

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

Approval Package for:

APPLICATION NUMBER:

89-096

Generic Name: Bethanechol Chloride Tablets USP,
50mg

Sponsor: Sidmak Laboratories, Inc.

Approval Date: December 19, 1985

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-096

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Administrative Document(s)	X
Correspondence	X

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-096

APPROVAL LETTER

ANDA 89-096

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
Post Office Box 371
East Hanover, New Jersey 07936

DEC 19 1985

Gentlemen:

Reference is made to your abbreviated new drug application dated December 19, 1984, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Bethanechol Chloride Tablets USP, 50 mg.

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.

Any significant change in the conditions outlined in this abbreviated application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 314.70 of the New Drug Regulations.

Postmarketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80 and 314.81 of the Regulations.

This Administration should be advised of any change in the marketing status of this drug.

For Initial Campaigns: We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your immediate 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 Advertising and Labeling (HFN-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

For Subsequent Campaigns: We call your attention to Section 314.81(b)(3) of the Regulations which requires that materials for any subsequent advertising or promotional campaign, at the time of their initial use, be submitted to our Division of Drug Advertising and Labeling (HFN-240) with a completed Form

NWK-~~10~~
FD-2253
HFN-250
HFN-83
HFN-10

REB
12/18/85
RBrown/JMeyer/MShih
R/D INITIALED BY: JMeyer/MSeife
D Utz: 12-17-85 (0139R)
APPROVAL

Sincerely yours,

Marvin Seife 12/19/85
Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-096

FINAL PRINTED LABELING

DEC 19 1985

APPROVED

BETHANECHOL
CHLORIDE
TABLETS, USP

OVERDOSAGE: Early signs of overdosage are abdominal discomfort, salivation, flushing of the skin ("hot feeling"), sweating, nausea, and vomiting.

Atropine is a specific antidote. The recommended dose for adults is 0.6 mg (1/100 grain). Repeat doses can be given every two hours, according to clinical response. The recommended dosage in infants and children up to 12 years of age is 0.01 mg/kg (to a maximum single dose of 0.4 mg.) repeated every two hours as needed until the desired effect is obtained or adverse effects of atropine preclude further usage. Subcutaneous injection of atropine is preferred except in emergencies when the intravenous route may be employed.

The oral LD50 of bethanechol chloride is 1510 mg/kg in the mouse.

DOSE AND ADMINISTRATION: Dosage and route of administration must be individualized, depending on the type and severity of the condition to be treated.

Preferably give the drug when the stomach is empty. If taken soon after eating, nausea and vomiting may occur.

The usual oral adult dose is 10 to 50 mg, three or four times a day. The minimum effective dose is determined by giving 5 or 10 mg, initially and repeating the same amount at hourly intervals until satisfactory response occurs or until a maximum of 50 mg. has been given. The effects of the drug sometimes appear within 30 minutes and usually within 60 - 90 minutes. They persist for about an hour.

HOW SUPPLIED: Bethanechol Chloride Tablets, USP.

5 mg.—White, round, scored tablets in bottles of 100 and 1000.

Imprint: SL/323

10 mg.—Pink, round, scored tablets in bottles of 100, 500 and 1000.

Imprint: SL/324

25 mg.—Yellow, round, scored tablets in bottles of 100, 500 and 1000.

Imprint: SL/325

50 mg.—Yellow, round, scored tablets in bottles of 100 and 1000.

Imprint: SL/326

Dispense in tight containers as defined in the USP.

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

CAUTION: Federal law prohibits dispensing without prescription.

Manufactured by

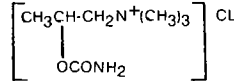
SIDMAK LABORATORIES, INC.
East Hanover, New Jersey 07936

323 - 26

Rev. 6/85 A

DESCRIPTION: Bethanechol chloride, a cholinergic agent, is a synthetic ester which is structurally and pharmacologically related to acetylcholine.

It is designated chemically as 2-[(aminocarbonyl)oxy]-N, N, N-trimethyl-1-propanaminium chloride. Its molecular formula is C₇H₁₇ClN₂O₂ and its structural formula is:



MCS

It is a white, hygroscopic crystalline compound having a slight amine-like odor, freely soluble in water, and has a molecular weight of 196.68.

Bethanechol chloride is available as 5 mg., 10 mg., 25 mg. and 50 mg. tablets intended for oral use.

CLINICAL PHARMACOLOGY: Bethanechol chloride acts principally by producing the effects of stimulation of the parasympathetic nervous system. It increases the tone of the detrusor urinae muscle, usually producing a contraction sufficiently strong to initiate micturition and empty the bladder. It stimulates gastric motility, increases gastric tone and often restores impaired rhythmic peristalsis.

Stimulation of the parasympathetic nervous system releases acetylcholine at the nerve endings. When spontaneous stimulation is reduced and therapeutic intervention is required, acetylcholine can be given, but it is rapidly hydrolyzed by cholinesterase and its effects are transient. Bethanechol chloride is not destroyed by cholinesterase and its effects are more prolonged than those of acetylcholine.

Effects on the GI and urinary tracts sometimes appear within 30 minutes after oral administration of bethanechol chloride, but more often 60 - 90 minutes are required to reach maximum effectiveness. Following oral administration, the usual duration of action of bethanechol is one hour, although large doses (300 - 400 mg.) have been reported to produce effects for up to six hours. Subcutaneous injection produces a more intense action on bladder muscle than does oral administration of the drug.

Labeling: ORIGINAL

NDA No: 89-0916 Rev'd. 8/20/85

Reviewed by: [Signature] 12/10/85

MCS

APPROVED DEC 19 1985

Because of the selective action of bethanechol, nicotinic symptoms of cholinergic stimulation are usually absent or minimal when orally or subcutaneously administered in therapeutic doses, while muscarinic effects are prominent. Muscarinic effects usually occur within 5 - 15 minutes after subcutaneous injection, reach a maximum in 15 - 30 minutes, and disappear within two hours. Doses that stimulate micturition and defecation and increase peristalsis do not ordinarily stimulate ganglia or voluntary muscles. Therapeutic test doses in normal human subjects have little effect on heart rate, blood pressure or peripheral circulation.

Bethanechol chloride does not cross the blood-brain barrier because of its charged quaternary amine moiety. The metabolic fate and mode of excretion of the drug have not been elucidated.

A clinical study (Diokno, AC, Lapides, J, Urol. 10:23-24, July 1977) was conducted on the relative effectiveness of oral and subcutaneous doses of bethanechol chloride on the stretch response of bladder muscle in patients with urinary retention. Results showed that 5 mg. of the drug given subcutaneously stimulated a response that was more rapid in onset and of larger magnitude than an oral dose of 50 mg., 100 mg. or 200 mg. All the oral doses, however, had a longer duration of effect than the subcutaneous dose. Although the 50 mg. oral dose caused little change in intravesical pressure in this study, this dose has been found in other studies to be clinically effective in the rehabilitation of patients with decompensated bladders.

INDICATIONS AND USAGE: For the treatment of acute postoperative and post-partum nonobstructive (functional) urinary retention and for neurogenic atony of the urinary bladder with retention.

CONTRAINDICATIONS: Hypersensitivity to bethanechol chloride, hyperthyroidism, peptic ulcer, latent or active bronchial asthma, pronounced bradycardia or hypotension, vasomotor instability, coronary artery disease, epilepsy and parkinsonism.

Bethanechol chloride should not be employed when the strength or integrity of the gastrointestinal or bladder wall is in question, or in the presence of mechanical obstruction; when increase muscular activity of the gastrointestinal tract or urinary bladder might prove harmful, as following recent urinary bladder surgery, gastrointestinal resection and anastomosis, or when there is possible gastrointestinal obstruction; in bladder neck obstruction, spastic gastrointestinal disturbances, acute inflammatory lesions of the gastrointestinal tract, or peritonitis; or in marked vagotonia.

PRECAUTIONS: General: In urinary retention, if the sphincter fails to relax as bethanechol chloride contracts the bladder, urine may be forced up the ureter into the kidney pelvis. If there is bacteriuria, this may cause reflux infection.

Information for patients: Bethanechol chloride tablets should preferably be taken one hour before or two hours after meals to avoid nausea or vomiting. Dizziness, lightheadedness or fainting may occur, especially when getting up from a lying or sitting position.

