

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

**APPLICATION NUMBER: 19-766/S040**

**ADMINISTRATIVE DOCUMENTS**

<b>DEPARTMENT OF HEALTH AND HUMAN SERVICES</b> <b>FOOD AND DRUG ADMINISTRATION</b>		Form Approved OMB No. 0910-0338. Expiration Date: April 30, 2000 See OMB Statement on last page.
<b>APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN</b> <b>ANTIBIOTIC DRUG FOR HUMAN USE</b> <i>(Title 21, Code Of Federal Regulations, 314)</i>		<b>FOR FDA USE ONLY</b>
		APPLICATION NUMBER
<b>APPLICANT INFORMATION</b>		
NAME OF APPLICANT <b>Merck &amp; Co., Inc.</b>		DATE OF SUBMISSION <b>30-JUN-1999</b>
TELEPHONE NO. (Include Area Code) <b>(610) 397-2850</b>		FACSIMILE (FAX) Number (Include Area Code) <b>(610) 397-2516</b>
APPLICANT ADDRESS (Number, Street, City, State, Country, Zip Code or Mail Code, and U.S. License number if previously issued): <b>Sumneytown Pike, P.O. Box 4          BLA-20          West Point, PA 19486</b>		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE:
<b>PRODUCT DESCRIPTION</b>		
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued) <b>19-766</b>		
ESTABLISHED NAME (e.g., Proper name, USPI/USAN name) <b>Simvastatin</b>		PROPRIETARY NAME (trade name) IF ANY <b>ZOCOR</b>
CHEMICAL/ BIOCHEMICAL/BLOOD PRODUCT NAME (if any) [1S-{1α, 3α, 7β, 8β(2S*, 4 S*), 8αβ}]-1,2,3,7,8a-hexahydro-3,7-dimethyl-6-[2-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl-2,2-dimethylbutanoate		CODE NAME (if any)
DOSAGE FORM <b>Tablet</b>	STRENGTHS: <b>5 mg, 10 mg, 20 mg, 40 mg, 80 mg</b>	ROUTE OF ADMINISTRATION <b>Oral</b>
(PROPOSED) INDICATION(S) FOR USE: Reduction of risk of total mortality by reducing coronary death, reduction of risk for non-fatal myocardial infarction and reduction of the risk for undergoing myocardial revascularization procedures in patients with coronary heart disease and hypercholesterolemia. Reduction of elevated total and LDL cholesterol levels in patients with primary hypercholesterolemia (Types Iia and Iib).		
<b>APPLICATION INFORMATION</b>		
APPLICATION TYPE (Check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input type="checkbox"/> ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR part 601)		
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b) (1) <input type="checkbox"/> 505 (b) (2) <input type="checkbox"/> 507		
IF AN ANDA, OR AADA, IDENTIFY THE REFERENCED LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug _____ Holder of Approved Application _____		
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input type="checkbox"/> AMENDMENT TO A PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> SUPAC SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input checked="" type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER		
<b>REASON FOR SUBMISSION</b>		
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)		
NUMBER OF VOLUMES SUBMITTED <b>5</b>	THIS APPLICATION IS <input type="checkbox"/> PAPER <input checked="" type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC	
<b>ESTABLISHMENT INFORMATION</b>		
Provide locations of all manufacturing, packaging and control sites for the drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.		
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)		

/S/

JUL 19 1999

NDA 19-766/S-040

Merck Research Laboratories, Inc.  
Attention: Charles Hyman, M.D.  
Director, Regulatory Affairs  
Sumneytown Pike, P.O. Box 4, BLA-20  
West Point, PA 19486

Dear Dr. Hyman:

We acknowledge receipt of your efficacy supplemental application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	Zocor™ (simvastatin) Tablets
NDA Number:	19-766
Supplement Number:	S-040
Therapeutic Classification:	Standard (S)
Date of Supplement:	June 30, 1999
Date of Receipt:	July 01, 1999

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on August 30, 1999, in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be May 01, 2000, and the secondary user fee goal date will be July 01, 2000.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within 120 days of receipt of your pediatric drug development plan, we will notify you of the pediatric studies that are required under section 21 CFR 314.55.

If you believe that this drug qualifies for a waiver of the study of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We

will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at [www.fda.gov/cder/pediatric](http://www.fda.gov/cder/pediatric)) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. If you do not submit a Proposed Pediatric Study Request within 120 days from the date of this letter, we will presume that you are not interested in obtaining pediatric exclusivity and will notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolic and Endocrine Drug Products, HFD-510  
Attention: Division Document Room, 14B-19  
5600 Fishers Lane  
Rockville, Maryland 20857

If you have any questions, contact Margaret Simoneau, R.Ph., Regulatory Management Officer, at (301) 827-6418.

Sincerely,

A rectangular box containing the handwritten initials "IST".

