CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 19787/S015

CORRESPONDENCE

Regulatory Affairs Division
Pfizer Inc
235 East 42nd Street
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ORIGINAL

Inna Kissen, PhD
Associate Director—Drug Regulatory Affairs

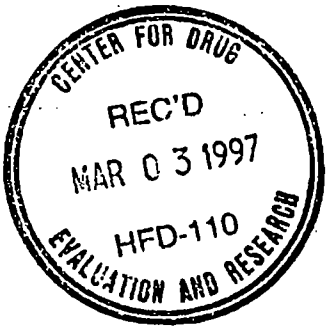
February 28, 1997

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW.

NDA NO. 19-787 REF. NO. 015

NDA SUPPL FOR SCM

Raymond Lipicky, M.D., Director
Division of Carodio-Renal
Drug Products (HFD-110)
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
1451 Rockville Pike
Rockville, MD 20852



RE: Norvasc (amlodipine besylate) Tablets
NDA #19-787
Special supplement - Changes being effected

Dear Dr. Lipicky;

This supplement requests approval for Pfizer's new organic synthesis building at our Groton Connecticut campus. The new organic synthesis building was designed and built to synthesize Pfizer's drug substances in accordance with Current Good Manufacturing Practices while providing the highest level of safety for employees as well as protection of the natural environment.

Reference is made to the November 17, 1994 meeting between Pfizer and the Agency regarding our new organic synthesis building, and to our letter to the FDA dated December 22, 1994.

A protocol for the approval of drug substances manufactured in this new facility was agreed to through discussions with FDA representatives at the meeting in November of 1994, and in subsequent telephone conversations and correspondences with the FDA. The protocol established the first drug substance to be manufactured in the facility (sertraline HCI) would be submitted as a supplement for prior approval. All subsequent drug substances introduced into the new facility would be submitted under section 314.70(c)(3) of the CFR, as Special Supplements - Changes being Effected. The sertraline HCI supplement was submitted to the FDA on April 4, 1995. A GMP inspection of the new facility was successfully conducted between July 25 and August 24, 1995. The new supplement was approved by the FDA on October 5, 1995.

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Amlodipine besylate drug substance has been manufactured in Pfizer's new organic synthesis building using the same methods and controls currently in use and on file in approved NDA #19-787. of the synthesis were performed in the new building. were performed in another approved facility on the Groton campus. The current Process Monograph Description and current In-Process Control Specification are provided in Appendix 1. The data presented in this supplement, obtained using currently approved test methods and a special test protocol, demonstrate that amlodipine besylate drug substance manufactured in the new building is physically and chemically equivalent to amlodipine besylate drug substance manufactured in the currently approved facility.

The first three lots of amlodipine besylate drug substance manufactured in the new building have been placed into stability studies. Three month drug substance stability data, including accelerated conditions, are included in this supplement. Norvasc drug product manufactured from amlodipine besylate drug substance synthesized in the new building will be monitored for stability. Data from the drug substance and drug product stability studies will be submitted in future Norvasc annual reports.

If you have any questions or comments on these data, please contact the undersigned at (212) 573-2503.

Sincerely,

I. Kissen

Inna Kissen, Ph.D.

IK:amw
Enclosure
NORSUUPP.DOC

ORIGINAL

Regulatory Affairs Division
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Inna Kissen, PhD
Associate Director—Drug Regulatory Affairs

April 15, 1997

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW.

Raymond Lipicky, M.D., Director
Division of Cardio-Renal
Drug Products (HFD -110)
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
1451 Rockville Pike
Rockville, MD 20852

SUPPL NEW CORRESP
(SNC 5-003)

RE: Norvasc (amlodipine besylate) Tablets
IND
Information amendment - Clinical - Final Study Report
* Norvasc (amlodipine besylate) Tablets
NDA # 19-787

Dear Dr. Lipicky:

Pursuant to 21 CFR 312.31, enclosed is a final study report entitled "The Effect of Grapefruit Juice on the Pharmacokinetics of Amlodipine in Normal Volunteers" (protocol #053-017).

The study showed no pharmacokinetic, pharmacodynamic, or clinical effect of grapefruit juice on intravenous or oral administration of amlodipine in healthy male volunteers.

Please include this information in the subject file.

Sincerely,

I. Kissen

Inna Kissen, Ph.D.

* Cover letter only

Enclosure
IK:amw
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