS section)

Nursing Mothers

It is not known whether neomycin is excreted in human milk but it has been shown to be excreted in cow milk following a single intramuscular injection. Other aminoglycosides have been shown to be excreted in human milk. Because of the potential for serious adverse reactions from the aminoglycosides in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

The safety and efficacy of oral neomycin in patients less than eighteen years of age have not been established. If treatment of a patient less than eighteen years of age is necessary, neomycin should be used with caution and the period of treatment should not exceed three weeks because of the absorption from the gastrointestinal tract.

ADVERSE REACTIONS

The most common adverse reactions to oral neomycin are nausea, vomiting, and diarrhea. The "Malabsorption Syndrome" characterized by increased fecal fat, decreased serum carotene and fall in xylose absorption has been reported with prolonged therapy. Nephrotoxicity, ototoxicity, and neuromuscular blockage have been reported
(see boxed WARNINGS and PRECAUTIONS section).

OVERDOSAGE

Because of low absorption, it is unlikely that acute overdosage would occur with oral neomycin. However, prolonged administration could result in sufficient systemic drug levels to produce neurotoxicity, ototoxicity, and/or nephrotoxicity. Hemodialysis will remove neomycin from the blood.

DOSAGE AND ADMINISTRATION

To minimize the risk of toxicity use the lowest possible dose and the shortest possible treatment period to control the condition. Treatment for periods longer than two weeks is not recommended.

Hepatic coma

For use as an adjunct in the management of hepatic coma, the recommended dose is 4-12 grams per day given in the following regimen:

1.Withdraw protein from diet. Avoid use of diuretic agents.

2.Give supportive therapy including blood products, as indicated.

3.Give NEO-FRADIN Oral Solution in doses of four to twelve grams of neomycin sulfate per day in divided doses. Treatment should be continued over a period of five to six days during which time protein should be returned incrementally to the diet.

4.If less potentially toxic drugs cannot be used for chronic hepatic insufficiency, neomycin sulfate in doses of up to four grams daily may be necessary. The risks for the development of neomycin induced toxicity progressively increase when the treatment must be extended to preserve the life of a patient with hepatic encephalopathy who has failed to fully respond. Frequent periodic monitoring of these patients to ascertain the presence of drug toxicity is mandatory (see PRECAUTIONS). Also, neomycin serum concentrations should be monitored to avoid potentially toxic levels. The benefits to the patient should be weighed against the risks of nephrotoxicity, permanent ototoxicity and neuromuscular blockade following the accumulation of neomycin in the tissues.

HOW SUPPLIED

NEO-FRADIN Oral Solution is available as a clear orange solution with a cherry flavor in 16 fl. oz, 4 fl. oz and 2 fl. oz bottles containing 125 mg of neomycin sulfate (equivalent to 87.5 mg of neomycin) per five mL.

NDC 39822-0330-5 for 16 fl. oz,
NDC 39822-0330-4 for 4 fl. oz and
NDC 39822-0330-2 for 2 fl. oz.

Store at controlled room temperature15° -30°C (59° -86°F).

Manufactured for:

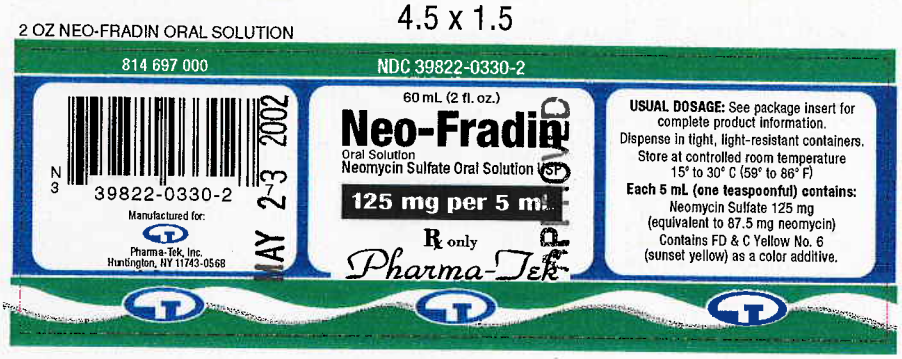
Pharma-Tek Inc.

Printed in U.S.A. HUNTINGTON, NY 11743-0568 Revised September 1999

NEO-FRADIN; Neomycin Sulfate Oral Solution USP 60 mL (2 fl. oz)

VIAL LABEL – 60 mL (2fl. oz)

4.5 x 1.5

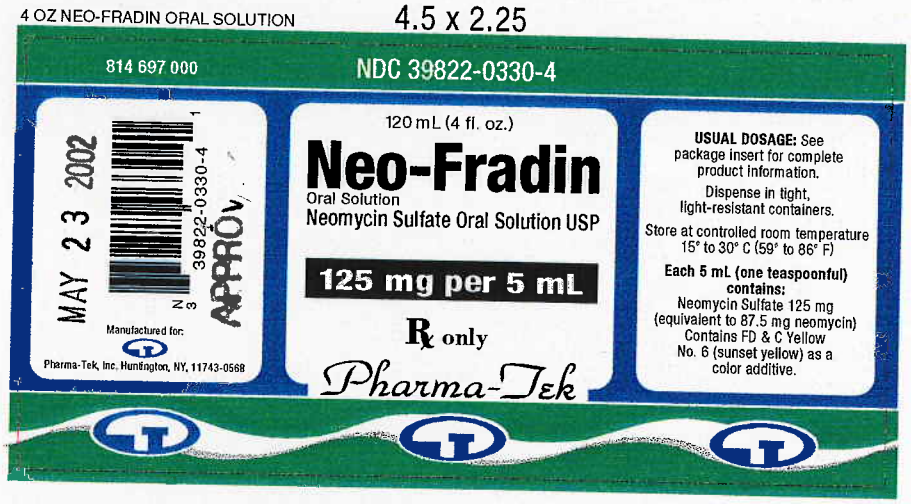


pms 354

NEO-FRADIN; Neomycin Sulfate Oral Solution USP 120 mL (4 fl. oz)

VIAL LABEL – 120 mL (4 fl. oz)

4 OZ NEO-FRADIN ORAL SOLUTION 4.5 x 2.25



pms 354

ORIGINAL

16 OZ NEO-FRADIN ORAL SOLUTION

5.75 x 4.5

NDC 39822-0330-5

480 mL (16 fl. oz)

Neo-Fradin

Oral Solution

APPROVED

Neomycin Sulfate
Oral Solution USP

125 mg per 5 mL

℞ only

Pharma-Tek, Inc.
Huntington, NY 11743-0568

Pharma-Tek

NDC 39822-0330-5

480 mL (16 fl. oz.)

Neo-Fradin

Oral Solution

Neomycin Sulfate Oral Solution USP

MAY 23 2002

USUAL DOSAGE: See package insert for complete product information.

Dispense in tight, light-resistant containers.

Store at controlled room temperature 15°-30° C (59°-86° F)

Each 5 mL (one teaspoonful) contains:
Neomycin Sulfate 125 mg
(equivalent to 87.5 mg neomycin)
Contains FD & C Yellow No. 6 (sunset yellow) as a color additive.

814 697 000

N 3 39822 0330 5 8

Manufactured for: Pharma-Tek

Made in USA

pms 354

57

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-010

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-010

Date of Submission: December 16, 1998

Applicant's Name: Pharma-Tek Inc.

Established Name: Neomycin Sulfate Oral Solution USP, 125 mg/5 mL

Labeling Deficiencies:

1. CONTAINER - 2 fl. oz, 4 fl. oz, & 16 fl. oz.

   a. For each size container, please state the metric volume first, e.g., "120 mL (4 fl. oz)"

   b. For the 2 fl. oz size, insert a space between "60" and "mL".

   c. For the 4 fl. oz size, insert a space between "120" and "mL".

2. INSERT

   a. DESCRIPTION

      i. Please include the pH range. We refer you to 21 CFR 201.57(a)(2).

      ii. When listing your inactive ingredients, we encourage you to specify which ingredients were used as pH adjusters.

      iii. In your list of inactive ingredients, use the established name instead of the brand name "[redacted]".

      iv. We encourage the inclusion of the specific flavor in the DESCRIPTION section.

   b. DOSAGE AND ADMINISTRATION

      i. First paragraph, last sentence: "...longer than two weeks is not recommended."

ii. Hepatic coma

A. Item 3., first sentence: "...four to twelve grams of neomycin sulfate per day..."

B. Item 4.

1) First sentence: "...insufficiency, neomycin sulfate in doses..."

2) Second sentence: Revise "reserve" to read "preserve".

3) Last sentence: "...blockade following the accumulation..."

c. HOW SUPPLIED

i. Second paragraph: "NDC...for 16 fl. oz,"

ii. We encourage that you relocate "Rx only" to appear immediately following the established name/title.

Please revise your labels and labeling, as instructed above, and submit in final print, or draft if you prefer.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

_____

Robert West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	x		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			z
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	x		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	x		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling (continued)	**Yes**	**No**	**N.A.**
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x

Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement? *See FTR and NOTE TO THE CHEMIST	*		
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?	x		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. *Not listed in RLD	*		
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T ½ and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

NOTES/QUESTIONS TO THE CHEMIST:

1. DESCRIPTION section:

   a. The firm added the molecular weight. Is the molecular weight accurate?

   b. The firm added the chemical name. Is the chemical name accurate?

   c. We note that the firm has listed "_____" as an inactive ingredient in the DESCRIPTION section and as a _____ in the composition statement. Is "_____" a brand name? If so, do you know the established name?

2. The following question is from the previous review/reviewer. [I am not sure if you answered this question. I did my review from the B/red jackets].

   The firm has proposed both PET and glass container for this product. Is it acceptable? Also, are the proposed containers light resistant?

FOR THE RECORD:

1. MODEL LABELING - Mycifradin; Approved 10/28/94; Revised 5/93, Upjohn Co.
   This is NDA 50-285/S-034.

2. This drug product is the subject of a USP monograph.

3. The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of Components and Composition appearing on page 60 (Volume B1.1). However, See comments under DESCRIPTION and the NOTES TO THE CHEMIST.

