CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 64-216

Name: Colistimethate for Injection USP, 150 mg (base) / vial

Sponsor: Pharma-Tek, Inc.

Approval Date: February 26, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 64-216

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 64-216

APPROVAL LETTER

ANDA 64-216

FEB 26 1999

Pharma-Tek, Inc.
Attention: Susan Badia
P. O. Box 1920
Huntington, NY 11743-0568

Dear Madam:

This is in reference to your abbreviated new drug application dated June 30, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Colistimethate for Injection USP, 150 mg (base)/vial. 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 amendments dated June 12, August 13, September 3, September 14, September 22, and October 14, 1998; and January 13 and 21, 1999.

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 Colistimethate for Injection USP, 150 mg (base)/vial, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Coly-Mycin® M Parenteral 150 mg (base)/vial of Parke Davis Pharmaceutical Research).

Under 21 CFR 314.70, 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 which 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,

D. L. Sporn 2/26/99

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 64-216
Division File
FIELD COPY
HFD-610/RLWest
HFD-92
HFD-210/B.Poole
HFD-330/
HFD-205/

Endorsements:
HFD-643/V.Walton/12/18/98 V. Walton 12/22/98
HFD-643/J.Harrison/12/18/98 J. Harrison 12/22/98
HFD-617/M.Anderson/12/21/98 Mark Anderson 12/22/98
HFD-640/J.McVey/12/22/98 J. McVey 12/22/98
HFD-613/J.White (C Hoppes for)/12/21/98 C Hoppes for/ 12/22/98
HFD-613/C.Hoppes (final only)/ C Hoppes 12/22/98

x:\new\firmsnz\pharmtek\ltrs&rev\64216.apd
F/T by: mda/12/22/98

APPROVAL

Robert L. Sept 2/25/99

1/21/99

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 64-216

LABELING

HOW SUPPLIED

Colistimethate for Injection USP is supplied in vials containing colistimethate sodium (150 mg colistin base equivalent per vial) as a white to slightly yellow lyophilized cake and is available as one vial per carton (NDC 39822-0615-1).

Store between 15° - 30° C (59° - 86° F).

Store reconstituted solution in refrigerator 2° - 8° C (36° - 46° F) or between 15° - 30° C (59° - 86° F) and use within 7 days.

TOXICOLOGY AND ANIMAL PHARMACOLOGY

Acute Toxicity: The intravenous LD_{50} was 41.5 mg/kg in the dog and 739 mg/kg in the mouse; intramuscular toxicity was 42 mg/kg in the dog and 267 mg/kg in the mouse.

Subacute Toxicity: In albino rabbits and beagle dogs, IV doses of 5, 10 and 20 mg/kg/day for 28 days resulted in elevated blood urea nitrogen in the dog (10 mg/kg/day dose group) and in both 20 mg/kg dose groups.

CLINICAL STUDIES

Clinically, Colistimethate for Injection has been of particular therapeutic value in acute and chronic urinary tract infections caused by sensitive strains of *Pseudomonas aeruginosa*. Colistimethate sodium is clinically effective in the treatment of infections due to other sensitive gram-negative pathogenic bacilli which have become resistant to broad spectrum antibiotics.

Colistimethate sodium has been used to treat bacteriuria and overt urinary infections in pregnant women during the third trimester. However, in view of the evidence of possible embryotoxic and teratogenic effectics of colistimethate sodium in pregnant rabbits, caution should be exercised in use of this drug in women of childbearing potential.

R_x only

Manufactured for:
Pharma-Tek Inc.
Huntington, NY 11743-0568

Printed in USA

Revised August 1998

Colistimethate for Injection USP

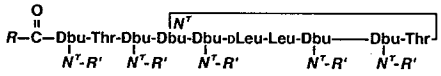
FOR INTRAMUSCULAR AND INTRAVENOUS USE

DESCRIPTION

Colistimethate for Injection is a sterile parenteral antibiotic product which, when reconstituted (see Reconstitution), is suitable for intramuscular or intravenous administration. Each vial contains: Sterile Colistimethate Sodium equivalent to 150 mg Colistin Base. Colistimethate for Injection USP is supplied in vials containing Colistimethate sodium (150 mg colistin base equivalent per vial) as a white to slightly yellow lyophilized cake. The sodium content is approximately 0.1 mg (0.004 mEq) of sodium per milligram of Colistin. Colistimethate sodium is a polypeptide antibiotic. The chemical name of colistimethate sodium is:

(Dbu is L-α,γ-diaminobutyric acid; *R* is $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}H(CH_2)_4$ in the colistin A component and $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}H(CH_2)_4$ in the colistin B component; *R'* is CH_2SO_3Na)

The molecular formula for colistin A component is $C_{58}H_{105}N_{16}Na_5O_{28}S_5$ and the molecular weight is 1749.85. The molecular formula for colistin B component is $C_{57}H_{103}N_{16}Na_5O_{28}S_5$ and the molecular weight is 1735.83. Colistimethate sodium has the following structural formula:



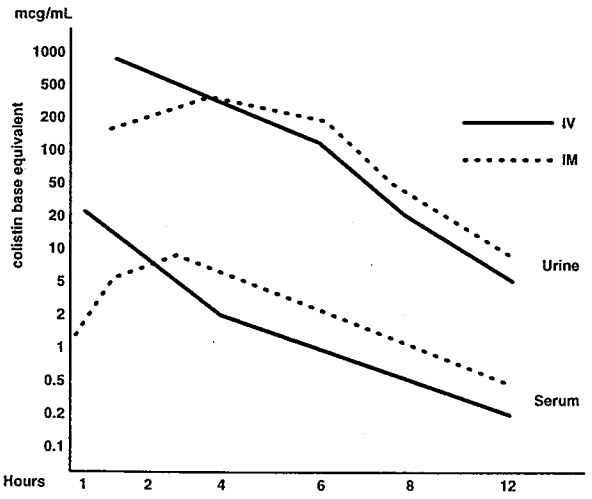
CLINICAL PHARMACOLOGY

Microbiology: Colistimethate for Injection has bactericidal activity against the following gram-negative bacilli: *Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*.

Human Pharmacology: Typical serum and urine levels following a single 150-mg dose of Colistimethate for Injection IM or IV in normal adult subjects are shown in Figure 1.

Figure 1

Urine and serum values in adults following Parenteral (IM or IV) administration of Colistimethate for Injection



Higher serum levels were obtained at 10 minutes following IV administration. Serum concentration declined with a half-life of 2-3 hours following either intravenous or intramuscular administration in adults and children including premature infants.

Colistimethate sodium is transferred across the placental barrier, and blood levels of about 1 mcg/mL are obtained in the fetus following intravenous administration to the mother.

Average urine levels ranged from about 270 mcg/mL at 2 hours to about 15 mcg/mL at 8 hours after intravenous administration and from 200 to about 25 mcg/mL during a similar period following intramuscular administration.

INDICATIONS AND USAGE

Colistimethate for Injection is indicated for the treatment of acute or chronic infections due to sensitive strains of certain gram-negative bacilli. It is particularly indicated when the infection is caused by sensitive strains of Pseudomonas aeruginosa. This antibiotic is not indicated for infections due to Proteus or Neisseria. Colistimethate for Injection has proven clinically effective in treatment of infections due to the following gram-negative organisms: *Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa.*

Pending results of appropriate bacteriologic cultures and sensitivity tests, Colistimethate for Injection may be used to initiate therapy in serious infections that are suspected to be due to gram-negative organisms.

CONTRAINDICATIONS

The use of Colistimethate for Injection is contraindicated for patients with a history of sensitivity to the drug.

WARNING

Maximum daily dose should not exceed 5 mg/kg/day (2.3 mg/lb) with normal renal function.

Transient neurological disturbances may occur. These include circumoral paresthesias or numbness, tingling or formication of the extremities, generalized pruritus, vertigo, dizziness, and slurring of speech. For these reasons, patients should be warned not to drive vehicles or use hazardous machinery while on therapy. Reduction of dosage may alleviate symptoms. Therapy need not be discontinued, but such patients should be observed with particular care. Overdosage can result in renal insufficiency, muscle weakness, and apnea. See PRECAUTIONS section for use concomitantly with curariform drugs and DOSAGE AND ADMINISTRATION section for use in renal impairment.

PRECAUTIONS

Since Colistimethate for Injection is eliminated mainly by renal excretion, it should be used with caution when the possibility of impaired renal function exists. The decline in renal function with advanced age should be considered.

When actual renal impairment is present, Colistimethate for Injection may be used, but the greatest caution should be exercised and the dosage should be reduced in proportion to the extent of the impairment. Administration of amounts of Colistimethate for Injection in excess of renal excretory capacity will lead to high serum levels and can result in further impairment of renal function, initiating a cycle which, if not recognized, can lead to acute renal insufficiency, renal shutdown, and further concentration of the antibiotic to toxic levels in the body. At this point, interference of nerve transmission at neuromuscular junctions may occur and result in muscle weakness and apnea.

Easily recognized signs indicating the development of impaired renal function are diminishing urine output, rising BUN and serum creatinine. If present, therapy with Colistimethate for Injection should be discontinued immediately.

If a life-threatening situation exists, therapy may be reinstated at a lower dosage after blood levels have fallen.

Certain other antibiotics (kanamycin, streptomycin, dihydrostreptomycin, polymyxin, neomycin) have also been reported to interfere with the nerve transmission at the neuromuscular junction. Based on this reported activity, they should not be given concomitantly with Colistimethate for Injection except with the greatest caution. The antibiotics with a gram-positive antimicrobial spectrum, eg, penicillin, tetracycline, sodium cephalothin, have not been reported to interfere with nerve transmission and, accordingly, would not be expected to potentiate this activity of Colistimethate for Injection.

Other drugs, including curariform muscle relaxants (ether, tubocurarine, succinylcholine, gallamine, decamethonium, and sodium citrate) potentiate the neuromuscular blocking effect and should be used with extreme caution in patients being treated with Colistimethate for Injection.

If apnea occurs, it may be treated with assisted respiration, oxygen, and calcium chloride injections.

Use in Pregnancy: The safety of colistimethate sodium during human pregnancy has not been established.

ADVERSE REACTIONS

Respiratory arrest has been reported following intramuscular administration of colistimethate sodium. Impaired renal function increases the possibility of apnea and neuromuscular blockade following administration of colistimethate sodium. This has been generally due to failure to follow recommended guidelines, usually overdosage, failure to reduce dose commensurate with degree of renal impairment, and/or concomitant use of other antibiotics or drugs with neuromuscular blocking potential.

A decrease in urine output or increase in blood urea nitrogen or serum creatinine can be interpreted as signs of nephrotoxicity, which is probably a dose-dependent effect of colistimethate sodium. These manifestations of nephrotoxicity are reversible following discontinuation of the antibiotic.

Increases of blood urea nitrogen have been reported for patients receiving Colistimethate for Injection at dose levels of 1.6 to 5 mg/kg per day. The BUN values returned to normal following cessation of Colistimethate for Injection administration.

Paresthesia, tingling of the extremities or tingling of the tongue, and generalized itching or urticaria have been reported by patients who received Colistimethate for Injection by intravenous or intramuscular injection. In addition, the following adverse reactions have been reported for colistimethate sodium: drug fever and gastrointestinal upset, vertigo, and slurring of speech.

The subjective symptoms reported by the adult may not be manifest in infants or young children, thus requiring close attention to renal function.

DOSAGE AND ADMINISTRATION

Important: Colistimethate for Injection is supplied in vials containing colistimethate sodium equivalent to 150 mg colistin base activity per vial.

Reconstitution: The **150-mg** vial should be reconstituted with **2 mL** Sterile Water for injection, USP. The reconstituted solution provides colistimethate sodium at a concentration of 75 mg/mL.

During reconstitution, swirl **gently** to avoid frothing.

Dosage—Adults and children—intravenous or intramuscular administration— Colistimethate for Injection should be given in 2 to 4 divided doses at dose levels of 2.5 to 5 mg/kg per day for patients with normal renal function, depending on the severity of the infection.

The daily dose should be reduced in the presence of any renal impairment, which can often be anticipated from the history.

