CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 19-898/S023

Trade Name: Pravachol Tablets

Generic Name: pravastatin sodium

Sponsor: Bristol Myers-Squibb

Approval Date: February 11, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-898/S023

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 19-898/S023

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-898/S-023

FEB 11 1999

Bristol-Myers Squibb
Attention: William J. Regan
Director, CMC, Regulatory Affairs
P.O. Box 5400
Princeton, NJ 08543-5400

Dear Mr. Regan:

Please refer to your supplemental new drug application dated August 13, 1998, received August 21, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pravachol (pravastatin sodium) Tablets.

We acknowledge receipt of your submissions dated January 4, 1999.

We note that this supplement was submitted as a 'Special Supplement - Changes Being Effected' under 21 CFR 314.70(c).

This supplemental new drug application provides for an alternate site to manufacture 20 mg, reduced-mass, tablets of Pravachol at the Squibb manufacturing facility in Humacao, P. R. Your submission stated September 13, 1998, as the implementation date for the change.

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

Sincerely,

Stephen K. Moore Feb. 11, 1999

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

cc:
Archival NDA 19-898
HFD-510/Div. Files
HFD-510/M. Simoneau/WBerlin/SMoore
HFD-95/DDMS (with labeling)
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: Mas/February 8, 1999
Initialed by:WBerlin2.8.99/HAhn2.8.99/SMoore2.8.99/EGalliers2.11.99
final:Mas2.11.99
filename: 19898.23

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-898/S023

CHEMISTRY REVIEW(S)

ORIGINAL FEB 4 1999

CHEMISTS REVIEW	1. ORGANIZATION	2. NDA NUMBER
	DMEDP II, HFD-510	19898
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
Bristol-Myers Squibb Co. P.O. Box 5400 Princeton NJ 08543-5400		SCM-023 13-AUG-1998
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Pravachol Tablets	Pravastatin sodium	4-JAN-1999

8. SUPPLEMENT PROVIDES FOR

An alternate site to manufacture 20 mg, reduced-mass, tablets of Pravachol at the Squibb manufacturing facility in Humacao, PR.

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 SNDA was filed as "Special Supplement-Changes Being Effected-SUPAC-IR", and is consistent with the SUPAC filing requirements. This application seeks approval for the use of an alternate site in Humacao PR to manufacture 20 mg-strength reduced-mass tablets of Pravachol, in batch sizes ranging from \ to \ kg. The sponsor has provided adequate descriptions of the raw material controls, the manufacturing process and controls, and the release and stability testing methods. The controls and testing methods for the proposed facility are the same as approved under this NDA and the manufacturing process is representative of the process at current sites. Adequate stability data were provided to support the alternate facility, and the sponsor has made acceptable stability commitments for future lots. The facility was found to be "Acceptable" by the Office of Compliance (see attached CDER EER dated 26-OCT-1998).

16. CONCLUSION AND RECOMMENDATION

The proposed facility at Humacao PR is acceptable for the manufacture of 20 mg-strength reduced-mass Pravachol Tablets. The facility has received an "Acceptable" recommendation by OC based on the District's Recommendation (see attached CDER EER dated 26-OCT-1998). Issue an approval letter.

17. NAME	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
WILLIAM K. BERLIN		1-27-99

DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE

D

AP

Stephen K. Moore
2/4/99

2 Page(s) Withheld

1 § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 19-898
5023

CDER Establishment Evaluation Report for October 26, 1998

Application: **NDA 19898/023**
Stamp: **21-AUG-1998** Regulatory Due: **21-FEB-1999**
Applicant: **BRISTOL MYERS SQUIBB**
RT 206 PROVINCE LINE RD
PRINCETON, NJ 085434000

Priority: **1S** Org Code: **510**
Action Goal: District Goal: **16-NOV-1998**
Brand Name: **PRAVACHOL TABLETS**
Established Name:
Generic Name: **PRAVASTATIN SODIUM**
Dosage Form: **TAB (TABLET)**
Strength: **10, 20, 40 MG**