4. PATENTS/EXCLUSIVITIES - None pending

5. STORAGE TEMPERATURE RECOMMENDATIONS

   Both RLD and the ANDA: Store at controlled room temperature 15° to 30°C (59° to 86°F).

6. DISPENSING STATEMENT

   RLD - Dispense in tight, light-resistant containers.

   ANDA - Dispense in tight, light-resistant containers.

   USP - Preserve in tight, light-resistant containers, preferably at controlled room temperature.

7. PACKAGING CONFIGURATIONS

   RLD: 1 pint.
   ANDA - 2 fl. oz, 4 fl. oz, 16 fl. oz.

8. CONTAINER/CLOSURE - 2 fl. oz, 4 fl. oz, 16 fl. oz.

   Closure - CRC

   Container - Amber PET & glass (see p.403, vol.B.1.2)

9. Bioequivalence:

The waiver of an *in vivo* bioequivalence study was granted on 6/23/98.

10. Nomenclature:

The proprietary name "NEO-FRADIN" was found to be acceptable by the Labeling and Nomenclature Committee on 9/3/98. (See Consult No. 1051 under y:\coorcom\cmccc\labelcom\names.xls.)

Date of Review: 6/25/99

Primary Reviewer: Jacqueline White Jacqueline White for Chmn Date: 7-2-99

Team Leader: Charlie Hoppes Date:

A. Vazza for C. Hoppes 7/2/99

Concur: John Grace 7/7/1999

cc:

ANDA: 65-010
DUP/DIVISION FILE
v:\firmsnz\pharmtek\ltrs&rev\65010NA2.L.doc
Review

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-010

Date of Submission: September 28, 1999

Applicant's Name: Pharma-Tek Inc.

Established Name: Neomycin Sulfate Oral Solution USP, 125 mg/5 mL

Labeling Deficiencies:

1. CONTAINER: 480 mL (16 fl. oz.)

   Side panel

   Following your proprietary name add the established name as seen on the front panel.

Please revise your labels and labeling, as instructed above, and submit

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes, http://www.fda.gov/cder/ogd/rid/labeling_review_branch.html.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Robert L. West, M.S., R.Ph.
Director Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? No, need blue jackets [from chemistry]

APPEARS THIS WAY
ON ORIGINAL

Container Labels: 2 fl. oz, 4 fl. oz, & 16 fl. oz.
Satisfactory in final print as of the ------, 1999 submission.

Professional Package Insert Labeling:
Satisfactory in final print as of the September 28, 1999 submission.

Future revisions:
1. INSERT:
a. General Comment
Throughout the text, revise so that the established name is used at least once in a column of running text in association with the proprietary name. We refer you 21 CFR 201.10(g)(1).
b. HOW SUPPLIED
Include the "Dispense in ..." statement as seen on your container labels."

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Mycifradin

NDA Number: 50-285

NDA Drug Name: Neomycin Sulfate Oral Solution

NDA Firm: The UpJohn Company

Date of Approval of NDA Insert and supplement #: S-034, approved 10/28/94; revised 5/93

Has this been verified by the MIS system for the NDA? yes

Was this approval based upon an OGD labeling guidance? No

If yes, give date of labeling guidance:
Basis of Approval for the Container Labels:
Basis of Approval for the Carton Labeling:

Other Comments:

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	x		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present?			z

Prefix or Suffix present?			
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	x		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	x		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x

Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement? *See FTR and NOTE TO THE CHEMIST	*		
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?	x		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. *Not listed in RLD	*		
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T □ and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

NOTES/QUESTIONS TO THE CHEMIST:

Portions of the DESCRIPTION section were revised with this submission.

1. The firm added the pH range. Do you concur?

   Chemist response: yes

2. The firm added the sentence, "Sodium phosphate dibasic heptahydrate and sulfuric acid are used as pH adjusters. Is this accurate?

   Chemist response: yes

3. The firm added "cherry flavor" as an inactive ingredient. Do you concur?

   Chemist response: yes

4. The firmed revised " [redacted] to read "diatomaceous earth". Is this accurate?

   Chemist response: yes

5. The following is from the previous review. [I am not sure if these questions were already answered, because I did my review from with the red volumes].

   DESCRIPTION section:

   a. The firm added the molecular weight. Is the molecular weight accurate?

      Chemist response: yes

   b. The firm added the chemical name. Is the chemical name accurate?

      Chemist response: yes

   c. We note that the firm has listed " [redacted] " as an inactive ingredient in the DESCRIPTION section and as [redacted] in the composition statement. Is " [redacted] " a brand name? If so, do you know the established name?

      Chemist response: - We will ask the firm to clarify it as " [redacted] ".
      [See chemistry comment #5 to the firm].
      - Brand name - yes

   d. The firm has proposed both PET and glass container for this product. Is it acceptable? Also, are the proposed containers light resistant?

      Chemist response: yes –from stability data

FOR THE RECORD: [portions from previous reviews]

1. MODEL LABELING - Mycifradin; Approved 10/28/94; Revised 5/93, Upjohn Co.
This is NDA 50-285/S-034.

2. This drug product is the subject of a USP monograph.

3. The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of Components and Composition appearing on page 60 (Volume B1.1 & B3.1-p.16). However, see NOTES TO THE CHEMIST.

4. PATENTS/EXCLUSIVITIES – None pending

5. STORAGE TEMPERATURE RECOMMENDATIONS

Both RLD and the ANDA: Store at controlled room temperature 15□ to 30□C (59□ to 86□F).

6. DISPENSING STATEMENT

RLD - Dispense in tight, light-resistant containers.

ANDA - Dispense in tight, light-resistant containers.

USP - Preserve in tight, light-resistant containers, preferably at controlled room temperature.

7. PACKAGING CONFIGURATIONS

RLD: 1 pint.
ANDA - 2 fl. oz, 4 fl. oz, 16 fl. oz.

8. CONTAINER/CLOSURE - 2 fl. oz, 4 fl. oz, 16 fl. oz.

Closure - CRC

Container - Amber PET & glass (see p.403, vol.B.1.2)

9. Bioequivalence:

The waiver of an *in vivo* bioequivalence study was granted on 6/23/98.

10. pH : NDA- not listed
ANDA - 5 to 7.5
USP – 5 to 7.5

11. Nomenclature:

The proprietary name "NEO-FRADIN" was found to be acceptable by the Labeling and Nomenclature Committee on 9/3/98. (See Consult No. 1051 under y:\coorcom\cmccc\labelcom\names.xls.)

Date of Review: 11/1/99

Primary Reviewer:
Jacqueline White, Pharm.D.
Jacqueline White Pharm.D.

Date:
11-4-99

Team Leader:

Date:
11/5/99

cc:

ANDA: 65-010
DUP/DIVISION FILE
v:\firmsnz\pharmtek\ltrs&rev\65010NA2.L.doc
Review

APPROVAL SUMMARY

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-010

Date of Submission: January 3, 2000

Applicant's Name: Pharma-Tek Inc.

Established Name: Neomycin Sulfate Oral Solution USP, 125 mg/5 mL

Proprietary Name: NEO-FRADIN

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? There are at least 9 of each piece.

Container Labels:

-2 fl. oz and 4 fl. oz
-Satisfactory in final print as of the September 28, 1999 submission.
-16 fl. oz.
-Satisfactory in final print as of the January 3, 2000 submission.

Professional Package Insert Labeling:
-Satisfactory in final print as of the September 28, 1999 submission.

Future revisions:

1. General Comment
   Following the storage temperature recommendations add the statement, "[See USP]".
2. INSERT:
   a. General Comment
      Throughout the text, revise so that the established name is used at least once in a column of running text in association with the proprietary name. We refer you 21 CFR 201.10(g)(1).
   b. HOW SUPPLIED
      Include the "Dispense in ..." statement as seen on your container labels."

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Mycifradin

NDA Number: 50-285

NDA Drug Name: Neomycin Sulfate Oral Solution

NDA Firm: The UpJohn Company

Date of Approval of NDA Insert and supplement #: S-034, approved 10/28/94; revised 5/93

Has this been verified by the MIS system for the NDA? yes

Was this approval based upon an OGD labeling guidance? No

If yes, give date of labeling guidance:

Basis of Approval for the Container Labels:
Basis of Approval for the Carton Labeling:

Other Comments:

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	x		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			z
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified? *See FTR.	*		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	x		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	

Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?.			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	

Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container? *See chemist response 5(d).	*		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. *Not listed in RLD	*		
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T □ and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

NOTES/QUESTIONS TO THE CHEMIST:

Portions of the DESCRIPTION section were revised with this submission.

1. The firm added the pH range. Do you concur?

   Chemist response: yes

2. The firm added the sentence, "Sodium phosphate dibasic heptahydrate and sulfuric acid are used as pH adjusters. Is this accurate?

   Chemist response: yes

3. The firm added "cherry flavor" as an inactive ingredient. Do you concur?

   Chemist response: yes

4. The firmed revised " ——————— " to read "diatomaceous earth". Is this accurate?

   Chemist response: yes

5. The following is from the previous review. [I am not sure if these questions were already answered, because I did my review from with the red volumes].

   DESCRIPTION section:

   a. The firm added the molecular weight. Is the molecular weight accurate?

      Chemist response: yes

   b. The firm added the chemical name. Is the chemical name accurate?

      Chemist response: yes

   c. We note that the firm has listed ' ——————— ' as an inactive ingredient in the DESCRIPTION section and as ——————— in the composition statement. Is ——————— ——— " a brand name? If so, do you know the established name?

      Chemist response: - We will ask the firm to clarify it as ——————— .
      [See chemistry comment #5 to the firm].
      - Brand name - yes

   d. The firm has proposed both PET and glass container for this product. Is it acceptable? Also, are the proposed containers light resistant?