Drug Interactions: Special care is required if this drug is given to patients receiving ganglion blocking compounds because a critical fall in blood pressure may occur. Usually severe abdominal symptoms appear before there is such a fall in the blood pressure.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have not been performed to evaluate the effects upon fertility, mutagenic or carcinogenic potential of bethanechol chloride.

Pregnancy: Pregnancy Category C. Animal reproduction studies have not been conducted with bethanechol chloride. It is also not known whether bethanechol chloride can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Bethanechol chloride should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk and because of the potential for serious adverse reactions from bethanechol chloride in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Adverse reactions are rare following oral administration of bethanechol, but are more common following subcutaneous injection. Adverse reactions are more likely to occur when dosage is increased.

The following adverse reactions have been observed: **Body as a Whole:** malaise; **Digestive:** abdominal cramps or discomfort, colicky pain, nausea and belching, diarrhea, borborygmi, salivation; **Renal:** urinary urgency; **Nervous System:** headache; **Cardiovascular:** a fall in blood pressure with reflex tachycardia, vasomotor response; **Skin:** flushing producing a feeling of warmth, sensation of heat around the face, sweating; **Respiratory:** bronchial constriction, asthmatic attacks; **Special Senses:** lacrimation, miosis.

Labeling: ORIGINAL

NDA No: 89-096 Rcd. 8/20/85

Reviewed by: MSL 12/10/85

APPROVED
NDC 50111-326-01

**Bethanechol Chloride
Tablets, USP
50 mg.**

CAUTION: Federal law prohibits
dispensing without prescription.

100 Tablets **DEC 1**
Sidmak[®]
LABORATORIES, INC.

EACH TABLET CONTAINS:
Bethanechol Chloride, USP 50 mg.
Dispense in tight containers

NDC 50111-326-01

**Bethanechol Chloride
Tablets, USP
50 mg.**

CAUTION: Federal law prohibits
dispensing without prescription.

100 Tablets **DEC 1**
Sidmak[®]
LABORATORIES, INC.

APPROVED
NDC 50111-326-01

**Bethanechol Chloride
SP**

EACH TABLET CONTAINS:
Bethanechol Chloride,
USP 50 mg.
Dispense in tight containers
as defined in the USP.

Store at controlled room tempera-
ture 15-30°C (59-86°F).
USUAL DOSAGE: See pack-
age insert.

Control No.:
Exp. Date:
SIDMAK LABORATORIES, INC.
East Hanover, N.J. 07936

prohibits
cription.

EACH TABLET CONTAINS:
Bethanechol Chloride,
USP 50 mg.
Dispense in tight containers
as defined in the USP.

Store at controlled room tempera-
ture 15-30°C (59-86°F).
USUAL DOSAGE: See pack-
age insert.

Control No.:
Exp. Date:
SIDMAK LABORATORIES, INC.
East Hanover, N.J. 07936

9 1985

APPROVED
APPROVED

NDC 50111-326-03

**Bethanechol Chloride
Tablets, USP
50 mg.**

CAUTION: Federal law prohibits
dispensing without prescription.

1000 Tablets **DEC 19 1985**

Sidmak[®]
LABORATORIES, INC.

50 mg.

CAUTION: Federal law prohibits
dispensing without prescription.

1000 Tablets **DEC 19 1985**

Sidmak[®]
LABORATORIES, INC.

50 mg.

CAUTION: Federal law prohibits
dispensing without prescription.

1000 Tablets **DEC 19 1985**

Sidmak[®]
LABORATORIES, INC.

EACH TABLET CONTAINS:
Bethanechol Chloride,
USP 50 mg.

Dispense in tight containers as
defined in the USP.

Store at controlled room tempera-
ture 15-30°C (59-86°F).

USUAL DOSAGE: See package
insert.

APPROVED

SIDMAK LABORATORIES, INC.
East Hanover, N.J. 07936

Control No.:
Exp. Date:

Store at controlled room tempera-
ture 15-30°C (59-86°F).

USUAL DOSAGE: See package
insert.

APPROVED

SIDMAK LABORATORIES, INC.
East Hanover, N.J. 07936

Control No.:
Exp. Date:

Store at controlled room tempera-
ture 15-30°C (59-86°F).

USUAL DOSAGE: See package
insert.

APPROVED

SIDMAK LABORATORIES, INC.
East Hanover, N.J. 07936

Control No.:
Exp. Date:

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-096

CSO LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING
Orig. Amendment - DRAFT

DATE OF REVIEW: 6/24/85

ANDA/NDA #89-095 (5 mg)
89-096 (50 mg)

NAME OF FIRM: Sidmak

NAME OF DRUG: Generic: Bethanechol Chloride Tablets USP

DATE OF SUBMISSION: 6/14/85

COMMENTS:

Insert: Not Satisfactory

1) DESCRIPTION

a)molecular formula...(rather than _____)

2. OVERDOSAGE

a) Add as the last sentence; The oral LD₅₀ of bethanechol chloride is 1510 mg/kg in the mouse.

3. DOSAGE AND ADMINISTRATION

a) Dosage and route of administration must be.....(rather than, _____)

4. HOW SUPPLIED

a) We encourage the inclusion of the National Drug Code for each product listed (not required).

RECOMMENDATIONS:

1. Inform firm of these comments.

2. Request that they revise then package insert labeling, then prepare and submit FPL.



Ron Brown

cc:

Orig.

RBrown/gp/6/26/85

0103g

REVIEW OF PROFESSIONAL LABELING

ANDA - DRAFT

DATE OF REVIEW: 3/8/85

ANDA #: 89-095 (5 mg)
89-096 (50 mg)

NAME OF FIRM: Sidmak

NAME OF DRUG: Generic: Bethanechol Chloride Tablets

DATE OF SUBMISSION: 12/19/84

COMMENTS:

Container: Not Satisfactory

(a) TITLE - should be that of the USP article.
BETHANECHOL CHLORIDE
TABLETS, USP

(b) Controlled Room Temperature - 15⁰-30⁰C (59⁰-86⁰F)

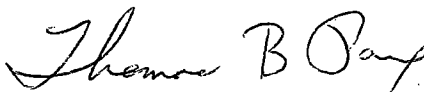
Insert: Not Satisfactory

(a) For consistency, the chemical name should be the second name listed in the USP monograph.

(b) Revise package insert labeling in accord with latest revision (7/84) of the package insert from the full NDA holder.

RECOMMENDATIONS:

1. Inform firm of above comments.
2. Request they revise container labels, then prepare and submit FPL.
3. Request they revise package insert labeling, then submit draft copy for our review and comment.


Thomas B. Poux

cc: Dup.
TPoux/mk/3/11/85
9752A

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-096

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW NDA 89-096

3. NAME AND ADDRESS OF APPLICANT
Sidmak Laboratories, Inc.
East Hanover, New Jersey 07936
6. NAME OF DRUG
Bethanechol Chloride
10. PHARMACOLOGICAL CATEGORY 11. HOW DISPENSED
Parasympathomimetic Rx
12. RELATED IND/NDA/DMF(s)
89-095 (5 mg)
89-096 (50 mg)
13. DOSAGE FORM(s) 14. POTENCY
Tablets 50 mg
17. COMMENTS
1. Bio - Satisfactory per Bio letter of June 5, 1985
2. Sidmak NDA 88-440 (10 mg) Approved May 29, 1984
 88-441 (25 mg) Approved May 29, 1984
18. CONCLUSIONS AND RECOMMENDATIONS
Approval
19. REVIEWER: DATE COMPLETED:
Maria Shih *MSH 12/18/85*

**APPEARS THIS WAY
ON ORIGINAL**

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Page(s) of trade

secret and /or

confidential

commercial

information

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3

Page(s) of trade

secret and /or

confidential

commercial

information

CHEMIST'S REVIEW NDA 89-096

3. NAME AND ADDRESS OF APPLICANT
Sidmak Laboratories, Inc.
East Hanover, New Jersey 07936
6. NAME OF DRUG
Bethanechol Chloride
8. SUPPLEMENT(s) PROVIDE(s) FOR:
Bio
9. AMENDMENTS AND OTHER DATES:
June 14, July 11, 1985
10. PHARMACOLOGICAL CATEGORY 11. HOW DISPENSED
Parasympathomimetic Rx
12. RELATED IND/NDA/DMF(s)
89-095 (5 mg)
89-096 (50 mg)
13. DOSAGE FORM(s) 14. POTENCY
Tablets 50 mg
17. COMMENTS
1. Bio under review
2. Sidmak NDA 88-440 (10 mg) Approved May 29, 1984
88-441 (25 mg) Approved May 29, 1984
18. CONCLUSIONS AND RECOMMENDATIONS
Not Approvable
19. REVIEWER: DATE COMPLETED:
Maria Shih MS 7/24/85

