CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-203

ADMINISTRATIVE DOCUMENTS
CORRESPONDENCE

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

draft labeling

103 pages

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

Abbott Laboratories
100 Abbott Park Road
Abbott Park, IL 60064-6108

ATTN: D-491, Bldg. AP6B-1
Pharmaceutical Products Division
Regulatory Affairs

2. TELEPHONE NUMBER *(Include Area Code)*

(847) 937-5091

3. PRODUCT NAME

Fenofibrate Tablets

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? 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 NDA 19-304 (APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

3823

6. LICENSE NUMBER / NDA NUMBER

N021203

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.

Please DO NOT RETURN this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
[signature]	Associate Director, Regulatory Affairs	

ABBOTT

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

November 10, 1999

Mellon Bank
Three Mellon Bank Center
27th Floor (FDA 360909)
Pittsburgh, PA 15259-0001

Subject: USER FEE I.D. NUMBER 3823

Dear Sir or Madam:

Enclosed is a check in the amount of $272,282 to cover the user fee payment for the following application:

Product Name:	Tricor
Generic Name:	Fenofibrate Tablets
Indication for Use:	Hyperlipidemia
Type of Submission:	New Drug Application
NDA Number:	NO21203
Name of Sponsor:	Abbott Laboratories
Address:	D-491, Building AP6B-1SW PPD Regulatory Affairs 100 Abbott Park Road Abbott Park, Illinois 60064-6108
Contact Person:	Peter Noblin
Telephone Number:	(847) 937-5091

We would appreciate receiving a receipt for this payment; for your convenience, I have enclosed a self-addressed, stamped envelope.

Sincerely,

Peter Noblin
Associate Director, Regulatory Affairs

Enclosures: Abbott Check Number ——— , User Fee Cover Sheet,
Self-Addressed, Stamped Envelope

cc: Peter Noblin, D-491, AP6B-1
Marilou Reed, D-491, AP6B-1
Paula Bourland, D-404, AP9A-1
Sandra Harder, D-387, AP6C-1
Kathy Christianson, D-344, AP6D-1

Division of Metabolic and Endocrine Drug Products

REGULATORY PROJECT MANAGER REVIEW

Application Number: NDA 21-203

Name of Drug: Tricor (fenofibrate) Tablets

Sponsor: Abbott Laboratories

Material Reviewed

Submission Date(s): August 13, 2001

Receipt Date(s): August 14, 2001

Background and Summary Description: This new NDA proposed a new tablet dosage form in 54mg, [redacted] and 160mg strengths. In the June 5, 2000, amendment the applicant indicated that they [redacted] "at the time of the approval of this application." The draft label reviewed in this document, therefore, does not include the [redacted] dosage form in the **DESCRIPTION** or **HOW SUPPLIED** sections.

Review

Package insert

The submitted package insert, identified as "August 13, 2001, Draft Industry", was compared to the final printed package insert for the capsule application NDA 19-304/S-005, identified as "03-5037-R4-Rev, April 2000", submitted March 7, 2001.

1. In the **DESCRIPTION** section:

APPROVED

TRICOR (fenofibrate capsules), micronized, is a lipid regulating agent available as capsules for oral administration. Each capsule contains 67 mg, 134 mg or 200 mg of micronized fenofibrate.

PROPOSED

TRICOR (fenofibrate tablets) is a lipid regulating agent available as tablets for oral administration. Each tablet contains 54 mg or 160 mg of fenofibrate.

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

2 pgs

6. In the **INDICATIONS AND USAGE** section:

PROPOSED

NCEP Treatment Guidelines: LDL-C Goals and Cutpoints for Therapeutic Lifestyle Changes and Drug Therapy in Different Risk Categories

Risk Category	LDL Goal (mg/dL)	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (mg/dL)	LDL Level at Which to Consider Drug Therapy (mg/dL)
CHD† or CHD risk equivalents (10-years risk >20%)	<100	≥100	≥130 (100-129:drug optional) ††
2+ Risk Factors (10-year risk ≤20%)	<130	≥130	10-year risk 10%-20%: ≥130 10-year risk <10%: ≥160
0-1 Risk Factor†††	<160	≥160	≥190 (160-189: LDL-lowering drug optional)

† CHD = coronary heart disease

†† Some authorities recommend use of LDL-lowering drugs in this category if an LDL-C level of <100 mg/dL cannot be achieved by therapeutic lifestyle changes. Others prefer use of drugs that primarily modify triglycerides and HDL-C, e.g., nicotinic acid or fibrate. Clinical judgment also may call for deferring drug therapy in this subcategory.

††† Almost all people with 0-1 risk factor have 10-year risk <10%; thus, 10-year risk assessment in people with 0-1 risk factor is not necessary.

After the LDL-C goal has been achieved, if the TG is still >200 mg/dL, non HDL-C (total-C minus HDL-C) becomes a secondary target of therapy. Non-HDL-C goals are set 30 mg/dL higher than LDL-C goals for each risk category.

7. In the **WARNINGS, Liver Function** subsection:

APPROVED

Fenofibrate at doses equivalent to 134 mg to 200 mg TRICOR per day has been associated with increases in serum transaminases [AST (SGOT) or ALT (SGPT)].

PROPOSED

Fenofibrate at doses equivalent to 107 mg to 160 mg TRICOR per day has been associated with increases in serum transaminases [AST (SGOT) or ALT (SGPT)].

8. In the **DOSAGE AND ADMINISTRATION** section

APPROVED

For the treatment of adult patients with primary hypercholesterolemia or mixed hyperlipidemia, the initial dose of TRICOR is 200 mg per day.

For adult patients with hypertriglyceridemia, the initial dose is 67 to 200 mg per day. Dosage should be individualized according to patient response, and should be adjusted if necessary following repeat lipid determinations at 4 to 8 week intervals. The maximum dose is 200 mg per day.

Treatment with TRICOR should be initiated at a dose of 67 mg/day in patients having impaired renal function, and increased only after evaluation of the effects on renal function and lipid levels at this dose. In the elderly, the initial dose should likewise be limited to 67 mg/day.

PROPOSED

For the treatment of adult patients with primary hypercholesterolemia or mixed hyperlipidemia, the initial dose of TRICOR is 160 mg per day.

For adult patients with hypertriglyceridemia, the initial dose is 54 to 160 mg per day. Dosage should be individualized according to patient response, and should be adjusted if necessary following repeat lipid determinations at 4 to 8 week intervals. The maximum dose is 160 mg per day.

Treatment with TRICOR should be initiated at a dose of 54 mg/day in patients having impaired renal function, and increased only after evaluation of the effects on renal function and lipid levels at this dose. In the elderly, the initial dose should likewise be limited to 54 mg/day.

9. In the **HOW SUPPLIED** section:

APPROVED

TRICOR® (fenofibrate capsules), micronized, is available as hard gelatin capsules in three strengths:

67 mg yellow capsules, imprinted with ⓐ on cap and Abbo-Code identification letters FR on body, available in bottles of 90 (**NDC** 0074-4342-90).

134 mg white capsules, imprinted with ⓐ on cap and Abbo-Code identification letters AR on body, available in bottles of 90 (**NDC** 0074-6447-90).

200 mg orange capsules, imprinted with ⓐ on cap and Abbo-Code identification letters SR on body, available in bottles of 90 (**NDC** 0074-6415-90).

PROPOSED

TRICOR™ (fenofibrate tablets) is available in two strengths:

54 mg yellow tablets, imprinted with ⓐ and Abbo-Code identification letters "TA", available in bottles of 90 (**NDC** 0074-4009-90).

160 mg white tablets, imprinted with ⓐ and Abbo-Code identification letters "TC", available in bottles of 90 (**NDC** 0074-4013-90).

10. No other changes were made except for the label identification code (new =) and the revision date (date).

Conclusions

The submitted labeling for the 54mg and 160mg formulations is acceptable. (and the application approved, pending medical officer review.)