      Chemist response: yes –from stability data

FOR THE RECORD: [portions from previous reviews]

1. MODEL LABELING - Mycifradin; Approved 10/28/94; Revised 5/93, Upjohn Co.
   This is NDA 50-285/S-034.

2. This drug product is the subject of a USP monograph.

3. The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of Components and Composition appearing on page 60 (Volume B1.1 & B3.1-p.16)

4. PATENTS/EXCLUSIVITIES – None pending

5. STORAGE TEMPERATURE RECOMMENDATIONS

   Both RLD and the ANDA: Store at controlled room temperature 15° to 30°C (59° to 86°F).
   See General Comment under Future Revisions.

6. DISPENSING STATEMENT

   RLD - Dispense in tight, light-resistant containers.

   ANDA - Dispense in tight, light-resistant containers.

   USP - Preserve in tight, light-resistant containers, preferably at controlled room temperature.

7. PACKAGING CONFIGURATIONS

   RLD: 1 pint.
   ANDA - 2 fl. oz, 4 fl. oz, 16 fl. oz.

8. CONTAINER/CLOSURE - 2 fl. oz, 4 fl. oz, 16 fl. oz.

   Closure - CRC

   Container - Amber PET & glass (see p.403, vol.B.1.2)

9. Bioequivalence:

   The waiver of an *in vivo* bioequivalence study was granted on 6/23/98.

10. pH : NDA- not listed
    ANDA - 5 to 7.5
    USP – 5 to 7.5

11. Proprietary:

    - The proprietary name "NEO-FRADIN" was found to be acceptable by the Labeling and Nomenclature Committee on 9/3/98. (See Consult No. 1051 under y:\coorcom\cmccc\labelcom\names.xls.)

    - E-mail to OPDRA.

Date of Review: 1/11/2000

Primary Reviewer:
Jacqueline Council, Pharm.D.
Jacqueline White, Pharm.D. [maiden name]
Jacqueline Council, PharmD

Date:
1/2, 2000

Team Leader:

Date:

4/12/00

Note:
OPDRA has no concern Re: Prop. Name: Neo-Fradin. (See e mail J. Phillips)

cc:

ANDA: 65-010
DUP/DIVISION FILE
v:\firmsnz\pharmtek\ltrs&rev\65010ap.l
Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-010

CHEMISTRY REVIEWS

1. CHEMIST'S REVIEW NO. 1

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Attention: Susan E. Badia
Tel.: 516-757-5522
Fax: 516-754-1550

Distributor:
Pharma-Tek Inc.
744 Baldwin St.
Elmira, NY 14901

Contact person: J.Robin Liles, Director of Operations
Tel.: 607-732-5555
Fax: 607-732-4382

Manufacturing Facility:

[redacted]

4. LEGAL BASIS for ANDA SUBMISSION:

Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator N50-285.

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES

Firm:

1. Original submission 2/10/1998
2. Correspondence including revised information to conform with 507 repeal. 3/11/98

FDA:

1. Acknowledgment letter 3/17/98
2. Review of request for Biowaiver by Division of Bioequivalence - granted 6/23/98
3. Labelling review - unacceptable 7/14/98

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)

TABLE 1: RELATED NDA'S/DMF'S

Firm	ANDA/DMF No.	Type	Function
		II	
		III	
		III	
		III	
		III	
		III	

DMF	III	
DMF	III	
DMF	III	
DMF	III	

13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE

APPEARS THIS WAY ON ORIGINAL

16. RECORDS AND REPORTS
N/A

17. COMMENTS
As noted above, Pharma-Tek has been distributing this product for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator N50-285.

This application formally reflects:

1. The drug product, formerly manufactured by the innovator (Pharmacia-Upjohn) for their own sale and for Pharma-Tek under private label, will now be manufactured by ——————— for Pharma-Tek.

2. Pharma-Tek will be the only approved application for this drug product.

The application is appropriate in format and content.

Major deficiencies are related to analytical methodology for the drug substance, Finished Drug Product Specifications, and Stability Specifications. The drug substance supplier utilizes HPLC for certain assays but does not use it for the official assay for potency for the drug substance. Neither the Acceptance Specifications nor the Stability program reflect the use of HPLC analytical methodology. No stress testing is reported for the stability program.

Minor deficiencies were found regarding potency calculations, raw material tests and specifications, holding times, and storage temperature interpretations. These deficiencies are detailed in the appropriate sections.

Other issues:

- Methods validation required on receipt of amendment with requested analytical methodology.
- Labelling review completed 7/14/98, unacceptable(Chan Park).
- Biowaiver granted, see review dated 6/23/98.
- Requested EER: 3/17/98.

18. CONCLUSIONS AND RECOMMENDATIONS

NOT APPROVABLE: MAJOR AMENDMENT REQUIRED

19. REVIEWER — DATE COMPLETED

R. C. Adams — 7/16/98

Redacted 23 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #1

1. CHEMIST'S REVIEW NO. 2

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Attention: Susan E. Badia
Tel.: 516-757-5522
Fax: 516-754-1550

Distributor:
Pharma-Tek Inc.
744 Baldwin St.
Elmira, NY 14901

Contact person: J.Robin Liles, Director of Operations
Tel.: 607-732-5555
Fax: 607-732-4382

Manufacturing Facility:

[ ]

4. LEGAL BASIS for ANDA SUBMISSION:

Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator NDA #50-285.

The manufacturer of this finished product is [redacted] at [redacted].

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate Oral solution

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES
Original submission: 2/10/98
Acknowledgment letter: 3/17/98
Amendment 12/16/98 to N/A (MAJOR) letter 8/26/98

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)
See under #37 DMF CHECKLIST

13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
N/A

16. RECORDS AND REPORTS
N/A

17. COMMENTS
This is the first Generic application.
The first comprehensive review was done by R. Adams (7/20/98). See CR #1 and the First Audit by K. Bernard (7/29/98).

In amendment 12/16/98 firm responds to our concerns in order (all are acceptable except Q1 and Q9&10. See also under **New Issues**):

Q1. [redacted]

A1. [redacted]

Redacted 5 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #2 (pp 3-7)

B. DMF #——— for ——————— was reviewed and found inadequate by me 6/23/99. N/A facsimile was issued, 7/14/99.

C. [redacted]

D. Clarification on Release Specification (pH) is needed.

Status Summary for #65-010:

DMFs:	DMF #——— inadequate (6/23/99)
Labeling:	Not acceptable 6/25/99
EER:	Withhold (Memo dated 2/3/99)
Sample:	Not requested (USP drug)
Bio:	Waiver granted 6/23/98

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (MINOR AMENDMENT)

19. REVIEWER: Maria C. Shih — DATE COMPLETED: 6/28/99

Redacted 12 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #2 (PP 9-20)

6. [ ]

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following:

A satisfactory compliance evaluation of your facility is required prior to approval. Please note the Office of Compliance currently considers _____ unacceptable based on inspection observations made during _____.

Sincerely yours,

Vilayat Sayal 7/21/99

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #65-010
Division File
Field Copy

Endorsements:
HFD-643/MShih/6/28/99/ 7/16/99
HFD-643/RAdams/7/14/99 R-C. Adams, 7/16/99
HFD-617/MAnderson/7/14/99 Mark Anderson 7/20/99
~~HFD-640/PFang~~/

F/T by;ps/7/16/99

V:\firmsnz\Pharmtek\ltrs&rev\65010.2r

NOT APPROVABLE - MINOR

1. CHEMIST'S REVIEW NO. 3

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Attention: Susan E. Badia
Tel.: 516-757-5522
Fax: 516-754-1550

Distributor:
Pharma-Tek Inc.
744 Baldwin St.
Elmira, NY 14901

Contact person: J.Robin Liles, Director of Operations
Tel.: 607-732-5555
Fax: 607-732-4382

Manufacturing Facility:

[redacted]

4. LEGAL BASIS for ANDA SUBMISSION:
Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator NDA #50-285.

The manufacturer of this finished product is [redacted] at [redacted].

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate Oral solution

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES
Original submission: 2/10/98
Acknowledgment letter: 3/17/98
Amendment 12/16/98 to N/A (MAJOR) letter 8/26/98
Amendment 9/28/99 to N/A (MINOR) letter 7/21/99

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)
See under #37 DMF CHECKLIST

13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
N/A

16. RECORDS AND REPORTS N/A

17. COMMENTS
This is the first Generic application.
The first comprehensive review was done by R. Adams (7/20/98). See CR #1 and the First Audit by K. Bernard (7/29/98).

In Amendment 9/28/99 Firm responds to our concerns in order (all are acceptable except DMF, stability, and Degradants issues.

Q1. [redacted]

A1. [redacted]

Q2. [redacted]

Redacted 2 page(s)

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confidential commercial

information from

CHEMISTRY REVIEW #3 (pp. 3-4)

[ ]

Status Summary for #65-010:

DMFs: DMF # [redacted] remains inadequate (10/29/99)
Labeling: Pending
EER: Pending
Sample: Not requested (USP drug)
Bio: Waiver granted 6/23/98

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (MINOR AMENDMENT)

19. REVIEWER: Maria C. Shih
DATE COMPLETED: 10/29/99

APPEARS THIS WAY
ON ORIGINAL

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confidential commercial

information from

CHEMISTRY REVIEW #3 (pp. 6-16)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following:

A satisfactory compliance evaluation for firms referenced in the ANDA is required prior to approval. Please note the Office of Compliance considers [redacted] unacceptable based on inspection observations made during [redacted].

Sincerely yours,

11/2/99.

for Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

cc: ANDA #65-010
DUP/Division File
Field Copy

Endorsements:
HFD-643/MShih/10/29/99/ 11/1/99
HFD-643/RAdams/10/29/99/ R.C. Adams, 11/1/99
HFD-617/MAnderson/11/1/99/ M Anderson 11/1/99
F/T by MCS 11/1/99
V:\firmsnz\pharma.tek\ltrs&rev\65010.rv3
NOT APPROVABLE - MINOR

APPEARS THIS WAY
ON ORIGINAL

1. CHEMIST'S REVIEW NO. 4

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Attention: Susan E. Badia
Tel.: 516-757-5522
Fax: 516-754-1550

Distributor:
Pharma-Tek Inc.
744 Baldwin St.
Elmira, NY 14901

Contact person: J.Robin Liles, Director of Operations
Tel.: 607-732-5555
Fax: 607-732-4382

Manufacturing Facility:

[redacted]

4. LEGAL BASIS for ANDA SUBMISSION:
Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator NDA #50-285.

The manufacturer of this finished product is [redacted] at [redacted].

