CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

89-095

Generic Name: Bethanechol Chloride Tablets USP, 5mg

Sponsor: Sidmak Laboratories, Inc.

Approval Date: December 19, 1985

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-095

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-095

APPROVAL LETTER

ANDA 89-095

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, 5 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 FD-2253.

Sincerely yours,

12/19/85

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

NWK-DO
HFN-230
HFN-83
HFN-10
RBrown/JMeyer/MShih
R/D INITIALED BY: JMeyer/MSeife
D Utz: 12-17-85 (0139R)
APPROVAL

12/18/85

12/18/85

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-095

FINAL PRINTED LABELING

Labeling: ORIGINAL

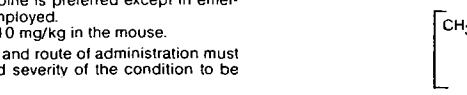
NDA No: 89-095 Rec'd: 8/20/85

Reviewed by: MLS 12/10/85

BETHANECHOL CHLORIDE TABLETS, USP

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 $C_7H_{17}ClN_2O_2$ and its structural formula is:



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 hydrolized 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.

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 repsonse that was more rapid in onset and of larger magnitude that an oral dose of 50 mg., 100 mg. or 200 mg. All the oral doses, however, had a longer duration of effect that 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 postpartum 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.

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 reponse. 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 proclude further usage. Subcutaneous injection of atropine is preferred except in emergencies when the intravenous route may be employed.

The oral LD_{50} of bethanechol chloride is 1510 mg/kg in the mouse.

DOSAGE 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

DEC 19 1985 APPROVED

DEC 19 1985 APPROVED MCS

Labeling: ORIGINAL

NDA No: 89-095 Rec'd. 8/20/85

Reviewed by: [signature] 12/10/85

APPROVED

NDC 50111-323-01

Bethanechol Chloride Tablets, USP 5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

100 Tablets

Sidmak® LABORATORIES, INC.

EACH TABLET CONTAINS: Bethanechol Chloride, USP ..... 5 mg.

Dispense in tight containers as defined in the USP.

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

USUAL DOSAGE: See package insert.

Control No.:

Exp. Date:

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

DEC 19 1985

APPROVED

NDC 50111-323-03

Bethanechol Chloride Tablets, USP 5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

1000 Tablets

Sidmak® LABORATORIES, INC.

5 mg.

EACH TABLET CONTAINS: Bethanechol Chloride, USP ..... 5 mg.

Dispense in tight containers as defined in the USP.

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

USUAL DOSAGE: See package insert.

Control No.:

Exp. Date:

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

DEC 19 1985

APPROVED

NDC 50111-323-03

Bethanechol Chloride Tablets, USP 5 mg.

CAUTION: Federal law prohibits dispensing without prescription.

1000 Tablets

Sidmak® LABORATORIES, INC.

5 mg.

EACH TABLET CONTAINS: Bethanechol Chloride, USP ..... 5 mg.

Dispense in tight containers as defined in the USP.

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

USUAL DOSAGE: See package insert.

Control No.:

Exp. Date:

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

DEC 19 1985

APPROVED

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-095

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 LD_{50} of bethanechol chloride is 1510 mg/kg in the mouse.

3. DOSAGE AND ADMINISTRATION

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

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

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 - 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.

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:

89-095

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW NDA 89-095

3. NAME AND ADDRESS OF APPLICANT
Sidmak Laboratories, Inc.
East Hanover, New Jersey 07936

6. NAME OF DRUG
Bethanechol Chloride

9. AMENDMENTS AND OTHER DATES
December 19, 1984

Original application

10. PHARMACOLOGICAL CATEGORY
Parasympathomimetic

11. HOW DISPENSED
Rx

12. RELATED IND/NDA/DMF(s)
89-095 (5 mg)
89-096 (50 mg)

13. DOSAGE FORM(s)
Tablets

14. POTENCY
5 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:
Maria Shih

DATE COMPLETED:
12/18/85

APPEARS THIS WAY
ON ORIGINAL

Redacted 3

Page(s) of trade secret and /or confidential commercial information

CHEMIST'S REVIEW NDA 89-095

3. NAME AND ADDRESS OF APPLICANT
Sidmak Laboratories, Inc.
East Hanover, New Jersey 07936

6. NAME OF DRUG
Bethanechol

8. SUPPLEMENT(s) PROVIDE(s) FOR:
Labeling revision

9. AMENDMENTS AND OTHER DATES:
August 16, 1985

10. PHARMACOLOGICAL CATEGORY
Parasympathomimetic

11. HOW DISPENSED
Rx

12. RELATED IND/NDA/DMF(s)
89-095 (5 mg)
89-096 (50 mg)

13. DOSAGE FORM(s)
Tablets

14. POTENCY
5 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
Not Approvable

19. REVIEWER:
Maria Shih

DATE COMPLETED:
9/11/85

APPEARS THIS WAY
ON ORIGINAL

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Page(s) of trade secret and /or confidential commercial information