**APPEARS THIS WAY
ON ORIGINAL**

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confidential

commercial

information

CHEMIST'S REVIEW NDA 89-096

3. NAME AND ADDRESS OF APPLICANT
Sidmak Laboratories, Inc.
East Hanover, New Jersey 07936
6. NAME OF DRUG
Bethanechol Chloride
8. SUPPLEMENT(s) PROVIDE(s) FOR:
1. Bio
2. Stability
9. AMENDMENTS AND OTHER DATES:
March 29, 1985
10. PHARMACOLOGICAL CATEGORY 11. HOW DISPENSED
Parasympathomimetic Rx
12. RELATED IND/NDA/DMF(s)
89-095 (5 mg)
89-096 (50 mg)
13. DOSAGE FORM(s) 14. POTENCY
Tablets 50mg
17. COMMENTS
1. Bio under review
2. Sidmak NDA 88-440 (10 mg) Approved May 29, 1984
88-441 (25 mg) Approved May 29, 1984
18. CONCLUSIONS AND RECOMMENDATIONS
Not Approvable
19. REVIEWER: DATE COMPLETED:
Maria Shih MSL - 6/10/85

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information

CHEMIST'S REVIEW <i>(If necessary, continue any item on 8" x 10 1/2" paper. Key continuation to item by number.)</i>		1. ORGANIZATION	2. NDA NUMBER 89-056096
3. NAME AND ADDRESS OF APPLICANT (City and State) Sidmak Laboratories, Inc. East Hanover, New Jersey 07936		4. AF NUMBER	5. SUPPLEMENT (S) NUMBER(S) DATE(S)
6. NAME OF DRUG Bethanechol Chloride	7. NONPROPRIETARY NAME	9. AMENDMENTS AND OTHER (Reports, etc.) DATES	
8. SUPPLEMENT(S) PROVIDES FOR:		12. RELATED IND/NDA/DMF(S) 89-095 (5 mg) 89-096 (50 mg)	
10. PHARMACOLOGICAL CATEGORY Parasympathomimetic	11. HOW DISPENSED <input checked="" type="checkbox"/> RX <input type="checkbox"/> OTC	13. DOSAGE FORM (S) Tablets	
14. POTENCY (see) 50 mg		15. CHEMICAL NAME AND STRUCTURE	
16. RECORDS AND REPORTS CURRENT <input type="checkbox"/> YES <input type="checkbox"/> NO REVIEWED <input type="checkbox"/> YES <input type="checkbox"/> NO		17. COMMENTS 1. Bio not acceptable per Bio letter of February 21, 1985 2. Sidmak NDA 88-440 (10 mg) Approved May 29, 1984 88-441 (25 mg) Approved May 29, 1984	
APPEARS THIS WAY ON ORIGINAL			
18. CONCLUSIONS AND RECOMMENDATIONS Not Approvable			
19. REVIEWER NAME Maria Shih		SIGNATURE <i>Maria Shih</i>	DATE COMPLETED 3/24/87
DISTRIBUTION <input type="checkbox"/> ORIGINAL JACKET <input type="checkbox"/> REVIEWER <input type="checkbox"/> DIVISION FILE			

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**CENTER FOR DRUG
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APPLICATION NUMBER:

89-096

**BIOEQUIVALENCE
REVIEW(S)**

5/29/85

Generic Name: Bethanechol Chloride

Firm Name: Sidmak Laboratories

Trade Name: _____

Firm Location: East Hamover, NY 07.

Dosage: 5 mg + 50 mg Tablets

Submission Date: March 29, 1985
March 29, 1985

ANDA #: 89-095 + 89-096

Reviewer: Agnest T. Wu

Wang #: 5362e

REVIEW OF DISSOLUTION DATA

Objective of Submission: The firm has submitted
comparative dissolution data in support
of these two ANDA's for approval.

Conditions for Dissolution Testing:

USP XXI Apparatus II Basket _____ Paddle RPM 50

Medium: 0.1 N HCl Volume: 900 ml

Number of (Tabs) Caps Tested: 12

Reference Drug: Urecholine 5mg + 50mg (MSD)

Assay Methodology: _____

Comments:

The firm has tested 12 tablets from each of their 5 mg and 50 mg products in comparison with the reference 5 mg and 50 mg products. The dissolution testing results are found acceptable.

Recommendations:

1. The dissolution testing conducted by Sidmak Laboratories on its Bethanechol Chloride 5 mg tablets, Lot # 84-181T and 50 mg tablets, Lot # 84-182T, is acceptable.
2. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 900 ml of 0.1N HCl at 37°C using USP XX apparatus II (paddle) at 50 rpm. The test product should meet the following specification:

Not less than 80% of the labeled amount of the drug
in the dosage form is dissolved in 30 minutes.

3. From the Bioequivalence point of view, the firm has met the requirement for bioavailability with in-vitro dissolution testing, and both applications on their 5 mg and 50 mg Bethanechol Chloride products are acceptable.

The above recommendations should be forwarded to the firm.

Agnes T. Wu 5/28/85

Agnes T. Wu, Ph.D.
Division of Bioequivalence, RB I

RD INITIALED CISE
FT INITIALED CISE

F. Pelton
AWu/dlp/05-23-85/Wang # 5362e

cc: ANDA # 89-095 and 89-096 original, HFN-230 (4), HFN-200 (Hare),
HFN-223 (Shah), HFN-252 (Wu, Ise), Drug File

2 / 08 / 85

Generic Name: Bethanechol Chloride

Firm Name: Sidmok Laboratories

Trade Name: _____

Firm Location: East Hanover, N.J. 079

Dosage: 5 mg + 50 mg Tablets

Submission Date: December 18, 1984

ANDA #: 89-095 + 89-096

Reviewer: AGNES T. WU

Wang #: 46500

REVIEW OF DISSOLUTION DATA

Objective of Submission: The firm presented composition information and dissolution data in support of their ANDA's for approval.

APPEARS THIS WAY
ON ORIGINAL

Conditions for Dissolution Testing:

USP XXI Apparatus II Basket _____ Paddle RPM 50

Medium: 0.1N HCl Volume: 900 ml

Number of Tabs/Caps Tested: 6

Reference Drug: NONE

Assay Methodology: ~~NOT SPECIFIED~~

Results

Time	Test Product		Reference Product	
	Lot No. <u>84-182 T (50mg)</u>	Mean % Range, (CV)	Lot No. <u>84-181 T (5mg)</u>	Mean % Range, (CV)
	Dissolved		Dissolved	
<u>30 min</u>	<u>100.1</u>	<u>(1.7%)</u>	<u>100.8</u>	<u>(2.1%)</u>
_____	_____	_____ ()	_____	_____ ()
_____	_____	_____ ()	_____	_____ ()
_____	_____	_____ ()	_____	_____ ()
_____	_____	_____ ()	_____	_____ ()
_____	_____	_____ ()	_____	_____ ()
_____	_____	_____ ()	_____	_____ ()
_____	_____	_____ ()	_____	_____ ()
_____	_____	_____ ()	_____	_____ ()

APPEARS THIS WAY
ON ORIGINAL

Composition:

	mg/tablet	
	<u>5 mg</u>	<u>50 mg</u>
Bethanechol Chloride, USP	—	—
—	—	—
—	—	—
—	—	—
—	—	—
—	—	—
—	—	—
—	—	—
total:	<u>320.0</u>	<u>490.0</u>

Dissolution Data:

The firm submitted dissolution data on 6 tablets each from their 5 mg and 50 mg products. The dissolution testing was conducted in 900 ml 0.1N HCl using USP II (paddle) method at 50 rpm with _____ monitoring at / _____ The firm submitted data only at 30 minutes and no data on reference products were submitted.