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate Oral solution

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES
Original submission: 2/10/98
Acknowledgment letter: 3/17/98
Amendment 12/16/98 to N/A (MAJOR) letter 8/26/98
Amendment 9/28/99 to N/A (MINOR) letter 7/21/99
Amendment 1/3/00 to N/A (MINOR) letter 11/5/99

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)
See under #37 DMF CHECKLIST

13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
N/A

16. RECORDS AND REPORTS N/A

17. COMMENTS
This is the first Generic application.
The first comprehensive review was done by R. Adams (7/20/98). See CR #1 and the First Audit by K. Bernard (7/29/98).

In Amendment 1/3/00 Firm responds to our concerns in order

Q1. [redacted]

A1.

Q2.

A2.

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confidential commercial

information from

CHEMISTRY REVIEW #4 (P.3)

Status Summary for #65-010:

DMFs:	DMF # [redacted] remains inadequate (2/7/00)
Labeling:	Acceptable 1/21/00
EER:	Pending
Sample:	Not requested (USP drug)
Bio:	Waiver granted 6/23/98

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (MINOR)

19. REVIEWER: Maria C. Shih — DATE COMPLETED: 2/7/00

APPEARS THIS WAY
ON ORIGINAL

Redacted 11 page(s)

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confidential commercial

information from

CHEMISTRY REVIEW #4 (PP. 5-15)

38. Chemistry Comments to be Provided to the Applicant

ANDA: 65-010 Applicant: Pharma-Tek Inc.

Drug Product: Neomycin Sulfate Oral Solution USP, 125 mg/5 mL (eq. 87.5 mg neomycin base/5 mL)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. DMF #——— for ——————————————————— remains inadequate because the holder, ——————————— has not yet responded to the deficiency letter dated July 15, 1999. The DMF deficiencies have to be addressed satisfactorily prior to approval of this application.

2. Regarding the submitted stability data:

a. [redacted]

b.

c.

Please comment.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following:

APPEARS THIS WAY
ON ORIGINAL

A satisfactory compliance evaluation for firms referenced in the ANDA is required prior to approval. Please note the Office of Compliance considers _____ unacceptable based on inspection observations made during _____.

Sincerely yours,

2/16/2000

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

for

APPEARS THIS WAY
ON ORIGINAL

cc: ANDA #65-010
DUP/Division File
Field Copy

Endorsements:
HFD-643/MShih/2/7/00 2/15/00
HFD-643/RAdams/2/8/00 R.C. Adams 2/15/00
HFD-617/MAnderson/2/14/00 M Anderson 2/16/00
F/T by mda/2/14/00
V:\firmsnz\pharma.tek\ltrs&rev\65010.rv4
NOT APPROVABLE - MINOR

1. CHEMIST'S REVIEW NO. 5

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Attention: Susan E. Badia
Tel.: 516-757-5522
Fax: 516-754-1550

Distributor:
Pharma-Tek Inc.
744 Baldwin St.
Elmira, NY 14901

Contact person: J.Robin Liles, Director of Operations
Tel.: 607-732-5555
Fax: 607-732-4382

Manufacturing Facility:

[redacted]

4. LEGAL BASIS for ANDA SUBMISSION:
Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator NDA #50-285.

The manufacturer of this finished product is [redacted] at [redacted].

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate Oral solution

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES
Original submission: 2/10/98
Acknowledgment letter: 3/17/98
Amendment 12/16/98 to N/A (MAJOR) letter 8/26/98
Amendment 9/28/99 to N/A (MINOR) letter 7/21/99
Amendment 1/3/00 to N/A (MINOR) letter 11/5/99
Amendment 3/17/00 to N/A (MINOR) letter 2/18/00
Amendment 4/12/00 to DMF deficiency letter

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)
See under #37 DMF CHECKLIST

13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
N/A

16. RECORDS AND REPORTS N/A

17. COMMENTS
This is the first Generic application.
The first comprehensive review was done by R. Adams (7/20/98). See CR #1 and the First Audit by K. Bernard (7/29/98).

In Amendment 3/17/00 Firm responds to our concerns in order:
(All acceptable)

Q1. DMF #——— for ———————————————
remains inadequate because the holder ————————
——— has not yet responded to the deficiency letter dated July 15, 1999. The DMF deficiencies have to be addressed satisfactorily prior to approval of this application.

A1. [redacted]

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information from

CHEMISTRY REVIEW #5 (P. 3)

Status Summary for #65-010:

DMFs: DMF # ———— is now adequate (4/26/00)
Labeling: Acceptable 1/21/00
EER: Pending
Sample: Not requested (USP drug)
Bio: Waiver granted 6/23/98

18. CONCLUSIONS AND RECOMMENDATIONS
Approval recommended (pending EER)

19. REVIEWER: Maria C. Shih
DATE COMPLETED: 4/26/00

APPEARS THIS WAY
ON ORIGINAL

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confidential commercial

information from

CHEMISTRY REVIEW #5 (PP. 5-14)

cc: ANDA #65-010
DUP/Division File
Field Copy

Endorsements:
HFD-643/MShih/4/26/00/ 5/9/00
HFD-643/RAdams/5/4/00/ R. C. Adams 5/10/00

F/T by MCS 5/9/00
V:\firmsnz\pharma.tek\ltrs&rev\65010.rv5
APPROVAL

APPEARS THIS WAY
ON ORIGINAL

1. CHEMIST'S REVIEW NO. 5a

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Manufacturing Facility:
[redacted]

4. LEGAL BASIS for ANDA SUBMISSION:
Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator NDA #50-285.

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate Oral solution

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES
Original submission: 2/10/98
Acknowledgment letter: 3/17/98
Amendment 12/16/98 to N/A (MAJOR) letter 8/26/98
Amendment 9/28/99 to N/A (MINOR) letter 7/21/99
Amendment 1/3/00 to N/A (MINOR) letter 11/5/99
Amendment 3/17/00 to N/A (MINOR) letter 2/18/00
Amendment 4/12/00 to DMF deficiency letter

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)
See under #37 DMF CHECKLIST

13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
N/A

16. RECORDS AND REPORTS N/A

17. COMMENTS
This is the first Generic application.
The first comprehensive review was done by R. Adams (7/20/98). See CR #1 and the First Audit by K. Bernard (7/29/98).

CMC issues for this application have been resolved (see CR #5) although we still have some reservation regarding [redacted] in-house HPLC method for potency and impurity assays.

According to Memo dated 6/14/2000, Preapproval Compliance Branch recommends "withhold" based on the cGMP observations. Agreement reached (conference call dated 7/13/00) between our review branch and the Compliance that a new batch should be made and new performance data generated to address all the concerns.

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (MAJOR)

19. REVIEWER: Maria C. Shih
DATE COMPLETED: 7/13/00

APPEARS THIS WAY
ON ORIGINAL

38. Chemistry Comments to be Provided to the Applicant

ANDA: 65-010 **Applicant:** Pharma-Tek Inc.

Drug Product: Neomycin Sulfate Oral Solution USP, 125 mg/5 mL (eq. 87.5 mg neomycin base/5 mL)

The deficiencies presented below represent MAJOR deficiencies.

A. Chemistry Deficiencies:

[ ]

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following:

A satisfactory compliance evaluation for firms referenced in the ANDA is required prior to approval.

Sincerely yours,

for Florence S. Fang 7/21/00
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #65-010
DUP/Division File
Field Copy

Endorsements:
HFD-643/MShih/7/13/00/
HFD-643/RAdams/
HFD-617/MAnderson/
F/T by
V:\firmsnz\pharma.tek\ltrs&rev\65010rv5a.doc
NOT APPROVABLE - MAJOR

R. C. Adams 7/21/00 7/20/00

APPEARS THIS WAY
ON ORIGINAL

1. CHEMIST'S REVIEW NO. 6

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Manufacturing Facility:
[ ]

4. LEGAL BASIS for ANDA SUBMISSION
Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator NDA #50-285.

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate Oral solution

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES

Original submission: 2/10/98
Acknowledgment letter: 3/17/98
Amendment 12/16/98 to N/A (MAJOR) letter 8/26/98
Amendment 9/28/99 to N/A (MINOR) letter 7/21/99
Amendment 1/3/00 to N/A (MINOR) letter 11/5/99
Amendment 3/17/00 to N/A (MINOR) letter 2/18/00
Amendment 4/12/00 to DMF deficiency letter
Amendment 7/17/01 to N/A (MAJOR) letter 7/24/00

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)
See under #37 DMF CHECKLIST