The recommended regulatory action for the proposed labeling is:

Package insert: DRAFT, submitted August 13, 2001, may be approved
Bottle/Vial label: Color FPL, submitted November 10, 1999, may be approved
Carton: Color FPL, submitted November 10, 1999, may be approved

{See appended electronic signature page}

William C. Koch, R.Ph. Date
Regulatory Project Manager

{See appended electronic signature page}

Enid Galliers Date
Chief, Project Management Staff

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

William Koch
8/23/01 03:51:42 PM
CSO

Enid Galliers
8/23/01 05:00:19 PM
CSO

Submitted
11/10/99

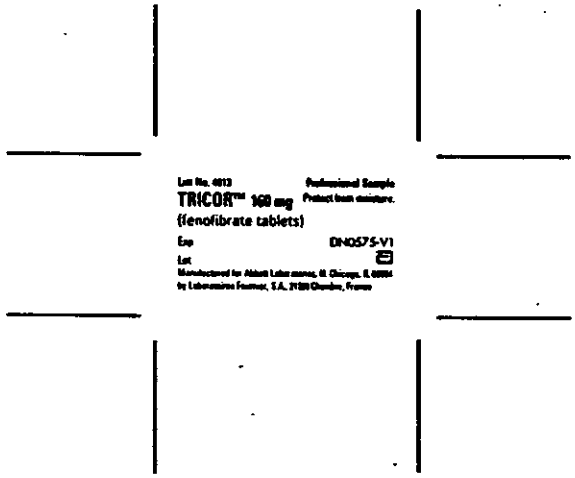
Blister Carton Label

TriCor™
(fenofibrate tablets)
160 mg

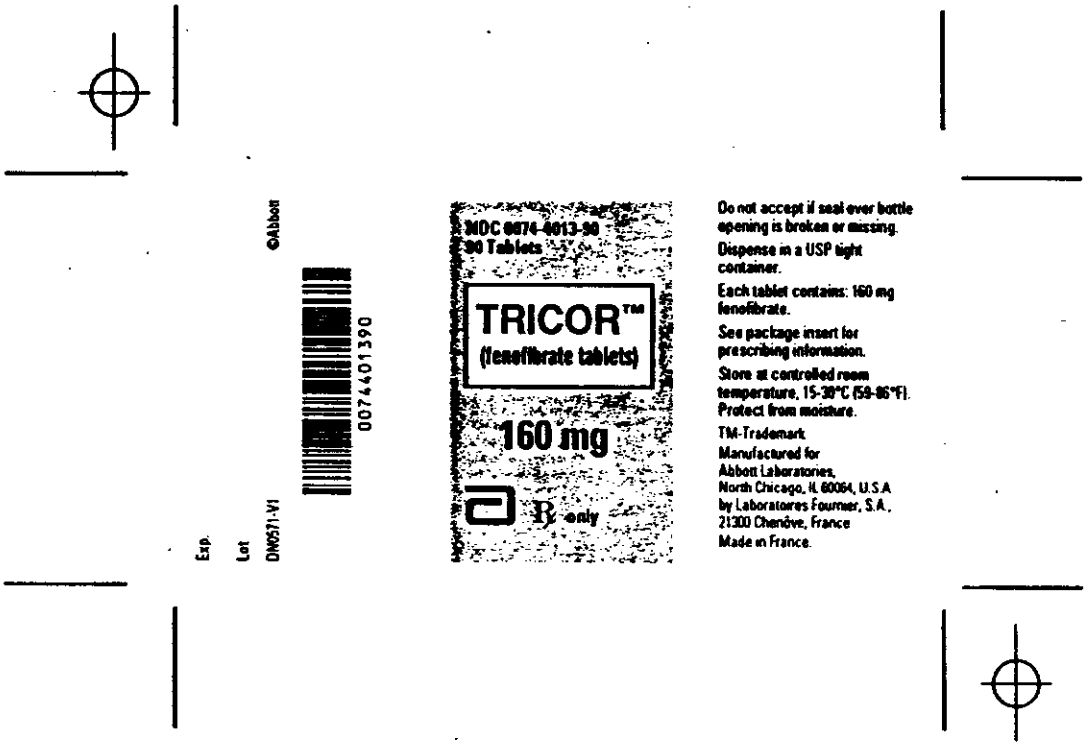
TriCor™
(fenofibrate tablets)
160 mg

TriCor™
(fenofibrate tablets)
160 mg

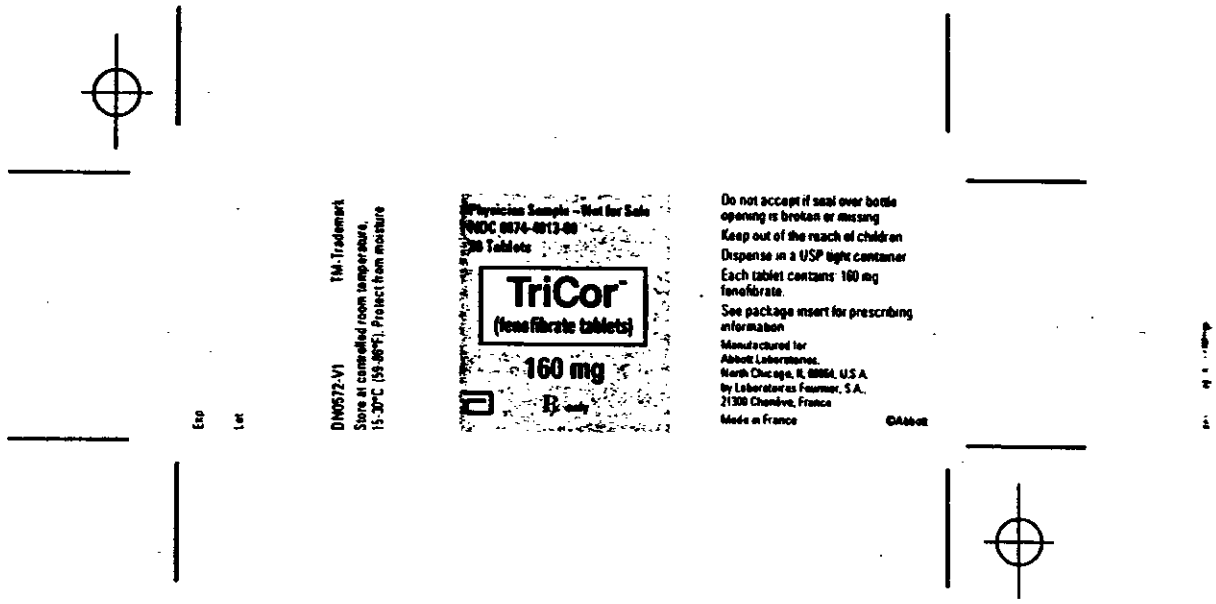
Blister Label



Bottle Label



Bottle Label



Blister Carton Label

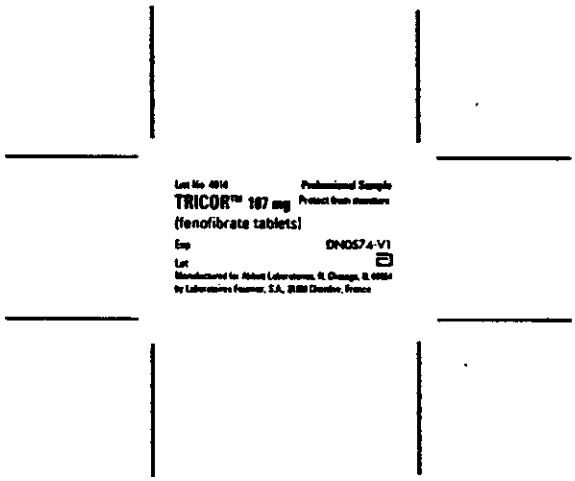
TriCor™
(fenofibrate tablets)
107 mg

TriCor™
(fenofibrate tablets)
107 mg

TriCor™
(fenofibrate tablets)
107 mg

TriCor™
(fenofibrate tablets)
107 mg

Blister Label



Bottle Label

Blister Carton Label

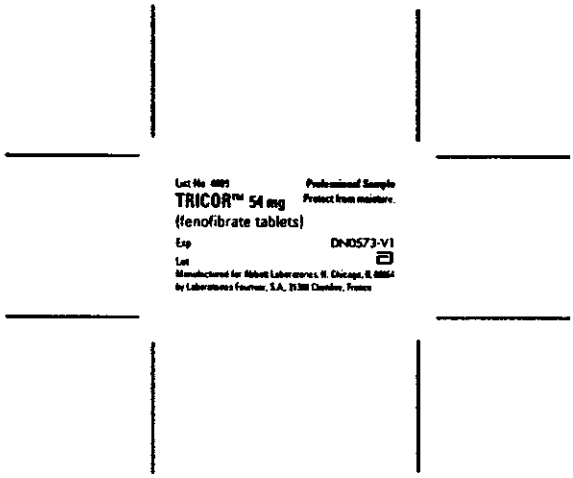
TriCor™
(fenofibrate tablets)
54 mg

TriCor™
(fenofibrate tablets)
54 mg

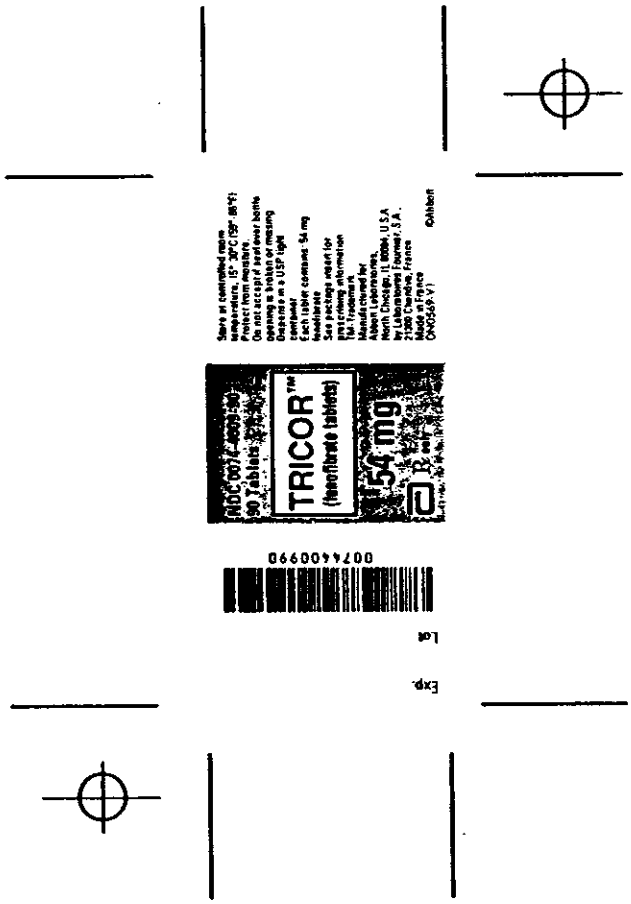
TriCor™
(fenofibrate tablets)
54 mg

TriCor™
(fenofibrate tablets)
54 mg

Blister Label



Bottle Label



DECLARATION

The undersigned declares that Patent No. 6,074,670 filed January 9, 1998 covers the formulation, composition, and or method of use of Tricor (fenofibrate) Tablets. This product is the subject of pending NDA 21-203 for which approval is being sought.

ABBOTT LABORATORIES
AGENT FOR LABORATOIRES FOURNIER SA

Marilou Reed
Associate Director, Regulatory Affairs

DEBARMENT STATEMENT

In compliance with the generic Drug Enforcement Act of 1992, Section 306(k)(1) of the Act (21 USC 355a(k)(1), we, Abbott Laboratories, certify the following with respect to this Supplemental New Drug Application:

> The applicant did not and will not use in any capacity the services of any person debarred under subsection (a) or (b) (sections 306(a) or (b) of the Federal Food, Drug and Cosmetic Act), in connection with this application for approval of a new drug product.

Marilou Reed

Marilou Reed, Associate Director
PPD Regulatory Affairs
D-491, AP6B/1
Abbott Laboratories
100 Abbott Park Road
Abbott Park, Illinois 60064-6108

2/27/01
Date

APPEARS THIS WAY
ON ORIGINAL

Exclusivity Checklist

NDA: 21-203				
Trade Name: Tricor Tablets				
Generic Name: fenofibrate				
Applicant Name: Abbott Laboratories				
Division: HFD-510				
Project Manager: William C. Koch, R.Ph.				
Approval Date: September 5, 2001				
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 questions about the submission.				
a. Is it an original NDA?	Yes	X	No	
b. Is it an effectiveness supplement?	Yes		No	X
c. If yes, what type? (SE1, SE2, etc.)				
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	X
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.				
Explanation: Submitted studies are pharmacokinetic comparing proposed tablets to approved capsules				
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:				
Explanation:				
d. Did the applicant request exclusivity?	Yes		No	X
If the answer to (d) is "yes," how many years of exclusivity did the applicant request?				
IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS.				
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?	Yes		No	X
If yes, NDA #				
Drug Name: Tricor (fenofibrate) Capsules				
IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS.				
3. Is this drug product or indication a DESI upgrade?	Yes		No	X
IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS (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.	Yes	X	No	
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	X	No	
If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).				
Drug Product	Tricor Capsules			
NDA #	19-304			
Drug Product				
NDA #				
Drug Product				
NDA #				
2. Combination product.	Yes		No	X
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).				
Drug Product				
NDA #				
Drug Product				
NDA #				
Drug Product				
NDA #				
IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS. 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	X
IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS.				

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. For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.				
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 BLOCKS.**				
Basis for conclusion:				
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	