Comments:

The firm has tested 6 tablets from each of their 5 mg and 50 mg products. The firm is advised to conduct comparative dissolution testing on 12 tablets from both their products (5 and 50 mg tablets) and the reference products (5 and 50 mg tablets) as follows:

Apparatus:	USP II (paddle)
RPM:	50 rpm
Medium:	900 ml of 0.1N HCl
Specification:	NLT 80% dissolution in 30 minutes.
Sampling times:	15 and 30 minutes

Recommendation:

The dissolution testing conducted by Sidmak Laboratories on Bethanechol Chloride 5 mg and 50 mg tablets is unacceptable. The firm should be advised to conduct comparative dissolution testing employing USP Apparatus II at 50 rpm in 900 ml 0.1N HCl with 12 units from both test products and reference products at each strength. The test products should meet the following specification:

Not less than 80% of the labeled amount of the drug in the dosage form is dissolved in 30 minutes.

The above recommendation should be forwarded to the firm.

Agnes T. Wu 2/4/85

Agnes T. Wu, Ph.D.
Division of Bioequivalence

RD INITIALED BY CISE
FT INITIALED BY CISE

C. M. Lee

AWu/cc/Wang #4650e/1-22-85

cc: ANDA 89-095, 89-096 orig., HFN-230 (4), HFN-227 (Wu, Ise-2), HFN-200
(Hare), HFN-223 (Shah-FOI), drug file

**APPEARS THIS WAY
ON ORIGINAL**

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-096

**ADMINISTRATIVE
DOCUMENTS**

RECORD OF TELEPHONE CONVERSATION/MEETING	DATE 12/17/85	
<p>To File:</p> <p>The firm submitted dissolution data for their Bethanechol Chloride Tablets 5mg and 50mg which was reviewed and found acceptable by the Division of Bioequivalence on May 29, 1985 (letter to firm dated June 5, 1985). Sidmak's Bethanechol Chloride Tablets 5mg and 50mg are thus deemed bioequivalent to the respective strengths of Urecholine manufactured by MSD.</p> <p>Bethanechol Chloride Tablets 5mg and 50mg are rated "AA" (non-bio problem drug) and therefore do not require any in-vivo bioavailability testing.</p> <p>The firm has met all of the Division of Bioequivalence's requirements for this drug.</p> <p style="text-align: center;">APPEARS THIS WAY ON ORIGINAL</p> <p>Prepared by: J J Sturm HFN-230 Concur: Charles M. De 12-17-85</p>	NDA NUMBER 88-095, 88-096	
	IND NUMBER	
	TELECON/MEETING	
	INITIATED BY <input type="checkbox"/> APPLICANT/ SPONSOR <input checked="" type="checkbox"/> FDA	MADE <input type="checkbox"/> BY TELE- PHONE <input type="checkbox"/> IN PERSON
	PRODUCT NAME Bethanechol Chloride Tablets 5mg and 50mg	
FIRM NAME Sidmak Labs 17 West Street P.O. Box 371 East Hanover, NJ 07936		
NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD		
TELEPHONE NO.		
SIGNATURE	DIVISION	

**NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT**

NDA NUMBER 89-096

DATE APPROVAL LETTER ISSUED
DEC 19 1985

TO: Press Relations Staff (HF1-40)

FROM: Bureau of Drugs
 Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION

ORIGINAL NDA SUPPLEMENT TO NDA ABBREVIATED ORIGINAL NDA SUPPLEMENT TO ANDA

CATEGORY

HUMAN VETERINA

TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG

Bethanechol Chloride

DOSAGE FORM

Tablets

ORIGINAL ABBREVIATED

HOW DISPENSED

RX OTC

ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)

Bethanechol Chloride, 50 mg

**APPEARS THIS WAY
ON ORIGINAL**

NAME OF APPLICANT (Include City and State)

Sidmak Labs
East Hanover, New Jersey 07936

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

Parasympathomimetic

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME Maria Shih

DATE

FORM APPROVED BY

NAME Jack Meyer

DATE

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE
Nov. 19, 1985

I'm ready to approve
 S. Amak's 4 NDAs

{ 88-958 Procaminite
 88-959

{ 88-895 Belhanech
 88-096

firm is on alert list. ^{for at least 2 wks} called
 Seymour Fishman today.
 (compliance)

He said the firm is on alert list
 We can not approve the NDAs

**APPEARS THIS WAY
 ON ORIGINAL**

NDA NUMBER

IND NUMBER
88-096

TELECON/MEETING

INITIATED BY
 APPLICANT/
 SPONSOR
 FDA

MAD:
 BY TELE-
 PHONE
 IN PERSON

PRODUCT NAME

FIRM NAME

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD

TELEPHONE NO.
443-7273

SIGNATURE
Man Stiel

DIVISION
Genetic



Memorandum

Date 4/4/85
From Director HFN-230
Division of Generic Drugs

Wm
DS

Subject

To Division of Bioequivalence (HFN-227)

PAPER NDA/ANDA/IND #: 89-096

COMPANY NAME: Sidmak Laboratories, Inc.

NAME OF DRUG: Bethanechol Chloride Tablets,
50mg.

Please review the dissolution data on the above drug.

Thank you,
Marvin Seife
Marvin Seife, M.D.

507

APPEARS THIS WAY
ON ORIGINAL



DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

shh

TO : Manufacturing Review Branch (HFN-322)
Division of Drug Quality Compliance

DATE: 1-3-84

FROM : Division of Generic Drugs
Requester's Name David Rosen PHONE: 443-4080

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 89-095 (5 mg); 89-096 (50 mg)

DRUG TRADE MARK (if any) _____

DRUG NONPROPRIETARY NAME: Bethanechloride Chloride Tablets USP

DOSAGE FORM AND STRENGTH(S): TCM

DRUG CLASSIFICATION: _____ PROFILE CLASS CODE: _____
(Priority) A or B 1C Other

APPLICANT'S NAME: Sidmak Laboratories, Inc.

ADDRESS: 17 West Street P.O. Box 371 East Hanover, NJ 07936

FACILITIES TO BE EVALUATED: (Name, Full Address, DMF# (if any), and Responsibility)

1. applicant _____

2. _____ DMF

3. _____

Comments: () See Attached.
() Actual on-site inspection requested.

Reason: _____

FOR HFN-322 USE ONLY:

Request Rec'd: _____ Inspection Requested: _____
(if applicable)

Firm(s) are in Compliance With GMPs: Approvable

Basis for Decision: GMPs of Firms Acceptable

Reviewing CSO: FF7 130-85 Concurrence: [Signature]

cc: HFN-_____
HFN-_____
HFN-322



(NBW)

on

12/19

Memorandum

D/11

Date

1/8/85

S/12/20

WM
DS

From

Director HFN-230
Division of Generic Drugs

Subject

To

Division of Bioequivalence (HFN-227)

~~PAPER NDA/ANDA/IND #:~~ 89-096

COMPANY NAME:

Sidmak Laboratories, Inc.

NAME OF DRUG:

Bethanechol Chloride Tablets, 50mg

Please review the dissolution data on the above drug.

Thank you,

Marvin Seife
Marvin Seife, M.D.

APPEARS THIS WAY
ON ORIGINAL

Instructions for Completing SF Software Survey

01. **Date Survey Prepared:** Indicate in YYYMM format
02. **Date Survey Completed or Last Updated:** Indicate in YYYMM format
03. **Agency Code:** Insert organization code from Appendix A of latest version of OCS Circular A-11
04. **Software Type:**
 - 1-individual program
 - 2-automated data system (assembly of computer programs)
05. **Type of Submission:**
 - 1-initial
 - 2-revision
 - 3-deletion
06. **Software Function:** Classify software in one of the following categories:

1-keyboard support/utility applications	1-data/file handlers
2-management/business applications	2-bibliographic applications
3-scientific applications	3-other (specify category)
07. **Software Identification:** Submitting agency's identification number or code for software. If none assigned, indicate none.
08. **Title:** Software title should be made as descriptive as possible.
09. **Acronym:** Commonly used abbreviation identifying software. (optional)
10. **Organization:** Identify organization responsible for software as completely as possible, including Agency (Department), Office, Service, Bureau, Corporation, Commission, or Council.
11. **Address:** Complete mailing address for responsible organization including building name, street address, city, state, and ZIP code. Include rail stop number if applicable.
12. **Technical Contact(s):** Name of person(s) to be contacted for technical information. Provide organization name and mailing address if different from those indicated in items 10 and 11.
13. **Telephone number(s):** Telephone number of technical contact(s). Provide area code, seven-digit commercial number, and extension.
14. **Computer Manufacturer and Model:** Identify mainframe computer on which software is operational. Use manufacturer, model, and abbreviations and codes provided in OCS Circular A-11.
15. **Computer Memory Requirements:** Maximum memory required to execute software other than that required for operating system. Specify bytes or words and numbers of bits per word.
16. **Computer Operating System:** Name, version, and release under which software is operating. Identify any operating system enhancements.
17. **Tape Drives:** Identify number needed to operate software. Specify, if critical, additional requirements such as manufacturer, model, recording density, number of tracks, etc.
18. **Disk/Drum Units:** Identify number needed to operate software. Specify manufacturer, model, etc., where critical.
19. **Keyboard Terminals:** Identify number of keyboard terminals used for inquiry and response, and/or remote operations. Specify manufacturer and model.
20. **Programming Language(s):** Identify programming language(s) used to generate software (include versions) e.g., MSB, COBOL, FORTRAN IV, SIMSCRIPT II.5.
21. **Other Operational Requirements:** Identify other peripheral devices, support software, or related equipment used, but not indicated above, e.g., optical character readers, facsimile, computer-output-microfilm, graphic plotters.
22. **Narrative:** Describe concisely what the software functionally accomplishes, its design characteristics, specific areas of application, relationship to other software, and other significant features.
23. **Keywords:** List significant words or phrases which reflect the functions, applications, and features of the software. Separate entries with semicolons.
24. **Status:** Enter code best describing software status:

1-planned	4-post operational
2-under development	5-other (explain in narrative)
3-operational	
25. **Software Availability:**

1-available	3-classified
2-proprietary	4-other (explain in narrative)
26. **Documentation:**

1-available
2-in preparation
3-unavailable

* In this draft, elements are numbered in groups for identification purposes. In the final form, elements will be numbered sequentially.

[FR Doc.73-18071 Filed 8-27-73; 8:45 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

(DESI 6536 Docket No. FDC-D-307; NDA 6-536)

BETHANECHOL CHLORIDE

Drugs for Human Use; Drug Efficacy Study Implementation; Followup Notice

In a notice (DESI 6536) published in the FEDERAL REGISTER of May 22, 1971 (36 FR 9341), the Commissioner of Food and Drugs announced his conclu-

sions pursuant to the evaluation of reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following drugs:

NDA 6-536; Urecholine Chloride Tablets and Injection containing bethanechol chloride; Merck Sharp & Dohme, Division of Merck and Co., Inc., West Point, PA 19486.

All identical, related, or similar products, not the subject of an approved new drug application, are covered by the new drug application(s) reviewed and are

subject to this notice. See 21 CFR 130. (37 FR 23185, Oct. 31, 1972). Any person who wishes to determine whether a specific product is covered by this notice should write to the Food and Drug Administration, Bureau of Drugs, Office of Compliance (BD-300), 5600 Fisher Lane, Rockville, MD 20852.

The notice stated that bethanechol injection was deemed effective for certain indications and the tablets probably effective for these indications and that the other labeled indications were possibly effective and lacking substantial evidence of effectiveness. The possible effective indications have been reclassified as lacking substantial evidence of effectiveness in that no new evidence of effectiveness has been received pursuant to the notice.

Based upon reevaluation of available information, the indications previously considered as probably effective are now regarded as effective. Also, the requirement that bioavailability data be submitted has been deferred and abbreviated rather than full new drug applications and supplements may be submitted.

Accordingly, the previous announcement is amended to read as follows:

A. Effectiveness classification.—The Food and Drug Administration has considered the Academy's reports, as well as other available evidence, and concludes that:

1. Bethanechol chloride injection and tablets are effective for treatment of acute postoperative and postpartum non-obstructive (functional) urinary retention and for neurogenic atony of the urinary bladder with retention.

2. These drugs lack substantial evidence of effectiveness for all their other labeled indications.

B. Conditions for approval and marketing.—The Food and Drug Administration is prepared to approve abbreviated new drug applications and abbreviated supplements to previously approved new drug applications under conditions described herein.

1. **Form of drug.**—These preparations are in sterile aqueous solution or tablet form suitable for subcutaneous or oral administration, respectively.

2. **Labeling conditions.**—a. The labels bear the statement, "Caution: Federal law prohibits dispensing without prescription."

b. The drugs are labeled to comply with all requirements of the Act and regulations, and the labeling bears adequate information for safe and effective use of the drug(s). The "Indications" are as follows:

INDICATIONS

For the treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention and for neurogenic atony of the urinary bladder with retention.

3. **Marketing status.**—Marketing of such drugs may be continued under the conditions described in the notice entitled *Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study*, published in the FEDERAL REGISTER July 14, 1970 (35 FR 11373), as follows:

NOTICES

For holders of "deemed approved" new drug applications (i.e., an application which became effective on the basis of safety prior to October 10, 1962), the submission of a supplement for revised labeling and an abbreviated supplement for updating information as described in paragraphs (a)(1)(i) and (iii) of the notice of July 14, 1970.

b. For any person who does not hold an approved or effective new drug application, the submission of an abbreviated new drug application as described in paragraph (a)(3)(i) of that notice.

c. For any distributor of the drug, the use of labeling in ~~accord~~ with this announcement for any such drug shipped within the jurisdiction of the Act as described in paragraph (b) of that notice.

C. Notice of opportunity for a hearing.—Notice is given to the holder(s) of the new drug application(s) and to any other interested person that the Commissioner proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355 (e)) withdrawing approval of the listed new drug application(s) and all amendments and supplements thereto providing for indications lacking substantial evidence of effectiveness referred to in paragraph A.2. of this notice on the grounds that new information before him with respect to the drug(s), evaluated together with the evidence available to him at the time of approval of the application(s), shows there is a lack of substantial evidence that the drug(s) will have all the effects purported or represented to have under the conditions of use prescribed, recommended, or suggested in the labeling. An order withdrawing approval will not issue with respect to any application(s) supplemented, in accord with this notice, to delete the claim(s) lacking substantial evidence of effectiveness.

Any manufacturer or distributor of such an identical, related, or similar product is an interested person who may in response to his notice submit data and information, request that the new drug application(s) not be withdrawn, request a hearing, and participate as a party in any hearing.

In accordance with the provisions of section 505 of the Act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Part 130), the Commissioner hereby gives the applicant(s) and any other interested person an opportunity for a hearing to show why approval of the new drug application(s) providing for the claim(s) involved should not be withdrawn.

On or before September 27, 1973 the applicant(s) and any other interested person may file with the Hearing Clerk, Food and Drug Administration, Room 6-86, 5600 Fishers Lane, Rockville, Maryland 20852, a written appearance electing whether or not to avail himself of the opportunity for a hearing. Failure of an applicant or any other interested person to file a written appearance of election within the specified time will constitute an election by him not to avail himself of the opportunity for a

hearing. No extension of time may be granted.

If no person elects to avail himself of the opportunity for a hearing, the Commissioner without further notice will enter a final order withdrawing approval of the application(s) which have not been supplemented to delete the indication(s) lacking substantial evidence of effectiveness.

If an applicant or any other interested person elects to avail himself of the opportunity for a hearing, he must file, on or before September 27, 1973, a written appearance requesting the hearing, giving the reasons why approval of the new drug application(s) should not be withdrawn, together with a well-organized and full-factual analysis of the clinical and other investigational data he is prepared to prove in support of his opposition. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing (21 CFR 130.14(b)).

If review of the data submitted by an applicant or any other interested person warrants the conclusion that there exists substantial evidence demonstrating the effectiveness of the product(s) for the labeling claim(s) involved, the Commissioner will rescind this notice of opportunity for hearing.

If review of the data in the application(s) and data submitted by the applicant(s) or any other interested person in a request for a hearing, together with the reasoning and factual analysis in a request for a hearing, warrants the conclusion that no genuine and substantial issue of fact precludes the withdrawal of approval of the application(s), the Commissioner will enter an order making findings and conclusions on such data and withdrawing approval of application(s) not supplemented to delete the claim(s) involved.