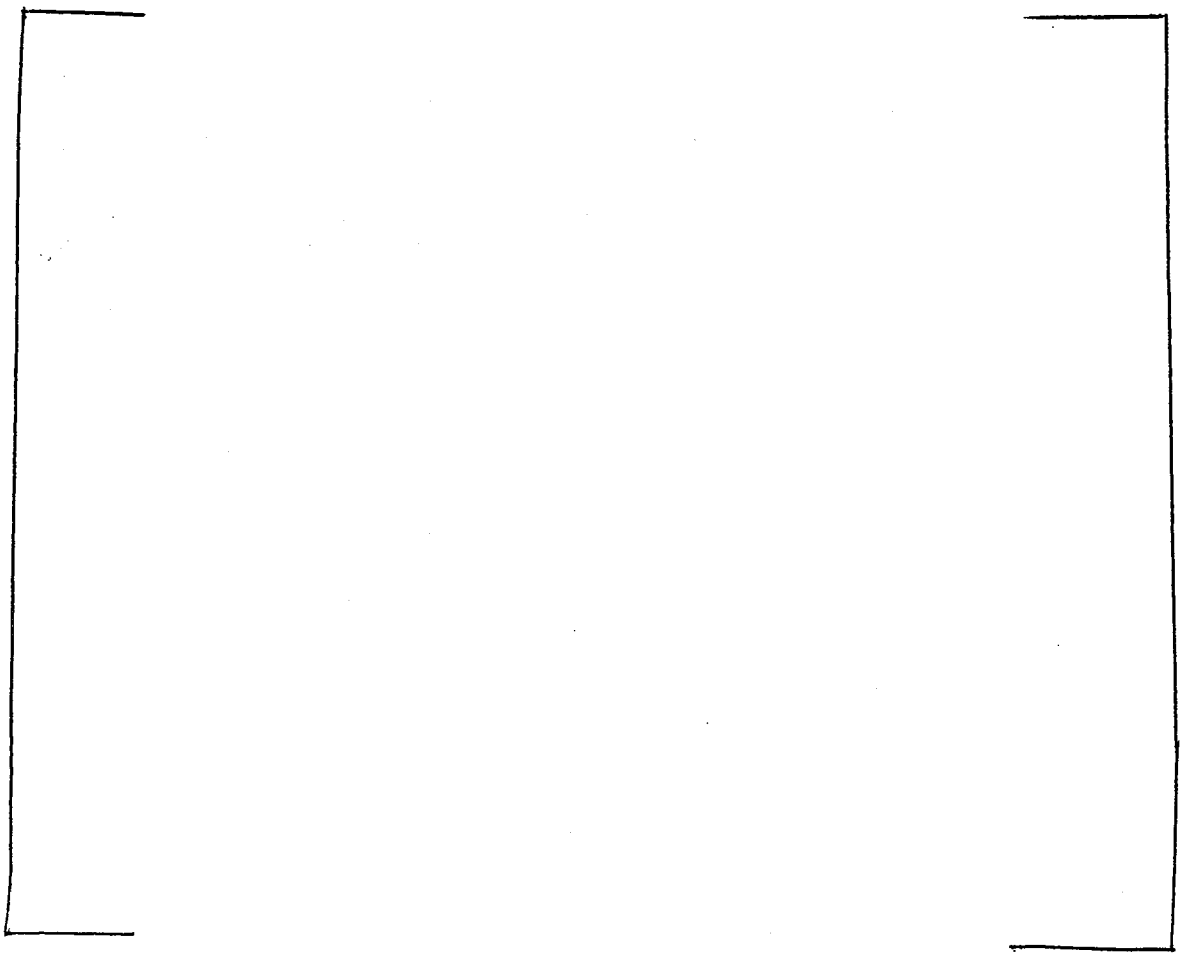
13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
N/A

16. RECORDS AND REPORTS N/A

17. COMMENTS
This is the first Generic application.
The first comprehensive review was done by R. Adams (7/20/98). See CR #1 and the First Audit by K. Bernard (7/29/98).



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CHEMISTRY REVIEW #6 (P.3)

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (FAX AMENDMENT)

19. REVIEWER: Maria C. Shih

DATE COMPLETED: 11/16/01

APPEARS THIS WAY
ON ORIGINAL

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confidential commercial

information from

CHEMISTRY REVIEW #6 (PP. 5-14)

38. Chemistry Comments to be Provided to the Applicant

ANDA: 65-010 **Applicant:** Pharma-Tek Inc.

Drug Product: Neomycin Sulfate Oral Solution USP, 125 mg/5 mL (eq. 87.5 mg neomycin base/5 mL)

The deficiencies presented below represent FAX deficiencies.

1. In the submitted Stability Summary Report, we note that there are no test results for "Related Compounds" as your stability protocol specified. Please explain.

2. Please indicate the equivalency in metric system (i.e., liters vs. gallons) for the batch size in the batch records and other documentation as provided in the original submission.

Sincerely yours,

12/5/01

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #65-010
DUP/Division File
Field Copy

Endorsements:
HFD-643/MShih/11/16/01 12/3/01
HFD-643/RAdams/11/27/01 R. C. Adams 12/3/01
HFD-617/MAnderson/ M Anderson 12/5-01

F/T by rad12/3/01
V:\firmsnz\pharma.tek\ltrs&rev\65010rv6.NADF.DOC

NOT APPROVABLE - FAX AMENDMENT

1. CHEMIST'S REVIEW NO.

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Manufacturing Facility:
[ ]

4. LEGAL BASIS for ANDA SUBMISSION
Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator NDA #50-285.

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate Oral Solution

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES

Original submission: 2/10/98
Acknowledgment letter: 3/17/98
Amendment 12/16/98 to N/A (MAJOR) letter 8/26/98
Amendment 9/28/99 to N/A (MINOR) letter 7/21/99
Amendment 1/3/00 to N/A (MINOR) letter 11/5/99
Amendment 3/17/00 to N/A (MINOR) letter 2/18/00
Amendment 4/12/00 to DMF deficiency letter
Amendment 7/17/01 to N/A (MAJOR) letter 7/24/00
Amendment 12/28/01 to N/A (FAX) letter 12/10/01

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)
See under #37 DMF CHECKLIST

13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
N/A

16. RECORDS AND REPORTS N/A

17. COMMENTS
This is a first Generic application for the finished drug product. The first comprehensive review was done by R. Adams (7/20/98). See CR #1 and the First Audit by K. Bernard (7/29/98).

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information from

CHEMISTRY REVIEW # 7 (PP. 3-4)

Status Summary for #65-010:

DMF:	# ——— (adequate 2/6/02)
Labeling:	Acceptable (1/21/00)
EER:	Withholding
Sample:	Not requested (USP drug)
Bio:	Acceptable (6/23/98)

18. CONCLUSIONS AND RECOMMENDATIONS

Not approvable (issues regarding impurities/degradants and cGMP status)

19. REVIEWER: Maria C. Shih

DATE COMPLETED: 2/6/02

APPEARS THIS WAY
ON ORIGINAL

Redacted 11 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #7 (PP. 6-16)

cc: ANDA #65-010
DUP/Division File
Field Copy

Endorsements:
HFD-643/MShih/2/6/02/ Susan Zuk for/ 2/13/02
HFD-643/RAdams/2/12/02
HFD-617/MAnderson/2/13/02 R.C. Adams 2/13/02

F/T by mda/2/13/02
V:\firmsnz\pharma.tek\ltrs&rev\65010RV7.NAD.DOC
NOT APPROVABLE - MINOR AMENDMENT

APPEARS THIS WAY
ON ORIGINAL

1. CHEMIST'S REVIEW NO. 8

2. ANDA # 65-010

3. NAME AND ADDRESS OF APPLICANT

Headquarters (assembly of submission):
Pharma-Tek Inc.
P.O. Box 1920
Huntington, NY
11743-0568

Manufacturing Facility:

[ ]

4. LEGAL BASIS for ANDA SUBMISSION
Pharma-Tek has been distributing this product under private label for the innovator firm under contract since 1996. Recently the innovator, Pharmacia-Upjohn, discontinued production and sale of the product. Pharma-Tek purchased the application and excess inventory from innovator and this application is for drug product identical in formulation to innovator NDA #50-285.

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
NEO-FRADIN®

7. NONPROPRIETARY NAME
Neomycin Sulfate Oral Solution

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES
Original submission: 2/10/98
Acknowledgment letter: 3/17/98
Amendment 12/16/98 to N/A (MAJOR) letter 8/26/98
Amendment 9/28/99 to N/A (MINOR) letter 7/21/99
Amendment 1/3/00 to N/A (MINOR) letter 11/5/99
Amendment 3/17/00 to N/A (MINOR) letter 2/18/00
Amendment 4/12/00 to DMF deficiency letter
Amendment 7/17/01 to N/A (MAJOR) letter 7/24/00
Amendment 12/28/01 to N/A (FAX) letter 12/10/01
Amendment 3/18/02 to N/A (MINOR) letter 2/14/02

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. HOW DISPENSED
R_x

12. RELATED IND/NDA/DMF(s)
See under #37 DMF CHECKLIST

13. DOSAGE FORM
Oral solution

14. POTENCY
125 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
N/A

16. RECORDS AND REPORTS N/A

17. COMMENTS
This is a first Generic application for the finished drug product. The first comprehensive review was done by R. Adams (7/20/98). See CR #1 and the First Audit by K. Bernard (7/29/98).

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confidential commercial

information from

CHEMISTRY REVIEW #8 (P.3)

Compliance status, this analytical methodology will not be the major constraint.

Note:
The official assay method is the USP Microbial Assay <81>.

B. In addition to responding to the deficiency presented above, please note and acknowledge the following comment in your response:

Q. A satisfactory compliance evaluation for firms referenced in the ANDA is required prior to approval. Please note that the Office of Compliance currently considers [redacted] unacceptable based on inspection observations.

A. See attached memo issued by Compliance dated 12/17/01.

Status Summary for #65-010:

DMF:	#[redacted] (adequate 2/6/02)
Labeling:	Acceptable (4/12/00)
EER:	Withhold
Sample:	Not requested (USP drug)
Bio:	Acceptable (6/23/98)

18. CONCLUSIONS AND RECOMMENDATIONS
Approval recommended pending EER

19. REVIEWER: Maria C. Shih — DATE COMPLETED: 4/24/02

Redacted 10 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #8 (pp. 5-14)

cc: ANDA #65-010
DUP/Division File
Field Copy

Endorsements:
HFD-643/MShih/4/24/02/
HFD-643/RAdams/4/29/02

F/T by: mda/5/1/02
V:\firmsnz\pharma.tek\ltrs&rev\65010RV8.APD.DOC

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-010

BIOEQUIVALENCE REVIEW

JUN 23 1998

Neomycin Sulfate
Oral Solution, EQ, 87.5 mg Base/5 mL
Reviewer: Gur J.P. Singh
ANDA #65-010
65010W.298

Pharma-Tek
P. O. Box 1920
Huntington, NY 11743
Submission Date:
February 10, 1998

Review of a Waiver-request

BACKGROUND: The reference listed drug for neomycin sulfate oral solution is Mycifradin® manufactured by Pharmcia-Upjohn (NDA #50285-001). The sponsor states that the innovator discontinued the sale of this product, and Pharma-Tek purchased the formulation and manufacturing procedure from the Pharmacia-Upjohn company. The same formulation and manufacturing process are utilized for preparation of the drug product that is subject of this application.

