CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 19-766/S022

Trade Name: Zocor Tablets

Generic Name: simvastatin

Sponsor: Merck Research Laboratories

Approval Date: July 18, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S022

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Approvable Letter	
Labeling	
Medical Review(s)	
Chemistry Review(s)	X
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S022

APPROVAL LETTER

NDA 19-766/S-022

JUL 18 1997

Merck Research Laboratories
Attention: Robert E. Silverman, M.D., Ph.D.
P.O. Box 4, BLA-20
Sumneytown Pike
West Point, PA 19486

Dear Dr. Silverman:

Please refer to your supplemental new drug application dated May 9, 1997, received May 12, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZOCOR™ (simvastatin) Tablets.

The User Fee goal date for this application is November 12, 1997.

The supplemental application provides for an alternate site for film-coating of the 10 mg strength tablet cores at your manufacturing division facility in Arecibo, Puerto Rico.

We have completed the review of this supplemental application and it is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Ms. Margaret Simoneau, Consumer Safety Officer, at 301-443-3510.

Sincerely yours,

Stephen K. Moore 7-18-97

Stephen K. Moore, Ph.D.
Chemistry Team Leader I, DNDC II
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 19-766
HFD-510/Div. Files
HFD-510/CSO/MSimoneau
HFD-510/ WBerlin/SMoore
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: JWeber/6/23/97/N19766.022

Initialed by:WBerlin 6/24/Smoore 6/24/EGalliers 7/17/HYAhn 6/25/97

final: JWeber/7/18/97

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-766/S022

CHEMISTRY REVIEW(S)

ORIGINAL

CHEMISTS REVIEW	1. ORGANIZATION	2. NDA NUMBER JUN 1 1997
	DMEDP II, HFD-510	19-766
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
Merck Research Labs. P.O. Box 4, BLA-20 West Point, PA 19486		SCS-022 5-9-97
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Zocor Tablets	Simvastatin	

8. SUPPLEMENT PROVIDES FOR

An alternate site for film-coating of 10 mg-strength tablet cores at the Merck Manufacturing Division facility in Arecibo, Puerto Rico.

9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
Antihypercholestremic	RX	
12. DOSAGE FORM	13. POTENCY	
Tablets	10, 20, 40 mg	

14. CHEMICAL NAME AND STRUCTURE

See Chemistry Review #1

15. COMMENTS

This supplement provides for a change in the site to film-coat 10-mg tablets of Zocor at Aricebo PR rather than Wilson NC. Essentially, this application is identical to N 19-766, S-019, submitted 11-26-96 for the 20-mg tablet site change for film coating, which was approved, subsequent to an acceptable Establishment Evaluation. The sponsor has provided adequate indication that the alternate facility will utilize the same equipment and procedures at the same scale for the process as is currently performed at the approved site of Wilson NC. The sponsor has also included comparative batch results, comparative multi-point dissolution data, and comparative stability data for tablets coated at both facilities, and the data are acceptable.

16. CONCLUSION AND RECOMMENDATION

The sponsor has provided adequate data to demonstrate equivalence of the tablets film-coated at both the current and proposed facilities. The Arecibo facility was inspected and found to be acceptable (see attached copy of the CDER Establishment Evaluation Report dated 11-June, 1997). Issue an approval letter.

17. NAME	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
WILLIAM K. BERLIN		6-11-97

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE

Stephen K. Moore
6/11/97

2 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 19-766
S022

CDER Establishment Evaluation Report
for June 11, 1997

Application: **NDA 19766/022**
Stamp: **12-MAY-1997** Regulatory Due: **12-NOV-1997**
Applicant: **MERCK**
SUMNEYTOWN PIKE
WEST POINT, PA 19486

Priority: **1S** Org Code: **510**
Action Goal: District Goal: **07-SEP-1997**
Brand Name: **ZOCOR (SIMVASTATIN)**
Established Name:
Generic Name: **SIMVASTATIN**
Dosage Form: **TAB (TABLET)**
Strength: **10, 20, 40 MG**

FDA Contacts:			
M. SIMONEAU	**(HFD-510)**	**301-443-3510**	**, Project Manager**
W. BERLIN	**(HFD-510)**	**301-443-3520**	**, Review Chemist**
S. MOORE	**(HFD-510)**	**301-443-3510**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 11-JUN-1997 by M. EGAS (HFD-322) 301-594-0095

Establishment: **2650235**
MERCK SHARP AND DOHME QUIMI
RD 2 KM 60.3 BO SAB HOYO
ARECIBO, PR 00688

DMF No: **9593**

Profile: **TCM** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATIO 11-JUN-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities:
FINISHED DOSAGE MANUFACTURER

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-766/S022

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-766/S-022

MERCK RESEARCH LABORATORIES, INC.
Sumneytown Pike, P.O. Box 4, BLA-20
West Point, PA 19486