If, upon the request of the new drug applicant(s) or any other interested person, a hearing is justified, the issues will be defined, a hearing examiner will be named, and he shall issue, as soon as practicable after September 27, 1973, a written notice of the time and place at which the hearing will commence. All persons interested in identical, related, or similar products covered by the new drug application(s) will be afforded an opportunity to appear at the hearing, file briefs, present evidence, cross-examine witnesses, submit suggested findings of fact, and otherwise participate as a party. The hearing contemplated by this notice will be open to the public except that any portion of the hearing that concerns a method or process the Commissioner finds entitled to protection as a trade secret will not be open to the public, unless the respondent specifies otherwise in his appearance.

Communications forwarded in response to this notice should be identified with the reference number DESI 6536, directed to the attention of the appropriate office listed below, and addressed

to the Food and Drug Administration: 5600 Fishers Lane, Rockville, MD 20852

Supplements (Identify with NDA number, Office of Scientific Evaluation (BD-10), Bureau of Drugs.

Original abbreviated new drug application (Identify as such):

Generic Drug Staff (BD-60), Bureau of Drugs.

Requests for the Academy's report: Drug Efficacy Study Information Cont (BD-66), Bureau of Drugs.

Request for Hearing (Identify with doct number):

Hearing Clerk, (CC-20), Room 6-86, Pat Lawn Building.

All other communications regarding announcement:

Drug Efficacy Study Implementation Project Manager (BD-101), Bureau of Drugs.

Received requests for a hearing may be seen in the office of the Hearing Clerk (address given above) during regular business hours, Monday through Friday.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (Sec. 502, 505, 512, 517, 1050-53, as amended; 21 U.S.C. 352, 355 and the Administrative Procedure Act (5 U.S.C. 554), and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated August 21, 1973.

SAM D. FINE,
Associate Commissioner
for Compliance

[FR Doc.73-18152 Filed 8-27-73; 8:45 am]

[DESI 5773 Docket No. FDC-D-642; NDA 15-773]

HOLLAND-RANTOS CO., INC.

Nylmerate Jelly; Notice of Opportunity for a Hearing on Proposal to Withdraw Approval of New Drug Application

In a notice (DESI 5773) published in the FEDERAL REGISTER of July 27, 1973 (37 FR 15030) the Commissioner of Food and Drugs announced his conclusion pursuant to the evaluation of a report received from the National Academy of Sciences-National Research Council Drug Efficacy Study Group, on the drug described below stating that the drug was regarded as possibly effective and lacking substantial evidence of effectiveness for the various labeled indications. The possibly effective indications have been reclassified as lacking substantial evidence of effectiveness in that no data have been submitted pursuant to this notice.

Nylmerate Jelly containing no oxynol 9 (previously listed as polyoxyethylenononylphenol), phenylmercuric acetate, and boric acid; marketed by Holland-Rantos Co., Inc., Enterprise Avenue, Trenton, N.J. 08638 (DESI 5-773).

Therefore, notice is given to the holder(s) of the new drug application(s) and to any other interested person that the Commissioner proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)) withdrawing approval

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-096

CORRESPONDENCE

ANDA 89-096

NOV 4 1985

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
Post Office Box 371
East Hanover, New Jersey 07936

Dear Dr. Patel:

Please refer to your abbreviated new drug application submitted pursuant to Section 505 of the Federal Food, Drug, and Cosmetic Act for Bethanechol Chloride Tablets USP, 50 mg.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

Your certification statement which pertains to Current Good Manufacturing Practices does not agree with an establishment inspection of your firm, March - April, 1985. When the problem is resolved, you will be notified.

The file is now closed. You are required to take one of the actions described at 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

Marvin Seife FOR

11-4-85

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

NWK-DO
HFN-83
HFN-230
JMeyer/MShih
R/D INITIALED BY: JMeyer/MSeife
D Utz: 11-1-85 (1048R)
NOT APPROVABLE

MS - 11/1/85

JMeyer 11/1/85

NDA 89-096

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
Post Office Box 371
East Hanover, New Jersey 07936

SEP 16 1985

Dear Dr. Patel:

Please refer to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Bethanechol Chloride Tablets USP, 50 mg.

Reference is also made to your communication dated August 16, 1985.

The application is deficient and therefore not approvable under Section 505(j)(3) of the Act for the following reasons:

Your samples for bulk material and finished dosage form are currently being validated by our district laboratories. We will correspond with you when the evaluation becomes available.

The file is now closed. You are required to take an action described under Section 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our conclusions for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

Kent C Johnson FOR

9-16-85

Harvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

NMK-DO
HFN-83
HFN-230

RB
9/12/85
RBrown/JMeyer/MShin
R/D INITIALED BY: JMeyer/MSeife
D Utz: 9-11-85 (0815R)
NOT APPROVABLE

MJ 9/13/85

JMeyer 9/13/85



17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

Orig

NDA 89-096

August 16, 1985

RESUBMISSION

NDA ORIG AMENDMENT

Marvin Seife, M.D.
Director
Division of Generic Drugs
Center for Drugs and Biologics
Room 16-70 (HFN-230)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

FPL

*FPL packet
insert label
and contain
labels sent
factory.
R.E. Bro
8/26/85*

Re: Bethanechol Chloride Tablets, 50 mg. NDA 89-096

Dear Dr. Seife:

Reference is made to your communication dated July 26, 1985 concerning the above referenced unapproved application. (Copy enclosed).

We are herewith submitting twelve copies of our revised printed labeling, revised as per your recommendations. However, we did not include our National Drug Code since our insert is also used for our private label customers.

Also enclosed are the revised test procedures and specifications for the dosage form with the test results for the lot to be submitted to your laboratory for evaluation. Three extra copies are also provided.

Thank you for your time and consideration in this matter.
Sincerely,

SIDMAK LABORATORIES, INC.

[Signature]
Satish P. Patèl, Ph.D.
President

RECEIVED

enc.

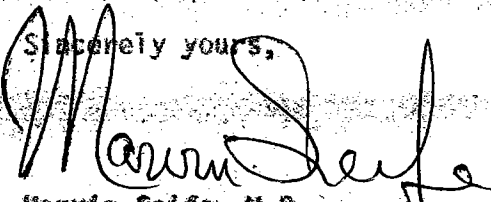
AUG 20 1985

SPP/G. Morrissey

GENERIC DRUGS

- 2. Submit three extra copies of the revised test procedures and specifications for the dosage form with the test results for the lot to be submitted to our laboratory for evaluation. All laboratory methods should be described in sufficient detail to permit their duplication in our laboratory.

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our conclusions for not approving this application, you may request an opportunity for a hearing.


Sincerely yours,


7/26/85

Marvin Seife, M.D.
 Director
 Division of Generic Drugs
 Office of Drug Standards
 Center for Drugs and Biologics

NWK-DO

HFN-83
 HFN-230
 RBrown/JMeyer/MShih
 R/D INITIALED BY: JMeyer/MSeife
 D Utz: 7-23-85 (0589R)
 NOT APPROVABLE


 JMeyer 7/25/85



17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

Drug

MAH US 7/22/85

*SOS J 2A
information
acceptable
DUL 12-17-85*

NDA 89-096

JUL 11 1985

ORIG NEW CORRES

Marvin Seife, M.D.
Director
Division of Generic Drugs
Center for Drugs and Biologics
Room 16-70 (HFN-230)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: Bethanechol Chloride Tablets, 50 mg. NDA 89-096

Dear Dr. Seife:

We are herewith amending the above referenced application to provide for the inclusion of the information required under the "Drug Price Competition and Patent Term Restoration Act of 1984.

Thank you for your time and consideration in this matter.

Sincerely,

SIDMAK LABORATORIES, INC.

Satish P. Patel, Ph.D.
President

enc.

gm

RECEIVED

JUL 12 1985

GENERIC DRUGS





17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

NDA 89-096

June 14, 1985

RESUBMISSION

NDA ORIG AMENDMENT

DRAFT LABELING

Marvin Seife, M.D.
Director
Division of Generic Drugs
Center for Drugs and Biologics
Room 16-70 (HFN-230)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: Bethanechol Chloride Tablets, 50 mg. NDA 89-096

Dear Dr. Seife:

Reference is made to your communication dated March 26, 1985 (copy attached) concerning the above unapproved abbreviated new drug application.