Modifications of dosage in the presence of renal impairment are presented in Table 1.

Table 1. Suggested Modification of Dosage Schedules of Colistimethate for Injection for Adults with Impaired Renal Function

Renal Function	Degree of Impairment			
	Normal	Mild	Moderate	Considerable
Plasma creatinine, mg/100 mL	0.7 to 1.2	1.3 to 1.5	1.6 to 2.5	2.6 to 4
Urea clearance, % of normal	80 to 100	40 to 70	25 to 40	10 to 25
Dosage				
Unit dose of Colistimethate for Injection, mg	100 to 150	75 to 115	66 to 150	100 to 150
Frequency times/day	4 to 2	2	2 or 1	every 36 hr
Total daily dose, mg	300	150 to 230	133 to 150	100
Approximate daily dose, mg/kg/day	5	2.5 to 3.8	2.5	1.5

Note: The suggested unit dose is 2.5 to 5 mg/kg; however, the time INTERVAL between injections should be increased in the presence of impaired renal function.

INTRAVENOUS ADMINISTRATION

1. Direct Intermittent Administration - slowly inject one-half of the total daily dose over a period of 3 to 5 minutes every 12 hours.

2. Continuous Infusion - slowly inject one-half of the total daily dose over 3 to 5 minutes. Add the remaining half of the total daily dose of Colistimethate for Injection to one of the following:

0.9% NaCl

5% dextrose in 0.9% NaCl

5% dextrose in water

5% dextrose in 0.45% NaCl

5% dextrose in 0.225% NaCl

lactated Ringer's solution

10% invert sugar solution

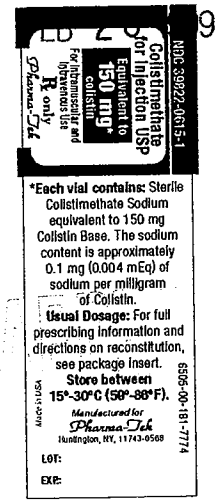
There are not sufficient data to recommend usage of Colistimethate for Injection with other drugs or other than the above listed infusion solutions.

Administer by slow intravenous infusion starting 1 to 2 hours after the initial dose at a rate of 5 to 6 mg/hr in the presence of normal renal function. In the presence of impaired renal function, reduce the infusion rate depending on the degree of renal impairment.

The choice of intravenous solution and the volume to be employed are dictated by the requirements of fluid and electrolyte management.

Any infusion solution containing colistimethate sodium should be freshly prepared and used for no longer than 24 hours.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.


Colistimethate
for Injection USP
Equivalent to
150 mg*
colistin
For Intramuscular and
Intravenous Use
℞ only
Pharma-Tek
NDC 59922-0615-1
*Each vial contains: Sterile Colistimethate Sodium equivalent to 150 mg Colistin Base. The sodium content is approximately 0.1 mg (0.004 mEq) of sodium per milligram of Colistin.
Usual Dosage: For full prescribing information and directions on reconstitution, see package insert.
Store between 15°-30°C (59°-86°F).
Manufactured for
Pharma-Tek
Huntington, NY, 11743-0568
LOT:
EXP:
6505-00-181-7774


NDC 39822-0615-1
NDC 39822-0615-1
NDC 39822-0615-1
6505-00-181-7774
Manufactured for:
Pharma-Tek, Inc.
Huntington, NY, 11743-0568
Pharma-Tek
*Each vial contains: Sterile Colistimethate Sodium equivalent to 150mg Colistin Base. The sodium content is approximately 0.1 mg (0.004 mEq) of sodium per milligram of Colistin.
Store between:
15° to 30°C (59° to 86°F).
Usual Dose -2 to 4 divided doses at dose levels of 2.5 to 5 mg/kg/day for patients with normal renal function,depending on the severity of the infection.
For full prescribing information and directions on reconstitution, see enclosed package insert.
Store reconstituted solution
In refrigerator 2°- 8°C (36°- 46°F) or at room temperature 15°- 30°C (59°- 86°F), and use within 7 days.
Pharma-Tek
COLISTIMETHATE FOR INJECTION USP
Equivalent to 150 mg* colistin
For Intramuscular and Intravenous Use
℞ only
Pharma-Tek
*Each vial contains: Sterile Colistimethate Sodium equivalent to 150mg Colistin Base. The sodium content is approximately 0.1 mg (0.004 mEq) of sodium per milligram of Colistin.
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Store reconstituted solution
In refrigerator 2°- 8° C (36°- 46° F) or at room temperature 15°- 30° C (59°- 86° F), and use within 7 days.
Pharma-Tek
Lot:
Exp.
MADE IN USA
FEB 2 6 2009
COLISTIMETHATE FOR INJECTION USP
Equivalent to 150 mg* colistin
For Intramuscular and Intravenous Use
NDC 39822-0615-1

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 64-216

LABELING REVIEWS

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

ANDA Number: 64-216

Date of Submission: June 30, 1997

Applicant's Name: Pharma-Tek, Inc.

Established Name: Colistimethate for Injection, USP, 150 mg (colistin base)/vials

Labeling Deficiencies:

1. General Comments

   a. Replace the "CAUTION: Federal law..." statement with the symbol "Rx only" or "℞ only" on your labels and labeling. We refer you to the Guidance for Industry, "Implementation of Section 126, Elimination of Certain Labeling Requirements...", at the internet site, **http://www.fda.gov/cder/guidance/index.htm** for guidance.

   b. On November 15, 1998, the official USP monograph title for "Sterile Colistimethate Sodium, USP" will be replaced with the title "Colistimethate for Injection, USP". Revise the established name on your container labels, carton labeling and insert labeling accordingly.

2. CONTAINER:

   a. Increase the prominence of the strength.

   b. Due to the USP title revision, make the following revisions:

      i. Add an asterisk following the strength, "150 mg*".

      ii. Delete the text "Colistin Base Equivalent".

      iii. Add the following statement to the side panel:

*Each vial contains: Sterile Colistimethate Sodium equivalent to 150 mg Colistin Base. The sodium content is approximately ___ mg (___ mEq) of sodium per milligram of Colistin.

3. CARTON: 1 vial/carton

a. Usual Dose

Delete the extra space between before the word "day" [... 5 mg/kg/day ...].

b. Delete the extra spaces in your storage statements and revise to read as follows:

Store between 15°-30°C (59°-86°F)

Store reconstituted solution in refrigerator 2°-8°C (36°-46°F) or at room temperature 15°-30°C (59°-86°F) and use within 7 days.

c. See comments 2(b)(i, ii and iii) under CONTAINER.

4. INSERT

a. General Comment

You may delete "USP" following the established name throughout the insert labeling, except in the TITLE and in the HOW SUPPLIED section.

b. DESCRIPTION

i. Revise the molecular formula to read, "1749.85"

ii. Add the chemical name and the structural formula. We refer you to USP 23 and 21 CFR 201.57(a)(vi) for further guidance.

iii. Revise your each vial contains statement to read as follows:

Each vial contains: Sterile Colistimethate Sodium equivalent to 150 mg Colistin Base. The sodium content is approximately ___ mg (___ mEq) of sodium per milligram of Colistin.

c. CLINICAL PHARMACOLOGY (Figure 1)

i. Figure 1 is difficult to read. Therefore, improve the readability and the print quality.

ii. Delete the terminal zero following a decimal point, [i.e., "1" instead of "1.0"].

d. ADVERSE REACTIONS

In the third paragraph replace the hyphen with the word "to".

e. DOSAGE AND ADMINISTRATION

i. General Comments

a. Delete the terminal zero following a decimal point.

b. Replace the hyphens with the word "to".

ii. Dosage

Delete the fifth paragraph, "(b) (4) ... (b) (4)".

iii. Intravenous Administration

Revise the fourth paragraph to read as follows:

> Administer by slow intravenous infusion starting 1 to 2 hours after the initial dose at a rate of 5 to 6 mg/hr in the presence of normal renal function. In the presence of impaired renal function, reduce the infusion rate depending on the degree of renal impairment.

iv. Add the following as the last paragraph:

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

We refer you to 21 CFR 201.57(j) for further guidance.

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.

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

ADDITIONAL - NOTE TO THE CHEMIST

1. Please note, we are requesting the following revision from the firm:

   On November 15, 1998, the official USP monograph title for "Sterile Colistimethate Sodium, USP" will be replaced with the title "Colistimethate for Injection, USP". Revise the established name on your container labels, carton labeling and insert labeling accordingly.

   Do you concur with comments 2(b)(i and ii) under CONTAINER?

NOTE TO THE CHEMIST

1. Should "Colistin A or B component" be listed in the DESCRIPTION section?

   Chemist response/V.W. - No

   The referenced drug is described (in the DESCRIPTION section) as a sterile parenteral antibiotic product which, when reconstituted, is suitable for intramuscular or intravenous administration. Each vial contains 150 mg colistin base equivalent. Colistimethate sodium is a polypeptide antibiotic with an approximate molecular weight of 1750, the empirical formula is $C_{58}H_{105}N_{16}Na_5O_{28}S_5$.

   Colistimethate sodium is described in Remington's Pharmaceutical Sciences, 17th Edition as follows: Colistimethate sodium contains the pentasodium salt of the penta (methanesulfonic acid) derivative of colistin A, $C_{58}H_{105}N_{16}Na_5O_{28}S_5$ as the major component, with a small proportion of the pentasodium salt of the same derivative of colistin B, $C_{57}H_{103}N_{16}Na_5O_{28}S_5$.

2. The firm listed "[redacted] (b) (4)" as an inactive ingredient in their component's statement. Should this be listed as an inactive ingredient in the DESCRIPTION section?

   Chemist response/V.W. - No

   [redacted] (b) (4) not listed as an inactive ingredient.

3. Has the firm submitted compatibility or stability data to adequately support the compatibility and stability claims which appear in the DOSAGE AND ADMINISTRATION/(INTRAVENOUS

ADMINISTRATION) section of the insert labeling? [See section V, p. 29].

Chemist response/V.W. - No

Firm has not submitted compatibility or stability to support the compatibility and stability claims which appear in the DOSAGE AND ADMINISTRATION/(INTRAVENOUS ADMINISTRATION) section of the insert labeling. We do not routinely require that data when the recommended Infusion Fluids are identical to those named in the innovator's labeling as in this ANDA. IV solutions must be prepared fresh every 24 hours.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's 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.	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			
PROPRIETARY NAME			
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?			X
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 -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.			
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	
Error Prevention Analysis: *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?			na
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. *See NOTE TO THE CHEMIST	*		
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? [See NOTE TO THE CHEMIST]	*		
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 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 the USP. Listed in the HOW SUPPLIED section of the RLD].	*		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.			
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. [See FTR].			

FOR THE RECORD:

1. Labeling model: Coly-Mycin-M by Parke-Davis, S-001 approved 10/7/82 and revised 10/81.

2. Patent/exclusivity: none pending

3. Manufacturing facility:

   - (b) (4)

4. Storage:

USP - Preserve in containers for sterile solids as described under Injections

NDA - Store between 15°-30°C (59°-86°F)

Store reconstituted solution in a refrigerator 2°-8°C(36°-46°F) or between 15°-30°C(59°-86°F) and use within 7 days.

ANDA - See comment in review.

5. Description section:

See NOTE TO THE CHEMIST.
[Vol. 1.1, p.43]

6. Container:

(b) (4) Vial/Gray (b) (4) Stopper/White flip-off aluminum seal
[Vol. 1.1, p.44]

7. Package size:

RLD - 1 vial/carton

ANDA - 1 vial/carton

8. Bioequivalence:

A waiver of <u>in-vivo</u> bioavailability/bioequivalence has been granted.
[Vol. 1.1, signed 1/15/98].

Date of Review: 10/22/97 and 3/20/98

Jacqueline White, Pharm.D. 3-15-98
Primary Reviewer Date
Jacqueline White, Pharm.D.

Team Leader 4/15/98
Date

cc:
ANDA: 64216
DUP/DIVISION FILE
HFD-613/JWhite/CHoppes (no cc)
x:\new\...64216na1.l
Review

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

ANDA Number: 64-216

Date of Submission: June 12, 1998

Applicant's Name: Pharma-Tek, Inc.