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	
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:				
Investigation #1, Study #:				
Investigation #2, Study #:				
Investigation #3, Study #:				
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.				
a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")				
Investigation #1	Yes		No	
Investigation #2	Yes		No	
Investigation #3	Yes		No	
If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:				
Investigation #1 -- NDA Number				
Investigation #2 -- NDA Number				
Investigation #3 -- NDA Number				

b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?				
Investigation #1	Yes		No	
Investigation #2	Yes		No	
Investigation #3	Yes		No	
If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:				
Investigation #1 -- NDA Number				
Investigation #2 -- NDA Number				
Investigation #3 -- NDA Number				
If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):				
Investigation #1				
Investigation #2				
Investigation #3				
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	Yes		No	
IND#:				
Explain:				
Investigation #2	Yes		No	
IND#:				
Explain:				
Investigation #3	Yes		No	
IND#:				
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		No	
IND#:				
Explain:				
Investigation #2	Yes		No	
IND#:				
Explain:				
Investigation #3	Yes		No	
IND#:				
Explain:				

c. Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)	Yes		No	
If yes, explain:				

{See appended electronic signature page}

Signature of PM

Date:

{See appended electronic signature page}

Signature of Division or Office Director

Date:

APPEARS THIS WAY
ON ORIGINAL

EXCLUSIVITY SUMMARY FOR NDA # 21-203 SUPPL # _____

Trade Name Tricor Generic Name fenofibrate tablets

Applicant Name Abbott Labs 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.

Tab 35

a) Is it an original NDA?

YES /✓/ NO /___/

b) Is it an effectiveness supplement?

YES /___/ NO /✓/

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

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:

_____

_____

d) Did the applicant request exclusivity?

YES /___/ NO /___/

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

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

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 /___/

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:

_____

_____

(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 /___/

(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 /___/

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:

_____

_____

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.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

_____ _____

_____ _____

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

_____ _____

_____ _____

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

_____ _____

_____ _____

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 # _____ YES /___/ NO /___/ Explain: _____

_____

Investigation #2

IND # _____ YES /___/ NO /___/ 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 /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

_____ _____

Signature Date

Title:_____

_____ _____

Signature of Office/ Date

Division Director

cc: Original NDA Division File HFD-85 Mary Ann Holovac

APPEARS THIS WAY
ON ORIGINAL

ADDENDUM TO MEDICAL REVIEW OF NDA 21-203
REVIEW OF FINANCIAL DISCLOSURE

Four clinical trials previously submitted to NDA 19-304 supplement 005 were referenced in NDA 21-203 for support of an HDL-raising indication. Review of financial disclosure information for these studies (CFEN 8104, 8502, 8802, 9116) were previously conducted under NDA 19-304.

Results of two clinical pharmacokinetic studies, M98-961 and M98-962 (see S. Johnson, biopharm review) were submitted with this application. The following financial disclosure summary pertains to these 2 studies.

Outcome Payment (payment dependent upon outcome of study)
none

Proprietary Interest (e.g. patents, trademark, copyright, licensing agreement in the product)
none

Equity Interest (e.g. stock ownership, stock options)
none

Significant Payment of Other Sorts (SPOOS)
none

Conclusions
In accordance with 21 CFR 54 the sponsor has submitted statements disclosing any information regarding financial interests and arrangements of clinical investigators, respective spouses, and dependent children of the investigators. There were no investigators who entered a financial arrangement with Groupe Fournier or Abbott Laboratories which could compromise the integrity of the trial results.

/S/ 9-7-01

Mary H. Parks, MD
Medical Officer
DMEDP (HFD-510)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	Lawrence A. Galitz, M.D.	