CHEMIST'S REVIEW NDA 89-095

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
Parasympathomimetic

11. HOW DISPENSED
Rx

12. RELATED IND/NDA/DMF(s)
89-095 (5 mg)
89-096 (50 mg)

13. DOSAGE FORM(s)
Tablets

14. POTENCY
5 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:
Maria Shih

DATE COMPLETED:
Maria Shih 7/24/85

APPEARS THIS WAY
ON ORIGINAL

Redacted 3

Page(s) of trade secret and /or confidential commercial information

CHEMIST'S REVIEW NDA 89-095

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
Parasympathomimetic

11. HOW DISPENSED
Rx

12. RELATED IND/NDA/DMF(s)
89-095 (5 mg)
89-096 (50 mg)

13. DOSAGE FORM(s)
Tablets

14. POTENCY
5 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:
Maria Shih

DATE COMPLETED:
6/10/85

APPEARS THIS WAY
ON ORIGINAL

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Page(s) of trade secret and /or confidential commercial information

CHEMIST'S REVIEW
(If necessary, continue any item on 8" x 10½" paper. Key continuation to item by number.)

1. ORGANIZATION	2. NDA NUMBER
	89-095

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	7. NONPROPRIETARY NAME
Bethanechol Chloride	

8. SUPPLEMENT(S) PROVIDES FOR:

9. AMENDMENTS AND OTHER *(Reports, etc.)* DATES

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF(S)
Parasympathomimetic	☒ RX ☐ OTC	89-095 (5 mg) 89-096 (50 mg)

13. DOSAGE FORM (S)	14. POTENCY *(Iea)*
Tablets	5 mg

15. CHEMICAL NAME AND STRUCTURE

16. RECORDS AND REPORTS

CURRENT ☐ YES ☐ NO

REVIEWED ☐ YES ☐ 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	SIGNATURE	DATE COMPLETED
Maria Shih	MS	3/28/85

DISTRIBUTION ☐ ORIGINAL JACKET ☐ REVIEWER ☐ DIVISION FILE

FORM FDH 2266 (7/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

Redacted 2

Page(s) of trade secret and /or confidential commercial information

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-095

BIOEQUIVALENCE REVIEW(S)

2/08/85

Generic Name: Bethanechol Chloride

Trade Name: _____

Dosage: 5 mg + 50 mg Tablets

ANDA #: 89-095 + 89-096

Reviewer: AGNES T. Wu

Firm Name: Sidmak Laboratories

Firm Location: East Hanover, N.J. 079.

Submission Date: December 18, 1984

Wang #: 465C

REVIEW OF DISSOLUTION DATA

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

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~~ J.

Results

Time	Test Product Lot No 84-182T (50mg) Mean % Dissolved	Range, (CV)	Reference Product Lot No. 84-181T (5mg) Mean % Dissolved	Range, (CV)
		( )		( )
30 min	100.1	1.7 ( )	101.8	2.1 ( )
		( )		( )
		( )		( )
		( )		( )
		( )		( )
		( )		( )
		( )		( )

APPEARS THIS WAY
ON ORIGINAL

Composition:

	mg/tablet	
	5 mg	50 mg
Bethanechol Chloride, USP	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
total:	320.0	490.0

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 [redacted] monitoring at [redacted] 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% dissolutin 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 Ise

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

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-095

ADMINISTRATIVE DOCUMENTS

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 89-095

DATE APPROVAL LETTER ISSUED: DEC 19 1985

TO: Press Relations Staff (HFI-40)

FROM:
- [XX] 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
- [XX] ABBREVIATED ORIGINAL NDA
- [ ] SUPPLEMENT TO ANDA

CATEGORY
- [XX] 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
- [XX] 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 5 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, 1987

NDA NUMBER:

IND NUMBER: 88-095

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☐ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME:

FIRM NAME:

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:

TELEPHONE NO.: 443-7273

I'm ready to approve Sidmak's 4 NDA's

88-958, 88-959 Procainamide

88-095, 88-096 Belladonna

Firm is on allert list. (at least 2 wks) called Seymour Fishman today. (compliance)

He said the firm is on allert list

We can not approve the NDA's

APPEARS THIS WAY ON ORIGINAL

SIGNATURE: Alan Stein

DIVISION: Generic

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 12/17/85

NDA NUMBER: 88-095, 88-096

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☒ FDA

MADE: ☐ BY TELEPHONE ☐ 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.