Established Name: Colistimethate for Injection, USP, 150 mg (colistin base)/vials

Labeling Deficiencies:

1. CONTAINER

   Start a new paragraph with the following text:

   Usual Dosage: For full...

2. CARTON

   Satisfactory in draft.

3. INSERT

   a. DESCRIPTION

      Include the physical description of the drug product, as it appears in the HOW SUPPLIED section, [... white to slightly yellow...].

   b. DOSAGE AND ADMINISTRATION (Table 1)

      i. Please ensure that the title of Table 1 appears on the same page as the table.

      ii. In second row and last column revise "2.5" to read "25".

Please revise your labels and labeling, as instructed above, and submit in final print.

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.

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

NOTE TO THE CHEMIST

DESCRIPTION section:

The firm has revised the molecular weight, added the chemical formula, and the structural formula. Do you concur?

Chemist response/V.W.: Yes-USP 23-7/25/98

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's 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.	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			
PROPRIETARY NAME			
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?			X
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 -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.			
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	
Error Prevention Analysis: *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?			na
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. *See NOTE TO THE CHEMIST	*		
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? [See NOTE TO THE CHEMIST]	*		
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 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 the USP. Listed in the HOW SUPPLIED section of the RLD. See comment under DESCRIPTION].	*		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.			
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. [See FTR].			

FOR THE RECORD:

1. Labeling model: Coly-Mycin-M by Parke-Davis, S-001 approved 10/7/82 and revised 10/81.

2. Patent/exclusivity: none pending

3. Manufacturing facility:

   - [redacted] (b) (4)

4. Storage:

   USP - Preserve in containers for sterile solids as described under Injections

   NDA - Store between 15°-30°C (59°-86°F)

   Store reconstituted solution in a refrigerator 2°-8°C(36°-46°F) or between 15°-30°C(59°-86°F) and use within 7 days.

   ANDA - Same as NDA.

5. Description section:

   This section is consistent with the firm's components and composition section.
   [See response from chemist for submission dated 6/30/97].
   [Vol. 1.1, p.43]

6. Container:

   [redacted] (b) (4) Vial/Gray [redacted] (b) (4) Stopper/White flip-off aluminum seal
   [Vol. 1.1, p.44]

7. Package size:

   RLD - 1 vial/carton

   ANDA - 1 vial/carton

8. Bioequivalence:

   A waiver of <u>in-vivo</u> bioavailability/bioequivalence has been granted.
   [Vol. 1.1, signed 1/15/98].

Date of Review: 6/30/98

Primary Reviewer
Jacqueline White, Pharm.D.

7-16-98
Date

Team Leader

7/16/98
Date

cc:

ANDA: 64216
DUP/DIVISION FILE
HFD-613/JWhite/CHoppes (no cc)
x:\new\...64216na2.l
Review

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

ANDA Number: **64-216**

Date of Submission: **August 13, 1998**

Applicant's Name: **Pharma-Tek, Inc.**

Established Name: **Colistimethate for Injection, USP, 150 mg (colistin base)/vials**

Labeling Deficiencies:

1. CONTAINER (150 mg)

   Revise the strength to read as follows:

   Equivalent to 150 mg colistin

2. CARTON LABELING (1 x 150 mg)

   See comment under container.

3. INSERT

   Satisfactory in final print.

Please revise your container labels and insert labeling, as instructed above, and submit final printed labels and labeling.

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.

Jerry Phillips
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? Yes

Container Labels: August 13, 1998 (150 mg).

Carton Labeling: August 13, 1998 (1 x 150 mg).

Professional Package Insert Labeling:
August 13, 1998 (Rev. August 1998).

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: COLY-MYCIN® M PARENTERAL

NDA Number: 50-108

NDA Drug Name: COLY -MYCIN® M PARENTERAL

NDA Firm: Parke-Davis

Date of Approval of NDA Insert and supplement #:
October 7, 1982/S-001

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

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Container Labels: side by sides submitted

Basis of Approval for the Carton Labeling: side by sides submitted

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's 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.	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?			X
Error Prevention Analysis			
PROPRIETARY NAME			
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?			X
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 -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.			
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	
Error Prevention Analysis: *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?			na
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling?		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	

FOR THE RECORD FROM PREVIOUS REVIEW:

1. Labeling model: Coly-Mycin-M by Parke-Davis, S-001 approved 10/7/82 and revised 10/81.

2. Patent/exclusivity: none pending

3. Manufacturing facility:

   - [redacted] (b) (4)

4. Storage:

   USP - Preserve in containers for sterile solids as described under Injections

   NDA - Store between 15°-30°C (59°-86°F)

   Store reconstituted solution in a refrigerator 2°-8°C(36°-46°F) or between 15°-30°C(59°-86°F) and use within 7 days.

   ANDA - Same as NDA.

5. Description section:

   This section is consistent with the firm's components and composition section.
   [See response from chemist for submission dated 6/30/97].
   [Vol. 1.1, p.43]

6. Container:

   [redacted] (b) (4) Vial/Gray [redacted] (b) (4) Stopper/White flip-off aluminum seal
   [Vol. 1.1, p.44]

7. Package size:

   RLD - 1 vial/carton

   ANDA - 1 vial/carton

8. Bioequivalence:

   A waiver of <u>in-vivo</u> bioavailability/bioequivalence has been granted.
   [Vol. 1.1, signed 1/15/98].

Date of Review: September 3, 1998

Date of Submission: August 13, 1998

Reviewer: C Holquist Date 9/10/98

Team Leader: John D. Grace Date 9/15/98

cc:

ANDA: 64-216
DUP/DIVISION FILE
HFD-613/CHolquist/JGrace (no cc)
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Review

APPROVAL SUMMARY

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

ANDA Number: 64-216

Date of Submission: September 14, 1998

Applicant's Name: Pharma-Tek, Inc.

Established Name: Colistimethate for Injection, USP, 150 mg (colistin base)/vials

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

Do you have 12 Final Printed Labels and Labeling? No, the blue volumes should be reviewed for additional labels and labeling.

Container Labels: - Satisfactory in final print as of the 9/14/98 submission.

Carton Labeling: 1s - Satisfactory in final print as of the 9/14/98 submission.

Professional Package Insert Labeling: Satisfactory in final print as of the 9/14/98 submission.

Revisions needed post-approval:

INSERT

1. DOSAGE AND ADMINISTRATION

   Relocate the "Parenteral drugs...", statement to follow the boxed statement, rather than appearing inside the box.

2. Encourage firm to relocate the Rx Only statement to appear beneath the Title of the insert.

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Coly-Mycin-M

NDA Number: 50-108

NDA Drug Name: Coly-Mycin-M Parenteral (Sterile Colistimethathe Sodium, USP)

NDA Firm: Parke-Davis

Date of Approval of NDA Insert and supplement #, S-001 approved 10/7/82 and revised 10/81

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: Coly-Mycin-M Parenteral
Basis of Approval for the Carton Labeling: Coly-Mycin-M Parenteral

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NOTE TO THE CHEMIST

The firm has included the sodium content in the DESCRIPTION section.

Is the sodium content accurate?

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's 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.	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			
PROPRIETARY NAME			
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?			X
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 -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.			
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	
Error Prevention Analysis: *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. *See NOTE TO THE CHEMIST	*		
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?			
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?		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 the USP. Listed in the HOW SUPPLIED section of the RLD. See comment under DESCRIPTION].	*		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) *See FTR.		*	
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.		x	

FOR THE RECORD:

1. Labeling model: Coly-Mycin-M by Parke-Davis, S-001 approved 10/7/82 and revised 10/81.

2. Patent/exclusivity: none pending

3. Manufacturing facility:

   - [redacted] (b) (4)

4. Storage:

   USP - Preserve in containers for sterile solids as described under Injections

   NDA - Store between 15°-30°C (59°-86°F)

   Store reconstituted solution in a refrigerator 2°-8°C(36°-46°F) or between 15°-30°C(59°-86°F) and use within 7 days.

   ANDA - Same as NDA.

5. Description section:

   This section is consistent with the firm's components and composition section.
   [See response from chemist for submission dated 6/30/97].
   [Vol. 1.1, p.43]

6. Container:

   [redacted] (b) (4) Vial/Gray [redacted] (b) (4) Stopper/White flip-off aluminum seal
   [Vol. 1.1, p.44]

7. Package size:

   RLD - 1 vial/carton

   ANDA - 1 vial/carton

8. Bioequivalence:

   A waiver of <u>in-vivo</u> bioavailability/bioequivalence has been granted.
   [Vol. 1.1, signed 1/15/98].

9. Labeling issue:

   The storage information for the reconstituted solution is listed in the HOW SUPPLIED section instead of the DOSAGE AND ADMINISTRATION section of the NDA and ANDA. There is a pending supplement [S-021] for the NDA. If the storage information is not relocated in the pending supplement, I

recommend that this issue is followed-up with the new drug division.

Date of Review: 10/2/98

Primary Reviewer
Jacqueline White, Pharm.D. *

10/7/98
Date

Team Leader

10/7/98
Date

cc:

ANDA: 64216
DUP/DIVISION FILE
HFD-613/JWhite/CHoppes (no cc)
x:\new\...64216ap.1
Review

* Reviewer is at a remote site

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 64-216

CHEMISTRY REVIEWS

1. CHEMISTRY REVIEW NO. 1

2. AADA # 64-216

3. NAME AND ADDRESS OF APPLICANT

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

4. BASIS OF SUBMISSION
21 CFR 448.220a and 448.20a
USP 23

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME

Sterile Colistimethate Sodium USP

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

9. AMENDMENTS AND OTHER DATES:

Date of Application: June 30, 1997
Amendment dated: August 21, 1997 the amendment contains the unexecuted batch record for Sterile Colistimethate Sodium USP reflecting the **maximum batch size of** (b) (4) **vials).**

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

(b) (4)
(b) (4)
DMF
DMF
DMF

15. CHEMICAL NAME AND STRUCTURE

$C_{58}H_{105}N_{16}Na_5O_{28}S_5$ (colistin A component) 1749.85

$C_{57}H_{103}N_{16}Na_5O_{28}S_5$ (colistin B component) 1735.83

16. RECORDS AND REPORTS
N/A

17. COMMENTS

Proposed Indications for use: Treatment of acute or chronic infections due to sensitive strains of certain gram-negative bacilli such as Pseudomonas aeruginosa.

Reference listed drug product: Coly-Mycin M Parenteral by Parke Davis

The contract manufacturer for this product is (b) (4) (b) (4)

Requirements for certification according to 21 CFR 448.20a:

Its **potency** is not less than 390 micrograms of colistin base equivalent per milligram. If it is packaged for dispensing, its potency is satisfactory if it is not less than 90 percent and not more than 120% of the number of milligrams of colistin base equivalent that it is represented to contain.

It is **sterile.**

It is **nonpyrogenic.**

Its **loss on drying** is not more than 7.0%.

Its **pH** in an aqueous solution containing 10 milligrams per milliliter is not less then 6.5 and not more than 8.5.

It gives a positive **identity** test for colistimethate sodium.

It passes the test for **free colistin.**

Its **heavy metals** content is not more than 30 parts per million.

18. CONCLUSIONS AND RECOMMENDATIONS
Not-Approvable (MAJOR)

19. REVIEWER: V.Walton
DATE COMPLETED: 9/18/97

20. COMPONENTS AND COMPOSITION - Satisfactory

Components of the Drug:

A. Sterile Colistimethate Sodium USP, 150 colistin base equivalent.

B. (b) (4)

C. (b) (4) (b) (4)

D. (b) (4) (b) (4)

Composition Statement

Each vial of Sterile Colistimethate Sodium USP contains a sterile lyophilized cake equivalent to 150 mg colistin base activity/vial.

Batch size

The proposed maximum production batch size will be approximately (b) (4) vials. The pilot production run was set at (b) (4) vials which represents (b) (4) of the proposed production runs.

21. FACILITIES AND PERSONNEL - Satisfactory

Pharma-Tex is utilizing (b) (4)

Following this page, 7 pages withheld in full - (b)(4)

next two digits, etc., etc...