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Lawrence E Roebel, Ph.D.	Vice President, PPD Regulatory Affairs and Research Quality Assurance
FIRM/ORGANIZATION	
Abbott Laboratories	
SIGNATURE	**DATE**
Lawrence E Roebel	2/23/01

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

3 pages

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-203

Abbott Laboratories
Attention: Marilou Reed
Associate Director
D-491/AP6B-1
100 Abbott Park Road
Abbott Park, IL 60064-6108

Dear Ms. Reed:

We acknowledge receipt on March 5, 2001, of your March 2, 2001, resubmission to your new drug application (NDA) for Tricor (fenofibrate) Tablets.

This resubmission contains additional new bioequivalence data, comparative dissolution method data, revised labeling, and a safety update submitted in response to our September 12, 2000, action letter.

We consider this a complete class 2 response to our action letter. Therefore, the user fee goal date is September 5, 2001. (WED)

If you have any questions, call me at (301) 827-6411.

Sincerely,

{See appended electronic signature page}

Margaret Simoneau, R.Ph.
Regulatory Project Manager
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

/s/

Margaret Simoneau
3/15/01 03:27:34 PM

APPEARS THIS WAY
ON ORIGINAL

ABBOTT

ORIGINAL

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

N 000 BL
ORIG AMENDMENT

August 13, 2001

Dr. David Orloff
Director, Division of Metabolic & Endocrine
Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

AMENDMENT TO A PENDING APPLICATION
Revised Draft Labeling

Dear Dr. Orloff,

Reference is made to our pending New Drug Application 21-203 for Tricor®, (fenofibrate tablets), and to a telefaxed communication from your Division dated August 9, 2001 in which several changes were requested to the draft labeling. We are herewith responding to the request for changes.

Abbott agrees with all the changes requested in your communication of August 9th. Appended are two copies of the revised draft labeling, one clean copy and one copy with the changes highlighted. A computer disc with this labeling is also provided. This labeling is being provided in a Blue Archival Folder and Red, Yellow and Tan Technical Review folders as well as a desk copy for Mr. William Koch.

Should you have questions concerning this submission, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002
e-mail: marilou.reed@secure.abbott.com

ABBOTT

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

April 20, 2001

Dr. David Orloff
Director, Division of Metabolic & Endocrine
Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

AMENDMENT TO A PENDING APPLICATION
Revised Draft Labeling

Dear Dr. Orloff,

Reference is made to our pending New Drug Application 21-203 for Tricor®, (fenofibrate tablets), to a telephone conference between Dr. Mary Parks and Ms. Margaret Simoneau of your Division and myself on April 9, 2001 and to a follow-up telephone conversation between Dr. Parks and myself on April 16, 2001. During those conversations several changes to the draft labeling were requested along with a request for a commitment regarding our intention on the marketing of the Tricor Capsule dosage form. We are herewith submitting revised draft labeling reflecting those changes.

Appended is a copy of the revised draft labeling highlighting the changes from the previous draft labeling submitted in our response to your Approvable letter dated March 2, 2001. Specifically, these changes include deletion of the word "———" from the name of the drug in the title (this was an oversight as all other references to ——— had previously been deleted), addition of HDL to the disclaimer of not being an independent risk factor for mortality, deletion of ———

———

———

Also appended is a clean copy of the draft labeling with the changes as listed above and a computer disc containing this clean copy. This labeling is being provided in a Blue Archival Folder and Red, Yellow and Tan Technical Review Folders as well as a desk copy for Ms. Simoneau.

Regarding the currently approved capsule dosage form, Dr. Parks had expressed a concern about possible confusion between the capsule and tablet dosage forms. Specifically there was a concern expressed about possibly titrating patients across all the potencies of the capsule and tablet dosage forms. Abbott Laboratories does not intend to [redacted]

Should you have questions concerning this submission, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002
e-mail: marilou.reed@secure.abbott.com

APPEARS THIS WAY
ON ORIGINAL

ABBOTT

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Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

NEW CORRESP
~~ORIG AMENDMENT~~
N-000-C

March 16, 2001

Dr. David Orloff
Director, Division of Metabolism & Endocrine
Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: TRICOR®, (fenofibrate capsules), micronized
NDA 19-304

RESPONSE TO FDA REQUEST FOR INFORMATION
Clinical

Dear Dr. Orloff

Reference is made to our approved New Drug Application 19-304 for Tricor® (fenofibrate capsules), to our letter of August 31, 1999 requesting a waiver of reporting of adverse events for a [redacted] and to your response dated September 10, 1999 in which you requested that serious unexpected events that are not endpoint ischemic events be reported. We are herewith responding to that request.

Appended a monthly summary of serious adverse events occurring in foreign studies reported to Abbott from February 1, 2001 through February 28, 2001. One report is for all studies except FIELD and the other report is for SAEs occurring only in FIELD.

Should you have any questions concerning this information, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002
e-mail: marilou.reed@secure.abbott.com

REVIEWS COMPLETED	
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO	
CSO INITIALS	DATE

ABBOTT

ORIGINAL

ORIG AMENDMENT

Pharmaceutical Products Division

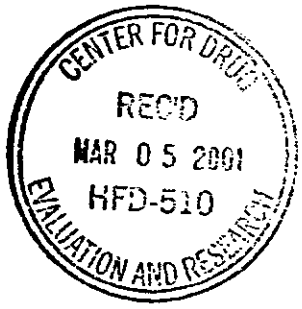
Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

N-020-AZ

Dated

/S/

3/19/01



March 2, 2001

Dr. David Orloff
Director, Division of Metabolic & Endocrine
Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.L. ☐ MEMO

CSO INITIALS DATE

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

AMENDMENT TO A PENDING APPLICATION
Complete Response to Approvable Letter

/S/

Peggy - I'd remove from the clinical jacket.
Thanks
3/16/01

Dear Dr. Orloff,

Reference is made to our pending New Drug Application 21-203 for Tricor®, (fenofibrate tablets), to your letter of September 12, 2000 in which your stated the application was approvable under certain conditions and to a telephone conversation on October 12, 2000 during which issues for responding to the Approvable Letter were discussed. For ease of review, the Abbott telecon minutes and your letter of September 12, 2000 are appended to this cover letter. In accordance with that letter and the telecon we are herewith submitting our complete response to that letter.

1. Concentration-Response Model

Further exploration of this path for approval of this application was not recommended and, we therefore, have not pursued this path.

2. Bioequivalence

Your letter of September 12, 2000 requested that we submit the results of a 2-way crossover bioequivalence study that compares the 160 mg tablet with the 200 mg Tricor capsule conducted under fasting conditions. In accordance with the request in your letter and the follow-up telecon we are herewith submitting the results of Study M00-253 entitled "Comparison of the Bioavailability of Fenofibric Acid From a 160 mg Tablet Formulation of Fenofibrate with that From a 200 mg Capsule Formulation of Fenofibrate Under Fasting Conditions". This study is a 2-way crossover study in 160 subjects.

This study is supported by a smaller study in 24 subjects, Study K 178 00 03 KH 0102, entitled "Comparative Bioavailability Study of One Tablet Containing 160 mg of Fenofibrate Ter Versus One Capsule Containing 200 mg of Micronised Fenofibrate After Single Administration in Fasting State, in 24 Healthy Subjects". The results of both studies demonstrate bioequivalence for AUC, but not for C_{max}. This difference in C_{max} is not expected to have any effect on the safety or efficacy of the 160 mg Tablet versus the 200 mg Capsule.

For ease of review, the data used to analyze the results of each these studies is included on CD at the end of each of the Clinical Summaries.

3. Dissolution

The September 12, 2000 letter requested additional information on the dissolution method used for the 160 mg tablets. In accordance with that letter and the follow-up telecon, we have included a Dissolution Profile Report using the two different paddle speeds requested.

4. Effects of fenofibrate on HDL-C

Since a complete labeling review did not take place, we have provided draft labeling in this submission which includes the HDL-C indication and deletes —— tablets which will not be launched at the time of approval of this application. The draft labeling is provided in three different formats, with the changes from the approved capsule labeling highlighted, with the changes annotated to original submission and to Supplement 005 of NDA 19-304 for Tricor Capsules, and as a clean copy which text is on an attached computer disc.

5. Additional information relating to safety and effectiveness

There are no on-going studies of Tricor tablets to be reported. However, there is new information included under Foreign Marketing History regarding the approval of Tricor Tablets in foreign countries. The approved labeling for those countries is also appended.

