

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**75-237**

**CORRESPONDENCE**



February 29, 2000

Mr. Robert A. Femia  
Vice President, Scientific & Regulatory Affairs  
Par Pharmaceutical, Inc.  
One Ram Ridge Road  
Spring Valley, New York, 10977  
USA

3/9/2000  
AM noted  
① To labeling for review. NAE approved 4/15/00  
② To CMC Review for review.  
[Signature]

3/8 02:00, 14:40 4/15/00

Re: **Minor Amendment to ANDA #75-237**  
**Sotalol Hydrochloride Tablets**  
**80 mg, 120 mg, 160 mg, 240 mg**

Dear Robert:

Please find enclosed Genpharm's **Minor Amendment** for the final approval of ANDA #75-237 for Sotalol. The following copies are enclosed:

- Archival Copy
- Review Copy
- Field Copy
- Par Copy

A form FDA-356h is included behind the cover letter of the amendment. Please date the cover page when it is time to send to FDA and also please sign and date page 2 of the form FDA 356h in the archival copy, and replace the unsigned page in the review and field copies and courier the package to FDA.

As usual, please send a copy of the signed form to Genpharm for our file.

If you have any questions, please let me know.

Kind regards,

*Ellen Comeau*  
Ellen Comeau  
Regulatory Affairs Assistant



NW  
7-8-00





GENPHARM

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food & Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

**MINOR AMENDMENT**  
*For Final Approval*

**Re: ANDA #75-237**  
**Sotalol Hydrochloride Tablets**  
**80 mg, 120 mg, 160 mg, 240 mg**

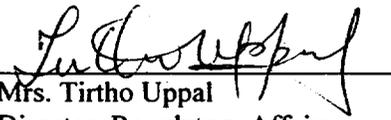
This **Minor Amendment** to our abbreviated new drug application is in response to the tentatively approved letter, dated October 21, 1999, from Douglas L. Sporn, Director, Office of Generic Drugs.

We are amending our application to identify and provide documents reflecting the changes made in the conditions under which the drug product was tentatively approved.

We have enclosed one (1) archival, one (1) review and one (1) field copy of the application in accordance with 21 CFR § 314.54. We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs.

We trust the information submitted is sufficient for this amendment to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm directly at 1-800-661-7134 or you may contact our U.S. agent, Mr. Robert A. Femia, at (914) 425-7100.

Yours sincerely

  
Mrs. Tirho Uppal  
Director, Regulatory Affairs  
GENPHARM INC.

Feb 29 | 2000  
(date)

cc: Mr. Robert A. Femia, PhD.  
Vice President, Scientific & Regulatory Affairs  
Par Pharmaceutical, Inc.  
One Ram Ridge Road,  
Spring Valley, NY  
USA 10977



BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-237

APPLICANT: Genpharm Inc.

DRUG PRODUCT: Sotalol Hydrochloride 80 mg, 120 mg, 160 mg,  
& 240 mg Tablets

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

The following dissolution testing will need to be incorporated into your stability and quality control programs:

The dissolution testing should be conducted in 900 mL of water, at 37° C using USP Apparatus II at 50 rpm. The test product should meet the following specifications, recommended by the Agency and based on the data submitted:

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

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

Sincerely yours,

*Barbara M. Davis*

*for*

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



GENPHARM

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

*Labeling review  
drafted 9/10/99  
A. Veza*

**LABELLING  
AMENDMENT**

**NDA ORIG AMENDMENT**

*N/A/F*

**RE: ANDA No. 75-237  
SOTALOL HCl TABLETS 80 mg, 120 mg, 160 mg & 240 mg**

Dear Sir/Madam:

This **LABELLING AMENDMENT** to our ANDA # 75-237 is in response to the faxed letter, dated Aug. 31/99 from Adolph Veza, FDA.

For the reviewers' convenience, we have:

- a) attached a copy of the deficiency letter dated Aug. 31/99;
- b) formatted our amendment such that each comment made by the reviewer has been restated, followed by our response to the comments;
- c) provided side-by-side comparison of the proposed labelling with the last submission, with all differences annotated and explained;
- d) enclosed 12 final printed insert.