To File:

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.

Bethanechol Chloride Tablets 5mg and 50mg are rated "AA" (non-bioproblem drug) and therefore do not require any in-vivo bioavailability testing.

The firm has met all of the Division of Bioequivalence's requirements for this drug.

APPEARS THIS WAY
ON ORIGINAL

Prepared by: J J Sturm HFN-230
Concur: Charles M Do 12-17-85

SIGNATURE

DIVISION

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

Redacted

Page(s) of trade secret and /or confidential commercial information

3/29/85

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

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 #: 89-095

COMPANY NAME: Sidmak Laboratories, Inc.

NAME OF DRUG: Bethanechol Chloride Tablets, 5mg

Please review the dissolution data on the above drug.

Thank you,

Marvin Seife

Marvin Seife, M.D.

506

DEPARTMENT OF HEALTH & HUMAN SERVICES

shh

Memorandum

TO :Manufacturing Review Branch (HFN-322) DATE: 1-3-84
:Division of Drug Quality Compliance

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: FRF 1-30-85 Concurrance: _____

cc: HFN-____
HFN-____
HFN-322

FORM FDA 3274 (1/83)

DEPARTMENT OF HEALTH & HUMAN SERVICES (NEW) one

Public Health Service

12/19

5/12/20

Memorandum

Date: 1/8/85

From: Director HFN-230
Division of Generic Drugs

Wm DS

Subject

To Division of Bioequivalence (HFN-227)

~~PAPER NDA~~/ANDA/~~IND~~ #: 89-095

COMPANY NAME: Sidmak Laboratories, Inc.

NAME OF DRUG: Bethanechol Chloride Tablets, 5 mg.

Please review the dissolution data on the above drug.

Thank you.

Marvin Seife, M.D.

APPEARS THIS WAY
ON ORIGINAL

Instructions for Completing SF ___, Software Summary *

01. Date Summary Prepared: Indicate in YYMMDD format

02. Date Summary Completed or Last Updated: Indicate in YYMMDD format

03. Agency Code: Insert organization code from Appendix A of latest version of OMB 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:
A=System support/utility applications
B=Management/business applications
C=Scientific applications
D=data/file handlers
E=bibliographic applications
F=other (specify category)

08. Software Identification: Submitting agency's identification number or code for software. If none assigned, indicate none.

11. Title: Software title should be made as descriptive as possible.

12. Acronym: Commonly used abbreviation identifying software. (optional)

13. Organization: Identify organization responsible for software as completely as possible, including Agency (Department), Office, Service, Bureau, Corporation, Commission, or Council.

14. Address: Complete mailing address for responsible organization including building name, street address, city, State, and ZIP code. Include mail stop number if applicable.

15. 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 13 and 14.

16. Telephone number(s): Telephone number of technical contact(s). Provide area code, seven-digit commercial number, and extension.

20. Computer Manufacturer and Model: Identify mainframe computer on which software is operational. Use manufacturer, model, and abbreviations and codes provided in OMB Circular A-11.

21. 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.

22. Computer Operating System: Name, version, and release under which software is operating. Identify any operating system enhancements.

23. Tape Drives: Identify number needed to operate software. Specify, if critical, additional requirements such as manufacturer, model, recording density, number of tracks, etc

24. Disk/Drum Units: Identify number needed to operate software. Specify manufacturer, model, etc., where critical.

25. Keyboard Terminals: Identify number of keyboard terminals used for inquiry and response, and/or remote operations. Specify manufacturer and model.

26. Programming Language(s): Identify programming language(s) used to generate software (include versions) e.g., ANSI COBOL, FORTRAN V, SIMSCRIPT II.5.

30. 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.

35. Narrative: Describe concisely what the software functionally accomplishes, its design characteristics, specific areas of application, relationship to other software, and other significant features.

40. Keywords: List significant words or phrases which reflect the functions, applications, and features of the software. Separate entries with semicolons.

45. Status: Enter code best describing software status:
1=planned
2=under development
3=operational
4=post operational
5=other (explain in narrative)

46. Software Availability:
1=available
2=proprietary
3=classified
4=other (explain in narrative)

47. 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 conclusions 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 pers who wishes to determine whether a sp cific product is covered by this not should write to the Food and Drug A ministration, Bureau of Drugs, Office Compliance (BD-300), 5600 Fish Lane, Rockville, MD 20852.