This submission also includes the Financial Disclosure and GCP Certification for the bioequivalence studies included herein.

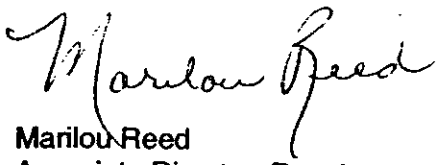
This complete response to an Approvable Letter consists of 14 volumes bound in Blue Archival folders. In addition, the following volumes are bound in Technical Review folders:

Volume 1 – Chemistry, Pharmacokinetics, Clinical, and Desk Copy for Margaret Simoneau
Volumes 2-3 – Chemistry
Volumes 4-14 – Pharmacokinetics, Clinical

In addition, a Field Copy of Volumes 2 and 3, certified to be an exact duplicate of this submission, has been sent to the Chicago District Office of the Food and Drug Administration.

Should you have questions concerning this submission, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES



Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002
e-mail: marilou.reed@secure.abbott.com

APPEARS THIS WAY
ON ORIGINAL

ABBOTT

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Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

Noted
Chemistry Reviews
completed (See
Clear. Rev. #4)
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NDA ORIG AMENDMEN
1S
4/9/01.

February 19, 2001

Dr. David Orloff
Director, Division of Metabolism & Endocrine
Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

AMENDMENT TO A PENDING APPLICATION
Chemistry

Dear Dr. Orloff,

Reference is made to our pending New Drug Application 21-203 for Tricor®, (fenofibrate tablets) and to a telephone conversation on October 12, 2001 during which we discussed, among other issues, a submission of additional stability data to provide for longer expiration dating. The conclusion of this conversation was that the stability data should be submitted separately from the response to the Approvable Letter for this application. Therefore at this time we wish to amend the application with additional stability data.

The appended tables provide 24 months real time stability data in blister and bottle packages in addition to the previously submitted accelerated and room temperature data. We are requesting [redacted] dating on the bottles and [redacted] dating on the blisters based on the kinetic analysis of the data. We are also proposing a [redacted] in bulk containers from the date of coating. The data for storage in bulk containers was submitted previously on June 5, 2000. The in-process control documents have been revised to indicate the change in expiration dating.

A Field Copy of this stability information, certified to be an exact duplicate of this submission, has been sent to the Chicago District Office of the Food and Drug Administration.

KDB
4/6/01

2/21/01

Should you have any questions concerning this submission, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002
e-mail: marilou.reed@secure.abbott.com

**APPEARS THIS WAY
ON ORIGINAL**

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☒ N.A.I. ☐ MEMO
Mun 4/9/01
CSO INITIALS DATE

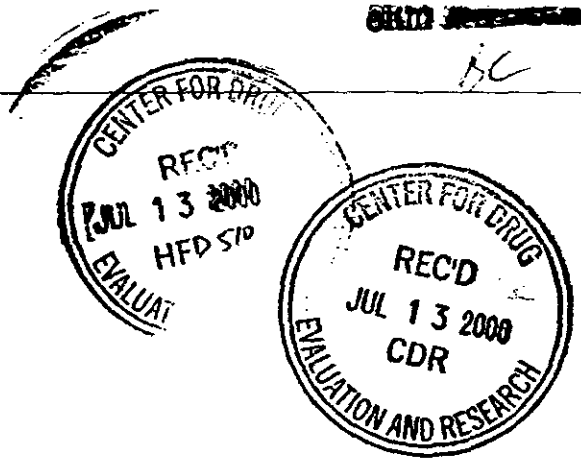
ABBOTT

DUPLICATE

[redacted]

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108



July 12, 2000

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
12229 Wilkins Avenue
Rockville, MD 20852

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

AMENDMENT TO PENDING APPLICATION
Patent Information

Dear Dr. Jenkins,

Reference is made to our pending New Drug Application 21-203 for Tricor® (fenofibrate tablets). At this time we wish to amend that application to provide for a new patent that covers Tricor Tablets.

In accordance with 21 CFR 314.60 and 314.53(c) we are submitting the required information on the patent and the required declaration that is appended.

Patent No.:	6,074,670 (filed January 9, 1998)
Issued:	June 13, 2000
Patent Expiration:	January 9, 2018
Type of Patent:	Drug Product
Patent Owner:	Laboratoires Fournier, SA
U.S. Agent:	Abbott Laboratories

An Archival Copy and a Technical Review Copy for chemistry, manufacturing and controls of this submission are being provided.

Should you have any questions concerning this information, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002

APPEARS THIS WAY
ON ORIGINAL

DECLARATION

The undersigned declares that Patent No. 6,074,670 filed January 9, 1998 covers the formulation, composition, and or method of use of Tricor (fenofibrate) Tablets. This product is the subject of pending NDA 21-203 for which approval is being sought.

ABBOTT LABORATORIES
AGENT FOR LABORATOIRES FOURNIER SA

Marilou Reed
Associate Director, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

ABBOTT

DUPLICATE

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

July 12, 2000

ORIG AMENDMENT

Dr. John Jenkins
Acting Director, Division of Metabolic & Endocrine Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUL 13 2000
HFD-510

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

RESPONSE TO FDA REQUEST FOR INFORMATION
Chemistry

Dear Dr. Jenkins,

Reference is made to our pending New Drug Application 21-203 for Tricor®, (fenofibrate tablets), to approved New Drug Application 19-304 for Tricor®, (fenofibrate capsules), micronized and to a telefax received from Dr. Stephen Moore, Ph. D. dated June 19, 2000. We are herewith responding to the requests for additional information.

Regarding the test methods, the questions from the telefax are repeated for ease of review followed by our response in the appended document.

Regarding the request for the change to add the word —— to the product name we have the following comments. Since this a different formulation of —— fenofibrate, not just the capsule formulation compressed into a tablet, we believe it is not correct to add the word —— to the product name. In addition, the reason "micronized" was added to the capsule formulation product name was because it was the second formulation approved under NDA 19-304 and it was used to distinguish the second formulation from the first formulation. In the case of the tablet formulation there is no other formulation.

We would propose to add the word —— to the product name to avoid confusion with capsule formulation. In the tablet formulation —— fenofibrate whereas in the capsule formulation the ——

We are therefore proposing the name of the product to be
TRICOR
(fenofibrate tablets), ——

insert. This revision will be included in a submission of final draft labeling at a later date after all comments have been received from the Division

Should you have any questions concerning this information, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002

APPEARS THIS WAY
ON ORIGINAL

ABBOTT

ORIGINAL

[redacted]

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

June 13, 2000

Dr. John Jenkins
Acting Director, Division of Metabolic & Endocrine
Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

RESPONSE TO FDA REQUEST FOR INFORMATION
Human Pharmacokinetics

Dear Dr. Jenkins,

Reference is made to our pending New Drug Application 21-203 for Tricor®, (fenofibrate tablets), and to a telephone conversation today between Dr. Steve Johnson of your Division and myself during which Dr. Johnson requested information on the pK report in this application to be sent on disc. We are herewith responding to that request.

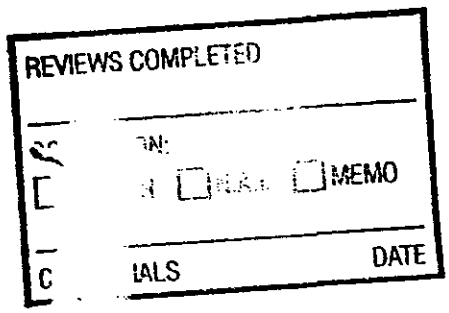
The pK/PD report is contained on seven discs labeled as follows:
NDA Document.doc
Appendix A & B
Win NonLin Files, Apolipoprotein B
Win NonLin Files, Cholesterol
Win NonLin Files. LDL-C
Win NonLin Files, LDL-HDL Ratios
Win NonLin Files, Triglycerides

We are providing a blue Archival Copy, an orange Technical Review Copy and a desk copy for Dr. Johnson. Should you have any questions concerning this information, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002



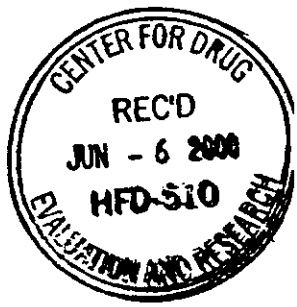
ABBOTT

ORIGINAL ORIG AMENDMENT

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

June 5, 2000



Dr. John Jenkins
Acting Director, Division of Metabolic & Endocrine
Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

AMENDMENT TO A PENDING APPLICATION
Labeling
Chemistry
Foreign Marketing History

Dear Dr. Jenkins,

Reference is made to our pending New Drug Application 21-203 for Tricor®, (fenofibrate tablets) and to approved NDA 19-304/S-005 for Tricor® (fenofibrate capsules), micronized. At this time we wish to amend that application with the following information.