31. SAMPLES AND RESULTS - Incomplete

Samples of the finished dosage form are available upon request.

Pharma-Tek will be asked to send samples from exhibit batch (Lot #846-20-0001) to our FDA lab for testing.

32. LABELING - Incomplete

33. ESTABLISHMENT INSPECTION - Incomplete

34. BIOEQUIVALENCY STATUS - Incomplete

In accordance with 21 CFR 320.22(a) Pharma-Tek requests a waiver of In-Vivo Biovailability requirement for Sterile Colistimethate Sodium USP, 150 colistin base equivalent to be manufactured by [redacted] (b) (4) A review by the Division of Bioequivalence is pending.

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

Satisfactory

[redacted] (b) (4) states that it is in compliance with all emission requirements set forth in permits, consent decrees and administrative orders applicable to the production of Colistimethate Sodium at its facilities in [redacted] (b) (4) as well as emission requirements set forth in all federal, state, and local statues and regulations applicable to the production of Colistimethate Sodium at its facilities in [redacted] (b) (4).

Pharma-Tek requests a categorical exclusion per Section 25.24 Categorical Exclusions, Paragraph (C)(1), 21 CFR Part 25 - Environmental Impact Considerations (4-1-91 Edition).

36. ORDER OF REVIEW:

The application submission(s) covered by this review was taken in the date order of receipt Yes X

No _____

37. DMF CHECKLIST FOR AADA # 64-216 REVIEW # 1

DMF #	DMF TYPE/SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED
(b) (4)	Type III/ (b) (4)			
	Comments: By S. Liu	3	Satis.	2/1/94
(b) (4)	Type III/ (b) (4)	3	Satis.	5/5/93
	Comments:			
	Comments:			
	Comments:			
	Comments:			
	Comments:			
	Comments:			
	Comments:			

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:

(2) Type 1 DMF;
(3) Reviewed previously and no revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under"Comments").

Page 1 of 1.

V.Walton — Reviewer

V.Walton — Signature

9/23/97 — Date

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 64-216

3. NAME AND ADDRESS OF APPLICANT

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

4. BASIS OF SUBMISSION
21 CFR 448.220a and 448.20a
USP 23

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME

Sterile Colistimethate Sodium USP

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

9. AMENDMENTS AND OTHER DATES:

Date of Application: June 30, 1997
Amendment dated: August 21, 1997 the amendment contains the unexecuted batch record for Sterile Colistimethate Sodium USP reflecting the **maximum batch size of** (b) (4) **vials).**
Amendment dated: February 12, 1998

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

(b) (4)

DMF (b) (4)
DMF
DMF

13. DOSAGE FORM
Sterile lyophilized powder for injection

14. POTENCY
150 mg (base)/vial

15. CHEMICAL NAME AND STRUCTURE

$C_{58}H_{105}N_{16}Na_5O_{28}S_5$ (colistin A component) 1749.85

$C_{57}H_{103}N_{16}Na_5O_{28}S_5$ (colistin B component) 1735.83

16. RECORDS AND REPORTS
N/A

17. COMMENTS

Proposed Indications for use: Treatment of acute or chronic infections due to sensitive strains of certain gram-negative bacilli such as Pseudomonas aeruginosa.

Reference listed drug product: Coly-Mycin M Parenteral by Parke Davis

The contract manufacturer for this product is [redacted] (b) (4)

Requirements for certification according to 21 CFR 448.20a:

Its **potency** is not less than 390 micrograms of colistin base equivalent per milligram. If it is packaged for dispensing, its potency is satisfactory if it is not less than 90 percent and not more than 120% of the number of milligrams of colistin base equivalent that it is represented to contain.

It is **sterile.**

It is **nonpyrogenic.**

Its **loss on drying** is not more than 7.0%.

Its **pH** in an aqueous solution containing 10 milligrams per milliliter is not less then 6.5 and not more than 8.5.

It gives a positive **identity** test for colistimethate sodium.

It passes the test for **free colistin.**

Its **heavy metals** content is not more than 30 parts per million.

The following comments are included in the Labeling review dated 10/22/97 and 3/20/98 under NOTE TO THE CHEMIST

2. Should "Colistin A or B component" be listed in the DESCRIPTION section? Answer No

   The referenced drug is described (in the DESCRIPTION section)as a sterile parenteral antibiotic product which, when reconstituted, is suitable for intramuscular or intravenous administration. Each vial contains 150 mg colistin base equivalent. Colistimethate sodium is a polypeptide antibiotic with an approximate molecular weight of 1750, the empirical formula is $C_{58}H_{105}N_{16}Na_5O_{28}S_5$.

   Colistimethate sodium is described in Remington's Pharmaceutical Sciences, 17th Edition as follows: Colistimethate sodium contains the pentasodium salt of the penta (methanesulfonic acid) derivative of colistin A, $C_{58}H_{105}N_{16}Na_5O_{28}S_5$, as the major component, with a small proportion of the pentasodium salt of the same derivative of colistin B, $C_{57}H_{103}N_{16}Na_5O_{28}S_5$.

3. The firm listed "(b)(4)" as an active ingredient in their component's statement. Should this be listed as an inactive ingredient in the DESCRIPTION section? Answer No

   (b)(4) not listed as an inactive ingredient.

4. Has the firm submitted compatibility or stability to adequately support the compatibility and stability claims which appear in the DOSAGE AND ADMINISTRATION/(INTRAVENOUS ADMINISTRATION) section of the insert labeling? [See section V, p. 29]. Answer No

   Firm has not submitted compatibility or stability to support the compatibility and stability claims which appear in the DOSAGE AND ADMINISTRATION/(INTRAVENOUS ADMINISTRATION) section of the insert labeling. We do not routinely require that data when the recommended Infusion Fluids are identical to those named in the innovator's labeling as in this ANDA. IV solutions must be prepared fresh every 24 hours.

18. CONCLUSIONS AND RECOMMENDATIONS

From the Chemistry and Manufacturing standpoint, the application is approvable.

19. REVIEWER:	DATE COMPLETED:
V.Walton	3/12/98

Following this page, 11 pages withheld in full - (b)(4)

31. SAMPLES AND RESULTS - Satisfaactory

Samples from Lot#846-20-0001 were tested by our laboratory and their results are reported below:

(b) (4)

(b) (4)

32. LABELING - Incomplete

33. ESTABLISHMENT INSPECTION - Satisfactory

Acceptable on 18-NOV-1997 for the following:

(b) (4) (Finished Dosage Manufacturer)

(b) (4) (Drug Substance Manufacturer)

(b) (4) (Finished Dosage Stability Tester)

34. BIOEQUIVALENCY STATUS - Satisfactory

In accordance with 21 CFR 320.22(a) Pharma-Tek requests a waiver of In-Vivo Biovailability requirement for Sterile Colistimethate Sodium USP, 150 colistin base equivalent to be manufactured by (b) (4). The waiver of in-vivo bioavailability/bioequivalence requirement has been granted.

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

Satisfactory

(b) (4) states that it is in compliance with all emission requirements set forth in permits, consent decrees and administrative orders applicable to the production of

Colistimethate Sodium at its facilities in [redacted] (b) (4) as well as emission requirements set forth in all federal, state, and local statues and regulations applicable to the production of Colistimethate Sodium at its facilities in [redacted] (b) (4).

Pharma-Tek requests a categorical exclusion per Section 25.24 Categorical Exclusions, Paragraph (C)(1), 21 CFR Part 25 - Environmental Impact Considerations (4-1-91 Edition).

36. ORDER OF REVIEW:

The application submission(s) covered by this review was taken in the date order of receipt Yes__X_____

No _____

37. **DMF CHECKLIST FOR ANDA # 64-216 REVIEW # 2**

DMF #	DMF TYPE/SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED
(b) (4)	Type III/ (b) (4)	3	Satis.	2/1/94
	Comments: By S. Liu			
(b) (4)	Type III/ (b) (4)	3	Satis.	5/5/93
	Comments:			
	Comments:			
	Comments:			
	Comments:			
	Comments:			
	Comments:			
	Comments:			

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:

(2) Type 1 DMF;
(3) Reviewed previously and no revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under"Comments").

Page 1 of 1 . V.Walton V. Walton 3/18/98

Reviewer Signature Date

cc: ANDA 64-216
DUP/Division File
FIELD COPY

Endorsements:

HFD-643/VWalton/3/12/98/ V. Walton 3/18/98
HFD-643/JHarrison/3/13/98 3/18/98 – 3/26/98
HFD-617/MAnderson/3/13/98 Mark Anderson 4/20/98

B:
F/T by pah/3/17/98
x:\new\firmsnz\pharmtek\ltrs&rev\64216no2.f

Addendum to Chemistry Review # 2

ANDA: 64-216

Product: Sterile Colistimethate Sodium USP

Applicant: Pharma-Tek, Inc.

<467> Organic Volatile Impurities

An examination of the list of raw materials used in the synthesis of the active ingredient indicates that the following organic compounds are not used:

(b) (4)

Therefore, the testing for Organic Volatile Impurities is unnecessary.

V.Walton/12/18/98 V.Walton 12/18/98
J.Harrison/ J.Harrison 12/18/98

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 64-216

BIOEQUIVALENCE REVIEWS

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

DRUG NAME:	Colistimethate Sodium	**ANDA #:**	64-216
SPONSOR:	Pharma-Tek Inc.		
DOSAGE FORM:	Lyophilized Powder For Reconstitution	**STRENGTH:**	150 mg
TYPE OF STUDY:	N/A		
STUDY SITE:	N/A		

Waiver request for Colistimethate Sodium Injection

Colistimethate Sodium is a sterile parenteral antibiotic product which, when reconstituted is suitable for intra-muscular and intravenous administration. Each vial contains 150 mg colistin base equivalent. Colistimethate is a polypeptide antibiotic with an molecular weight of 1750. High serum levels were obtained at 10 minutes following IV administration. Serum concentration declined with a half-life of about 2 -3 hours following IV administration.

Colistimethate is indicated for the treatment of acute or chronic infections due to sensitive strains of certain gram negative bacilli, particularly against Pseudomonas aeruginosa.

The Sponsor, Pharma-Tek, Inc., is filing this ANDA for Colistimethate Sodium Injection, 150 mg in lyophilized powder vials. The Sponsor requests that the in-vivo bioequivalence requirement for this drug product be waived based on the fact that this product is identical to the innovator's product Coly-Mycin M^{R} by Parke-Davis Pharmaceuticals. The Sponsor cited the 21 CFR 320.22(b)(1) as the grounds for the waiver request.

Both test and reference products are identical with respect to the formulation. Both contain colistimethate sodium (150 mg colistin base equivalent per vial) in lyophilized powder form. When reconstituted with 2 ml sterile water for injection, the reconstituted solution has a concentration of 75 mg/ml.

The Division of Bioequivalence agrees that the information submitted by Pharma - Tek demonstrates that its colistimethate injection falls under 21 CFR 320.22(b)(1) of the bioavailability/bioequivalence regulations. Therefore, from bioequivalence perspective, the waiver of in-vivo bioavailability/bioequivalence requirements is granted.

DISSOLUTION: N/A

PRIMARY REVIEWER: Nhan L. Tran, Ph.D. **BRANCH:** II

INITIAL: _____ DATE: 11/07/97

Team Leader: Shrinivas Nerurkar, Ph.D. **BRANCH:** II

INITIAL: _____ DATE: 1/15/1998

~~**ACTING** DIRECTOR, DIVISION OF BIOEQUIVALENCE:~~ ~~Rabindra Patnaik, Ph.D.~~

INITIAL: _____ DATE: 1/15/98

DIRECTOR, OFFICE OF GENERIC DRUGS:

INITIAL: _____ DATE: _____

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 64-216 APPLICANT: Pharma-Tek

DRUG PRODUCT: Colistimethate Sodium For Injection

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 P. Conner

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

CC: ANDA 64-216
ANDA DUPLICATE
DIVISION FILE
HFD-655/ S. Nerurkar for Office Level BIOSign Off Queue
HFD-651/ Bio Secretary - Bio Drug File
HFD-655/ nlt, Reviewer
HFD-655/ Bio Team Leader

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Printed in final on / /

Endorsements: (Final with Dates)
HFD-655/ Reviewer
HFD-655/ Bio team Leader 1/15/98
HFD-617/ L. Sanchez or N.Chamberlin
HFD-650/ D. Conner 1/15/98

BIOEQUIVALENCY - ACCEPTABLE submission date: 6/30/97

1. **WAIVER** (WAI) Strengths: 150 mg
Outcome: AC

2. **DISSOLUTION WAIVER** (DIW) N/A

Outcome Decisions: **AC** - Waiver Acceptable

WINBIO COMMENTS:

Colistimethate Sodium Injection, 150mg
Lyophilized Powder For Reconstitution
ANDA 64-216
Reviewer: Nhan L. Tran

Pharma-Tek Inc.
Huntington, NY
Submission Date:
June 30, 1997.

