CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 19-766/S044

Trade Name: Zocor Tablets

Generic Name: simvastatin

Sponsor: Merck & Company, Inc.

Approval Date: December 11, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-766/S044

CONTENTS

Reviews / Information Included in this NDA Review.

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Chemistry Review(s)	**X**
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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/S044

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-766/S-044

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

Dear Dr. Elia:

Please refer to your supplemental new drug application dated August 11, 2000, received August 14, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zocor (simvastatin) Tablets.

This supplemental new drug application provides for already approved packaging configurations containing new drug product counts.

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 Project Manager, at (301) 827-6411.

Sincerely,

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

/s/

Stephen Moore
12/11/00 11:37:10 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-766/S044

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW

1. ORGANIZATION CDER/HFD-510
Division of Metabolism and Endocrine Drug Products

2. NDA # 19-766
Original NDA approved: 23-DEC-1991

3. NAME AND ADDRESS OF APPLICANT
Merck & Co., Inc.
P.O. Box 4
West Point PA 19486 (Phone): 610-397-2944

4. SUPPLEMENT SCP -044
11-AUG-99
(Rec'd 15-NOV-99)

5. Name of the Drug
ZOCOR™

6. Nonproprietary Name
Simvastatin

7. SUPPLEMENT PROVIDES for already approved packaging configurations containing new drug product counts.

8. AMENDMENT --

9. PHARMACOLOGICAL CATEGORY
HMG-CoA inhibitor used to treat hyperlipidemia

10. HOW DISPENSED
Oral

11. RELATED
-N. A. -

12. DOSAGE FORM Tablet

13. POTENCY 5, 10, 20, 40 & 80 mg

14. CHEMICAL NAME AND STRUCTURE

Butanoic acid, 2,2-dimethyl-,1,2,3,7,8,8α-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl]-1-naphthalenyl ester, [1S-[1α,3α,7β,8β(2S*,4S*),-8αβ]]; $C_{25}H_{38}O_5$, F.W. = 418.57, CAS 56180-94-0 (For the structure, see Chemistry Review #1, dated 16-MAR-1988 in Vol. 3.1 of NDA 19-766).

15. COMMENTS See next page

16. CONCLUSIONS AND RECOMMENDATIONS The CMC information provided in this Prior Approval Supplement is satisfactory. The request for a Categorical Exclusion to prepare an EA under 21 CFR §25.31(b) is acceptable. From a Chemistry point of view, this supplement can be approved. Issue approval letter.

17. REVIEWER NAME (AND SIGNATURE) **DATE**
COMPLETED 07-DEC-2000
Sharon Kelly, PhD
R/D INITIATED BY

filename: 19766#044

DISTRIBUTION: Original: sNDA 19-766 cc: HFD-510 Division File CSO Reviewer

AP

2 Page(s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 19-766
5044

/s/

Sharon Kelly
12/7/00 12:30:07 PM
CHEMIST

paper copy signed Dec. 7

Stephen Moore
12/7/00 04:10:27 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-766/S044

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES 98 95)

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-766/S-044

Merck & Co, Inc.
Sumneytown Pike
P.O. Box 4, BL A-20
West Point, PA 19486

AUG 24 2000

Attention: Michael C. Elia, Ph.D.
Director, Regulatory Affairs

Dear Dr. Elia:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Zocor™ (simvastatin)

NDA Number: 19-766

Supplement Number: S-044

Date of Supplement: August 11, 2000

Date of Receipt: August 14, 2000

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on October 13, 2000, 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-044
HFD-510/Div. Files
HFD-510/CSO/Simoneau

filename: C:\DATA\WPFILES\19766S44.WPD

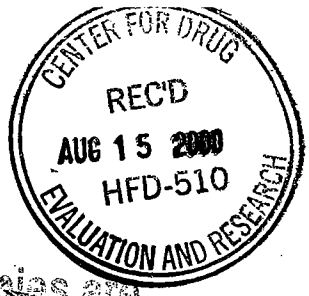
SUPPLEMENT ACKNOWLEDGEMENT

Michael C. Elia, Ph.D.
Director
Regulatory Affairs

ORIGINAL

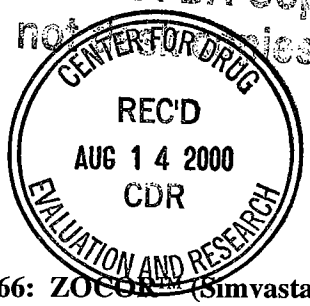
NDA NO. 19-766 REF. NO. 044

SUPPL FOR SCP



Merck & Co., Inc.
BLA-20
P.O. Box 4
West Point PA 19486
Tel 610 397 3180
215 652 5000
Fax 610 397 2516