The draft labeling for Tricor tablets has been revised in accordance with the final approved labeling for Tricor capsules under NDA 19-304 Supplement 005. A revised copy of the annotated labeling has been provided highlighting the changes for the change in dosage form as well as the changes approved under NDA 19-304/S-005. A clean copy of the labeling with all the proposed changes is also appended along with a computer disc of the copy. The "Description" and "How Supplied" sections include the [redacted] However, we do not intend to [redacted] at the time of the approval of this application.

The stability data for the tablet dosage forms and packages has also been updated. At this time we are providing 12 months real time data in blister and bottle packages in addition to original accelerated and room temperature data. We are requesting [redacted] dating for the bottles and [redacted] for the blister packages based on the kinetic analysis of the data. The in-process control documents have been revised to indicate the change in the expiration dating and are appended.

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

The foreign marketing history section of the application summary is being revised at this time to include the approval of Tricor Tablets in [redacted]. The revised table is appended.

Should you have any questions concerning this submission, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002

APPEARS THIS WAY
ON ORIGINAL

ABBOTT

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

June 1, 2000

Dr. John Jenkins
Acting Director, Division of Metabolic & Endocrine
Drug Products
Food and Drug Administration, HFD-510
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: TRICOR®, (fenofibrate tablets)
NDA 21-203

RESPONSE TO FDA REQUEST
FOR INFORMATION
Chemistry

Dear Dr. Jenkins,

Reference is made to our pending New Drug Application 21-203 for Tricor®, (fenofibrate tablets), to approved New Drug Application 19-304 for Tricor®, (fenofibrate capsules), micronized and to a telephone conversation between Dr. Chien-Hua Niu of your Division and myself during which Dr. Niu requested information regarding the formulations used in the clinical studies supporting this NDA. We are herewith responding to that request.

Support for approval of this application is based a pK/PD analysis using data from five bioequivalence studies, three of which were previously submitted to NDA 19-304, and two clinical studies which were previously submitted to NDA 19-304. The following is a list of the studies and the appended documents or references that provide the formulation information requested by Dr. Niu.

Study K178 9501 was a single dose comparative bioavailability study used to support a new formulation of micronized fenofibrate. This new formulation was approved under NDA 19-304/S-001. Appended is the Certificate of Analysis for the two formulations, the quantitative formulations, and the dissolution results of the two formulations.

Study K178 8902 is a repeat dose study comparing the standard formulation of fenofibrate approved under NDA 19-304 and a micronized formulation of fenofibrate. This study was previously submitted to NDA 19-304. Appended are the Certificates of Analysis for the micronized and standard formulations used in this study.

Study M98-961 is a bioequivalence study to compare the 54 mg tablet that is the subject of this NDA with the 67 mg capsule that is approved under NDA 19-304. The Certificate of Analysis for Lot No. 47-800 AL of 54 mg tablets used in this bioequivalence study can

be found in this application in Volume 9, page SEC. 4 V.8 Pg 219. The executed batch record for this lot can be found in Volume 3 beginning on page SEC. 4 V. 2 Pg 186. The 67 mg capsules used in this study were from Lot 47-032-3T-21 of commercial product distributed under NDC 0074-4342-90.

Study M98-962 is a comparative study comparing the 160 mg tablet under fed and fasting conditions with three 67 mg capsules under fed conditions. The Certificate of Analysis for Lot 47-813-AL of 160 tablets can be found in this application in Volume 9 on page SEC. 4 V. 8 Pg 259. The executed batch record for this lot of 160 mg tablets can be found in Volume 4 beginning on page SEC. 4 V. 3 Pg 140. The same of lot of commercial 67 mg capsules was used in this study as was used in Study M98-961.

Study K178 9601 is a study to investigate the effect of food on the bioavailability of the micronized formulation of fenofibrate. This study was used to support the approval of the micronized formulation under NDA 19-304/S-001. The Certificate of Analysis, quantitative formulation and dissolution curves of the lot 67 mg capsules used in this study are appended.

Study CFEN 8802 is a placebo-controlled study comparing the standard formulation of fenofibrate and the micronized formulation of fenofibrate. This study was previously submitted to NDA 19-304. The 200 mg capsule formulation was approved under NDA 19-304/S-003. The Certificates of Analysis for the 200 mg micronized formulation, the 100 mg standard formulation and placebo capsules are appended.

Study CFEN 8906 is a dose ranging study comparing various doses of standard formulation fenofibrate in patients with hypertriglygeridemia. This study was previously submitted to NDA 19-304. The Certificates of Analysis of the standard formulation of fenofibrate are appended.

Should you have any questions concerning this information, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002

APPEARS THIS WAY
ON ORIGINAL

NDA 21-203

FEB - 4 2000

Abbott Laboratories
Attention: Marilou Reed
Associate, Director
D-491/ AP6B-1
100 Abbott Park Road
Abbott Park, IL 60064-6108

Dear Ms. Reed:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Tricor® (fenofibrate) 57, ~, 160 mg Tablets

Therapeutic Classification: Standard (S)

Date of Application: November 10, 1999

Date of Receipt: November 12, 1999

Our Reference Number: NDA 21-203

This application was filed under section 505(b) of the Act on January 11, 2000, in accordance with 21 CFR 314.101(a). The primary user fee goal date will be September 12, 2000, and the secondary user fee goal date will be November 12, 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 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) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will proceed with the pediatric drug development plan that you submit and 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. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA 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

APPEARS THIS WAY
ON ORIGINAL

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

Sincerely,

/S/ 01.04.00

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

APPEARS THIS WAY
ON ORIGINAL

cc:
Archival NDA 21-203
HFD-510/Div. Files
HFD-510/M. Simoneau
HFD-510/Reviewers and Team Leaders
DISTRICT OFFICE

Drafted by: ddk/February 3, 2000
Initialed by: Galliers 2.3.00
final: ddk/February 4, 2000
filename: 21203ACK

ACKNOWLEDGEMENT (AC)

ABBOTT

Pharmaceutical Products Division

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

November 10, 1999

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
12229 Wilkins Avenue
Rockville, MD 20852-1833

Re: Tricor™ (fenofibrate tablets)
NDA 21-203

ORIGINAL APPLICATION

Dear Sir or Madam,

Abbott Laboratories hereby submits this original New Drug Application 21-203 for Tricor™ (fenofibrate tablets) for treatment of Type II, IV and V hyperlipidemia in accordance with section 505 (b)(2) of the Food, Drug and Cosmetic Act. Reference is made to a pre-NDA meeting held September 9, 1999 with the Division of Metabolic and Endocrine Drugs during which agreement on the content and format of this application was reached. A copy of the minutes of this meeting is provided as an attachment to this letter.

This application consists of 40 volumes submitted as a complete set in Blue Archival Copy folders. The Technical Review sections are divided as follows:

Volume 1	Chemistry, Pharmacokinetics, Clinical
Volumes 2-10	Chemistry
Volumes 11-40	Pharmacokinetics, Clinical

In addition, a Field Copy of the Chemistry, Manufacturing and Controls Section, certified to be an exact duplicate of the CMC section in this application, has been sent to the Chicago District Office of the Food and Drug Administration.

The basis of approval of this application will be based on pK/PD data and not on bioequivalence to the previously approved capsule dosage form approved under NDA 19-304. A report on the concentration-response relationship is found in Volume 11, page Sec. 6 V.1 Pg 017. This report is based on five bioequivalence studies and two previously conducted clinical trials. The bioequivalence study reports can be located in Section 6 of this application and the two clinical studies can be located in Section 8 of this application. For ease of review, Sections 6 and 8 have been provided in both Orange Pharmacokinetic Technical Review folders and Light Brown Clinical Data Review folders.

Draft labeling has been provided in Volume 1 which is bound in Blue, Red, Orange and Light Brown folders for the Archival Copy and each of the Technical Review Sections contained in this application.

We believe we have provided all the information necessary for review and approval of this application. Should you have any questions concerning this submission, please do not hesitate to contact me directly.