7.16.99

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

**EER**

**APPEARS THIS WAY  
ON ORIGINAL**

**NOT NEEDED**

**Item 19**      **Financial Disclosure Information**

**A. Introduction**

In compliance with the U.S. Food and Drug Administration's regulation *Financial Disclosure by Clinical Investigators* published February 2, 1998 and revised December 31, 1998, this item details the requested information concerning the financial interests of and compensation to investigators participating in the clinical trials presented in this application.

Data from two clinical trials provide the primary information in support of this application:

*A Multicenter Study to Compare the Safety, Tolerability and Efficacy of Synvinolin and Cholestyramine in the Treatment of Hypercholesterolemia and to Study the Concomitant Use of the Two Drugs (Protocol 004)*

*A Multicenter Study to Compare the Safety, Tolerability and Efficacy of Synvinolin and Probucol in the Treatment of Hypercholesterolemia (Protocol 005).*

Both of these Clinical Study Reports were submitted to the FDA as part of the original New Drug Application (submitted October 16, 1987; resubmitted December 9, 1988) and were approved on December 13, 1991. As discussed with Ms. Enid Galliers, FDA and Dr. Robert Silverman, Merck Research Laboratories on March 31, 1999, financial disclosure information is not required to be presented for either of these trials as the data have already been submitted, reviewed and approved by the Agency.

Additional supportive safety information is provided in this submission in the form of a publication for a clinical trial currently in progress (*MRC/BHF Heart Protection Study of Cholesterol-Lowering Therapy and of Antioxidant Vitamin Supplementation in a Wide Range of Patients at Increased Risk of Coronary Heart Disease Death: Early Safety and Efficacy Experience* [European Heart Journal 1999, 20, 725-741]). This study is funded through four independent organizations (UK Medical Research Council, British Heart Foundation, Merck & Co., Inc. and Hoffmann-La Roche). This study was designed independent of either pharmaceutical company and neither company has representation in its organization.

**B. Discussion**

Information regarding the financial interest of and the compensation to the clinical investigators/subinvestigators participating in the Heart Protection Study as directly related to Merck & Co., Inc. is currently being compiled. As the supportive information being presented in this application is an early evaluation of safety from this on-going study, full collection of this information has not been completed. Efforts are currently underway to collect and provide such details to Merck & Co., Inc.; this information along with the payments of other sorts requirements will be provided to the FDA when completed.

Please note that the Steering Committee, investigators and funding organizations involved with the Heart Protection Study remain blinded to study endpoints.

Section C in this item provides the names of all investigators/subinvestigators participating in the Heart Protection Study; none of these individuals is employed by Merck & Co., Inc. or its subsidiary (MSD - UK).

**C. Table of All Clinical Investigators/Subinvestigators**



Redacted 2

pages of trade

secret and/or

confidential

commercial

information

D. Certification and Disclosure Forms

Certification and Disclosure Forms (3454 and 3455, respectively) are not provided with this submission; these will be provided when the required financial information for the investigators/subinvestigators identified in Table C-1 has been received and tabulated by Merck & Co., Inc.

**APPEARS THIS WAY  
ON ORIGINAL**

Patent Department

Merck & Co., Inc.  
P.O. Box 2000  
Rahway NJ 07065-0907  
Fax 732 594 4720  
Tel 732 594 4000  
Cable MERCKRAH  
Telex 138825

June 7, 1999



ZOCOR®  
NDA 19-766  
Simvastatin

ITEM 13

Pursuant to the provisions of Section 505(b)(1) of the Federal Food, Drug and Cosmetic Act 21 U.S.C. § 355 (b)(1) and in accordance with Title 21 C.F.R. 314.70(b), attached hereto please find the patent information for the above-identified application.

The undersigned declares that U.S. Patent No. 4,444,784 covers the formulation, composition, and/or method of use of ZOCOR® (simvastatin 5 mg, 10 mg, 20 mg, 40 mg and 80 mg tablets), the subject of this application for which approval is being sought.

U.S. Patent No. 4,444,784 has an expiration date of December 23, 2005, as extended by granted Patent Term Restoration under 35 U.S.C. § 156. This patent claims a genus of chemical compounds including simvastatin. This patent is exclusively licensed to Merck & Co., Inc.

The undersigned declares that U.S. Patent No. 4,444,784 covers the composition ZOCOR®. This product is the subject of this application for which approval is being sought.

A claim of infringement could be asserted if a person not licensed by the owner of U.S. Patent No. 4,444,784 engaged in the manufacture, use or sale of ZOCOR®.

Sincerely,

A handwritten signature in cursive script that reads "Carol S. Quagliato".