We would like to respond in the following manner:

In response to:

Comment 1 - We have revised the container labels according to your recommendations and will submit final printed labels when available. We are submitting draft copy of the package insert revised according to the latest revision (7/84) from the full NDA holder. (See Exhibit A).

Comment 2 - An amendment providing for the inclusion of three months stability data at both normal and challenge conditions, proposing a 24 month expiration period, was submitted March 29, 1985. (See Exhibit B for Sampling Procedures).

Comment 3 - Characteristics and test methods for the container/closure system. (See Exhibit C).



NDA 89-096

June 14, 1985

We believe that this amendment, and the subsequent submission of final printed labeling, represents the information necessary to remove the deficiencies that you have outlined and we look forward to a prompt review and comment.

Thank you for your time and consideration in this matter.

Sincerely,

SIDMAK LABORATORIES, INC.



Satish P. Patel. Ph.D.
President

enc.

SPP/gm

RECEIVED
JUN 18 1985
GENERIC DRUGS



NDA 89-096

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
Post Office Box 371
East Hanover, New Jersey 07936

MAR 26 1985

Gentlemen:

Please refer to your abbreviated new drug application dated December 19, 1984, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for the preparation Bethanechol Chloride Tablets, USP, 50 mg.

The application is deficient and therefore not approvable under Section 505(j)(3) of the Act as follows:

1. It fails to include the correct labeling information. In this regard:

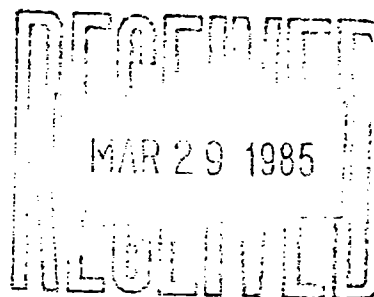
Container: Not Satisfactory

- (a) TITLE - should be that of the USP article
BETHANECHOL CHLORIDE
TABLETS, USP
- (b) Controlled Room Temperature - 15^o-30^oC
(59^o-86^oF)

Insert: Not Satisfactory

- (a) For consistency, the chemical name should be the second name listed in the USP Monograph.
- (b) Revise package insert labeling in accord with latest revision (7/84) of the package insert from the full NDA holder.

- A. Revise container labels, then prepare and submit Final Printed Labeling.
- B. Revise package insert labeling, then submit draft copy for our review and comment.



2. It fails to submit adequate stability information. In this regard:

- A. Your intent with respect to the expiration dating: We are unable to reach any conclusion based on the limited data submitted. It is recommended that data be obtained for production lots at challenge conditions, to justify the proposed expiration dating prior to approval.
- B. Sampling procedures
- C. The report format:

The report format should include information on the drug product under test that specifies:

- a. Name and Potency
- b. Formulation
- c. Lot/Batch Number
- d. Manufacturing procedure (e.g., research, pilot or production batch).
- e. Container/closure system
- f. Storage conditions (e.g. temperature, humidity, light).
- g. Mode of storage (e.g. liquids and creams should be stored such that the drug product is in contact with the closure).
- h. A continuous tabulation of data generated at the desired test stations.
- i. Data should include an assay (stability indicating) and such criteria as appearance, microbial testing, viscosity, and dissolution were applicable.

3. It fails to include a satisfactory description of containers and materials used for packaging and adequate information with respect to the characteristics of, and test methods employed for, the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

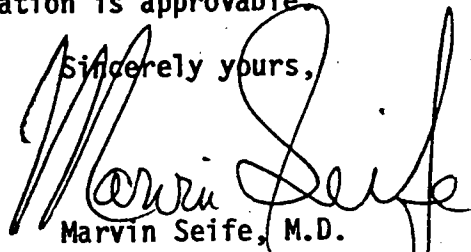
In this regard:

- a. Description of desiccant (if appropriate)
- b. Compatibility
- c. Sampling
- d. Acceptance specifications

The file is now closed. If you wish to reopen it, the submission should be in the form of an amendment to this application, adequately organized, which represents the information necessary to remove all deficiencies we have outlined.

If you do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.110(d). If you do so, the application shall be re-evaluated and within 90 days of the date of receipt of such request (or additional period as we may agree upon), the application shall be approved or you shall be given a written notice of opportunity for a hearing on the question of whether the application is approvable.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Marvin Seife". The signature is written in black ink and is positioned above the typed name and title.

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

MSL
NDA 89-095
89-096

JUN 5 1985

Sidmak Laboratories, Inc.
Attention: Satish P. Patel
17 West Street
East Hanover, NJ 07936

Gentlemen:

Reference is made to the dissolution data you submitted on March 29, 1985 for Bethanechol Chloride Tablets, 5 mg and 50 mg.

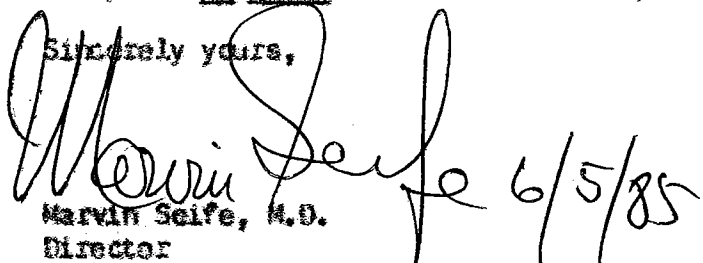
The data have been reviewed by our Division of Bioequivalence and they have the following comments:

1. The dissolution testing conducted by Sidmak Laboratories on its Bethanechol Chloride 5 mg tablets, Lot #84-181T and 50 mg tablets, Lot #84-182T, is acceptable.
2. The dissolution testing should be incorporated into your manufacturing controls and stability program. The dissolution testing should be conducted in 900 ml of 0.1N HCl at 37°C using USP XXI apparatus II (paddle) at 50 rpm. The test product should meet the following specification:

Not less than 80% of the labeled amount of the drug in the dosage form is dissolved in 30 minutes.

3. From the Bioequivalence point of view, the firm has met the requirement of bioavailability and in-vitro dissolution testing."

Sincerely yours,


Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

cc: NWK-DO
HFN-230
SHIH *js*
MSEIFE/JSTURM/jt/6-3-85
BIO LETTER 0587A

NDA 89-096

JUN 11 1985

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
Post Office Box 371
East Hanover, New Jersey 07936

Gentlemen:

Please refer to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for the preparation Bethanechol Chloride Tablets USP, 50 mg.

Reference is also made to your two communications dated March 29, 1985 and our letter dated March 26, 1985.

The application is deficient and therefore not approvable under Section 505(j)(3) of the Act as follows:

1. Please reply to our letter referenced above.
2. Your bioavailability study is currently under review by our Division of Bioequivalence. We will correspond with you when the evaluation becomes available.

The file is now closed. If you wish to reopen it, the submission should be in the form of an amendment to this application, adequately organized, which represents the information necessary to remove all deficiencies we have outlined.

If you do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.110(d). If you do so, the application shall be re-evaluated and within 90 days of the date of receipt of such request (or additional period as we may agree upon), the application shall be approved or you shall be given a written notice of opportunity for a hearing on the question of whether the application is approvable.

Sincerely yours,

NWK-DO

HFN-83

HFN-230

JMeyer/MShih

R/D INITIALED BY: JMeyer/MSeife

D Utz: 6-5-85 (0330R)

NOT APPROVABLE

JMeyer 6/10/85

MS - 6/10/85
Marvin Seife, M.D.

Director

Division of Generic Drugs

Office of Drug Standards

Center for Drugs and Biologics



17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

Drug

NDA m/c 4/15/85

NDA 89-096

March 29, 1985

ORIG NEW CORRES

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics
Room 16-70 (HFN-530)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

BIOAVAILABILITY MATERIAL

Re: Bethanechol Chloride Tablets, 50 mg. NDA 89-096

Dear Dr. Seife:

We are herewith amending the above referenced unapproved abbreviated new drug application with the inclusion of comparative dissolution testing conducted according to comments in your communication dated February 21, 1985.

We believe that the dissolution testing and data meet the criteria as outlined in your letter and we look forward to a prompt review and comment.

Thank you for your time and consideration in this matter.

Sincerely,

SIDMAK LABORATORIES, INC.

Satish P. Patel
President

SP/gm

Enc.