FDA Contacts:			
M. SIMONEAU	**(HFD-510)**	**301-827-6418**	**, Project Manager**
W. BERLIN	**(HFD-510)**	**301-827-6370**	**, Review Chemist**
S. MOORE	**(HFD-510)**	**301-827-6430**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 19-OCT-1998 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: **2623458**
SQUIBB MANUFACTURING INC
STATE RD #3 KM775
HUMACAO, PR 00791

DMF No:
AADA No:

Profile: **TCM** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **19-OCT-1998**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-898/S023

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-898/S-023

Bristol Myers Squibb
P.O. Box 4000
Princeton, NJ 08543-4000

AUG 27 1998

Attention: William J. Regan
Director

Dear Mr. Regan:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Pravachol ® (pravastatin sodium) Tablets

NDA Number: 19-898

Supplement Number: S-023

Date of Supplement: August 13, 1998

Date of Receipt: August 21, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on October 20, 1998, 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 19-898/S-023
HFD-510/Div. Files
HFD-510/CSO/M. Simoneau

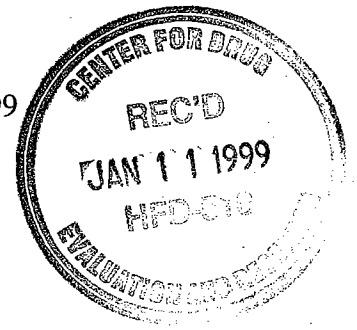
filename: C:\DATA\WPFILES\19898ACK

SUPPLEMENT ACKNOWLEDGEMENT

ORIGINAL

Bristol-Myers Squibb
Pharmaceutical Research Institute

P.O. Box 5400 Princeton, NJ 08543-5400
609 818-4732 Fax: 609 818-5832



January 4, 1999

William J. Regan
Director, CMC
North American Regulatory Affairs

Amendment to
Special Supplement--Changes Being Effected--SUPAC-IR
NDA 19-898, S-023
PRAVACHOL® (pravastatin sodium) Tablets

NDA SUPP AMEND
SCM-023 BC

Solomon Sobel, M.D., Director
Division of Metabolism and Endocrine Drug Products (HFD-150)
Center of Drug Evaluation and Research
Food and Drug Administration
Department of Health & Human Services
5600 Fishers Lane
Rockville, MD 20857

REVIEWS COMPLETED
AP 2-11-99
CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO
Mas 2-17-99
CSO INITIALS DATE

Attention: Document Control Room (14B-03)

Dear Dr. Sobel:

Reference is made to our approved New Drug Application, NDA 19-898, for PRAVACHOL® (pravastatin sodium) Tablets, and specifically to our "Changes Being Effected" Supplement dated 8-13-98, S-023. The supplement informs FDA of our intention to manufacture and control PRAVACHOL® (pravastatin sodium) Reduced Mass Tablets, 20mg, at Squibb Manufacturing, Inc., a subsidiary of the Bristol-Myers Squibb Company in Humacao, Puerto Rico, as permitted by SUPAC-IR.

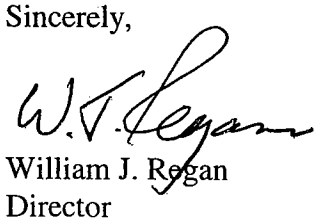
In accordance with a request by William Berlin, Ph.D., we are amending our supplement to revise the stability commitment to specify samples from a [redacted] batch will be entered into the marketed product stability testing program when such a batch size is produced.

Bristol-Myers Squibb Company certifies that field copies of this amendment have been provided to the North Brunswick office (120 North Center Drive, North Brunswick, NJ 08902) and to the San Juan, P. R. Office (466 Fernandez Juncos Avenue, Puerta de Tierra, San Juan, Puerto Rico 00901) of the Food and Drug Administration. We further certify that the field copies are true copies of this amendment.

h:\mg-sup\prava.amd

Should you have any questions concerning this supplement, please contact me at (609) 818-4732.