Compositions of the Test and Reference Products (Not to be released under FOI)

INGREDIENT	*AMOUNT (PER 5 ML)*	
	Pharmacia-Upjohn	*Pharma-Tek*
Neomycin Sulfate	[redacted]	[redacted]
Glycerin		
[redacted] Cherry flavor		
Sodium Phosphate, Dibasic		
Dye FDC Yellow #6		
Benzoic Acid		
Methylparaben		
Propylparaben		
Water, Purified		
Sulfuric Acid	Adjust pH	Adjust pH

1. *The reference product composition listed above is based on the March 6, 1998, E-mail from HFD-520.*
2. [redacted] *the label claim (87.5 mg Base). However, the concentration of the active ingredient remains with the USP specifications (90-125% of the label claim).*

COMMENTS

Compositions of the test and reference products are identical. The concentration of the active ingredient in these products is ——— the label claim (87.5 mg Base). However, it is within the acceptable limit of 90-125% of the label claim, based on the USP monograph. Therefore, the waiver of *in vivo* bioequivalence study requirements for the Pharma-Tek's neomycin sulfate oral solution (87.5 mg Base/5 mL) may be granted pursuant to 21 CFR section 320.22(b)(3).

RECOMMENDATION

The Division of Bioequivalence agrees that the information submitted by Pharma-Tek demonstrates that neomycin sulfate oral solution, 87.5 mg Base/5 mL, falls under 21 CFR Section 320.22(b) (3) of Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence study requirements for neomycin sulfate oral solution, 87.5 mg Base/5 mL, of the test product is granted. From the Bioequivalence point of view, the Division of Bioequivalence deems the proposed test formulation to be bioequivalent to Mycifradin® oral solution, 87.5 mg Base/5 mL, manufactured by Pharmacia-Upjohn.

Gur J.P. Singh, Ph.D.
Division of Bioequivalence
Review Branch II.

RD INITIALED SNERURKAR
FT INITIALED SNERURKAR 6/18/98

CONCUR: Date: 6/23/98
Dale P. Conner, Pharm.D
Director
Division of Bioequivalence.

GJP SINGH 6/17/98 65010W.298
cc. ANDA # 65010, original, HFD-650 (Division Director), HFD-630 (OGD), HFC-130 (Jallen), HFD-600 (Hare), HFD-655 (Nerurkar, Singh), Drug file, Division file.

BIOEQUIVALENCY COMMENTS

ANDA: 65010 APPLICANT: Pharma-Tek

DRUG PRODUCT: Neomycin Oral Solution (87.5 mg/5 mL)

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale Conner

Dale Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

CC: ANDA: 65-010
ANDA DUPLICATE
DIVISION FILE
HFD-651/ Bio Secretary - Bio Drug File
HFD-655 / Reviewer (GJP Singh)

X:\NEW\FIRMSNZ\PHARMTEK\65010W.298
Printed in final on 6/18/98

Endorsements: (Final with Dates)
HFD-655 / GJP Singh GJPS 6/18/98
HFD-655 / S. Nerurkar
HFD-617/ L. Sanchez or N. Chamberlin AS 6/23/98
HFD-65 / D. Conner DMC 6/23/98

BIOEQUIVALENCY - ACCEPTABLE SUBMISSION DATE: 2/10/98

6. **WAIVER** (WAI)

Strengths: 87.5 mg Base/5 mL

Outcome: AC

WINBIO COMMENTS: Waiver Request may be granted.

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #: 65-010 **SPONSOR:** Pharma-Tek
DOSAGE FORM: Neomycin Sulphate Oral Solution..
STRENGTHS(s): EQ. 87.5 mg Base/5 mL.
TYPE OF STUDY: NA
STUDY SITE: NA

STUDY SUMMARY: NA

DISSOLUTION: NA

WAIVER: A waiver of *in vivo* bioequivalence study requirements is granted

PRIMARY REVIEWER: Gur J.P. Singh, Ph.D. **BRANCH:** II

INITIAL: Gurjpsingh DATE 6-18-98

BRANCH CHIEF: Shriniwas G. Nerurkar, Ph.D. **BRANCH:** II

INITIAL: SGNerurkar DATE 6/18/1998

DIRECTOR, DIVISION OF BIOEQUIVALENCE: Dale P. Conner, Pharm. D.

INITIAL: Dale Conner DATE 6/23/98

DIRECTOR, OFFICE OF GENERIC DRUGS

INITIAL:_____ DATE_____

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-010

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

OGD APPROVAL ROUTING SUMMARY

ANDA # 65-010 Applicant Pharma-Tek Inc
rug Neomycin Oral Solution USP Strength 125 mg/5 mL

APPROVAL ☐ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐ OTHER ☐

REVIEWER:

DRAFT RECEIPT

FINAL ACTION

1. Project Manager M Anderson
   Review Support Br G
   Date 4/30/02 Initials MA
   Date 5/8/02 Initials MA

   Application Summary:
   Original Rec'd date 2/11/98
   Date Acceptable for Filing 2/11/98 ✓
   Patent Certification (type) —
   Date Patent/Exclus.expires —
   Citizens Petition/Legal Case Yes ☐ No ☒
   (If YES, attach email from PM to CP coord)
   First Generic Yes ☐ No ☐
   (If YES, check PETS)
   Pediatric Exclusivity Tracking PETS)
   Date checked _____ NDA# _____
   Nothing Submitted ☐
   Written request issued ☐
   Study Submitted ☐

   EER Status Pending ☒ Acceptable ☐ OAI ☐
   Date of EER Status 6/14/02
   Date of Office Bio Review 6/23/98
   Date of Labeling Approv. Sum 4/12/00
   Date of Sterility Assur. App. N/A
   Methods Val. Samples Pending Yes ☐ No ☒
   30 Day Clock Start _____ End _____
   Commitment Rcd. from Firm Yes ☐ No ☐
   Modified-release dosage form: Yes ☐ No ☒
   Interim Dissol. Specs in AP Ltr: Yes ☐

   Previously reviewed and tentatively approved ☐ Date _____
   Previously reviewed and CGMP def./N/A Minor issued ☐ Date _____
   Comments:

2. Div. Dir./Deputy Dir.
   Chemistry Div. I or II
   Comments:
   Date 5/8/02 Initials ~~HS~~
   Date 5/9/02 Initials ~~HS~~
   cmc satisfactory
   cGMP pending

3. Frank Holcombe fpv
   Assoc. Dir. For Chemistry
   Comments: (First generic drug review) FH was consulted about the USP specifications
   Inspections related problems / Essentially this DP has been bought from the Innovator through purchase of Upjohn's NDA. Commitments have been sought to develop a method (HPLC) and monitor degradants in DP until appropriate
   Date 5/22/02 Initials RAC
   Date 5/23/02 Initials RAC

4. Pat Beers Block
   Supv., Review Support Branch
   EER Status: Refer to DLS review below
   Date _____ Initials _____
   Date _____ Initials _____

   Bioequivalence sites:
   Clinical site:
   Inspection needed: ☐ yes ☐ no
   Status: ☐acceptable ☐unacceptable ☐ pending
   Date of status: _____
   Reason:
   Bioequivalence office level sign off:

   Analytical site:
   Inspection needed: ☐ yes ☐ no
   Status: ☐acceptable ☐unacceptable ☐pending
   Date of status: _____
   Reason:

   Labeling Status:

   Microbiology status:
   Patent Certification:
   Controlled Correspondence/Cit.Pet.
   Comments: RLD =

Request 5/23/2002

REVIEWER: | DRAFT RECEIPT | FINAL ACTION

5. Greg Davis
Supv., Reg. Support Branch
Date 5/23/02 Initials RW | Date 5/23/02 Initials RW for

Contains GDEA certification: Yes ☒ No ☐ Determ. of Involvement? Yes ☐ No ☒
(required if sub after 6/1/92) Pediatric Exclusivity System
Patent/Exclusivity Certification: Yes ☒ No ☐ Date Checked N/A
If Para. IV Certification- did applicant PI Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☐ N/A No ☐ Written request issued ☐
Was applicant sued w/in 45 days: Yes ☐ N/A No ☐ Study Submitted ☐
Has case been settled: Yes ☐ No ☐ RLD-Hycitrad IN Oral Solution
Date settled: N/A
Is applicant eligible for 180 day Pharmacia + Upjohn Co. 125mg/5mL
Generic Drugs Exclusivity for each strength: Yes ☐ No ☒ NDA 50-285/000 (187.5mg(base)/5mL)
Comments: There are no unexpired patents or exclusivity currently listed in the Orange Book for this products RLD. This is a former 505 drug product.

6. Peter Rickman
Acting Director, DLPS
Date 5/23/02 Initials RW | Date 5/23/02 Initials Robert West for
Comments: Acceptable ETS dated 5/20/02 (Verified 5/23/02). No OAI. Labels noted. Bioequivalence waiver granted under 320.22(b)(3) Office-Level bio granted 6/23/98. FPL acceptable 4/2/00 (as endorsed 5/2/02). Proprietary name is acceptable to ODRA. CMC acceptable 5/6/02. Methods validation is not required.

7. Robert L. West
Acting Deputy Director, OGD
Date 5/23/02 Initials RW | Date 5/23/2002 Initials Robert West

Para.IV Patent Cert: Yes ☐ No ☒; Pending Legal Action: Yes ☐ No ☒; Petition: Yes ☐ No ☒
Comments: This ANDA is recommended for approval.