RECEIVED
APR 2 1985

GENERIC DRUGS



17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

Handwritten signature

NDA mfg 4/5/85

NDA 89-096

RESUBMISSION

March 29, 1985

NDA ORIG AMENDMENT

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics
Room 16-70 (HFN-530)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: Bethanechol Chloride Tablets, 50 mg. NDA 89-096

Dear Dr. Seife:

We are herewith amending our abbreviated, unapproved New Drug Application for the above referenced product to provide for the inclusion of three months stability data at both normal and challenge conditions.

We are also amending the application with the inclusion of a spec sheet for _____
At the time of submission, a spec sheet for _____
was inadvertently included in Section 11
as a packaging component, whereas we are actually using _____

Stability testing was conducted on the product in the same container/closure system and sizes in which the drug will be marketed.

We propose a 24 month expiration period for the product based on the results of the stability study.



NDS 89-096

March 29, 1985

We believe that the inclusion of the data herein completes our Abbreviated New Drug Application and we look forward to a prompt review and comment.

Thank you for your time and consideration in this matter.

Sincerely,

SIDMAK LABORATORIES, INC.

Geraldine Morrissey

Geraldine Morrissey
Regulatory Associate

Enc.
gm

APR 2 1985
GENERIC DRUGS

NDA 89-096

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
Post Office Box 371
East Hanover, New Jersey 07936

MAR 26 1985

Gentlemen:

Please refer to your abbreviated new drug application dated December 19, 1984, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for the preparation Bethanechol Chloride Tablets, USP, 50 mg.

The application is deficient and therefore not approvable under Section 505(j)(3) of the Act as follows:

1. It fails to include the correct labeling information. In this regard:

Container: Not Satisfactory

- (a) TITLE - should be that of the USP article
BETHANECHOL CHLORIDE
TABLETS, USP
- (b) Controlled Room Temperature - 15°-30°C
(59°-86°F)

Insert: Not Satisfactory

- (a) For consistency, the chemical name should be the second name listed in the USP Monograph.
- (b) Revise package insert labeling in accord with latest revision (7/84) of the package insert from the full NDA holder.

- A. Revise container labels, then prepare and submit Final Printed Labeling.
- B. Revise package insert labeling, then submit draft copy for our review and comment.

APPEARS THIS WAY
ON ORIGINAL

2. It fails to submit adequate stability information. In this regard:

A. Your intent with respect to the expiration dating: We are unable to reach any conclusion based on the limited data submitted. It is recommended that data be obtained for production lots at challenge conditions, to justify the proposed expiration dating prior to approval.

B. Sampling procedures

C. The report format:

The report format should include information on the drug product under test that specifies:

- a. Name and Potency
- b. Formulation
- c. Lot/Batch Number
- d. Manufacturing procedure (e.g., research, pilot or production batch).
- e. Container/closure system
- f. Storage conditions (e.g. temperature, humidity, light).
- g. Mode of storage (e.g. liquids and creams should be stored such that the drug product is in contact with the closure).
- h. A continuous tabulation of data generated at the desired test stations.
- i. Data should include an assay (stability indicating) and such criteria as appearance, microbial testing, viscosity, and dissolution were applicable.

3. It fails to include a satisfactory description of containers and materials used for packaging and adequate information with respect to the characteristics of, and test methods employed for, the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

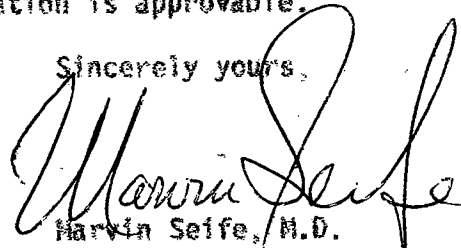
In this regard:

- a. Description of desiccant (if appropriate)
- b. Compatibility
- c. Sampling
- d. Acceptance specifications

The file is now closed. If you wish to reopen it, the submission should be in the form of an amendment to this application, adequately organized, which represents the information necessary to remove all deficiencies we have outlined.

If you do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.110(d). If you do so, the application shall be re-evaluated and within 90 days of the date of receipt of such request (or additional period as we may agree upon), the application shall be approved or you shall be given a written notice of opportunity for a hearing on the question of whether the application is approvable.

Sincerely yours,

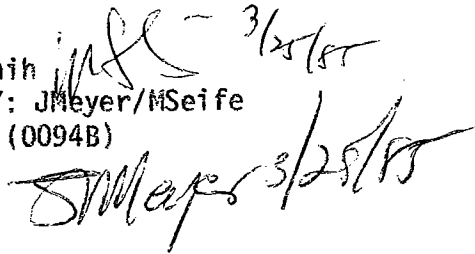


3/26/85

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

NWK-DO
HFN-83
HFN-230

TPoux/JMeyer/MShih
R/D INITIALED BY: JMeyer/MSeife
D Utz: 3-22-85 (0094B)
NOT APPROVABLE



3/25/85
3/25/85

7

NDA 89-095

89-096

FEB 21 1985

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
Post Office Box 371
East Hanover, New Jersey 07936

Gentlemen:

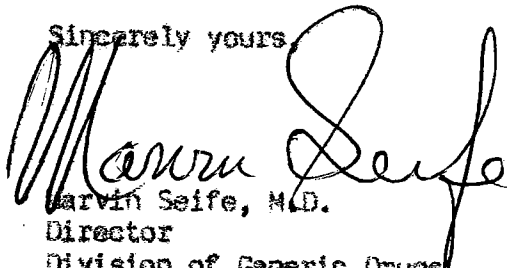
Reference is made to the dissolution data you submitted on December 19, 1984 for Bethanechol Chloride Tablets, USP, 5 mg and 50 mg.

The data have been reviewed by our Division of Bioequivalence and they have the following comments:

"The dissolution testing conducted by Sidmak Laboratories on Bethanechol Chloride 5 mg and 50 mg tablets is unacceptable. The firm should be advised to conduct comparative dissolution testing employing USP Apparatus II at 50 rpm in 900 ml 0.1N HCl with 12 units from both test products and reference products at each strength. The test products should meet the following specification:

Not less than 80% of the labeled amount of the drug in the dosage form is dissolved in 30 minutes."

Sincerely yours,



Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

2/21/85

cc:

NWK-DO

HFN-230

HFN-227

MSeife/BPollock/gp/2/20/85

9099A

B Pollock
2/21/85

JAN 8 1985

NDA 89-096

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
P.O. Box 371
East Hanover, NJ 07936

Gentlemen:

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

NAME OF DRUG: Bethanechol Chloride Tablets USP, 50 mg

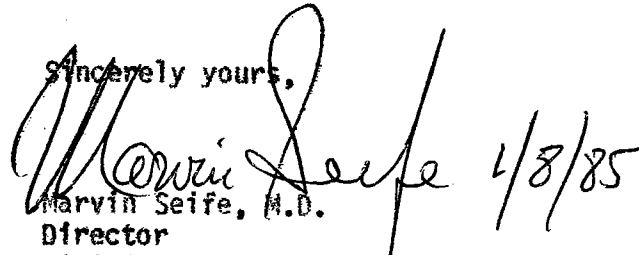
DATE OF APPLICATION: December 19, 1984

DATE OF RECEIPT: December 20, 1984

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

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

Sincerely yours,

 4/8/85

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

NWK-DO DUP HFN-230
JLMeyer/mlb/1-3-85
Ack
(1471A)

JMS 1-3-85
JLMeyer 1/7/85



17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

December 19, 1984

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics
Room 16-70 (HFN-530)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

ABBREVIATED
NEW DRUG APPLICATION

89-096

Product: Bethanechol Chloride Tablets, USP 50 mg.
Re: Abbreviated New Drug Application

Dear Dr. Seife:

Pursuant to Section 505 (b) of the Federal Food, Drug and Cosmetic Act, we are herewith submitting in triplicate an Abbreviated New Drug Application for the above referenced product.

Included in the submission are:

1. Form 356H
2. Volume No. 1 - Copy No. 1 (Blue folder)
3. Volume No. 1 - Copy No. 2 (Red folder)
4. Volume No. 1 - Copy No. 3 (Yellow folder)

Also included with this application are three additional copies of the analytical method.

Respectfully submitted,

SIDMAK LABORATORIES, INC.

Satish P. Patel, Ph.D.
President

SPP/gm

Enclosures

RECEIVED

DEC 20 1984

GENERIC DRUGS