MAY 16 1997

Attention: Robert E. Silverman, M.D., Ph.D., Director, Regulatory Affairs

Dear Dr. Silverman:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Z0COR (Simvastatin) Tablets

NDA Number: 19-766

Supplement Number: S-022

Date of Supplement: May 9, 1997

Date of Receipt: May 12, 1997

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on July 11, 1997 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Attention: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine
Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 19-766/S-022
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

filename: C:\WPFILES\19766ACK.WPD

SUPPLEMENT ACKNOWLEDGEMENT

NDA NO. 19766 REF. NO. 022
NDA SUPPL FOR SCM

ORIGINAL
NDA SUPPLEMENT

Robert E. Silverman, M.D., Ph.D.
Senior Director
Regulatory Affairs

Merck & Co., Inc.
P.O. Box 4
West Point PA 19486
Fax 610 397 2516
Tel 610 397 2944
215 652 5000

These copies are OFFICIAL FDA Copies
not desk copies.

May 9, 1997

MERCK
Research Laboratories

Solomon Sobel, M.D. - Director
Division of Metabolism and Endocrine
Drug Products HFD-510, Room 14B-04
Office of Drug Evaluation II (CDER)
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAY 12 1997
HFD-510

Supplemental New Drug Application: NDA 19-766
ZOCOR ™ (Simvastatin)

Dear Dr. Sobel:

Pursuant to Section 505(b) of the Food Drug and Cosmetic Act and in accordance with 21 CFR 314.70(b), we submit, for your approval, a supplement to NDA 19-766.

As indicated on the attached Form FDA 356h, the supplemental application provides for changes in Item 3 of the approved New Drug Application for ZOCOR™.

The attached prior-approval supplement provides for the alternate film-coating of Tablets ZOCOR™10 mg at the Merck Manufacturing Division (MMD) facility in Arecibo, Puerto Rico.

The location of the Arecibo facility is:

Merck Manufacturing Division
Division of Merck and Co., Inc.
Road #2, Kilometer 60.3
Bo. Sabana Hoyos
Arecibo, PR 00688

The mailing address of the Arecibo facility is:

Merck Sharp & Dohme, Quimica de Puerto Rico
P.O. Box 6060
Barceloneta, PR 00617

Currently, [redacted] The film-coated tablets are subsequently

[redacted] Merck & Co., Inc. requests approval for film-coating the core tablets at MMD Arecibo, in addition to the currently approved Wilson facility.

This supplement contains CMC information similar to that which was provided previously in Supplement 019 (submitted on November 20, 1996 and approved on March 17, 1997) to support the use of MMD, Arecibo as an alternate site for the film-coating of Tablets ZOCOR™, 20 mg. The following chemistry documentation is provided:

- An Updated Film-Coating Manufacturing Process Description of the Arecibo facility.
- [redacted] accelerated stability data for [redacted] lot of Tablets ZOCOR™10 mg film-coated at the Arecibo facility (these samples will also be retained for long-term stability data to be provided in subsequent Annual Reports).
- Multi-point dissolution profiles for Tablets ZOCOR™ 10 mg film-coated at the Arecibo and Wilson facilities.
- Data comparison of [redacted] batches film-coated at Wilson and Arecibo.

The Arecibo facility was inspected by the San Juan District Office from February 5 through February 21, 1997 as part of the Preapproval Inspection for the manufacture of Tablets [redacted] and the film-coating of Tablets ZOCOR™, 20 mg. All observations issued as a result of this inspection were successfully resolved.

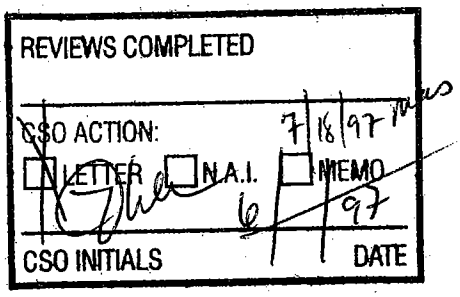
Please note that CMC information for [redacted]

Pursuant to 21 CFR 314.70(a), a complete field copy of this supplement has been submitted to the FDA Philadelphia District Office.

As required by Section 306(k)(l) of the Generic Drug Enforcement Act [21 U.S.C. 335a (k)(l)], we hereby certify that in connection with this application, Merck & Co., Inc. did not and will not use in any capacity the services of any person debarred under subsections 306(a) or (b) of the Act.

We consider the filing of this Supplemental New Drug Application to be a confidential matter, and request the Food and Drug Administration not to make its content, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this supplemental application should be directed to Robert E. Silverman, M.D., Ph.D. (610/397-2944) or, in my absence, to Bonnie J. Goldmann, M.D. (610/397-2383).



Sincerely,

Robert E. Silverman, M.D. Ph.D.
Senior Director
Regulatory Affairs

Attachments

Federal Express #1
Desk Copy: Philadelphia District Office, FDA
U. S. Customs House, Room 900
2nd & Chestnut Streets
Philadelphia, PA 19106-2973

Q/young766.doc