Sincerely,



William J. Regan
Director
CMC - Marketed Products
Worldwide Regulatory Affairs

h:\mg-sup\prava.amd

NDA NO. 19898 REF. NO. 023

NDA SUPPL FOR SCH

Bristol-Myers Squibb
Pharmaceutical Research Institute

P.O. Box 5400 Princeton, NJ 08543-5400
609 818-4732 Fax: 609 818-5832

NDA SUPPLEMENT

ORIGINAL

William J. Regan
Director, CMC
North American Regulatory Affairs

August 13, 1998

Special Supplement--Changes Being Effected--SUPAC-IR
NDA 19-898
PRAVACHOL® (pravastatin sodium) Tablets

Solomon Sobel, M.D., Director
Division of Metabolism and Endocrine Drug Products (HFD-510)
Center of Drug Evaluation and Research
Food and Drug Administration
Department of Health & Human Services
5600 Fishers Lane
Rockville, MD 20857

Attention: Document Control Room (14B-03)

Dear Dr. Sobel:

Reference is made to our approved New Drug Application, NDA 19-898, for PRAVACHOL® (pravastatin sodium) Tablets, and specifically to Supplement S-008, which approved the reduced mass formulation. We are currently approved to manufacture, package and control PRAVACHOL® (pravastatin sodium) Reduced Mass Tablets, 10 mg, 20 mg and 40 mg, at Bristol Laboratories Corporation, a subsidiary of the Bristol-Myers Squibb Company at Mayagüez, Puerto Rico. We are also approved to package in HDPE bottles and in unit-dose foil pouches at the Bristol-Myers Squibb facilities in Evansville, Indiana; Mt. Vernon, Indiana; and Humacao, Puerto Rico; and in unit-dose foil pouches at several contract-packaging sites. In addition, the contract packagers are also approved to perform secondary packaging operations of bottles of tablets filled, closed, sealed, labeled and released in our approved facilities.

Based on SUPAC-IR guidance, section IV, C, we are submitting this level 3 changes being effected supplement in order to manufacture and control PRAVACHOL® (pravastatin sodium) Reduced Mass Tablets, 20 mg, at Squibb Manufacturing, Inc., a subsidiary of the Bristol-Myers Squibb Company in Humacao, Puerto Rico. We plan to implement these changes 30 days from the date of this supplement.

noted
Ahn 11/10/98

Based on 21 CFR Part 25.31(a), we request a waiver of the requirement for an environmental assessment.

Bristol-Myers Squibb Company certifies that field copies of this supplemental application have been provided to the North Brunswick office (120 North Center Drive, North Brunswick, NJ 08902) and to the San Juan, P. R. Office (466 Fernandez Juncos Avenue, Puerta de Tierra, San Juan, Puerto Rico 00901) of the Food and Drug Administration. We further certify that the field copies are true copies of this supplemental application.

A detailed summary of this supplement may be found in the Introduction and Summary Section. In addition, a Table of Contents describing the components of this submission follows this letter.

Should you have any questions concerning this supplement, please contact me at (609) 818-4732.

Sincerely,

W. J. Regan

William J. Regan
Director
CMC - Marketed Products
Worldwide Regulatory Affairs

jgm/WJR

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. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Bristol-Myers Squibb
P.O. Box 4000
Princeton, New Jersey 08543-4000

2. TELEPHONE NUMBER *(Include Area Code)*

(609) 252-4000

3. PRODUCT NAME

PRAVACHOL (pravastatin sodium) Tablets

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

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

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ 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

19-898

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

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. 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

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
W. J. Regan	William J. Regan Director of Regulatory Affairs	8/13/98

FORM FDA 3397 (5/98)

Created by Electronic Document Services/USDHHS: (301) 443-2454 EF