Carol S. Quagliato  
Senior Patent Attorney

ZOCOR®  
NDA 19-766  
Simvastatin

Item 13  
June 7, 1999

ITEM 13  
PATENT AND EXCLUSIVITY INFORMATION  
MERCK RESEARCH LABORATORIES

- |    |  |   |
|----|--|---|
| 1) | Active Ingredient(s)                                     | Simvastatin                                       |
| 2) | Strength(s)  | 10 mg, 20 mg and 40 mg                            |
| 3) | Trade Name   | ZOCOR®  |
| 4) | Dosage Form, Route<br>of Administration                  | Tablets, Oral                                     |
| 5) | Applicant Firm Name                                      | Merck Research Laboratories                       |
| 6) | NDA Number   | 19-766  |
| 7) | Approval Date  |   |
| 8) | Exclusivity - Date First<br>ANDA could be approved       | Three (3) Years from this sNDA ✓<br>approval date |
|    | Length of Exclusivity Period                             | Three (3) years                                   |
| 9) | Applicable patent numbers<br>and expiration date of each | 4,444,784<br>Expiration Date: 12/23/2005 w/PTR    |

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EXCLUSIVITY SUMMARY FOR NDA # 19-766 SUPPL # 40

Trade Name Zocor Generic Name SIMVASTATIN

Applicant Name Merck HFD # 510

Approval Date If Known \_\_\_\_\_

## PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA? YES /  / NO /  /

b) Is it an effectiveness supplement? YES /  / NO /  /

If yes, what type? (SE1, SE2, etc.) SE2

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES /  / NO /  /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

\_\_\_\_\_  
\_\_\_\_\_  
If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:  
\_\_\_\_\_  
\_\_\_\_\_

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d) Did the applicant request exclusivity?

YES /  / NO /  /

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 yrs

e) Has pediatric exclusivity been granted for this Active Moiety?

no

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO-please indicate as such)

YES /  / NO /  /

If yes, NDA # \_\_\_\_\_ Drug Name \_\_\_\_\_

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES /  / NO /  /

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

## PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

### 1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved.

Answer "no"-if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /  / NO /  /

**APPEARS THIS WAY  
ON ORIGINAL**

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# \_\_\_\_\_  
NDA# \_\_\_\_\_  
NDA# \_\_\_\_\_

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /\_\_\_/ NO /\_\_\_/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# \_\_\_\_\_  
NDA# \_\_\_\_\_  
NDA# \_\_\_\_\_

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

**PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS**

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /  / NO /  /

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /  / NO /  /

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

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(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /  / NO /  /

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(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /  / NO /  /

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /  / NO /  / N/A

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval: N/A

\_\_\_\_\_  
\_\_\_\_\_

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.



4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1		!	
IND #	<input type="text"/>	YES / <input checked="" type="checkbox"/> /	NO / <input type="checkbox"/> / Explain: _____
		!	_____
		!	_____
Investigation #2		!	
IND #	<input type="text"/>	YES / <input checked="" type="checkbox"/> /	NO / <input type="checkbox"/> / Explain: _____
		!	_____
		!	_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1		!	
YES / <input type="checkbox"/> / Explain	_____	!	NO / <input type="checkbox"/> / Explain _____
	_____	!	_____
	_____	!	_____
Investigation #2		!	
YES / <input type="checkbox"/> / Explain	_____	!	NO / <input type="checkbox"/> / Explain _____
	_____	!	_____
	_____	!	_____



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## PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

NDA/BLA # 19-766/ Supplement # 040 Circle one: SE1  SE2 SE3 SE4 SE5 SE6

HFD 510 Trade and generic names/dosage form: Zocor (simvastatin) Action:  AP  AE  NA

Applicant Meck Therapeutic Class lipid lowering drugs

Indication(s) previously approved \_\_\_\_\_

Pediatric information in labeling of approved indication(s) is adequate  inadequate

Proposed indication in this application new starting dose (optimal)

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.

IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS?  Yes (Continue with questions)  No (Sign and return the form)

WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)

Neonates (Birth-1month)  Infants (1month-2yrs)  Children (2-12yrs)  Adolescents (12-16yrs)

1. PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS. Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.
2. PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS. Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.
3. PEDIATRIC STUDIES ARE NEEDED. There is potential for use in children, and further information is required to permit adequate labeling for this use.
  - a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.
  - b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.
  - c. The applicant has committed to doing such studies as will be required.
    - (1) Studies are ongoing.
    - (2) Protocols were submitted and approved.
    - (3) Protocols were submitted and are under review.
    - (4) If no protocol has been submitted, attach memo describing status of discussions.
  - d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.
4. PEDIATRIC STUDIES ARE NOT NEEDED. The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.
5. If none of the above apply, attach an explanation, as necessary.

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER?  Yes  No

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from Med Team LOR (e.g., medical review, medical officer, team leader)

SI  
Signature of Preparer and Title

4-20-02  
Date

Orig NDA/BLA # 19-766/S-040  
HFD 510 /Div File  
NDA/BLA Action Package  
HFD-006/ KRoberts

(revised 10/20/97)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, KHYATI ROBERTS, HFD-8 (ROBERTSK)

**Simvastatin 40-mg Alternative Starting Dose  
Debarment Certification**

As required by §306(k)(1) of 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.

**APPEARS THIS WAY  
ON ORIGINAL**