CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 19-766/S043

Trade Name: Zocor Tablets

Generic Name: simvastatin

Sponsor: Merck & Company, Inc.

Approval Date: April 14, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S043

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APPLICATION NUMBER:

NDA 19-766/S043

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

APR 14 2000

NDA 19-766/S-043

Merck & Co., Inc.
Attention: Michael Elia, M.D.
Director, Regulatory Affairs
Sumneytown Pike, P.O. Box 4
BLA-20
West Point, PA 19486

Dear Dr. Elia:

Please refer to your supplemental new drug application dated November 16, 1999, received November 17, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zocor (simvastatin) Tablets.

This "Changes Being Effected" supplemental new drug application provides for correcting the inconsistency noted between the NDA and the Caguas, Puerto Rico lubrication parameters for 5 mg tablets.

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, call Margaret Simoneau, R.Ph., Regulatory Management Officer, at (301) 827-6418.

Sincerely,

Stephen K. Moore 3/14/00

Stephen K. Moore, Ph.D.
Chemistry Team Leader I for
Division of Metabolic and
Endocrine Drug Products, (HFD-510)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 19-766
HFD-510/Div. Files
HFD-510/M. Simoneau
HFD-510/SKelly/SMoore
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: Mas/April 14, 2000
Initialed by: SKelly4.14.00/SMoore4.14.00/EGalliers4.14.00
final:Mas4.14.00
filename: 19766.43

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-766/S043

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

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

These copies are ORIGINAL
SPECIAL FILE
desk copies

NDA NO. 19766 REF NO. 043
NDA SUPPL FOR SCM

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

November 16, 1999

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

MERCK
Research Laboratories

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
NOV 17 1999
HFD-510

Dear Dr. Sobel:

NDA 19-766: Tablets ZOCOR™ (Simvastatin)
SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED (CBE)
Chemistry Section: Tablets ZOCOR™, 5 mg

Pursuant to Section 505(b) of the Food, Drug and Cosmetic Act and in accordance with *21 CFR 314.70(c),* Merck Research Laboratories (MRL), a division of Merck & Co., Inc., submits a supplement to NDA 19-766.

As indicated on the attached Form FDA 356h, this supplemental application provides for changes in the Chemistry section of the approved New Drug Application (NDA) for Tablets ZOCOR™ (simvastatin).

In 1996, Tablets ZOCOR® 5 mg was initiated and validated utilizing the modified lubrication parameters provided in the attached supplement at the Merck Manufacturing Division (MMD) facility located in Caguas, Puerto Rico. The validated manufacturing process of the Wilson, North Carolina facility utilizes the NDA filed lubrication parameters. During the validation in 1996, Caguas and Wilson validation data were reviewed and found to be acceptable. During the recent annual review of the NDA, it was determined that this site dichotomy was not reflected in the filed manufacturing process description. Therefore, with this letter, MRL is providing a CBE supplement to NDA 19-766 correcting the inconsistency noted between the NDA filed with the Agency and the Caguas manufacturing lubrication parameters.

Attachment 1 contains the following CMC information:

- An Updated Tablets ZOCOR® 5 mg Manufacturing Process Description.
- Multi-point dissolution profiles for Tablets ZOCOR® 5 mg film-coated at the Caguas and Wilson facilities.
- Batch analysis of representative batches of film-coated tablets at Caguas and Wilson.
- Stability data for one lot of Tablets ZOCOR® 5 mg film-coated at the Caguas facility (Long-term stability data will be provided in subsequent Annual Reports).

Attachment 2 contains Merck's request for a categorical exclusion from the requirements to prepare an Environmental Assessment under *21 CFR 25.31(a)*.

Unless otherwise notified, Merck & Co. would like to continue distribution of Tablets ZOCOR® 5 mg manufactured at the Caguas facility on or about November 18, 1999.

In accordance with the Food and Drug Administration Modernization and Accountability Act of 1997, as indicated on the attached Form 3397, no fee is required for this supplemental application.

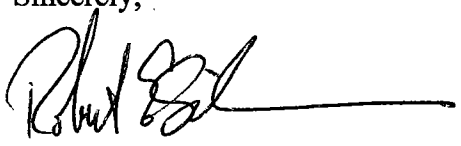
Pursuant to *21 CFR 314.70(a)*, a complete field copy of this amendment to the above-referenced supplemental application has been submitted to the FDA Philadelphia District Office.

As required by Section 306(k)(1) of the Generic Drug Enforcement Act [21 U.S.C. 335a (k) (1)], 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 to be a confidential matter, and request that the Food and Drug Administration not 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 information should be directed to Robert E. Silverman, MD, PhD (610-397-2944) or, in my absence, to Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely,



Robert E. Silverman, MD, PhD
Senior Director, Regulatory Affairs

RES/ped
Attachments
Federal Express #1, HFD-510, Room 14B-04
Desk Copy: FDA Philadelphia District Office
Federal Express #2

Q:\deans\zocor\cmc\5 mg_11-12-99.doc

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Merck & Co., Inc.
Sumneytown Pike, BLA-10
P. O. Box 4
West Point, PA 19486

2. TELEPHONE NUMBER *(Include Area Code)*

(610) 397-2383

3. PRODUCT NAME

ZOCOR (Simvastatin)

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP I AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICAT

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

6. LICENSE NUMBER / NDA NUMBER

N019766

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE **EXCLUSIONS**? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☒ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See Item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☐ NO *(See reverse side if answered YES)*

A completed form must be signed and accompany each new drug or biologic product application and each n supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with paym

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DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please **DO NOT RETURN** this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Bonnie J Goldmann	Bonnie J. Goldmann, M.D. Vice President, Domestic Liaison Regulatory Affairs	November 6, 1

FORM FDA 3397 (5/98)

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