# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER 74941

## CORRESPONDENCE

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

June 18, 1997

NEW CORRESP
NC

Noted:
PAS
M Anderson
7/29/97

CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF GENERIC DRUGS, HFD #630
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Douglas Spom, Director

RE: ANDA 74-941 Diltiazem HCl Injection, 5mg/mL

Abbott Laboratories hereby provides notification per 21 CFR 314.72 that on June 10, 1997, a change in ownership of the subject approved application has taken place. As of that day, the ownership has been transferred from Sanofi Pharmaceuticals, New York, New York to Abbott Laboratories, North Chicago, Illinois.

Per 21 CFR 314.72(a)(2), Abbott Laboratories commits to agreements, promises, and conditions made by the former owner and has obtained and has on file, a copy of the application including supplemental applications.

Please use the address below for further correspondence:

David T. Guzek, Director HPD Regulatory Affairs
Abbott Laboratories
200 Abbott Park Road, D-389, AP30
Abbott Park, IL 60064

We trust that this information application is complete.

Sincerely,

ABBOTT LABORATORIES

David T. Guzek

David T. Guzek, Director, Regulatory Affairs
Hospital Products Division
Phone: (847) 937-3216
FAX: (847) 938-7867

RECEIVED
JUN 20 1997
GENERIC DRUGS

DTG/dg
g:\gms\sanofi.gms
Attachment

ANDA 74-941

Sanofi Winthrop, Inc.
Attention: Gregory M. Torre
90 Park Ave.
New York, NY 10016

OCT 18 1996

Dear Sir:

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 our "Refuse to File" letter dated September 20, 1996, and your amendment dated September 27, 1996.

NAME OF DRUG: Diltiazem Hydrochloride Injection, 5 mg/mL, 5 mL and 10 mL vials

DATE OF APPLICATION: August 13, 1996

DATE OF RECEIPT: August 15, 1996

DATE ACCEPTABLE FOR FILING: September 30, 1996

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) 594-0305

Sincerely yours,

/S/ 10/18/96

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

SANOFI WINTHROP, INC.
90 PARK AVENUE
NEW YORK, NY 10016-1389
TELEPHONE 212 551 4000

505(b)(2)(a) ok
Anne Marie H. Weikel
10/4/96
10/4/96 ISL

sanofi WINTHROP

September 27, 1996

**VIA TELEFAX AND FEDERAL EXPRESS**

Mr. Douglas Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

NDA 3RD AMENDMENT
RECEIVED N/AC
SEP 3 1996
GENERIC DRUGS

**Re: ANDA 74-941**

Dear Mr. Sporn:

Reference is made to our abbreviated new drug application dated August 13, 1996, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Diltiazem Hydrochloride Injection, 5 mg/mL, 5 mL and 10 mL vials.

Reference is also made to Mr. Jerry Phillips' correspondence dated September 20, 1996 which detailed a reason for refusing to file this ANDA. Contained herein, please find our response to this inquiry.

Page 318 of the August 13, 1996 submission declares total compounding losses of for exhibit batch PD5-083. The low percentage of bulk converted to usable filled units , noted with an asterisk, was accompanied by the following explanation:

> *Low yield due to the amount of bulk solution sampled in compounding for validation studies (i.e.

A more detailed explanation of the accountability of the bulk solution and justification for the sampling losses can be found on the table in Attachment 1.

We would also like to point out the significance of batch size and subsequent impact on the vial yield specification as noted in great detail on page 319 of the August 13, 1996 submission, fixed losses on the ng line, as well as fixed losses at several stages of the manufacturing process, justify the above referenced specification. That is, on a percentage basis, the fixed losses will have a greater impact on a batch than on a er batch. Please refer to page 319 for a quantitative illustration of this justification.

Sanofi Winthrop, Inc. hereby certifies that we have sent a true copy of this letter to Mr. Edward T. Warner, District Director of the New York FDA District Office, and a true copy of this submission to Mr. W. Michael Rogers of the Lenexa, Kansas FDA District Office, as per Mr. Warner's instructions.

This document consists of Confidential and/or Trade Secret information subject to 18 U.S.C. 1905 and to which all claims of Privilege and Confidentiality are asserted in both statutory and common law.

If you require any clarification or further information, please contact Mr. John Purpura, Manager CMC, at (212) 551-4261.