REVIEW OF A WAIVER REQUEST

I. Background:

Colistimethate Sodium is a sterile parenteral antibiotic product which, when reconstituted, is suitable for intra-muscular and intravenous administration. Each vial contains 150 mg colistin base equivalent. Colistimethate sodium is a polypeptide antibiotic with an molecular weight of 1750.
High serum levels were obtained at 10 minutes following IV administration.
Serum concentration declined with a half-life of about 2 -3 hours following IV administration.
Colistimethate is indicated for the treatment of acute or chronic infections due to sensitive strains of certain gram negative bacilli, particularly against Pseudomonas aeruginosa.

II. Objective

The Sponsor, Pharma-Tek, Inc., is filing this ANDA for Colistimethate Sodium Injection, 150 mg in lyophilized powder vials. The Sponsor requests that the in-vivo bioequivalence requirement for this drug product be waived based on the fact that this product is identical to the innovator's product Coly-Mycin M^R by Parke-Davis Pharmaceuticals. The Sponsor cited the 21 CFR 320.22(b)(1) as the grounds for the waiver request.

III. Formulation

Both test and reference products are identical with respect to the formulation. Both contain colistimethate sodium (150 mg colistin base equivalent per vial) in lyophilized powder form. When reconstituted with 2 ml sterile water for injection, the reconstituted solution has a concentration of 75 mg/ml.

IV. Comments

1. The test and the innovator products are solutions which are intended for intramuscular or intravenous injection.

2. The formulations of the test and the innovator's products are identical with respect to the active and inactive ingredients.

3. According to the Merck Index and Remmington, Colistimethate sodium is stable in powder form and is completely soluble in water. A SOLUTION is obtained after reconstitution with water.

4. To the best of the reviewer's knowledge, nothing unusual about this drug can be found (checked EXCALIBUR Files and other references).

III. Recommendation

The Division of Bioequivalence agrees that the information submitted by Pharma - Tek demonstrates that its colistimethate injection falls under 21 CFR 320.22(b)(1) of the bioavailability/bioequivalence regulations. Therefore, from bioequivalence perspective, the waiver of in-vivo bioavailability/bioequivalence requirements is granted.

Nhan L. Tran

Nhan L. Tran, Ph.D.
Division of Bioequivalence
Review Branch II

RD INITIALED BY SNERURKAR
FT INITIALED BY SNERURKAR

1/15/1998

Concur: Dale P. Conner Date: 1/15/98
Dale P. Connor, Pharm.D.
Director, Division of Bioequivalence

cc: ANDA 64-216, HFD-655 (Nerurkar, Tran), Drug File, Division File

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 64-216

MICROBIOLOGY REVIEWS

OFFICE OF GENERIC DRUGS
Microbiologists Review #1
February 25, 1998

A. 1. ANDA: **64-216**

APPLICANT: Pharma-Tek Inc.
Attn. Susan B. Badia
P.O. Box 1920
Huntington, NY

2. PRODUCT NAME: **Colistimethate Sodium For Injection**
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 150 mg Colistin Base/ 6 cc vial. Freeze Dried. Reconstitute with Water For Injection. For IV or IM Use.
4. METHOD(S) OF STERILIZATION: (b) (4)
5. PHARMACOLOGICAL CATEGORY: Peptide - Antibiotic

B. 1. DATE OF INITIAL SUBMISSION: June 30, 1997
2. DATE OF AMENDMENT: None.
3. RELATED DOCUMENTS: 21CFR 448.220a and 448.20a, now extinct, were referenced for this application.
4. ASSIGNED FOR REVIEW: February 12, 1998

C. REMARKS: Volume 1.4 contains the Lyophilization Process Validation Package for (b) (4).

D. CONCLUSIONS: The submission is not recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes" and "Microbiologist's Draft of Letter to Applicant".

2/27/98
James L. McVey

3/5/96

initialed by F. Fang or F. Holcombe

cc:
Original ANDA
Duplicate ANDA
Field Copy
drafted by: J. McVey

Following this page, 9 pages withheld in full - (b)(4)

OFFICE OF GENERIC DRUGS
Microbiologists Review #2
July 8, 1998

A. 1. ANDA: **64-216**

APPLICANT: Pharma-Tek Inc.
Attn. Susan B. Badia
P.O. Box 1920
Huntington, NY

2. PRODUCT NAME: **Colistimethate Sodium For Injection**
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 150 mg Colistin Base/ 6 cc vial. Freeze Dried. Reconstitute with Water For Injection. For IV or IM Use.
4. METHOD(S) OF STERILIZATION: (b)(4)
5. PHARMACOLOGICAL CATEGORY: Peptide - Antibiotic

B. 1. DATE OF INITIAL SUBMISSION: June 30, 1997
2. DATE OF AMENDMENT: **June 12, 1998. - Subject of this review.**
3. RELATED DOCUMENTS: 21CFR 448.220a and 448.20a, now extinct, were referenced for this application.
4. ASSIGNED FOR REVIEW: July 7, 1998

C. REMARKS: Volume 1.4 contains the Lyophilization Process Validation Package for (b)(4).

D. CONCLUSIONS: The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes".

James L. McVey

7/8/98

initialed by F. Fang or F. Holcombe

cc:

Original ANDA
Duplicate ANDA
Field Copy
drafted by: J. McVey 64216na2.m

Following this page, 3 pages withheld in full - (b)(4)

AADA/ANDA: 64-216 APPLICANT: Pharma- Tek Inc.

DRUG PRODUCT: Sterile Colistimethate Sodium, USP

A. Microbiology Deficiencies:

1. (b) (4)

2.

3.

4.

5.

Please clearly identify your amendment to this facsimile as

"RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in the cover page/letter.

Sincerely yours,

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

OFFICE OF GENERIC DRUGS

Microbiologists Review #3
October 7, 1998

A. 1. ANDA: **64-216**

APPLICANT: Pharma-Tek Inc.
Attn. Susan B. Badia
P.O. Box 1920
Huntington, NY

2. PRODUCT NAME: **Colistimethate Sodium For Injection**
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 150 mg Colistin Base/ 6 cc vial. Freeze Dried. Reconstitute with Water For Injection. For IV or IM Use.
4. METHOD(S) OF STERILIZATION: (b) (4)
5. PHARMACOLOGICAL CATEGORY: Peptide - Antibiotic

B. 1. DATE OF INITIAL SUBMISSION: June 30, 1997
2. DATE OF AMENDMENT: June 12, 1998.
September 2, 1998 - Subject of this review.
September 22, 1998 - Subject of this review.
3. RELATED DOCUMENTS:
4. ASSIGNED FOR REVIEW: October 7, 1998.

C. REMARKS: Volume 1.4 contains the Lyophilization Process Validation Package for (b) (4).

D. CONCLUSIONS: The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes".

James L. McVey 10/7/98

initialed by F. Fang or F. Holcombe 10/13/98

cc:

Original ANDA
Duplicate ANDA
Field Copy
drafted by: J. McVey 64216na3.m

E. REVIEW NOTES: The questions asked in the not approvable letter are listed in bolded and italicized print for convenience. A summary of the applicants response is provided in normal print. Comments by the reviewer are bolded.

1. (b) (4)

Acceptable

2. (b) (4)

Not Acceptable

Comment. No (b) (4) data or calculations were included in your response to Question 5 of the FAX dated April 20, 1998 or question 2 of the July 14, 1998 Amendment. Please provide this information.

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

1. ***Please do not make incomplete submissions. They do not speed up your review time and may cause delay.*** This comment was not acknowledged.

Comment. 1. Please do not make incomplete submissions. They do not speed up your review time and may cause delay.

2 1 Andersen

OFFICE OF GENERIC DRUGS
Microbiologists Review #4
November 3, 1998

A. 1. ANDA: **64-216**

APPLICANT: Pharma-Tek Inc.
Attn. Susan B. Badia
P.O. Box 1920
Huntington, NY

2. PRODUCT NAME: **Colistimethate Sodium For Injection**
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 150 mg Colistin Base/ 6 cc vial. Freeze Dried. Reconstitute with Water For Injection. For IV or IM Use.
4. METHOD(S) OF STERILIZATION: (b) (4)
5. PHARMACOLOGICAL CATEGORY: Peptide - Antibiotic

B. 1. DATE OF INITIAL SUBMISSION: June 30, 1997
2. DATE OF AMENDMENT: June 12, 1998.
September 2, 1998
September 22, 1998
October 14, 1998 - Subject of this review.
3. RELATED DOCUMENTS:
4. ASSIGNED FOR REVIEW: October 7, 1998.

C. REMARKS:

D. CONCLUSIONS: The submission is **recommended** for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes".

11/3/98
James L. McVey

initialed by M. Fanning 11/5/98

cc:
Original ANDA
Duplicate ANDA
Field Copy
drafted by: J. McVey 64216a4.m

E. REVIEW NOTES: The question asked in the not approvable FAX dated 10/2/98 is listed in bolded and italicized print for convenience. A summary of the applicants response is provided in normal print. Comments by the reviewer are bolded.

1. [redacted] (b) (4)

Acceptable

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 64-216

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Pharma-Tek Inc.
PHARMACEUTICALS

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

JUN 3 0 1997

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

Re: AADA for Sterile Colistimethate Sodium USP, 150 mg colistin base equivalent

Dear Mr. Sporn:

We are submitting an archival copy and review copy of an abbreviated antibiotic drug application (AADA) covering Sterile Colistimethate Sodium USP, 150 mg colistin base equivalent, 21 CFR 448.20a in accordance with the regulations promulgated under Section 507 of the Federal, Food, Drug and Cosmetic Act. When this product is manufactured in accordance with cGMP's the FDA certifies that this drug is safe and effective as per 21 CFR 448.20a.

This AADA submission contains five (5) volumes with the table of contents at the beginning of each volume.

The contract manufacturer for this product is (b) (4)

Your early review of this submission is most appreciated.

Sincerely yours,

Susan E. Badia

Susan E. Badia
Assistant to the President

Enclosures

RECEIVED
JUL 0 3 1997
GENERIC DRUGS

RECORD OF TELEPHONE CONVERSATION

In order to file this AADA, I called to firm to request some additional information. It is not stated in the application what the master production record for maximum-size (10X) production. In addition, the firm should provide a side-by-comparison of the inactive ingredients of RDL and the proposed product. The firm is requested to submit the information within 10 working days.

DATE

August 13, 1997

APPLICATION NUMBER

64-216

IND NUMBER

TELECON

INITIATED BY **MADE**

_ **APPLICANT/ SPONSOR** _ **BY TELE.**

XFDA _ **IN PERSON**

PRODUCT NAME

Sterile Colistimethate Sodium USP, 150 mg

FIRM NAME

Pharma-Tek Inc.