We have enclosed one (1) archival copy, one (1) chemistry review copy, one (1) bioequivalence section copy, and one (1) field copy of the application in accordance with 21 CFR § 314.96. We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs. Along with our responses, a signed form FDA 356h by our US agent, Dr. Robert A. Femia of Par Pharmaceutical, Inc., New York, NY. is submitted. The number of volumes in the archival, chemistry review, and field copies of the ANDA are as follows:

Archival Copy	1 volume
Chemistry Review Copy	1 volume
Field Copy	1 volume
Pharmacokinetic Review Copy	1 volume

We trust the information submitted is sufficient for this amendment to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm Inc. at 1-800-661-7134 or you may contact our US agent, Dr. Robert A. Femia, at (914) 425-7100, Ext. 708.

Thank you for your prompt handling of this submission.

*[Signature]*  
Mrs. Tirto Uppal  
Director, Regulatory Affairs  
GENPHARM INC.

**SEP 09 1999**  
(date)



4.1      J. 227

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-237

APPLICANT: Genpharm Inc.

DRUG PRODUCT: Sotalol Hydrochloride 80 mg, 120 mg, 160 mg,  
& 240 mg Tablets

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

The following dissolution testing will need to be incorporated into your stability and quality control programs:

The dissolution testing should be conducted in 900 mL of water, at 37° C using USP Apparatus II at 50 rpm. The test product should meet the following specifications, recommended by the Agency and based on the data submitted:

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

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

Sincerely yours,

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



GENPHARM

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

**BIO & TELEPHONE  
AMENDMENT**

**NDA ORIG AMENDMENT**

N/A  
N/A

**RE: ANDA No. 75-237  
SOTALOL HCl TABLETS 80 mg, 120 mg, 160 mg & 240 mg**

Dear Sir/Madam:

This **BIO AMENDMENT** to our ANDA # 75-237 is in response to the faxed letter, dated Aug. 4/99 from Elain Hu, Project Manager. Since this amendment also affects the chemistry review (revised dissolution method & specification), it is also treated as **TELEPHONE AMENDMENT** as discussed with Tim Ames at the chemistry department on Aug. 9/99.

For the reviewers' convenience, we have:

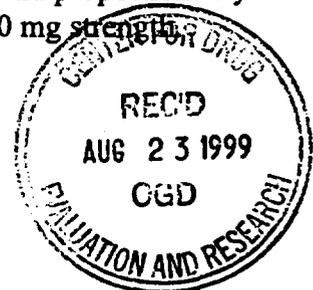
- a) attached a copy of the letter dated June 14/99;
- b) formatted our amendment such that each comment made by the reviewer has been restated, followed by our response to the comments.

We have enclosed one (1) archival copy, one (1) review copy, and one (1) field copy of the application in accordance with 21 CFR § 314.96. We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs. Along with our responses, a signed form FDA 356h by our US agent, Dr. Robert A. Femia of Par Pharmaceutical, Inc., New York, NY. is submitted. The number of volumes in the archival, chemistry review, and field copies of the ANDA are as follows:

Archival Copy	1 volume
Chemistry Review Copy	1 volume
Field Copy	1 volume
Pharmacokinetic Review Copy	1 volume

Since method validations are currently being performed at the FDA laboratory, Genpharm will work with the district laboratory to resolve any issues which may arise pending method validation.

Since the waiver information submitted in the Oct. 14/98 Major Amendment for the 120 mg was not reviewed by the bioequivalence department, the waiver request including comparative dissolution using "water" as medium, components & composition statements, and proportionality data of the formulation have been resubmitted with this amendment for the 120 mg strength.





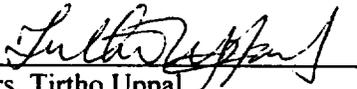
GENPHARM

Page 2 of 2

Office of Generic Drugs, CDER, FDA

We trust the information submitted is sufficient for this amendment to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm Inc. at 1-800-661-7134 or you may contact our US agent, Dr. Robert A. Femia, at (914) 425-7100, Ext. 708.

Thank you for your prompt handling of this submission.

  
Mrs. Tirtho Uppal  
Director, Regulatory Affairs  
GENPHARM INC.

Aug 17/99  
(date)





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Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

**TELEPHONE  
AMENDMENT**

**ORIG AMENDMENT**

**RE: ANDA No. 75-237  
SOTALOL HCl TABLETS 80 mg, 120 mg, 160 mg & 240 mg**

N/FA

Dear Sir/Madam:

This **TELEPHONE AMENDMENT** to our ANDA # 75-237 is in response to the telephone request on Oct. 07/99 by Tim Ames, FDA, Project Manager to Tirtho Uppal, Regulatory Affairs, Genpharm Inc..