The notice stated that bethanech injection was deemed effective for ce tain indications and the tablets probab effective for these indications and th the other labeled indications were po sibly effective and lacking substanti evidence of effectiveness. The possib effective ind...ations have been reclass fied as lacking substantial evidence effectiveness in that no new eviden of effectiveness has been received pu suant to the notice.

Based upon reevaluation of availabl information, the indications previous considered as probably effective are no regarded as effective. Also, the require ment that bioavailability data be sub mitted has been deferred and abbrevi ated rather than full new dru applications and supplements may b submitted.

Accordingly, the previous announce ment is amended to read as follows:

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

1. Bethanechol chloride injection and tablets are effective for treatment of acute postoperative and postpartum nonobstructive (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 11273), as follows:

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 new labeling 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 theevidence 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 Administrati 5600 Fishers Lane, Rockville, MD 2085

Supplements (identify with NDA numb Office of Scientific Evaluation (BD-1 Bureau of Drugs.

Original abbreviated new drug applicati (identify as such): Generic Drug Staff (BD-5 Bureau Drugs.

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

Request for Hearing (identify with doc number): Hearing Clerk, (CC-20), Room 6-86, Pa lawn Building.

All other communications garding announcement: Drug Efficacy Study Implementation I ject Manager (BD-101), Bureau of Dr

Received requests for a hearing n be seen in the office of the Hearing Cl (address given above) during regu business hours, Monday throu Friday.

This notice is issued pursuant to p visions of the Federal Food, Drug, a Cosmetic Act (Sec. 502, 505, 52 S 1050–53, as amended; 21 U.S.C. 352, 3 and the Administrative Procedure (5 U.S.C. 554), and under the autho delegated to the Commissioner of F 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 a

[DESI 5773 Docket No. FDC-D-642; NDA 5-773]

HOLLAND-RANTOS CO., INC.

Nylmerate Jelly; Notice of Opportunity Hearing on Proposal To Withdraw proval of New Drug Application

In a notice (DESI 5773) published the FEDERAL REGISTER of July 27, 1 (37 FR 15030) the Commissioner of F and Drugs announced his conclusi pursuant to the evaluation of a rep received from the National Academy Sciences-National Research Coun Drug Efficacy Study Group, on the d described below stating that the d was regarded as possibly effective and lacking substantial evidence of effecti ness for the various labeled indicatio The possibly effective indications h been reclassified as lacking substant evidence of effective in that no d have been submitted pursuant to t notice.

Nylmerate Jelly containing no oxynol 9 (previously listed as po oxyethylenenonylphenol), phenylm curic acetate, and boric acid; marke by Holland-Rantos Co., Inc., Enterpr Avenue, Trenton, N.J. 08638 (N 5-773).

Therefore, notice is given to t holder(s) of the new drug applicatio and to any other interested person th the Commissioner proposes to issue order under section 505(e) of the Fe eral Food, Drug, and Cosmetic Act U.S.C. 355(e)) withdrawing approval

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-095

CORRESPONDENCE

ANDA 89-095

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, 5 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,

Robert C. Johnson for 11-1-85

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 11/1/85
R/D INITIALED BY: JMeyer/MSeife
D Utz: 11-1-85 (1048R)
NOT APPROVABLE

idmak
LABORATORIES, INC.

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

September 19, 1985

Mr. Marty Finkelson
NY Regional Laboratory
850 Third Avenue
Brooklyn, NY 11232

Re: Bethanechol Chloride Tablets, USP 5 mg., NDA 89-095

Dear Mr. Finkelson:

As requested by Ms. Maria Shih of the FDA, enclosed you will find a bottle of 100 tablets of Bethanechol Chloride 5 mg., Lot No. 84-181T to be tested in support of NDA 89-095.

Should anything else be required, please do not hesitate to contact me.

Sincerely,

SIDMAK LABORATORIES, INC.

Geraldine Morrissey

Geraldine Morrissey
Regulatory Associate

enc.

gm

COPY - Ms. Maria Shih

NDA 89-095

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

[redacted] 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, 5 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,

Marvin Seife 9/13/85

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

NWK-DO
HFN-83
HFN-230
R[redacted]/JMeyer/MShih 9/11/85
R/D INITIALED BY: JMeyer/MSeife
D Utz: 9-11-85 (0815R)
NOT APPROVABLE JMeyer 9/12/85

idmak
LABORATORIES, INC.

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

Orig

NDA 89-095

RESUBMISSION

August 16, 1985

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 package insert labeling and container labels satisfactory. R.S. Brown 8/26/85

FPL

Re: Bethanechol Chloride Tablets, 5 mg. NDA 89-095

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.

Satish P. Patel, Ph.D.
President

enc.