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD

Dan Badia
Susan Badia

TELEPHONE NUMBER

516-757-5522

SIGNATURE

Harvey Greenberg

HGreenberg

ANDA CHECKLIST FOR COMPLETENESS and ACCEPTABILITY of the APPLICATION

AADA / ANDA # 64-216 FIRM NAME PharmaTek Inc

DRUG NAME: Sterile Colistimethate Sodium USP

DOSAGE FORM: 150mg/Base/Vial

Supervisory Chemist (Harrison) Labeling Reviewer (Angela Payne)

Random Assignment (Random IV) AMP

	YES	NO
Comments EC1 ✓ On Cards ✓		
Therapeutic Code 4010700 ✓ Peptides - antibiotic	6/30/97 7/3/97	
Methods Validation Package (3 copies) (NO) Required for Non-USP drugs	✓	
Cover Letter	✓	
Letter of Authorization	✓	
U.S. Agent (If needed, Countersignature on 356h)	N/A	
DMF Referral(s)	✓	
356 Form - Completed /Original Signature	✓	
Table of Contents	✓	
Listed Drug/Firm Coly-Mycin M Parke Davis	✓	
AADA Monograph 448.220 a	✓	
Information to show proposed product is the same as the listed product: (i) (a) indications (ii) active ingredients(s) iii (a) route (b) dosage form (c) strength (iv) labeling -- side by side comparison - insert:		
Container:		
Same Formulation? need to provide side by side	✓	
Ophthalmics/Otics/Externals/Parenterals	✓	
Parenteral: Same Size Container / (strength/volume)	✓	
Petition Required	N/A	
Debarment Certification	✓	
List of Convictions	✓	
Third Copy Certification	✓	
Patent Certification	✓	
Use Patent Statement? Exclude Use in labeling / indications?	N/A	
Exclusivity Addressed	✓	

Five year exclusivity? If yes, cannot be filed until expiration of exclusivity or after 4 years if patent challenged.		
Labeling: 4 copies of draft (✓) or 12 copies of FPL ( )	✓	
Statement re Rx/OTC Status	✓ 356h	
Components & Composition (Unit Composition)		
Specifications and Tests for Active Ingredients and Dosage Form	✓	
Source of Active Ingredient(s)	✓	
COA from Manufacturer of Active Ingredient(s)	✓	
Applicant COA	✓	
COA for finished product	✓	
Specifications and Tests for Inactive Ingredients	✓	
Source of Inactive Ingredients Identified	✓	
Applicant COA for Inactive Ingredient	✓	
COA from Manufacturer of Inactive Ingredients	✓	
Manufacturing Controls	✓	
Batch Formulation (b) (4)	✓	
Master Production Batch Record for largest batch size intended for production (No more than 10x pilot batch) (b) (4)	✓	
Certification of GMP	✓	
Description of Facilities (b) (4)	✓	
Address of Manufacturing Site for Production Batches	✓	
Manufacturing Procedures (Batch Records)	✓	
Package entire test batch	✓	
Batch Number(s)	✓	
Mfg. Facility (b) (4)	✓	
If Sterile product: (b) (4)		
Stability Profile Including stability Data (Use of Stability Indication Method)	✓	
3 months Accelerated Stability Data	✓	
Batch Number(s) Listed on Stability Records (Batch number(s) the same as the test batch	✓	
Sample Statement Plus Data	✓	
Bioavailability/Bioequivalence Study		
In Vivo Study/Waiver Request	✓	
Comparative Dissolution Data		

Paragraph IV bio study acceptable for filing		
Date acceptable for filing		
Computer Disk Submitted		
Environmental Impact Analysis	✓	
Compliance Statement	✓	

Reviewing CSO / CST (Harvey A Theeler **)**

Date 8/13/97

Recommendation: (FILE) **REFUSE to FILE**

Supervisory Concurrence / Date _____

Duplicate copy sent to Bio:
(Hold if RF and send when acceptable)

Duplicate copy to HFD _____ **for Consult**

Type of Consult:

Micro Assignment:

Pharma-Tek Inc.
PHARMACEUTICALS

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

August 21, 1997

NEW CORRESP

Harvey Greenberg
Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs (HFD-615)
7500 Standish Place
Rockville, MD 20855

64-216

Re: Telephone Amendment
Sterile Colistimethate Sodium USP

Dear Mr. Greenburg:

As per our conversation I am enclosing in duplicate a telephone amendment to our application for Sterile Colistimethate Sodium USP, 150 mg Colistin base equivalent.

The amendment contains a comparison between the generic drug Pharma-Tek is filing for and the reference listed drug. Also enclosed is the unexecuted batch record for Sterile Colistimethate Sodium USP reflecting the maximum batch size of (b) (4)

If you have any questions regarding this amendment or the original submission please call me at 516-757-5522. Thank you.

Sincerely yours,

Susan E. Badia

Susan E. Badia
Assistant to the President

RECEIVED
AUG 25 1997
GENERIC DRUGS

Enclosures

pc: FDA - (b) (4) District
(b) (4)

AADA 64-216

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

AUG 27 1997

Dear Madam:

We acknowledge the receipt of your abbreviated antibiotic application submitted pursuant to Section 507 of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Sterile Colistimethate Sodium USP, 150 mg (base)/vial

DATE OF APPLICATION: June 30, 1997

DATE OF RECEIPT: July 3, 1997

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

Please be advised that during the AADA approval process, samples of the active and inactive ingredients, and the AADA exhibit batch(es) (which should be the same as the biobatch if a bioequivalence study was conducted) may be requested by the FDA district office staff and tested by FDA district or headquarters laboratory staff. Drug substance standards and manufacturer's documentation of the impurity profile should be made available. In addition, batch records, certificates of analysis and specifications and tests for the drug substance, drug product and inactive ingredients may be requested.

The subject product of an AADA must conform to the current official compendial monograph requirements and be compatible with the test and assay methods described in that monograph. You must submit adequate documentation and laboratory data in your AADA that prove that any non-official alternate procedures that you choose to use for the analytical control (release) of your product are equivalent to the official compendial procedures. If this information is not submitted, the review of the application will be delayed.

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

Should you have questions concerning this application contact:

Mark Anderson
Project Manager
(301) 827-5848

Sincerely yours,

8/22/97

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

cc: AADA 64-216
DUP/Jacket
Division File
HFD-92
Field Copy
HFD-600/Reading File
HFD-610/JPhillips
HFD-615/MBennett
HFD-473/Antimicrobial Drugs Branch
HFD-324/Mark Lynch

Endorsements: HFD-615/PRickman, Chief, RSB 8/26/97 date
HFD-615/HGreenber, CSO 8/18/97 date
HFD-643/JHarrison, Sup. Chem. _____ date
WP File

x:\new\firmsnz\pharmtek\ltrs&rev\64216.ack
FT/njg/8/14/97
AADA Acknowledgement Letter!

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

Date: 16-Sep-1997 06:51am EDT
From: Melissa Egas
EGASM
Dept: HFD-322 MPN1 272
Tel No: 301-594-0095 FAX 301-594-2202

TO: Mark Anderson (ANDERSONM)

Subject: 64-216

We received a response from BUF-DO for Pharma Tek, listed in the EER as a stability tester. Response says stability testing is not performed at this location. Elmira only packages. Tell me what to do.

Mimi

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

Date: 18-Sep-1997 10:27am EDT
From: Mark Anderson
ANDERSONM
Dept: HFD-617 MPN2 E210
Tel No: 301-827-5848 FAX 301-443-3839

TO: Melissa Egas (EGASM)

CC: John Harrison (HARRISONJ)
CC: Vernon Walton (WALTON)

Subject: FWD: 64-216

Mimi,

This may or may not help. I checked the application for responsibilities and found the following (I presume the field also has access to same info):

"Pharma-Tek is responsible for the storage, sale and distribution of the finished product from its Elmira plant and is responsible for the management of [redacted] ability studies" (p. 90 of application).

Under Description of Manufacturing Facility (p. 91):

Pharma-Tek is responsible for the storage of stability samples in environmental controlled chambers for accelerated and long term testing. Pharma-Tek is also responsible for submitting accelerated and long term stability samples at appropriate intervals to the proper laboratories."

Elsewhere on p. 91 it describes [redacted] (b) (4) and [redacted] (b) (4) as doing testing.

Thus, the wording is a little vague which probably led the regulatory support staff to list PharmaTek as a testing site. It appears they only store samples and send them out for testing. Don't you think this was explained to the investigator during his or her inspection?

Mark

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

Date: 12-Nov-1997 04:47pm EST
From: Mark Anderson
ANDERSONM
Dept: HFD-617 MPN2 E210
Tel No: 301-827-5848 FAX 301-443-3839

TO: Jacqueline White (WHITEJ)

CC: Charles Hoppes (HOPPESC)

Subject: Labeling comments for Pharmatek's Colistimethate 64-216

Jackie/Charlie,

I decided to go ahead and fax the chemistry comments for this application. It is going out as a Major NA for chemistry.

Please forward the labeling comments when they are complete and I will fax them out.

ks,

Mark

MAJOR AMENDMENT

NOV 1 3 1997

AADA 64-216

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Pharma-Tek, Inc. PHONE: 516-757-5522

ATTN: Susan Badia FAX: 516-754-1550

FROM: Mark Anderson PROJECT MANAGER (301) 827–5848

Dear Madam:

This facsimile is in reference to your abbreviated antibiotic application dated June 30, 1997, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act for Sterile Colistimethate Sodium USP, 150 mg (base)/mL.

The application is deficient and, therefore, Not Approvable under Section 507 of the Act for the reasons provided in the attachments (____ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, norwill the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If this represents a socond or greater occassion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

SPECIAL INSTRUCTIONS:

Labeling and Microbiology Comments will follow separately when the reviews are completed.

X:\new\ogdadmin\macros\faxmaj.frm

NOV 13 1997

38. **CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT**

AADA: 64-216

APPLICANT: Pharma-Tek, Inc.

DRUG PRODUCT: Sterile Colistimethate Sodium USP, 150 mg (base)/vial.

The deficiencies presented below represent MAJOR deficiencies

A. Deficiencies:

1. [redacted] (b) (4)

2. [redacted] (b) (4)

3. [redacted] (b) (4)

4. [redacted] (b) (4)

5. [redacted] (b) (4)

6. [redacted] (b) (4)

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

1. Please submit 12 immediate containers from exhibit lot #846-20-0001 to:

   Food and Drug Administration
   Beltsville Research Facility
   Attention: Valerie Flournoy (HFD-910)
   8501 Muirkirk Road
   Laurel, MD 20708

   (Telephone: 301-827-8054)

   Copies of the latest Certificate of Analysis should accompany the samples. The samples will be tested to verify the quality of the product.

2. If available, long term stability data should be included in your next amendment.

Sincerely yours,

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Pharma-Tek Inc.
PHARMACEUTICALS

PHONE (607) 732-5555
P.O. BOX 1148
ELMIRA, NY 14902

December 1, 1997

Food and Drug Administration
Beltsville Research Facility
Attention: Valerie Flournoy (HFD-910)
8501 Muirkirk Road
Laurel, MD 20708

RE: OGD/CDER Letter Dated Nov 13, 1997
Chemistry Comments AADA 64-216 (para B.1.)

Dear Madam:

The reference letter requested that we "submit 12 immediate containers from exhibit batch #846-20-0001." Enclosed with this letter are twelve (12) vials of Sterile Colistimethate Sodium USP **Lot #846-20-0001.** These vials represent 11 month samples of our long term stability study. Also as per your request the latest Certificate of Analysis is enclosed.

If you have any questions or need additional samples, please do not hesitate to contact our office at (607)732-5555 or pharmatk@servtech.com.

Sincerely,

RC Park
Manager of Quality Assurance

Enclosure

STERILE COLISTIMETHATE SODIUM USP
150mg ACTIVITY/ VIAL
LOT # 846-20-0001
11 MONTH SAMPLES
STORED AT 27.5°C & 60% RH 12-1-97

Pharma-Tek Inc.
PHARMACEUTICALS

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

FEB 12 1998

AADA 64-216

ORIG AMENDMENT
N/AC

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
OGD, Center of Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, MPN II
Rockville, MD 29857

Dear Dr. Holcombe:

We are submitting herewith, in duplicate, an amendment to our AADA 64-216 dated June 30, 1997 for Sterile Colistimethate Sodium USP, 150mg (base)/mL.

The amendment is in response to your faxed letter dated November 13, 1997 outlining certain deficiencies in our original application.

So as to facilitate your review we have included a table of contents listing our responses which correspond numerically to each of the deficiencies listed in your letter.