8. Gary Buehler
Director, OGD
Comments:
Date 5/23/02 Initials GB | Date 5/23/02 Initials GB

First Generic Approval ☒ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐

9. Project Manager Mark Anderson
Review Support Branch
Date 5/23/02 Initials MA | Date 5/23/02 Initials MA

N/A Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
2:45 Time notified of approval by phone 2:50 Time approval letter faxed

FDA Notification:
5/23 Date e-mail message sent to "OGD approvals" account
5/23 Date Approval letter copied to"//cder/drugapp" directory

v:\reports\approval\approvrou

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (516) 757-5522
FAX (516) 754-1550

P. O. BOX 1920
HUNTINGTON, NY 11743-0568

Douglas L. Sporn, Director
Office of Generic Drugs
CDER -- FDA Metro Park North II
HFD600
7500 Standish Place
Rockville, MD 20855-2773

FEB 10 1998

505(j)(11)a OK
3/11/98

Dear Director Sporn:

RE: Neomycin Sulfate Oral Solution USP; 125mg/5mL (87.5mg base/5mL)

The Pharmacia-Upjohn Company discontinued the production of the subject product (N50285 001) in 1996. At that time it was manufactured for their company and under private label for Pharma-Tek.

Pharmacia-Upjohn has subsequently discontinued the sale of Neomycin Oral Solution USP. However, Pharma-Tek purchased excess inventory so as to supply this drug without interruption to the medical profession until it has had an opportunity to gain approval of its own ANDA from the FDA.

In order to provide the medical profession with identical product, Pharma-Tek purchased the formulation and manufacturing procedure from the Pharmacia-Upjohn Company which is utilized in this ANDA.

Therefore we are submitting herewith, in duplicate, an abbreviated new drug application covering NEO-FRADIN; Neomycin Sulfate Oral Solution USP; 125mg/5mL equivalent to 87.5mg/5mL neomycin base (containing 4 volumes). This product is identical in content to the product previously manufactured by the Pharmacia-Upjohn Company, which is presently being marketed by Pharma-Tek.

This ANDA provides for 3 sizes; 2 ounce, 4 ounce and pint bottles.

When approved, Pharma-Tek will be the **only** FDA approved source of this product.

Your expedited review and approval is most urgently needed.

RECEIVED
FEB 11 1998
GENERIC DRUGS

Sincerely,

Susan E. Badia

Susan E. Badia
Assistant to the President

Pharma-Tek Inc.
PHARMACEUTICALS

NEW CORRESP
NC

PHONE (516) 757-5522
FAX (516) 754-1550
P. O. BOX 1920
HUNTINGTON, NY 11743-0568

Greg Davis
Office of Generic Drugs
CDER - FDA Metro Park North II
HFD 600
7500 Standish Place
Rockville, MD 20855-2773

Re: ANDA # 65-010 (Neomycin Sulfate Oral Solution USP) Amendment

Dear Mr. Davis:

Following this letter is an updated Form FDA 3439 and amendments to application 65-010 as per our conversation.

I contacted _____, the supplier of the bulk material, to obtain an exact address for the submission. They suggested I also list the registration number and a contact person.

All future submissions will reflect the changes of the Repeal of Section 507 of the Federal Food, Drug, and Cosmetic Act. I apologize for any inconvenience in not originally listing this submission as an ANDA.

If you require additional information please call me at 516-757-5522.

Sincerely yours,

Susan E. Badia

Susan E. Badia
Asst. to the Pres.

Enclosures

cc: FDA - Brooklyn District

RECEIVED
MAR 1 1 1999
GENERIC DRUGS

ANDA 65-010

Pharma-Tek Inc.
Attention: Susan E. Badia
P.O. Box 1920
Huntington, NY 11743

MAR 17 1998

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the telephone conversation dated March 9, 1998 and your correspondence dated March 9, 1998.

NAME OF DRUG: Neomycin Sulfate Oral Solution USP, 125 mg/5 mL

DATE OF APPLICATION: February 10, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: February 11, 1998

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Mark Anderson
Project Manager
(301) 827-5849

Sincerely yours,

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 65-010
cc: DUP/Jacket
Division File
Field Copy
HFD-610/J.Phillips
HFD-92
HFD-615/M.Bennett
Endorsement:
HFD-615/PRickman, Chief, RSB _____ date 3/17/98
HFD-615/GDavis, CSO _____ 3/11/98 date
HFD-643/JHarrison, Sup. Chem._____date
WP File x:\new\firmsnz\pharmtek\ltrs&rev\65010.ack
FT/njg/3/10/98
ANDA Acknowledgment Letter!

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (516) 757-5522
FAX (516) 754-1550
P. O. BOX 1920
HUNTINGTON, NY 11743-0568

Noted:
NDE
Mark Anderson 4/20/99
see E mails attached

February 23, 1999

NEW CORRESP

NC

RE: ANDA 65-010

Harvey A. Greenberg
OGD, Center of Drug Evaluation and Research
Food and Drug Administration
HFD-615, MPN2/113
5600 Fishers Lane
Rockville, MD 20857-1706

EXPEDITED REVIEW REQUEST

Dear Mr. Greenberg:

Confirming our telecon, Pharma-Tek is the only supplier of Neomycin Sulfate Oral Solution USP. Our inventory is [redacted]. This inventory was manufactured by Pharmacia & Upjohn for Pharma-Tek and they have subsequently discontinued its production. They no longer manufacture this product for themselves or for Pharma-Tek.

Pharma-Tek purchased the formulation and manufacturing procedure from Pharmacia & Upjohn and has utilized [redacted] to produce future batches for us. The batches are identical to Pharmacia & Upjohn's product in content and manufacturing procedure. Our ANDA was filed on February 10, 1998 utilizing the USP bio-assay procedures to monitor the stability batch.

The FDA in their letter of August 26, 1998 requested, in part, that we develop and utilize a stability indicating assay although the USP only recognizes the bio-assay procedure. The innovator, Pharmacia & Upjohn, was never required to develop and utilize a stability assay to produce this product.

In the spirit of cooperation and rather than request a hearing, Pharma-Tek developed a stability indicating assay and amended our application on December 16, 1998 with this data.

RECEIVED
MAR - 1 1999
GENERIC DRUGS

If the FDA had accepted our bio-assay data which was acceptable for the innovator Pharma-Tek would have had FDA approval for this product and [redacted]

[redacted]

Please expedite the review of our amendment to ANDA 65-010 in order [redacted] We agree to a post-approval commitment to resolve any deficiencies that may still exist.

Thank you for your consideration in this matter.

Sincerely,

Dan J. Badia
President

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (516) 757-5522
FAX (516) 754-1550

P. O. BOX 1920
HUNTINGTON, NY 11743-0568

F.C
ANDA
65-010

March 24, 1999

NEW CORRESP
NC

Noted:
NAE
Mark Anderson
4/20/99
review of major amendment is pending and EER reports with withhold recommendation

Harvey A. Greenberg
OGD, Center of Drug Evaluation and Research
Food and Drug Administration
HFD-615, MPN2/113
5600 Fishers Lane
Rockville, MD 20857-1706

Dear Mr. Greenberg:

As we discussed by telephone the unfair playing field rules on ANDAs for old generic drugs will have to be reviewed at the Congressional level if we can not work out fair procedures with the FDA's Office of Generic Drugs.

Sincerely,

Dan J. Badia
President

DJB/aap

Enclosure

RECEIVED
MAR 3 1 1999
GENERIC DRUGS

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (516) 757-5522
FAX (516) 754-1550
P. O. BOX 1920
HUNTINGTON, NY 11743-0568

September 28, 1999

ORIG AMENDMENT

MINOR AMENDMENT - ANDA# 65-010

Florence Fang, Ph.D.
Director, Division of Chemistry II
Office of Generic Drugs
Food and Drug Administration, CDER
7500 Standish Place
Rockville, MD 20855

RE: MINOR AMENDMENT
ANDA # 65-010
Neo-Fradin, Neomycin Sulfate Oral Solution USP, 125 mg/5mL

Dear Dr. Fang:

We are submitting herewith, in duplicate, an amendment to our ANDA #65-010 (Neomycin Sulfate Oral Solution USP; 125 mg/5mL) in response to MINOR deficiencis outlined in Dr. Fang's letter of July 21, 1999.

In addition to the responses to the deficiencies of July 21, 1999, appended to this submission are updated stability data covering our stability batch of Neomycin Sulfate Oral Solution USP.

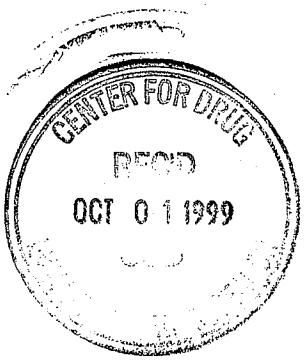
As the sole source of this product Pharma-Tek has now been

Your early review and approval of our application will be most appreciated.

Sincerely yours,

Susan E. Badia
Susan E. Badia
Assistant to the President

cc: FDA, Brooklyn District Office



10-5-99

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (516) 757-5522
FAX (516) 754-1550
P. O. BOX 1920
HUNTINGTON, NY 11743-0568

Noted To Jackie C. Maria S. 1/5/00

ORIG AMENDMENT
N/AM

MINOR AMENDMENT

RESPONSES TO CHEMISTRY & LABELING DEFICIENCIES

January 3, 2000

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs, CDER
7500 Standish Place, Room 150
Rockville, MD 20855

RE: ANDA# 65-010; Neo-Fradin; Neomycin Sulfate Oral Solution USP
Minor Amendment – Responses to Chemistry and Labeling Deficiencies

Dear Dr. Fang:

We are submitting herewith, in duplicate, an amendment to ANDA# 65-010 (Neomycin Sulfate Oral Solution; 125 mg/5mL) in response to minor deficiencies outlined in FDA's November 5, 1999 correspondence.

The responses to FDA's November 5, 1999 deficiencies cover both chemistry and labeling. Responses to the labeling deficiencies start on page 49 of this submission.

Your early review of this amendment and approval would be most appreciated.