Sincerely,

John Purpura /for

Gregory M. Torre, Ph.D., J.D.
Senior Director
Drug Regulatory Affairs

SANOFI WINTHROP, INC.
90 PARK AVENUE
NEW YORK, NY 10016-1389
TELEPHONE 212 551 4000

sanofi WINTHROP

August 13, 1996

**VIA FEDERAL EXPRESS**

Mr. Douglas Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

**ORIGINAL ANDA SUBMISSION;
MICRO/STERILITY ASSURANCE
DOCUMENTATION ENCLOSED**



Dear Mr. Sporn:

Submitted herewith, in duplicate, under § 505(j) of the Federal Food, Drug, and Cosmetic Act, is an original Abbreviated New Drug Application for Diltiazem Hydrochloride Injection, 5 mg/mL.

Diltiazem Hydrochloride Injection is listed in "Approved Drug Products with Therapeutic Equivalence Evaluations," 16th Edition, page 3-107. A copy appears in Section II.

The active ingredient, indications, route of administration, dosage form, and strength for Diltiazem Hydrochloride Injection are the same as those of the innovator's product, Cardizem® Injectable, sponsored by Hoechst Marion Roussel (formerly Marion Merrell Dow). Comparative information is contained in Section IV.

The labeling is the same in content as that of the reference drug, Cardizem® Injectable, except for changes that are necessary due to a change in manufacturer. A copy of the innovator's package insert is provided in Section V.

The first three production batches of Diltiazem Hydrochloride Injection, 5 mg/mL, in each vial fill will be placed into our stability program and reported at regular intervals for as long as necessary to support the proposed 24-month expiration date. Furthermore, we agree to withdraw from the market any batch found to fall outside the established specifications for this product. Our complete stability protocol and post-approval commitments are contained in Section XVII.

Documentation for Sterilization Process Validation is contained in a separate volume with a dedicated table of contents.

The sponsor of the Abbreviated New Drug Application is The product

is manufactured at the facility, which is registered under the name , Inc. However, the approved product will be marketed by Pharmaceuticals, which is an affiliate of

hereby certifies that we have sent a true copy of this letter to Mr. Edward T. Warner, District Director of the New York FDA District Office, and a true copy of this submission to Mr. W. Michael Rogers of the Lenexa, Kansas FDA District Office, as per Mr. Warner's instructions.

This document consists of Confidential and/or Trade Secret information subject to 18 U.S.C. 1905 and to which all claims of Privilege and Confidentiality are asserted in both statutory and common law.

If you require any clarification of further information, please contact Mr. John Purpura, Manager CMC, at (212) 551-4261.

Sincerely,

Gregory M. Torre, Ph.D., J.D.
Senior Director
Drug Regulatory Affairs

ANDA 74-941

Sanofi Winthrop, Inc.
Attention: Gregory M. Torre, Ph.D., J.D.
90 Park Avenue
New York, NY 10016-1389

SEP 20 1996

Dear Sir:

Please refer to your abbreviated new drug application (ANDA) dated August 13, 1996, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Diltiazem Hydrochloride Injection, 5 mg/mL, 5 mL and 10 mL vials.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reason:

> You are required to completely package your exhibit batches in the containers proposed for marketing. Regarding Batch #PD5-083, you have failed to completely fill the batch as indicated on page 317 of your application. Please provide a more detailed explanation of the accountability of the bulk solution and a justification for the bulk sampling losses. Please refer to the letter to industry dated August 4, 1993, regarding parenteral scale-up requirements. We also refer you to the OGD Policy & Procedure Guide #41-95 for guidance on the packaging of test batches.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3)If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Anna Marie H. Weikel
Project Manager
(301) 594-0315

Sincerely yours,

/S/

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

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9/20/96

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

**DATE:** September 9, 1996

**FROM:** Anna Marie H. Weikel
Consumer Safety Officer
HFD-615

/S/

**SUBJECT:** ANDA 74-941

**TO:** The File

Upon cursory review of this application I noted that the packaging yield for Lot # PD5-083 was only as indicated on page 317 of the application. Based on our policies and procedures regarding parenteral scale-up requirements, this is unacceptable for filing.

I consulted John Simmons and in his opinion, the removal of 30% of the bulk solution requires more justification and explanation, prior to the filing of this application.