August 11, 2000



MERCK
Research Laboratories

Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20850

NDA 19-766: ZOCOR™ (Simvastatin)

Prior Approval Supplement - Chemistry

Pursuant to Section 505(b) of the Food, Drug and Cosmetic Act and in accordance with 506A(c)(1) of the Food and Drug Administration Modernization Act, we submit, for the Agency's review and approval, 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 for ZOCOR™.

The attached prior approval supplements providing additions are listed below.

- 30 count, HDPE Bottle packaging configuration for ZOCOR™, 5 mg tablets.
- 30 count, HDPE Bottle packaging configuration for ZOCOR™, 10 mg tablets.
- 30 and 90 count, HDPE Bottle packaging configuration for ZOCOR™, 20 mg tablets.
- 30 and 90 count, HDPE Bottle and [redacted] packaging configuration for ZOCOR™, 40 mg tablets.
- 30 and 90 count, HDPE Bottle and [redacted] packaging configurations for ZOCOR™, 80 mg tablets.

Supporting USP XXIV <671> Test results for the new packaging configurations and three months accelerated and long term stability data for ZOCOR™ tablets packaged in the new packaging configurations are also provided in this supplement. All information is in an electronic format as indicated in the Table of Contents for this supplemental application.

This supplemental application is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations. This supplemental application is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the supplemental application. All documents requiring signatures for certification are included as paper for archival purposes.

All of the information is contained on one CD and is not more than 100MB We have taken precautions to insure that any software on the CD is free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorize the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Metabolic and Endocrine Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Margaret Simoneau, Regulatory Project Manager, Division of Metabolic and Endocrine Drug Products. MRL will follow-up with Ms. Simoneau to ensure that the appropriate reviewers have been given access to this electronic submission.

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

Pursuant to 21 CFR 314.50 a complete field copy of this supplement has been submitted to the FDA Philadelphia District Office.

Merck & Co., Inc. is requesting a categorical exclusion for the requirements to prepare an Environmental Assessments under 21 CFR 25.31(a). This supplement meets the requirements of a categorical exclusion under 21 CFR 25.31(a) because it will not increase the use of the active moiety. To the best of the firm's knowledge no extraordinary circumstances exist in regard to this action.

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 Application 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 supplemental application should be directed to Michael C. Elia, Ph.D. (610-397-3180) or, in my absence, to Bonnie J. Goldmann, M.D. (610-397-2383).

Sincerely,

Michael C. Elia, Ph.D.
Director, Regulatory Affairs

Attachment: One Compact Disk

Federal Express #1

Desk Copies:

Margaret Simoneau, R.Ph., Regulatory Project Manager (cover letter)
HFD-510, Room 14B-04 Federal Express #2

With Administrative and Chemistry Documentation:
Philadelphia District Office
Food and Drug Administration
U.S. Custom House Room 900
2nd & Chestnut Streets
Philadelphia, PA 19106-2973
Federal Express #3

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

Expiration Date [illegible]

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

APPLICANT'S NAME AND ADDRESS

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

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 HI AND SIGN THIS FORM.

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

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATI

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

2. TELEPHONE NUMBER *(Include Area Code)*
(610) 397-2383

5. USER FEE I.D. NUMBER

6. ~~LICENSE NUMBER~~ / NDA NUMBER
19-766

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 ne supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with paym

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for rev instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of inform Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

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

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

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Bonnie Goldmann	Bonnie J. Goldmann, M.D. Vice President, Domestic Liaison Regulatory Affairs	Aug 11, 2000

FORM FDA 3397 (5/98)

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