Your early review and approval of this amendment is appreciated.

Sincerely,

Susan E. Badia

Susan E. Badia
Assistant to the President

SEB/aap
cc: FDA (b) (4) District Office

RECEIVED
FEB 13 1998
GENERIC Drugs

FACSIMILE AMENDMENT

APR 20 1998

ANDA 64-216

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Pharma-Tek Inc PHONE: 516-757-5522

ATTN: Susan Badia FAX: 516-754-1550

FROM: Mark Anderson PROJECT MANAGER (301) 827–5849

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated June 30, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Sterile Colistimethate Sodium USP.

Reference is also made to your amendment dated February 12, 1998.

Attached are 7 pages of minor deficiencies and/or comments that should be responded to within 30 calendar days from the date of this document. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your complete response should be (1) faxed directly to our document control room at 301- 827-4337, (2) mailed directly to the above address, and (3) the cover sheet should be clearly marked a FACSIMILE AMENDMENT.

Please note that if you are unable to provide a complete response within 30 calendar days, the file on this application will be closed as a MINOR AMENDMENT and you will be required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Accordingly, a response of greater than 30 days should be clearly marked MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. Facsimiles or incomplete responses received after 30 calendar days will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data.

SPECIAL INSTRUCTIONS:

We note that this product is subject to the exception provisions of Section 125(d) (2) of Title I of the FDA Modernization Act of 1997. MICRO, labeling and Bioequivalency comments attached.

X:\new\ogdadmin\macros\faxfax.frm

AADA/ANDA: 64-216 APPLICANT: Pharma- Tek Inc.

DRUG PRODUCT: Sterile Colistimethate Sodium, USP

A. Microbiology Deficiencies:

1. (b) (4)

2.

3.

4.

5.

Please clearly identify your amendment to this facsimile as

"RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in the cover page/letter.

Sincerely yours,

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

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

ANDA Number: 64-216

Date of Submission: June 30, 1997

Applicant's Name: Pharma-Tek, Inc.

Established Name: Colistimethate for Injection, USP, 150 mg (colistin base)/vials

Labeling Deficiencies:

1. General Comments

   a. Replace the "CAUTION: Federal law..." statement with the symbol "Rx only" or "℞ only" on your labels and labeling. We refer you to the Guidance for Industry, "Implementation of Section 126, Elimination of Certain Labeling Requirements...", at the internet site, **http://www.fda.gov/cder/guidance/index.htm** for guidance.

   b. On November 15, 1998, the official USP monograph title for "Sterile Colistimethate Sodium, USP" will be replaced with the title "Colistimethate for Injection, USP". Revise the established name on your container labels, carton labeling and insert labeling accordingly.

2. CONTAINER:

   a. Increase the prominence of the strength.

   b. Due to the USP title revision, make the following revisions:

      i. Add an asterisk following the strength, "150 mg*".

      ii. Delete the text "Colistin Base Equivalent".

      iii. Add the following statement to the side panel:

*Each vial contains: Sterile Colistimethate Sodium equivalent to 150 mg Colistin Base. The sodium content is approximately ___ mg (___ mEq) of sodium per milligram of Colistin.

3. CARTON: 1 vial/carton

a. Usual Dose

Delete the extra space between before the word "day" [... 5 mg/kg/day ...].

b. Delete the extra spaces in your storage statements and revise to read as follows:

Store between 15°-30°C (59°-86°F)

Store reconstituted solution in refrigerator 2°-8°C (36°-46°F) or at room temperature 15°-30°C (59°-86°F) and use within 7 days.

c. See comments 2(b)(i, ii and iii) under CONTAINER.

4. INSERT

a. General Comment

You may delete "USP" following the established name throughout the insert labeling, except in the TITLE and in the HOW SUPPLIED section.

b. DESCRIPTION

i. Revise the molecular formula to read, "1749.85"

ii. Add the chemical name and the structural formula. We refer you to USP 23 and 21 CFR 201.57(a)(vi) for further guidance.

iii. Revise your each vial contains statement to read as follows:

Each vial contains: Sterile Colistimethate Sodium equivalent to 150 mg Colistin Base. The sodium content is approximately ___ mg (___ mEq) of sodium per milligram of Colistin.

c. CLINICAL PHARMACOLOGY (Figure 1)

i. Figure 1 is difficult to read. Therefore, improve the readability and the print quality.

ii. Delete the terminal zero following a decimal point, [i.e., "1" instead of "1.0"].

d. ADVERSE REACTIONS

In the third paragraph replace the hyphen with the word "to".

e. DOSAGE AND ADMINISTRATION

i. General Comments

a. Delete the terminal zero following a decimal point.

b. Replace the hyphens with the word "to".

ii. Dosage

Delete the fifth paragraph, "(b) (4) ... (b) (4)".

iii. Intravenous Administration

Revise the fourth paragraph to read as follows:

> Administer by slow intravenous infusion starting 1 to 2 hours after the initial dose at a rate of 5 to 6 mg/hr in the presence of normal renal function. In the presence of impaired renal function, reduce the infusion rate depending on the degree of renal impairment.

iv. Add the following as the last paragraph:

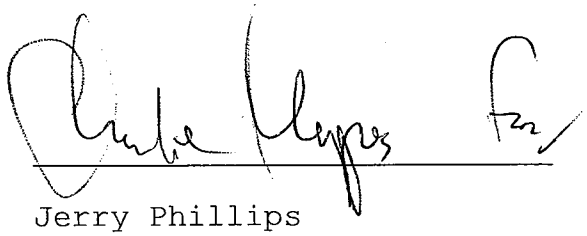
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

We refer you to 21 CFR 201.57(j) for further guidance.

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.



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

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 64-216 APPLICANT: Pharma-Tek

DRUG PRODUCT: Colistimethate Sodium For Injection

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 P. Conner

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

Pharma-Tek Inc.
PHARMACEUTICALS

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

JUN 12 1998

DR. Label
NDA ORIG AMENDMENT
AM

ANDA 64-216

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
OGD, Center of Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, MPN II
Rockville, MD 20855

FACSIMILE AMENDMENT

RESPONSE TO MICROBIOLOGY DEFICIENCIES
and
RESPONSE TO LABELING DEFICIENCIES

Dear Dr. Holcombe:

In response to the FDA FAX dated April 20, 1998 we are amending, in duplicate, our ANDA 64-216 "Colistimethate for Injection USP".

The amendment provides for responses to Microbiology Deficiencies and Labeling Deficiencies.

Your early review and approval will be appreciated.

Sincerely,

Susan E. Badia

Susan E. Badia
Assistant to the President

RECEIVED
JUN 15 1998
GENERIC DRUGS

SEB/aap
pc: FDA (b) (4) District Office

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS (HFD-600)
7500 STANDISH PLACE, ROCKVILLE, MD 20855

From:

Mark Anderson
Project Manager
Office of Generic Drugs
(301) 827-5849 Fax # (301) 443-3839

Date: **July 14, 1998**

To: **Susan Badia**

FAX #: 516-754-1550 Phone # 516-757-5522

Comments: Attached are Microbiology comments based on review of your June 12, 1998 amendment. Please respond when requested data are available. please respond as a Minor Telephone Amendment

Microbiology Comments to be Provided to the Applicant

ANDA: **64-216** APPLICANT: **Pharma-Tek Inc.**

DRUG PRODUCT: **Colistimethate for Injection, USP**

A. Microbiology Deficiencies:

1. [redacted] (b) (4)

2. No [redacted] (b) (4) data or calculations were included in your response to Question 5 of the FAX dated April 20, 1998. Please provide this information.

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

1. Please do not make incomplete submissions. They do not speed up your review time and may cause delay.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in the cover page/letter.

Sincerely yours,

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Pharma-Tek Inc.
PHARMACEUTICALS - FINE CHEMICALS

PHONE (516) 757-5522
P.O. BOX 1920
HUNTINGTON, N.Y. 11743-0568

ORIG AMENDMENT

N/AF

FPL satisfactory
C. Hudgens
for
J. White
8/13/98

August 13, 1998

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry
OGD, Center of Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, MPN II
Rockville, MD 20855

RE: ANDA# 64-216, Colistimethate for Injection USP, 150 mg(colistin base)/vial
Response to Labeling Deficiencies

Dear Dr. Holcombe:

In response to the FDA FAX for labeling deficiencies dated July 1998 we are amending, in duplicate, our ANDA 64-216 "Colistimethate for Injection USP".

The amendment provides responses to Labeling Deficiencies.

Your early review of this amendment will be appreciated. Thank you.

Sincerely yours,

Susan E. Badia

Susan E. Badia
Assistant to the President

SEB/aap
pc: FDA (b) (4) District Office

RECEIVED
AUG 17 1998
GENERIC DRUGS

8/17/98

Pharma-Tek Inc.
PHARMACEUTICALS

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

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

September 3, 1998

ORIG AMENDMENT

ANDA 64-216

N/A
Post approval commitments for product stereligation are not appropriate.
Jim Nelson
Sept. 21, 1998

Frank O. Holcombe, Jr., Ph.D.
Director, Division of Chemistry II
OGD, Center of Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, MPN II
Rockville, MD 20855

MINOR TELEPHONE AMENDMENT
RESPONSE TO MICROBIOLOGY DEFICIENCIES

Dear Dr. Holcombe:

We are submitting herewith, in duplicate, an amendment to our ANDA 64-216 "Colistimethate for Injection USP, in response to the Microbiology Deficiencies listed in your FAX dated July 14, 1998.

It is important to Pharma-Tek to make complete submissions and acknowledge your comment accordingly. We are finding that (b) (4)

As a small generic company, Pharma-Tek continually runs into low priority problems when our older generic drug products are competing with newer patentable drugs developed by PMA companies. (b) (4) test and will still require several weeks to complete the test.

On this note we would appreciate your approving the ANDA with our commitment to provide results of the (b) (4) test post-approval.

Your early review of this amendment and approval of the ANDA is requested.

Sincerely,

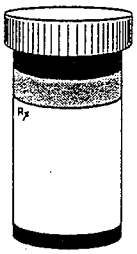
Susan E. Badia

Susan E. Badia
Assistant to the President

RECEIVED
SEP 0 4 1998
GENERIC DRUGS

SEB/aap
pc: FDA, (b) (4) District Office

Fax Cover Sheet



Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Rockville, Maryland

Date: 9/10/98

To: Susan E Badia

Phone: 516-757-5522 **Fax:** 516-754-1550

From: Labeling Review Branch

Phone: (301) 827-5846 **Fax:** (301) 443-3847

Number of Pages: 2
(Including Cover Sheet)

Comments:

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

ANDA Number: **64-216**

Date of Submission: **August 13, 1998**

Applicant's Name: **Pharma-Tek, Inc.**

Established Name: **Colistimethate for Injection, USP, 150 mg (colistin base)/vials**

Labeling Deficiencies:

1. CONTAINER (150 mg)

   Revise the strength to read as follows:

   Equivalent to 150 mg colistin

2. CARTON LABELING (1 x 150 mg)

   See comment under container.

3. INSERT

   Satisfactory in final print.

Please revise your container labels and insert labeling, as instructed above, and submit final printed labels and labeling.

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.

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

Pharma-Tek Inc.
PHARMACEUTICALS - FINE CHEMICALS

PHONE (516) 757-5522
P.O. BOX 1920
HUNTINGTON, N.Y. 11743-0568

September 14, 1998

AMENDMENT
N/AF

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs, CDER
Food and Drug Administration
7500 Standish Place, MPN II
Rockville, MD 20855

RE: ANDA# 64-216: Colistimethate for Injection USP, 150 mg (colistin base)/vial
Responses to Labeling Deficiencies and Final Printed Labeling

Dear Mr. Phillips:

In response to the FDA fax for labeling deficiencies dated September 10, 1998, we are amending, in duplicate our application ANDA # 64-216 entitled "Colistimethate for Injection USP".

The amendment provides responses to the labeling deficiencies to the container label and the single vial carton. Also enclosed are final printed labeling for the container, single vial carton and insert.

Your early review of this amendment will be appreciated. Thank you.

