We consider the filing of this amendment to be a confidential matter, and request 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 Charles L. Hyman, M.D. (610/397-2850) or, in my absence, Bonnie Goldmann, M.D., Ph.D. (610/397-2383).

Sincerely,

Charles L. Hyman, M.D.
Director, Regulatory Affairs

Attachment
Federal Express #1

Desk Copy (cover letter with attachments):
Federal Express #1 Margaret Simoneau HFD-510, Room 14B-04
Federal Express #1 Mary Parks, M.D. HFD-510, Room 14B04
Federal Express #2 Joyce Mele, Ph.D. HFD-715, Room 14B45

q/Corrado/Murakami/nda19643

APPEARS THIS WAY ON ORIGINAL

Charles L. Hyman, M.D.
Director
Regulatory Affairs

Merck & Co., Inc.
P.O. Box 4
West Point PA 19486
Fax 610 397 2516
Tel 610 397 2850
215 652 5000

July 1, 1998

DESK COPY

MERCK
Research Laboratories

Dr. H. W. Ju
Division of Scientific Investigations Clinical Branch
HFD-344, Room 125
Food and Drug Administration
7520 Standish Place
Rockville, Maryland 20855

Dear Dr. Ju:

NDA 19-643/S-055
MEVACOR™ (Lovastatin)

RESPONSE TO REQUEST FOR INFORMATION

Reference is made to the above Supplemental New Drug Application (SNDA) submitted on April 28, 1998. Reference is also made to telephone conversations between Dr. H. W. Ju, Division of Scientific Investigations (DSI) and Dr. Charles L. Hyman, Merck Research Laboratories (MRL) on June 19, 1998 and June 23, 1998 requesting additional patient information the Lovastatin - Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) SNDA/S-055. With this letter and attachments, MRL is providing the additional requested information concerning AFCAPS/TexCAPS (Protocol 042).

This submission consists of Table 1 containing the requested data for AFCAPS patients and Table 2 containing the requested data for TexCAPS patients. As requested, both tables are also provided as Microsoft Excel 5.0/95 Workbook documents on the enclosed diskette.

We consider the information included in this submission 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 Charles L. Hyman, M.D. (610/397-2850) or, in my absence, to Robert E. Silverman, M.D., Ph.D. (610/397-2944).

Sincerely,

Charles L. Hyman, M.D.
Director, Regulatory Affairs

Attachments: Tables 1 and 2 (paper copy)
Diskette (electronic version)

Federal Express #1

Facsimile: Dr. H. W. Ju (301-594-1204), July 1, 1998

Desk Copy: Ms. Margaret Simoneau, HFD-510 (letter only)
Federal Express #2

Official File: NDA 19-643, HFD-510 (with attachments + 1 diskette)
Federal Express #2

q:\murakami\mevacor\afcaps\dsi\req61998.doc

Charles L. Hyman, M.D.
Director
Regulatory Affairs

DESK COPY

Merck & Co., Inc.
P.O. Box 4
West Point PA 19486
Fax 610 397 2516
Tel 610 397 2850
215 652 5000

June 18, 1998

Dr. H. W. Ju
Division of Scientific Investigations Clinical Branch
HFD-344, Room 125
Food and Drug Administration
7520 Standish Place
Rockville, Maryland 20855

MERCK
Research Laboratories

Dear Dr. Ju:

NDA 19-643/S-055
MEVACOR™ (Lovastatin)

GENERAL CORRESPONDENCE

Reference is made to the above Supplemental New Drug Application (SNDA) submitted on April 28, 1998. Reference is also made to a Merck Research Laboratories (MRL) response to a FDA request submitted on June 12, 1998 containing additional information for DSI's site inspection regarding the Lovastatin - Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS).

MRL has identified corrections to the letter and attachments submitted on June 12, 1998. In Volume 1, on page 1 of the cover letter, the fourth paragraph contained incorrect data concerning the number of patients randomized and number of patients completed at the AFCAPS Clinic and at the TexCAPS Clinic.

The corrected numbers are bolded in the following revised paragraph:

"At the AFCAPS Clinic, the number of patients randomized was 3737 and the number of patients completed was **2482** (not 2335). At the TexCAPS Clinic the number of patients randomized was **2868** (not 2863 -typo) and the number of patients completed was **1934** (not 2081)"

Inadvertently, 2335 was given as the number of patients completed at the AFCAPS Clinic. However, 2335 was the total number of patients on lovastatin who completed the study. Also, 2081 was given as the number of patients completed at the TexCAPS Clinic. However, 2081 was total number of patients on placebo who completed the study.

Corrections to two additional attachment pages due to this error in the number of patients completed at the AFCAPS Clinic and at the TexCAPS Clinic have been identified, and the revised replacement pages are enclosed. The pages to be replaced are located in Volume 1, behind the tab "AFCAPS Clinic Site No. 042-001 J.R. Downs" (see attachment 1) and in Volume 2, behind the tab "TexCAPS Clinic Site No. 042-001 Clearfield/Weis." (see attachment 2).

MRL has also identified a correction on the first page of Monitoring Log for the TexCAPS Clinic Location located in Volume 1, behind the tab "Monitoring Log TexCAPS Clinic." The third entry under Monitoring Period should be **06/04/92** (not 06/07/92) for L. Saidt. This revised replacement page is also enclosed (see attachment 3).