SPP/G. Morrissey

RECEIVED
AUG 20 1985
GENERIC DRUGS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 89-095

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

JUL 26 1985

Gentlemen:

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, 5 mg.

Reference is also made to your two communications dated June 14 and July 11, 1985 and our letter dated June 5, 1985.

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

1. Labeling:
   Insert: Not Satisfactory

   1) DESCRIPTION
      a) . . . molecular formula . . . (rather than

   2) OVERDOSAGE
      a) Add as the last sentence; The oral LD_{50} 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).

Revise the package insert labeling, then prepare and submit final printed labeling.

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,

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

APPEARS THIS WAY
ON ORIGINAL

idmak
LABORATORIES, INC.

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

NDA mfc 8/15/85

NDA 89-095

August 5, 1985

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

Attn: Ms. Maria Shih

Dear Dr. Seife:

Enclosed please find two copies of the methodology, according to USP XXI, as amended by Supplement A, to be employed to evaluate the Bethanechol Chloride 5 mg. Tablets which were sent to the NY District Laboratory for testing in support of NDA 89-095.

Should you have any questions, please do not hesitate to contact me.

Sincerely,

SIDMAK LABORATORIES, INC.

Geraldine Morrissey

Geraldine Morrissey
Regulatory Associate

enc.

gm

Orig

idmak
LABORATORIES, INC.

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

NDA mfg 7/22/85
505 J 2A information is Acceptable DJR 12-17-85

NDA 89-095

ORIG NEW CORRES

JUL 11 1985

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, 5 mg. NDA 89-095

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

idmak
LABORATORIES, INC.

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

NDA 89-095

RESUBMISSION

June 14, 1985

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

DRAFT LABELING

Re: Bethanechol Chloride Tablets, 5 mg., NDA 89-095

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 89-095

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

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 89-095

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, 5 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.

RECEIVED
MAR 29 1985

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,

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

M?

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 6/5/85

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

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

5/29/85

Generic Name: Bethanechol Chloride

Trade Name: _____

Dosage: 5 mg + 50 mg Tablets

ANDA #: 89-095 + 89-096

Reviewer: Agnes T. Wu

Firm Name: Sidmak Laboratories

Firm Location: East Hanover, NJ 07

Submission Date: March 29, 1985
March 29, 1985

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.

APPEARS THIS WAY
ON ORIGINAL

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 5 mg + 50 mg (MSD)

Assay Methodology: _____

Results

Time	Test Product			Reference Product		
30 min	Lot # 84-181T (5 mg)			Lot # L0339 (Urecholine) 5.0mg Merck		
	Mean % Dissolved	Range	(CV) %	Mean % Dissolved	Range	(CV) %
	99.23		(5.12)	94.40		(5.44)
			( )			( )
			( )			( )
			( )			( )
			( )			( )
			( )			( )
			( )			( )
		APPEARS THIS WAY ON ORIGINAL				
			( )			( )
			( )			( )
	Sidmak Lot # 84-182T (50mg)			Lot # K2881 (Urecholine) 50mg Merck		
	102.77		(4.3)	102.24		(3.93)
			( )			( )
			( )			( )
			( )			( )
			( )			( )
			( )			( )
		APPEARS THIS WAY ON ORIGINAL				
			( )			( )
			( )			( )

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. Pelsor

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

NDA 89-095

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, 5 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 6/10/85
R/D INITIALED BY: JMeyer/MSeife
D Utz: 6-5-85 (0329R)
NOT APPROVABLE

Marvin Seife, M.D. 6/11/85
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

JMeyer 6/10/85

sidmak
LABORATORIES, INC.

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

NDA 89-095

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, 5 mg. NDA 89-095

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

GENERIC DRUGS

idmak
LABORATORIES, INC.

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

Drug

NDA mfg: 4/15/85

NDA 89-095

March 29, 1985

RESUBMISSION

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, 5 mg. NDA 89-095

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.

NDA 89-095

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

NDA 89-095

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, 5 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.

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 60 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,

Marvin Seife 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 MS 3/25/85
R/D INITIALED BY: JMeyer/MSeife
D Utz: 3-22-85 (0089B)
NOT APPROVABLE
JMeyer 3/25/85

JAN 8 1985

NDA 89-095

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, 5 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,

Marvin Seife 1/8/85

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)

JMeyer 1/7/85

idmak
LABORATORIES, INC.

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

December 19, 1984

ABBREVIATED
NEW DRUG APPLICATION
89-095

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

Product: Bethanechol Chloride Tablets, USP 5 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

RECEIVED
DEC 20 1984
GENERIC DRUGS

SPP/gm

Enclosures