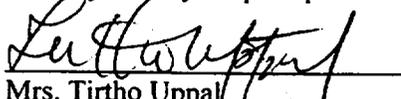
For the reviewers' convenience, we have formatted our amendment such that each comment made by the FDA has been restated, followed by our response to the comments. Please note that the response to comment 2 (Blister Leak Test) was submitted in the major amendment which was submitted on Oct. 14/98, however the corresponding pages from the major amendment are resubmitted with this submission again for your information.

We have enclosed one (1) archival copy, one (1) chemistry review copy and one (1) field copy of the application in accordance with 21 CFR § 314.96. We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs. Along with our responses, a signed form FDA 356h by our US agent, Dr. Robert A. Femia of Par Pharmaceutical, Inc., New York, NY. is submitted. The number of volumes in the archival, chemistry review, and field copies of the ANDA are as follows:

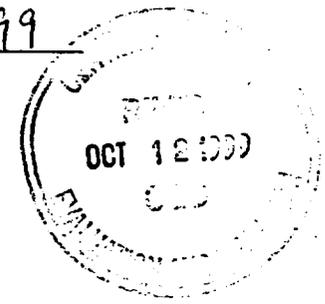
Archival Copy	1 volume
Chemistry Review Copy	1 volume
Field Copy	1 volume

We trust the information submitted is sufficient for this amendment to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm Inc. at 1-800-661-7134 or you may contact our US agent, Dr. Robert A. Femia, at (914) 425-7100, Ext. 708.

Thank you for your prompt handling of this submission.

  
Mrs. Tirtho Uppal  
Director, Regulatory Affairs  
GENPHARM INC.

Oct 8/99  
(date)



AUG 4 1999

APR 1-8-94-  
Supm

BIOEQUIVALENCY DEFICIENCIES

ANDA: 75-237            APPLICANT: Genpharm Inc.

DRUG PRODUCT: Sotalol Hydrochloride Tablets,  
80 mg, 160 mg, & 240 mg

The Division of Bioequivalence has previously (March 25, 1998) recommended the following dissolution method for your sotalol hydrochloride tablets:

Apparatus: USP 2 (Paddle), 50 rpm  
Medium: 0.1N HCL, 900 mL  
Sampling Times: 5, 15, 30 and 60 minutes  
Tolerance: Not less than            n 30 minutes

For consistency in the dissolution testing of this drug product, your are advised to repeat the dissolution testing using the following method and submit the dissolution data to the Agency for review:

Apparatus: USP 2 (Paddle), 50 rpm  
Medium: Water, 900 mL  
Sampling Times: 5, 15, 30 and 60 minutes  
Tolerance: Not less than            30 minutes

Sincerely yours,



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

BIOEQUIVALENCY DEFICIENCIES

ANDA: 75-237            APPLICANT: Genpharm Inc.

DRUG PRODUCT: Sotalol Hydrochloride Tablets,  
80 mg, 160 mg, & 240 mg

The Division of Bioequivalence has previously (March 25, 1998) recommended the following dissolution method for your sotalol hydrochloride tablets:

Apparatus: USP 2 (Paddle), 50 rpm  
Medium: 0.1N HCL, 900 mL  
Sampling Times: 5, 15, 30 and 60 minutes  
Tolerance: Not less than            .n 30 minutes

For consistency in the dissolution testing of this drug product, your are advised to repeat the dissolution testing using the following method and submit the dissolution data to the Agency for review:

Apparatus: USP 2 (Paddle), 50 rpm  
Medium: Water, 900 mL  
Sampling Times: 5, 15, 30 and 60 minutes  
Tolerance: Not less than            in 30 minutes

Sincerely yours,



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



GENPHARM

7/5/99 FA noted,  
To CMC Reviewer  
for Review.  
JCS

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7500 Standish Place, Room 150  
Rockville, Maryland 20855

**FAX  
AMENDMENT**

**RE: ANDA No. 75-237  
SOTALOL HCl TABLETS 80 mg, 120 mg, 160 mg & 240 mg**

Dear Sirs/Madam:

This **FAX AMENDMENT** to our ANDA # 75-237 is in response to your faxed letter, dated June 14/99 from Timothy Ames, Project Manager.

For the reviewers' convenience, we have:

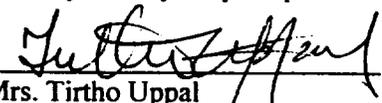
- a) attached a copy of the letter dated June 14/99;
- b) formatted our amendment such that each comment made by the reviewer has been restated, followed by our response to the comments.