Sincerely,

Susan E. Badia

Susan E. Badia
Asst. to the President

pc: FDA, Brooklyn District Office

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JAN 05 2000
OGD

Pharma-Tek Inc.
PHARMACEUTICALS

b31
PHONE (516) 757-5522
FAX (516) 754-1550
P. O. BOX 1920
HUNTINGTON, NY 11743-0568

ANDA 65-010

March 17, 2000

Florence S. Fang, Ph.D.
Director
OGD, Center of Drug Evaluation and Research
FDA, Division of Chemistry II
7500 Standish Place, MPN II
Rockville, MD 20855

MINOR AMENDMENT NDA ORIG AMENDMENT

Dear Dr. Fang:

We are submitting herewith, in duplicate, an amendment to our ANDA 65-010 covering Neomycin Sulfate Oral Solution USP, 125 mg/5 mL, dated February 10, 1998 – 2 years ago.

This amendment is in response to the Chemistry Comments contained in your letter of February 18, 2000 that were listed as Minor deficiencies.

Our responses are in the same order as the comments raised and follow this letter.

Your early review of this ANDA, which has been under review for 2 years, will be greatly appreciated.

Sincerely,

Susan E. Badia

Susan E. Badia
Assistant to the President

SEB/aap
Pc: FDA, Jamaica District Office

CENTER FOR DRUG
REC'D
MAR 21 2000
OGD
EVALUATION AND RESEARCH

Fde 65-010

E L E C T R O N I C M A I L M E S S A G E

Sensitivity: COMPANY CONFIDENTIAL

Date: 11-Apr-2000 03:00pm EDT
From: Jerry Phillips
PHILLIPSJ
Dept: HFD-400 PKLN 15B03
Tel No: 301-827-3242 FAX 301-480-8173

TO: Charles Hoppes (HOPPESC)

CC: Peter Honig (HONIGP)
CC: Robert West (WESTR)
CC: Sammie Beam (BEAMS)

Subject: OPDRA Consult 00-0113; Neo-Fradin

Charlie:

OPDRA has no objection to the use of the proprosed proprietary name Neo-Fradin for Neomycin Oral Solution by PharmaTek. This is considered a final review and need not be resubmitted to OPDRA. If you have any questions, please contact Sammie Beam. Thanks.

Jerry

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (631) 757-5522
FAX (631) 754-1550
P. O. BOX 1920
HUNTINGTON, NY 11743-0568

Mtg request denied - a Subsequent - Teleconfer was held on 8/1/00
NEW CORRESP M Anderson
NC

July 25, 2000

Director
Office of Generic Drugs
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

Re: ANDA 65-010
Neomycin Sulfate Oral Solution USP, 125 mg/5mL
REQUEST FOR A MEETING

Dear Sir:

Reference is made to the above cited ANDA and the agency's major amendment dated July 24, 2000. In this major amendment the agency recommended that a new batch be manufactured and all performance data (COA, executed batch records, and accelerated stability data) be submitted to the agency. Additionally, the agency indicated that current USP Microbial Assay <81> should be used for potency determination.

In view of the above, we respectfully request a meeting with members of your staff on Wednesday, August 2, 2000 or Thursday, August 10, 2000.

The following people will attend the meeting on behalf of Pharma-Tek:

Dan J. Badia, President, Pharma-Tek

We acknowledge that a satisfactory compliance evaluation for firms referenced in the ANDA is required prior to approval.

Sincerely,

Dan J. Badia

Dan J. Badia
President

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUL 26 2000
OGD

RECORD OF TELEPHONE CONVERSATION/MEETING

Richard Adams, Maria Shih, Pat Alcock (from Office of Compliance), and I spoke to Dan Badia and several representatives from ——— (PharmaTek's contract manufacturer) in a pre arranged Teleconference. Discussion was a result of our Not Approvable letter sent to PharmaTek on 7/24/00 in which we requested a new exhibit batch and testing thereof using USP <81> microbial assay due to concerns about the validity of the data from the original exhibit batch. Compliance has concurred with district recommendation for withhold status due to inconsistent information about analytical methodology provided by ——— to investigator.

Mr.——— and others from ——— provided a lengthy explanation and attempted to clarify the chronology of events concerning the manufacture of the Neomycin Sulfate Oral Solution and testing which occurred initially in the micro lab and later in the chemistry lab. Inconsistent data which led to the need to repeat analyses was explained by the fact that the micro lab analyst was using an incorrect calculation based on Neomycin Sulfate content instead of Neomycin (base). They stressed the fact that the actual method used including the "draft method" cited by the investigator is identical to the CFR method (repealed with passage of FDAMA) and USP method (i.e., all 3 are identical). It is ——— feeling that this fact was made clear to the investigator.
We explained the importance of satisfactory documentation and that if documentation can not be produced then we have to assume work was not done.

Agreement was reached that the firm would provide data for product at release and at 1, 2, and 3 month test points for batch on accelerated stability along with all raw data and we would look this over in conjunction with Office of Compliance and investigator, as needed. We provided no assurance that this would lead to a reversal of our recommendation for a new batch and testing thereof.

We will contact ——— (via PharmaTek) when we reach a conclusion.

This concluded our conversation.
V:\firmsnz\pharma.tek\telecons\65010.002

DATE
8/1/00

ANDA NUMBER
65-010

IND NUMBER

TELECON

INITIATED BY — **MADE**
_ **APPLICANT/ SPONSOR** — X **BY TELE.**
X **FDA** — _ **IN PERSON**

PRODUCT NAME
Neomycin Oral Solution

FIRM NAME
Pharma-Tek
———

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Dan Badia, ———
———, etc

TELEPHONE NUMBER

SIGNATURE
Mark Anderson

R.C. Adams

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (631) 757-5522
FAX (631) 754-1550

P. O. BOX 1920
HUNTINGTON, NY 11743-0568

August 28, 2000

Director
Office of Generic Drugs
Food and Drug Administration
Metro Park North
7500 Standish Place
Room 150
Rockville, MD 20855

NEW CORRESP
NC

RE: ANDA # 65-010
Neomycin Sulfate Oral Solution USP, 125 mg/5mL

Dear Sir:

On August 8, 2000 ———— submitted information in our behalf in connection with the subject ANDA covering Neomycin Sulfate Oral Solution USP, 125 mg/5mL.

Please incorporate their submission as part of our ANDA for your review. Anything you can do to expedite the review and approval will be greatly appreciated.

Sincerely,

Susan E. Badia

Susan E. Badia
Assistant to the President

Enclosure: Form FDA 356h

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (631) 757-5522
FAX (631) 754-1550

P. O. BOX 1920
HUNTINGTON, NY 11743-0568

ANDA # 65-010 – Neomycin Sulfate Oral Solution USP, 125mg/5mL
MAJOR AMENDMENT (Response to Chemistry Deficiencies)

July 17, 2001

Florence S. Fang
Director, Division of Chemistry II
OGD, CDER
7500 Standish Place
Rockville, MD 20855-2773

N/AC

ORIG AMENDMENT

Dear Ms. Fang:

We are submitting herewith, in duplicate, an amendment to our ANDA dated Februrary 10, 1998.

The information contained herein is in response to FDA's facsimile dated July 24, 2000, which cited major chemistry deficiencies. These deficiencies have been corrected and we are including data from the contract manufacturer. A new batch of Neomycin Sulfate Oral Solution was manufactured and we have submitted all performance data (COA, executed batch records and accelerated stability data) as requested in your July 24th letter.

Also, the current USP Microbial Assay <81> was used for potency determination as per your letter.

Pharma-Tek acknowledges that a satisfactory compliance evaluation for firms referenced in the ANDA is required prior to approval. We believe this has been accomplished.

Following this cover letter is a brief summary of events leading up to this submission.

Your early review and approval of this three (3) year and five (5) month old ANDA will be greatly appreciated.

Sincerely,

Dan J. Badia

Dan J. Badia
President
pc: FDA, Jamaica District Office

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUL 20 2001
OGD

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (516) 757-5522
FAX (516) 754-1550
P. O. BOX 1920
HUNTINGTON, NY 11743-0568

FAX AMENDMENT
ANDA # 65-010 (Neomycin Sulfate Oral Solution USP, 125 mg/5mL)

December 28, 2001

N/FA

ORIG AMENDMENT

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs, CDER
7500 Standish Place, Room 150
Rockville, MD 20855-2772

Dear Ms. Fang:

We are submitting herewith, in duplicate (archival and review copies), a FAX amendment in response to FDA's deficiencies and/or comments dated December 10, 2001 for ANDA# 65-010 entitled Neomycin Sulfate Oral Solution USP, 125 mg/5mL (eq. 87.5 mg neomycin base/5mL).

Pharma-Tek has responded to the FDA's Chemistry comments and has listed its responses to the deficiencies/comments in the same number sequence as received by the FDA.

If you have any questions please do not hesitate to call me at 631-757-5522. Thank you.

Sincerely,

Susan E. Badia

Susan E. Badia
Asst. to the President

pc: FDA, Jamaica District Office

CENTER FOR DRUG
JAN 03 2002
EVALUATION AND RESEARCH

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (631) 757-5522
FAX (631) 754-1550

P. O. BOX 1920
HUNTINGTON, NY 11743-0568

Noted:
M Anderson

MINOR AMENDMENT
ANDA# 65-010; Neomycin Sulfate Oral Solution USP

March 18, 2002

ORIG AMENDMENT

Office of Generic Drugs
FDA, CDER
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: Response to Chemistry Deficiencies for ANDA 65-010

Dear Ms. Fang:

We are submitting herewith, in duplicate, a Minor Amendment to ANDA# 65-010, Neomycin Sulfate Oral Solution USP, 125 mg/mL (eq. to 87.5 mg neomycin base/5mL). This Minor Amendment is in response to your letter dated February 14, 2002.

The following pages contain the chemistry deficiencies cited by FDA followed by Pharma-Tek's responses.

Please note that we have been waiting more than four (4) years for approval of this product. Your earliest review and approval would be appreciated.

If you have any questions please call me at 631-757-5522. Thank you.

Sincerely,

Susan E. Badia

Susan E. Badia
Assistant to the President

Enclosures
pc: FDA, Jamaica District Office

RECEIVED
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OGD / CDER

3/23/02