Sincerely yours,

Susan E. Badia

Susan E. Badia
Asst. to the Pres.

pc: FDA (b) (4) District Office

RECEIVED
SEP 16 1998
GENERIC DRUGS

Pharma-Tek Inc.
PHARMACEUTICALS - FINE CHEMICALS

PHONE (516) 757-5522
P.O. BOX 1920
HUNTINGTON, N.Y. 11743-0568

September 22, 1998

YOUR ORIG AMENDMENT
N/AS

ANDA 64-216

Frank O. Holcombe, Jr., Ph.D.
Director, Division of Chemistry II
OGD, Center of Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, MPN II
Rockville, MD 20855

MINOR AMENDMENT
RESPONSE TO MICROBIOLOGY DEFICIENCY

Dear Dr. Holcombe:

We are submitting herewith, in duplicate, an amendment to ANDA 64-216 entitled "Colistimethate for Injection USP", in response to Microbiology Deficiency (question A(1)) listed in your fax dated July 14, 1998.

On September 3, 1998 we filed an amendment responding to the July 14th microbiology deficiencies. We indicated that the (b) (4) test for Sterile Colistimethate for Injection USP was being performed by (b) (4) and would be ready in several weeks. The (b) (4) test has been completed and is enclosed for your review.

The (b) (4) test results completes Pharma-Tek's amendment to the microbiology deficiencies as set forth in FDA's July 14, 1998 fax.

We would appreciate your early review of this amendment.

RECEIVED
SEP 23 1998
GENERIC DRUGS

Sincerely,

Susan E. Badia

Susan E. Badia
Assistant to the President

pc: FDA, (b) (4) District Office

Pharma-Tek Inc.
PHARMACEUTICALS

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

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

October 14, 1998

NDA ORIG AMENDMENT
AS

ANDA# 64-216

Frank O. Holcombe, Jr., Ph.D.
Director, Division of Chemistry II
OGD, Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, MPN II
Rockville, MD 20855

Re: RESPONSE TO MICROBIOLOGY DEFICIENCIES

Dear Dr. Holcombe:

We are submitting herewith, in duplicate, an amendment to ANDA 64-216 entitled "Colistimethate for Injection USP", in response to Microbiology Deficiencies from your facsimile dated October 2, 1998.

Your early review of the enclosed responses would be most appreciated. If there are any questions, please call me at (516) 757-5522. Thank you.

Sincerely,

Susan E. Badia

Susan E. Badia
Asst. to the President

pc: FDA, (b) (4) District Office

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: December 23, 1998

NDA NUMBER: 64-216

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☑ FDA

MADE: ☑ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Sterile Colistimethate Sodium

FIRM NAME: Pharma-Tek, Inc. Huntington, N.Y.

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD

Dan Badea
President

TELEPHONE NO.

(516) 757-5522

I called Mr. Badea about 3:30 PM and requested that he submitted a "Telephone amendment" to his pending ANDA. I gave him the information on the attached sheet prepared by Florence Fang ---- He said he would work on filing the requested changes next week -- December 28th. I gave him our FAX number [(301) 443-3839]. He will follow up FAX with hard copy for filing with the application.

SIGNATURE: John D. Harman

DIVISION:

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

U. S. GOVERNMENT PRINTING OFFICE - 1984-432-976/7126

Pharma-Tek Inc.
PHARMACEUTICALS - FINE CHEMICALS
PHONE (516) 757-5522
P.O. BOX 1920
HUNTINGTON, N.Y. 11743-0568

January 13, 1999

ANDA 64-216

Florence S. Fang

FDA DRUG AMENDMENT

OGD, Center of Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, MPN II
Rockville MD 20855

TELEPHONE AMENDMENT
Colistimethate for Injection USP
150 mg colistin base equivalent/vial

Dear Ms. Fang:

In response to comments telephoned to our attention by Mr. John Harrison on December 23, 1998, we are submitting herewith, in duplicate and by facsimile, an amendment to our ANDA 64-216 covering Colistimethate for Injection USP; 150 mg colistin base equivalent/vial.

One the following 3 pages we have responded to these comments:

1. Bulk Active Ingredient testing for Particle Size and Constituted Solutions Confirms telephone conversation with Ms. Fang.

2. Listing of the Components of the Drug per vial and batch sizes

3. Long Term Stability Revision and Commitment

Your early inclusion of this information into our ANDA and approval will be most appreciated.

Sincerely,

Dan J. Badia
President

pc: FDA, (b) (4) District Office

RECEIVED
JAN 14 1999
GENERIC DRUGS

RECORD OF TELEPHONE CONVERSATION

Jon Clark and I called Dan Badia with regard to his 1/13/99 amendment and asked that he provide revised composition statement in terms of amount of colistimethate sodium content rather than only in terms of base content.

Mr. Badia said he would submit as requested.

V:\new\firmsnz\pharmtek\telecons\64216.001

DATE

1/20/99

APPLICATION NUMBER

64-216

TELECON

INITIATED BY FDA

PRODUCT NAME

Colistimethate for Injection

FIRM NAME

Pharmatek

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD

Dan Badia

TELEPHONE NUMBER

516-757-5522

SIGNATURE

Mark Anderson

Pharma-Tek Inc.
PHARMACEUTICALS

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

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

January 21, 1999

NDA ORIG AMENDMENT

ANDA 64-216

N-AM

Florence S. Fang
Deputy Director
OGD, Center of Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place, MPN II
Rockville, MD 20855

TELEPHONE AMENDMENT
Colistimethate for Injection USP
150 mg colistin base equivalent/vial

Dear Ms. Fang:

Please refer to our telephone amendment dated January 13, 1999. The amendment responded to 3 comments previously telephoned to us by Mr. John Harrison on December 23, 1998.

We are submitting herewith, in duplicate and by facsimile, an amendment to our ANDA 64-216 covering Colistimethate for Injection USP; 150 mg colistin base equivalent/vial.

This amendment further elaborates Comment 2 which was contained in our January 13, 1999 amendment based upon a telephone conversation with Mark Anderson and John Clark on January 20, 1999. Enclosed is a revision of Comment 2.

Your early review of this information into our ANDA and approval will be most appreciated.

Sincerely,

Dan J. Badia
President

RECEIVED
JAN 26 1999
GENERIC DRUGS

DJB/aap
pc: FDA, (b) (4) District Office

OGD APPROVAL ROUTING SUMMARY

ANDA # 64-216 Applicant Pharmatek

Drug Strength 150 mg (base)/Vial Sterile Colistimethate Sodium

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

REVIEWER:

1. Project Manager M Anderson
   Review Support Br 4

DRAFT RECEIPT
Date 11/18/98
Initials MA

FINAL ACTION
Date 12/22/98
Initials MA

Application Summary:
Original Rec'd date 7/3/97
Date Acceptable for Filing 7/3/97
Patent Certification (type) _____
Date of Office Bio Review _____
Methods Val. Samples Pending Yes ☐ No ☒
30 Day Clock Start NA End _____
Commitment rcd. from Firm NA Yes ☐ No ☐
First Generic ☒ Yes ☒ No ☐

EER Status Pending ☐ Acceptable ☒ OAI ☐
Date of EER Status 11/30/98
Date Patent in effect NA
Citizens Petition/Legal Case Yes ☐ No ☒
(If YES, attach email from PM to Pet. Coord. notifying of pending approval)
Pediatric Exclusivity Tracking System
Date checked 12/22
Nothing Submitted ☒
Written request issued ☐
Study Submitted ☐

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

2. Div. Dir./Deputy Dir.
   Chemistry Div. I or II
   Date 12/22/98
   Initials _____
   Date 1/21/99
   Initials _____
   Comments:
   12/23 Time to review composition statement, drug substance testing spec + stability protocol.
   Amendments dated 1/13/99 and 1/21/99 addressed the concerns. Chemistry is satisfactory.

3. Office Level Chem Review **(1st Generic Only)**
   Chemistry Div. I or II
   Date _____
   Initials _____
   Date 2/24/99
   Initials _____
   Comments: CONTROLS & SPECIFICATIONS ARE SATISFACTORY

4. Pat Beers Block
   Supv., Review Support Branch
   Date _____
   Initials _____
   Date _____
   Initials _____
   Comments:
   Refer to DLPS review. 2/25/99

REVIEWER:	DRAFT RECEIPT	FINAL ACTION

5. Peter Rickman
Supv., Reg. Support Branch
Contains certification Yes ☒ No ☐
(required by the GDEA if sub after 6/1/92)
Paragraph 4 Certification Yes ☐ No ☒
Comments:

Date 2/25/99 Date 2/25/99
Initials [illegible] Initials [illegible]
Determ. of involvement? Yes ☐ No ☒
Pediatric Exclusivity Tracking System
Date Checked N/A 2/25/99 Rec'd
Nothing Submitted ☒
Written request issued ☐
Study Submitted ☐

patent and exclusivity issues N/A Title II Drug Product (antibiotic)

EER acceptable 11/30/98
Office Label Bio 1/15/98

FIRST GENERIC!

6. Jerry Phillips
Dir. Div. Labeling & Prog. Support
Comments: Acceptable EES 11/30/98 (verified 2/25/99). No D.A.I. alerts noted. Bioequivalence waiver granted under 320.22(b)(1)(2+2 to RLD) on 1/15/98. Office-level bio endorsed 1/15/98 (D. Conner). FPL Acceptable for approval 10/7/98 (as endorsed 12/22/98). Microbiology/Sterility assurance acceptable 1/5/98. CMC Acceptable. Field analysis acceptable 2/13/98.

Date 2/25/99 Faxed Date 2/25/99 Faxed
Initials [illegible] Initials [illegible]

Recommend: Approval

7. Gordon Johnston
Deputy Director, OGD
Patent Cert - P_4 Yes ☐ No ☒
Pend. Legal Action Yes ☐ No ☒
Comments: No patent or exclusivity issues. No Controlled correspondence or Citizens Petitions currently pending. First-generic CMC audit completed.

Date 2/25/99 Faxed Date 2/25/99 Faxed for
Initials [illegible] Initials [illegible]
Petition Status N/A

8. Doug Sporn
Dir., OGD
Comments:

Date 2/26/99 Date 2/26/99
Initials [illegible] Initials [illegible]

Roger Williams, M.D.
Dep.Dir., CDER

Date [illegible] Date [illegible]
Initials [illegible] Initials [illegible]

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

9. Project Manager Mark Anderson
Review Support Branch

Date 2/26/99 Date 2/26/99
Initials MA Initials MA

RW DTA Pediatric Exclusivity Tracking System (check just prior to notification to firm)

Applicant notification:
12:30 Time notified of approval by phone 12:30 Time approval letter faxed

FDA Notification:
2/26/99 Date e-mail message sent to "OGD approvals" account
2/26 Date Approval letter copied to "//cder/drugapp" directory

x:\wpfile\beersbl\aprovrou.wp

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: **ANDA 64216/000**
Stamp: **03-JUL-1997** Regulatory Due:
Applicant: **PHARMA TEK**
1920
HUNTINGTON, NY 11743

Priority: Org Code: **600**
Action Goal: District Goal: **03-SEP-1998**
Brand Name:
Established Name: **STERILE COLISTIMETHATE SODIUM**
Generic Name:
Dosage Form: **INJ (INJECTION)**
Strength: **150 MG BASE/VIAL**

FDA Contacts: **M. ANDERSON (HFD-617) 301-827-5848 , Project Manager**
ID = 101009 , Team Leader

Overall Recommendation:

ACCEPTABLE on 30-NOV-1998 by J. D AMBROGIO (HFD-324) 301-827-0062
ACCEPTABLE on 18-NOV-1997 by M. EGAS (HFD-322) 301-594-0095

Establishment: (b) (4)
DMF No:
AADA No:

Profile: **SVS** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date (b) (4)
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
Responsibilities: **FINISHED DOSAGE MANUFACTURER**

Establishment: (b) (4)
DMF No:
AADA No: (b) (4)

Profile: **CFN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date (b) (4)
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**
Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Establishment: (b) (4)
DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date (b) (4)
Responsibilities: **FINISHED DOSAGE STABILITY TESTER**

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Decision: **ACCEPTABLE**

Reason: **BASED ON PROFILE**