We have enclosed one (1) archival copy, one (1) review copy, and one (1) field copy of the application in accordance with 21 CFR § 314.55. As required, three (3) additional separately bound copies of the analytical methods and descriptive information needed to perform the tests on the samples (both bulk active ingredient and finished dosage form) are included as one the volumes of the archival copy of this submission. We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs. Along with our responses, a signed form FDA 356h by our US agent, Dr. Robert A. Femia of Par Pharmaceutical, Inc., New York, NY. is submitted. The number of volumes in the archival, chemistry review, and field copies of the ANDA are as follows:

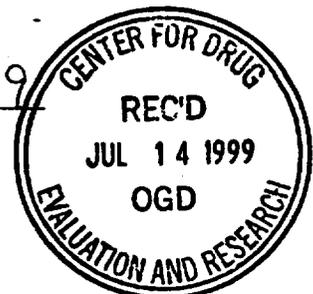
Archival Copy	1 volume
Chemistry Review Copy	1 volume
Field Copy	1 volume.

We trust the information submitted is sufficient for this amendment to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm Inc. at 1-800-661-7134 or you may contact our US agent, Dr. Robert A. Femia, at (914) 425-7100, Ext. 708.

Thank you for your prompt handling of this submission.

  
Mrs. Tirho Uppal  
Director, Regulatory Affairs  
GENPHARM INC.

July 8/99  
(date)



JUN 14 1999

**Chemistry deficiencies to be provided to the applicant:**

ANDA: 75-237 APPLICANT: Genpharm Co.

DRUG PRODUCT: Sotalol HCl Tablets 80, 120, 160, 240 mg

The deficiencies presented below represent Facsimile Deficiencies.

Chemistry Deficiencies:

1. Your response to our request regarding Blend Uniformity Analysis (BUA) is not acceptable. Please note that the active constitutes only 40% of the total tablet weight. To ensure adequate control of dosage uniformity we request that an in-process BUA test be instituted for post-approval production batches. Please revise and resubmit the appropriate pages of the blank batch records.

We recommend the analysis of a minimum six blend samples from the blender or a single container, which are representative of the entire batch. The BUA acceptance criteria should be % (mean of individual tests) with a relative standard deviation (RSD) of

We acknowledge data submitted in support of the 80 mg, 160 mg and 240 mg product. Please submit BUA data for the 120 mg product.

2. The blank batch record lists many tablet presses. Please document which one was used in the manufacture of test batches. Are they all equivalent?

3. Please submit a method validation package.
  
4. You have provided room temperature stability data for bulk storage of the 160 mg and 240 mg products supporting a 3 month expiration date in this container closure system. Please comment on your intentions with regard to the 80 mg and 120 mg products.

Sincerely yours,



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



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Office of Generic Drugs, CDER, FDA  
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7500 Standish Place, Room 150  
Rockville, Maryland 20855

MAJOR AMENDMENT

N/AC

**MAJOR  
AMENDMENT**

**RE: ANDA No. 75-237  
SOTALOL HCl TABLETS  
80 mg, 120 mg, 160 mg & 240 mg**

Dear Sirs/Madam:

This **MAJOR AMENDMENT** to our ANDA # 75-237 is in response to your faxed letter, dated Aug. 07/98 from Timothy Ames, Project Manager.

For the reviewers' convenience, we have:

- a) attached a copy of the letter dated Aug. 07/98;
- b) formatted our amendment such that each comment made by the reviewer has been restated, followed by our response to the comments.
- c) provided side-by-side comparison of the proposed labelling with the last submission, with all differences annotated and explained.
- d) enclosed 12 final printed, container labels, unit dose lables (printed foil), cartons, and insert.

Together with this submission we are submitting an **amendment to add a new strength 120 mg** to our existing ANDA.

We have enclosed one (1) archival copy, one (1) review copy, one (1) bioequivalence section copy, and one (1) field copy of the application in accordance with 21 CFR § 314.55. We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs. Along with our responses, a signed form FDA 356h by our US agent, Dr. Robert A. Femia of Par Pharmaceutical, Inc., New York, NY. is submitted. The number of volumes in the archival, chemistry review, pharmacokinetic review and field copies of the ANDA are as follows:

Archival Copy	3 volumes
Pharmacokinetic Review Copy	1 volume
Chemistry Review Copy	3 volumes
Field Copy	2 volumes.

**This application contains an amendment to Bioequivalence electronic submission ESD.**

OCT 21 1998



GENPHARM INC.