We apologize for any inconvenience the replacement of these pages may have caused your personnel. Questions concerning this information should be directed to Charles L. Hyman, M.D. (610/397-2850) or, in my absence, to Robert E. Silverman, M.D., Ph.D. (610/397-2944).

Sincerely,

Charles L. Hyman, M.D.
Director, Regulatory Affairs

Attachment
Federal Express #1

Official File: NDA 19-643/S-055: MEVACOR™/w att (2)
HFD-510, Rm. 14B-04, Federal Express #2

Desk Copy (cover letter only) Ms. Margaret Simoneau, HFD-510, Rm. 14B-04
Federal Express #2

q\robinson\murakami\S_055

Charles L. Hyman, M.D.
Director
Regulatory Affairs

Merck & Co. Inc
P.O. Box 4
West Point PA 19486
Fax 610 397 2516
Tel 610 397 2850
215 652 5000

June 12, 1998

DESK COPY

MERCK
Research Laboratories

Dr. H. W. Ju
Division of Scientific Investigations Clinical Branch
HFD-344, Room 125
Food and Drug Administration
7520 Standish Place
Rockville, Maryland 20855

Dear Dr. Ju:

NDA 19-643/S-055
MEVACOR™ (Lovastatin)

RESPONSE TO REQUEST FOR INFORMATION

Reference is made to the above Supplemental New Drug Application (SNDA) submitted on April 28, 1998. Reference is also made to telephone conversations between Dr. H. W. Ju, Division of Scientific Investigations (DSI) and Dr. Charles L. Hyman, Merck Research Laboratories (MRL) on May 14, 22, 26 and 28, 1998. During these conversations, required information for DSI's site inspection regarding the Lovastatin - Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) SNDA/S-055 was discussed. In addition, reference is made to a MRL Response to a FDA Request for information dated May 20, 1998.

With this letter and attachments, MRL is providing the additional requested information concerning AFCAPS/TexCAPS (Protocol 042), the only study contained in S-055 which is entitled, "A Randomized, Double-Blind, Placebo-Controlled Trial of the Effect of Lovastatin on the Incidence of Primary Coronary Heart Disease in Patients with Mild to Moderate Elevations in Total and LDL-Cholesterol in Combination with Low HDL-Cholesterol".

The study site number is 042-001. The study is a single site study with two clinical locations in the United States. The primary investigator for this study is Lt. Col. John R. Downs, M.D., 59th MDW/MMCCP, AFCAPS Clinic, Building 3746, 2449 Pepperrell Street, Lackland Air Force Base, San Antonio, TX 78236-5316. Michael B. Clearfield, D.O. and Stephen E. Weis, D.O. are subinvestigators for this study at the TexCAPS Clinic, University of North Texas Health Sciences Center, 3500 Camp Bowie, Fort Worth, TX 76107 location. Please note that the TexCAPS Clinic has been closed, and the records from the TexCAPS Clinic have been transferred to the AFCAPS Clinic.

At the AFCAPS Clinic, the number of patients randomized was 3737 and the number of patients completed was 2335. At the TexCAPS Clinic the number of patients randomized was 2863 and the number of patients completed was 2081.

This submission consists of two Volumes. Volume 1 contains data concerning the AFCAPS Clinic in San Antonio, TX, and Volume 2 contains data concerning the TexCAPS Clinic in Forth Worth, TX. Each volume contains the following information:

- Copy of Original Protocol 042 with cover letter.
- Copies of the cover letters for each protocol amendment for Protocol 042.
- Form 1572 for the principal investigator (Lt. Col. John R. Downs, M.D. for AFCAPS Clinic) Form documenting the addition or substitution of secondary/subinvestigator to a clinical study (Michael B. Clearfield, D.O. and Stephen E. Weis, D.O. for TexCAPS Clinic).
- List of Subjects with Primary Endpoint Events.
- List of Subjects who did not complete the study.
- List of Subjects Reported as Protocol Violators per Protocol Analysis and Nature of Violation. PLEASE NOTE, this list and categories of violations would apply if a Per Protocol Analysis were performed. However, the analysis that supported this application was an Intent-to-Treat analysis, and therefore included all randomized participants.

  This list includes three categories:

  I. Pre-Existing Documented Cardiovascular Atherosclerotic Disease

  II. Compliance <75% - Non-Compliance (<75 compliant to prescribed dosage regimen) or those that took one or fewer doses of study medication.

  III. CRX Use of Lipid Lowering Medication (Discontinuation due to concomitant use of lipid lowering medication.)

- Monitoring Log
- Worldwide Clinical Quality Assurance Resources (WCQAR) Investigator Site Audit Standard Operating Procedures (SOP).
- Clinical Research Guidelines For Monitoring an Ongoing Study.
- Case Report Forms for four randomized patients from Protocol 042.

Questions concerning this information should be directed to Charles L. Hyman, M.D. (610/397-2850) or, in my absence, to Robert E. Silverman, M.D., Ph.D. (610/397-2944).

Sincerely,

Charles L. Hyman, M.D.
Director, Regulatory Affairs

Attachment

Federal Express #1

Desk Copies (cover letter only) Ms. Margaret Simoneau, HFD-510, Rm. 14B-04
Federal Express #2

FDA File: FDA 19-643/S-055: MEVACOR™ (Lovastatin), Dr. Sobel
HFD-510, Rm. 14B-04, Federal Express #2

q\robinson\murakami\ndaaftx1