Sincerely,
ABBOTT LABORATORIES

Marilou Reed

Marilou Reed
Associate Director, Regulatory Affairs
(847) 937-6844, fax (847) 937-8002

APPEARS THIS WAY
ON ORIGINAL

RECORD OF TELEPHONE CONVERSATION/MEETING	Date: April 9, 2001
Date: April 9, 2001 Location: 14B45 Time: 11:30 to 12 noon Format: Telconference FDA Attendees: Dr. Parks M. Simoneau 1. **Meeting Objective** T-con with the sponsor to discuss labeling and nomenclature issues. 2. **Discussion Points** • Sponsor was told to change the geriatric use section of the proposed package insert to reflect that which was submitted for the approvable letter. This would be a separate efficacy supplement (SE8) after approval of the NDA for the tablets and would require payment. • In the CLIN PHARM section, regarding the HDL, a disclaimer statement needed to be put back in the labeling. Sponsor was requested to send in an amendment to the label. • After Tricor tablets gets approved. —— —— —— • The nomenclature, '—— was not a safety issue but an efficacy concern. This would be taken into consideration during the review process. (*See appended electronic signature page*) **Name:** ---------- Margaret Simoneau, R.Ph., Reg. Project Manager	**IND/NDA#:** 21-203 **Telecon/Meeting initiated by:** O FDA **By:** Telephone **Product Name:** Tricor (fenofibrate) **Firm Name:** Abbott **Name and Title of Person with whom conversation was held:** Marilou Reed **Phone:** 847-937-6844

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Margaret Simoneau
7/23/01 11:27:42 AM

APPEARS THIS WAY ON ORIGINAL

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 11 September 2000

FROM: Enid Galliers /S/
Chief, Project Management Staff
Division of Metabolic and Endocrine Drug Products

SUBJECT: Classification of NDA 21-203 under section 505 of the FFDC Act
Tricor (fenofibrate) tablets

TO: NDA 21-203 FILE
THROUGH: David G. Orloff, M.D.,
Director, Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II, CDER

At a September 7, 1999, pre-NDA meeting with Abbott Laboratories, the firm inquired whether a proposed new NDA for a new dosage form, i.e., tablets, of fenofibrate could be submitted as a 505(b)(2) application. At that time FDA agreed to that designation.

Upon further investigation, it appears that FDA erred in that statement. NDA 21-203 relies, in part, on data contained in NDA 19-304 for fenofibrate capsules, micronized, an application that is also owned by Abbott Laboratories. Apparently, Abbott Laboratories believed that the new application for the tablets would have to be a 505(b)(2) application because some of the studies in the referenced NDA 19-304 were conducted for Laboratoires Fournier, the previous owner of NDA 19-304, and not by Abbott.

Abbott owns both applications, and NDA 21-203 does not rely on additional literature or any other applications. Because Abbott has "right of reference" to all the data submitted in NDA 19-304, NDA 21-203 must be considered a 505(b)(1) application.

Cc: Orig. NDA
HFD-510/Div. File
HFD-510/M.Simoneau

C:\data\wordfiles\21203mem.doc

Meeting Minutes

Division of Metabolic and Endocrine Drug Products
Pre-NDA for Fenofibrate Tablets

Date: Tuesday, September 7, 1999
Location: Parklawn, 3rd floor, Conference Room L
Time: 1:00-2:30 PM

FDA and Abbott Attendees:
See enclosure 1

1. Meeting Objective

This was a Pre-NDA meeting requested by Abbott to discuss a tablet dosage form of fenofibrate (enclosure 2).

2. Discussion Points and Decisions

Enclosure 3, submitted August 12, 1999, is the briefing package including the proposed agenda.

Discussion and responses to the agenda questions are included in your meeting minutes, faxed September 22, 1999 (enclosure 4). These minutes have been reviewed by FDA attendees with no additional comments or notations other than those items listed below.

- The NDA can be filed under section 505(b)(2) of the FD&C Act as a stand alone NDA. The sponsor will generate concentration-response relationship and approvability of the NDA will be based on PK/PD, not a bioequivalence claim. This comment clarifies and replaces the second item listed on the fax.

- With respect to stability, the sponsor should provide

Minutes preparer: Margaret Simoneau /S/ 10-6-99

Concurrence Chairman: Dr. Orloff /S/ 10-7-99

SAFETY UPDATE REVIEW
NOT REQUIRED

APR - 6 2000

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: 1/ 27/ 2000	DUE DATE: 4/ 1/ 2000	OPDRA CONSULT #: 00-0031

TO:

John Jenkins, M.D.
Acting Director, Division of Metabolic and Endocrine Drug Products
(HFD-510)

THROUGH:

Margaret Simoneau
Project Manager
(HFD-510)

PRODUCT NAME:	MANUFACTURER: Abbott Laboratories
ricor (Fenofibrate Tablets) icronized NDA #: 21-203	

SAFETY EVALUATOR: Lauren Lee, Pharm.D.

OPDRA RECOMMENDATION:

OPDRA recommends that the word, ——— ' be included on the label in conjunction with the name.
See review for other safety concerns.

/S/ 4/5/2000
Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
ffice of Post-Marketing Drug Risk Assessment
.one: (301) 827-3242
ax: (301) 480-8173

/S/ - 4/6/00
Peter Honig, MD
Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

MEMORANDUM OFFICE OF POST-MARKETING DRUG RISK ASSESSMENT
CENTER FOR DRUG EVALUATION AND RESEARCH
HFD-400; Rm 15B-03

CONSULT#: 00-0031/ 00-0185

DATE: August 2, 2000

FROM: Lauren Lee, Pharm.D., Safety Evaluator
Medication Error Prevention, HFD-400

THROUGH: Jerry Phillips, R.Ph., Associate Director for
Medication Error Prevention, HFD-400 /S/ 8/11/2000

TO: John Jenkins, M.D., Acting Director
Division of Metabolic and Endocrine Drug Products, HFD-510

SUBJECT: NDA No. 21-203; Tricor (Fenofibrate Tablets) ——

I. INTRODUCTION:

This memorandum is in response to a request received on July 19, 2000, from the Division of Metabolic and Endocrine Drug Products, to review the applicant's proposal "to add the word, —— to the product name."

According to the applicant, "the tablet formulation ' —— fenofibrate whereas in the capsule formulation, the —— and then —— ' Since a Tricor tablet does not consist of "capsule formulation compressed into a tablet, it is not correct to add the word, —— to the product name. Therefore, in order to avoid confusion with the capsule formulation, the applicant proposes to add the word, —— to the product name.

II. BACKROUND:

The proposed proprietary name, Tricor (fenofibrate tablets), was previously reviewed by the Office of Post-Marketing and Drug Risk Assessment (OPDRA) on April 5, 2000, at the request of the Division to address the concern regarding the exclusion of the word, —— from the trademark even though the tablets are manufactured —— fenofibrate.

OPDRA recommended the following:

——

——

——

——

TRICOR
(Fenofibrate Tablets) ——

III. RISK ASSESSMENT:

Since our last review, we've received *new* information from the Division regarding fenofibrate tablets and capsules as follows:

According to the chemist, "The manufacturing processes for these two formulation are not the same. The same is used as starting material to manufacture both capsule and tablet formulations. The difference in the manufacturing processes for both capsule and tablet formulation is the

The tablets should not be considered to be

According to this new information, fenofibrate tablets are *not* , but instead Therefore, adding the word, in conjunction with the name is not appropriate. The following presentation of the name is recommended:

TRICOR
(Fenofibrate Tablets)

, to further distinguish the two formulations.

RECOMMENDATION

OPDRA does not recommend adding the term, ' , in conjunction with the name. We recommend the above presentation of the name.

If you have further questions or need clarification, please contact Sammie Beam at 301-827-3161.

/S/
Lauren Lee, Pharm.D.

Concur:

/S/
Jerry Phillips, RPh

CC:

NDA: 21-203
Office Files
HFD-510; DivFiles; Margaret Simoneau, Project Manager
HFD-510; John Jenkins, Acting Division Director
HFD-440; Mary Dempsey, Project Manager, DDRE II, OPDRA (Electronic Only)
HFD-400; Sammie Beam, Project Manager, Medication Errors, OPDRA (Electronic Only)
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Peter Honig, Director, OPDRA (Electronic Only)
HFD-002; Mac Lumpkin, Deputy Center Director for Review Management
(Electronic Only)

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B-03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE RECEIVED: January 27, 2000

NDA#: 21-203

NAME OF DRUG: Tricor (Fenofibrate Tablets) ———

NDA HOLDER: Abbott Laboratories

I. INTRODUCTION:

This OPDRA consult is in response to a January 27, 2000 request by the Division of Metabolic and Endocrine Drug Products, to review the name, Tricor (fenofibrate tablets). Container label and container labeling were also reviewed for possible interventions in minimizing medication errors.