85 ADVANCE ROAD • ETOBICOKE • ONTARIO • CANADA M8Z 2S9 • (416) 236-2631 • FAX (416) 236-2940 • TOLL FREE: 1-800-668-3174



GENPHARM

Since the 120 mg strengths is added as an amendment to the existing ANDA, we have enclosed a computer diskette containing an amendment to Bioequivalence electronic submission ESD (BA/BE EVA) in the format prescribed by the FDA. The diskettes (2 copies) are located at the beginning of Volume 1 of the Archival Copy of this application. We certify that, to the best of our knowledge, the data entered into the BA/BE EVA ESD are identical to or can be derived from the information contained in the hard copy submission.

We trust the information submitted is sufficient for this amendment to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm Inc. at 1-800-661-7134 or you may contact our US agent, Dr. Robert A. Femia, at (914) 425-7100, Ext. 708.

Thank you for your prompt handling of this submission.

Mrs. Tirho Uppal  
Director, Regulatory Affairs  
GENPHARM INC.

Oct 14/98  
(date)



BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-237

APPLICANT: Genpharm Inc.

DRUG PRODUCT: Sotalol Hydrochloride 80 mg, 160 mg, & 240 mg  
Tablets

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

The following dissolution testing will need to be incorporated into your stability and quality control programs:

The dissolution testing should be conducted in 900 mL of 0.1 N HCl , at 37° C using USP Apparatus II at 50 rpm. The test product should meet the following specifications, recommended by the Agency and based on the data submitted:

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

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

Sincerely yours,



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



BIOAVAILABILITY

ORIG AMENDMENT

N / AB

Dr. Dale Conner  
Office of Generic Drugs  
CDER, FDA  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

**TELEPHONE  
AMENDMENT**

**Re: Telephone Amendment, dated November 20, 1997, to ANDA #75-237  
Sotalol Tablets  
80 mg, 160 mg and 240 mg**

The enclosed copies of the **Telephone Amendment**, dated November 20, 1997, to our abbreviated new drug application are being re-sent in response to a telephone conversation on March 3, 1998, between Lizzie Sanchez, Project Manager, and Jo-anne Richardson, Regulatory Affairs Associate, Genpharm Inc.

The original amendment was not included with the copies of the ANDA and the reviewer did not have access to the additional information. As requested by Lizzie Sanchez, we have enclosed two copies of the amendment for your files.

If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm at 1-800-661-7134 or you may contact our U.S. agent, Ms. Anita M. Goodman, at (212) 223-1282.

Yours sincerely

  
Jo-anne Richardson  
Associate, Regulatory Affairs  
GENPHARM INC.

  
\_\_\_\_\_  
(date)

**RECEIVED**

MAR U 4 1998

**GENERIC DRUGS**



GENPHARM INC.

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ANDA #75-237

AB

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Center for Drug Evaluation and Research  
Food & Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

**BIOEQUIVALENCE  
AMENDMENT**

**Re: Bioequivalence Amendment to ANDA #75-237  
Sotalol Tablets  
80 mg, 160 mg and 240 mg**

We are pleased at this time to submit an amendment to our ANDA for our product - Sotalol Tablets. 80 mg, 160 mg and 240 mg.

The purpose of this amendment is to submit the electronic submission of the bioequivalence section. Two diskettes are submitted, each one contains: Electronic Submission Document (ESD) file (GPM9701.001), the companion document (GPM9701.002) and twenty-two data files (ASCII files).

The analytical method validation report has been revised to include the long-term stability. Hard copies of the revised reports are included.

We certify that the Electronic Copy is an identical copy of the bioequivalence section contained in the archival and review copies of this application.

We trust the information submitted is sufficient for this application to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm directly at 1-800-661-7134 or you may contact Ms. Anita M. Goodman at (212) 223-1282.

Yours sincerely

  
Jo-anne Richardson  
Regulatory Affairs Associate  
GENPHARM INC.

NOV 24 1997

(date)

RECEIVED

NOV 25 1997

GENERIC DRUGS



AUG 7 1999

38. Chemistry Comments to be Provided to the Applicant

ANDA: 75-237

APPLICANT: GENPHARM, INC.

DRUG PRODUCT: Sotalol Hydrochloride Tablets, 80 mg, 160 mg and  
240 mg

The deficiencies presented below represent MAJOR deficiencies.

A. Chemistry Deficiencies:

1.

sts  
ard

2.

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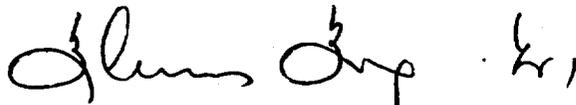
e. Please submit copies of the British Pharmacopoeia tests for

f. referenced on p. 3632 st

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

1. Please be advised that for the manufacture of the drug substance Sotalol Hydrochloride has been reviewed and found inadequate. The holder of the DMF has been notified of the deficiencies. All deficiencies must be satisfactorily resolved prior to the approval of this ANDA.
2. Since Sotalol Hydrochloride drug substance and Sotalol Hydrochloride Tablets are non-USP, methods validation will be performed by an FDA laboratory.

Sincerely yours,



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

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-237

APPLICANT: Genpharm Inc.

DRUG PRODUCT: Sotalol Hydrochloride 80 mg, 160 mg, & 240 mg  
Tablets

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

The following dissolution testing will need to be incorporated into your stability and quality control programs:

The dissolution testing should be conducted in 900 mL of 0.1 N HCl , at 37° C using USP Apparatus II at 50 rpm. The test product should meet the following specifications, recommended by the Agency and based on the data submitted:

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

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

Sincerely yours,



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

Lipha Pharmaceuticals Inc.  
U.S. Agent for: Genpharm Inc.  
Attention: Anita M. Goodman, M.D.  
9 West 57th Street  
Suite 3825  
New York, NY 10019-2701

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Dear Madam:

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

Reference is also made to the telephone conversation dated November 19, 1997 and your correspondence dated November 20, 1997.

NAME OF DRUG: Sotalol Hydrochloride Tablets, 80 mg, 160 mg and 240 mg

DATE OF APPLICATION: October 30, 1997

DATE (RECEIVED) ACCEPTABLE FOR FILING: October 31, 1997

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

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

Should you have questions concerning this application, contact:

Tim Ames  
Project Manager  
(301) 827-5849

Sincerely yours,

*Handwritten notes:*  
see the white copy but  
the pink copy  
is a copy  
of the original signature  
of the original  
I would be good  
to see by  
11/26/98

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

cc:

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ack



505(j)(ii) OK  
11/24/97  
Happaj S. Dantz

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food & Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

ANDA

Re: **Abbreviated New Drug Application**  
**Sotalol Tablets**  
**80 mg, 160 mg and 240 mg**

We are pleased at this time to submit an original Abbreviated New Drug Application for our product - Sotalol Tablets, 80 mg, 160 mg and 240 mg.

The purpose of this application is to gain FDA approval to market Sotalol Tablets, 80 mg, 160 mg and 240 mg, in the U.S.A. The drug product described above is the same as Betapace®, manufactured by Berlex. We have submitted comparative information to indicate that our product is the same as the reference listed drug product. This information is presented in tabular form, comparing active ingredient, conditions of use, route of administration, dosage form, strength, bioequivalence, and labeling for the products as supplied by Genpharm Inc. and by Berlex.

We have enclosed one (1) archival, one (1) review, and one (1) field copy of the application in accordance with 21 CFR § 314.55. As required, three (3) additional separately bound copies of the analytical methods and descriptive information needed to perform the tests on the samples (both the bulk active ingredient and finished dosage form) are included as one of the volumes of the archival copy of this ANDA. The number of volumes in the archival, review and field copies of the ANDA are as follows:

Blue Archival Copy	7 volumes
Orange Review Copy	5 volumes
Red Review Copy	4 volumes
Burgundy Field Copy	4 volumes.

We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs.

**RECEIVED**

**OCT 31 1997**

**GENERIC DRUGS**



re: *Sotalol Tablets*  
*80 mg, 160 mg and 240 mg*  
*Page 2 of 2*

In addition, for the Bioequivalence Section, we have enclosed a computer diskette with the analytical data and bioavailability parameters in the format prescribed by the FDA. A hard copy of the diskette data is also included in this section. The diskettes and hard copy of the data is located at the beginning of Section VI of the Orange Review Copy of this application.

We trust the information submitted is sufficient for this Abbreviated New Drug Application to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm directly at 1-800-661-7134 or you may contact Ms. Anita M. Goodman at (212) 223-1282.

A letter of authorization, allowing Ms. Anita M. Goodman to act as our U.S. agent, is included in Section XX.2.b of this application.

Yours sincerely



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Richard Pike  
Director, Regulatory Affairs  
GENPHARM INC.

**OCT 30 1997**

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(date)