Tricor (fenofibrate capsules) ——— was approved on February 9, 1998 under the NDA 19-304 for the 67 mg strength. On June 30, 1999, the 134 mg and 200 mg strengths were also approved.

According to the Division, the concern is that the same proprietary name, Tricor, will be used for both the tablets and capsules, but the sponsor has removed the word ——— from the name for the tablets. Both the tablets and capsules are ———

PRODUCT INFORMATION

Tricor is a lipid regulating agent. Fenofibric acid, the active metabolite of fenofibrate, produces reductions in total cholesterol, LDL cholesterol, apolipoprotein B, total triglycerides and triglyceride rich lipoprotein (VLDL) in treated patients. In addition, treatment with fenofibrate results in increases in high density lipoprotein (HDL) and apoproteins, apoAI and apoAII. Tricor is indicated as adjunctive therapy to diet for the reduction of LDL cholesterol, total cholesterol, triglycerides, and Apo B, as well as for the elevation of HDL cholesterol in adult patients with primary hypercholesterolemia or mixed dyslipidemia (Frederickson Types IIa and IIb) with triglycerides less than 250 mg/dL. Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol when response to diet and non-pharmacological interventions alone has been inadequate.

Proprietary Name	Established Name	Usual Dose	How Supplied
Tricor	(Fenofibrate Capsules) Micronized	Primary Hypercholesterolemia or Mixed Hyperlipidemia 200 mg per day Hypertriglyceridemia 67 mg per day	67 mg, 134 mg, & 200 mg
Tricor	(Fenofibrate Tablets)	Primary Hypercholesterolemia or Mixed Hyperlipidemia 160 mg per day Hypertriglyceridemia 54 mg per day	54 mg ——— & 160 mg

RISK ASSESSMENT

A. A search of the Adverse Event Reporting System (AERS) database was conducted to find any previously reported medication errors for Tricor (fenofibrate capsules) micronized. The AERS database was searched for reports using the Meddra term, DRUG MALADMINISTRATION, where Tricor% and fenofibrate% were listed as the suspect drugs. *There were no reports located using this search.*

B. According to the NDA 21-203 Sec 3 V.1 Page 24 *(for fenofibrate tablets)*, "the mixing of fenofibrate and sodium laurylsulfate followed by [redacted] is identical to that described for the manufacture of Tricor capsules (NDA 19-304)." Since fenofibrate tablets are [redacted], the product name should indicate [redacted] (See comments in section III). If the product is not labeled [redacted] health professionals could assume that both micronized and nonmicronized fenofibrate are available.

C. According to the Division, the Agency is currently reviewing the bioequivalence of Tricor tablets (54 mg, [redacted], & 160 mg) to Tricor capsules (67 mg, 134 mg, & 200 mg) per NDA 21-203. Furthermore, it has not been determined as to whether the [redacted] Although this consult request does not involve addressing the safety perspective of this issue, we request a follow-up regarding the outcome of this issue since there is a safety concern if bioequivalent capsules and tablets with the same name but with different strengths become available on the market. For example, if the capsules and the tablets are found to be bioequivalent, a patient could be prescribed 160 mg Tricor capsules and switched to 200 mg tablets with a false sense of increased titration regarding this drug, when in fact, they are identical in vivo.

In addition, regardless of whether Tricor [redacted] ts, the problem between the capsules and the tablets could still occur if generic fenofibrate capsules become available on the market. [redacted] Unless the NDA is taken off the market due to safety reasons (e.g. Seldane), a generic firm could submit an ANDA regardless of the availability of the NDA product on the market.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container label, carton and insert labeling of Tricor, OPDRA has attempted to focus on safety issues relating to possible medication errors. OPDRA has reviewed the current container label and carton and insert labeling and has identified several areas of possible improvement, which might minimize potential user error.

A. CONTAINER LABEL (54 mg, [redacted], & 160 mg)

1. We recommend the following presentation for the proprietary and established names on the container label, carton labeling, and package insert:

TRICOR
(Fenofibrate Tablets) [redacted]

2. The "Each tablet contains..." statement should be revised to read:

3. The color of the container label [redacted] is different than the color of the physician sample carton labeling [redacted] In fact, the color of the container label for [redacted] strength is very close in shade to the color of the unit dose carton labeling for 67 mg capsules (yellow). Furthermore, the color of the container label for 200 mg capsules (orange) is very close in shade to the color of the physician sample carton labeling for [redacted]. We recommend consistency in the use of the color to differentiate the different strengths and that the shade of the colors should not be close among the different strengths.

IV. RECOMMENDATIONS:

A. OPDRA recommends that the word, [redacted] be included on the label in conjunction with the name.

B. OPDRA recommends the above labeling revisions that might lead to safer use of the product.

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Lauren Lee, Pharm.D. at 301-827-3243.

/S/ 4/4/00

Lauren Lee, Pharm.D.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur:

/S/

Jerry Phillips, RPh
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

CC:

NDA: 21-203
Office Files
HFD-510; DivFiles; Margaret Simoneau, Project Manager
HFD-510; John Jenkins, Acting Division Director
HFD-042, Mark Askine, Senior Regulatory Review Officer, DDMAC (Electronic Only)
HFD-400; Lanh Green, Safety Evaluator, DDRE II, OPDRA
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Peter Honig, Director, OPDRA (Electronic Only)
HFD-002; Mac Lumpkin, Deputy Center Director for Review Management (Electronic Only)

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

REQUEST FOR CONSULTATION

TO (Division/Office): HFD-Hou OPDRA
ATTN: Sammie Beam Rm 15B07

FROM: HFD-510 Metabolic and Endocrine Drug Products

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
7/19/00		21-203		July 12, 2000

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Tricor (fenofibrate tablets)	High	Lipid Altering Agent	August 11, 2000

NAME OF FIRM: UF-9-12-00

REASION FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER (SPECIFY BELOW): Tradename Review

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISION RICK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Please review the enclosed Submission.
If there are any questions please contact:
Chemist - Chien-Hua Niu, PhD 301-827-6390
Project Manager - /S/ 76418

Note:
This is a Second Consult for Tricor tablets. First one was OPDRA Consult # OD-0031 (See attached)

SIGNATURE OF REQUESTER /S/

METHOD OF DELIVERY (Check one) ☐ MAIL ☒ HAND

SIG[illegible] OF RECEIVER 0

SIGNATURE OF DELIVERER

/S/ 7-19-00
DEPUTY DIRECTOR, DMEDP

FDA Links Searches Check Lists Tracking Links Calendars Reports Help

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements)

View as Word Document

NDA Number:	021203	**Trade Name:**	TRICOR (FENOFIBRATE)54/107/160MG TABLETS
Supplement Number:	000	**Generic Name:**	FENOFIBRATE
Supplement Type:	N	**Dosage Form:**	
Regulatory Action:	AE	**COMIS Indication:**	TREATMENT OF TYPE II/IV/V HYPERLIPIDEMIA
Action Date:	9/12/00		

Indication # 1 Treatment of hypercholesterolemia and hypertriglyceridemia

Label Adequacy: Inadequate for ALL pediatric age groups

Formulation Needed: NO NEW FORMULATION is needed

Comments (if any): Waiver of pediatric studies requested; granted.

Ranges for This Indication

Lower Range	Upper Range	Status	Date
Tanner1	Tanner5	Waived	9/5/01

Comments: Meaningful therapeutic benefit over existing treatments for the pediatric populations does not appear likely.

This page was last edited on 8/28/01

/S/

Signature

08/28/01

Date

Request for Waiver of Requirement for Pediatric Studies

Background:

According to FDA regulations, a full waiver of the requirement for studies in pediatric can be requested if the applicant certifies that:
1. The drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients and is not likely to be used in a substantial number of pediatric patients;
2. Necessary studies are impossible or highly impractical because, e.g., the number of such patients is so small or geographically dispersed; OR
3. There is evidence strongly suggesting that the drug product would be ineffective or unsafe in all pediatric age groups.

Introduction:

Studies of hypercholesterolemia in children have provided evidence of early findings of atherosclerotic disease. Post mortem studies in children have demonstrated that atherosclerotic plaque formation is evident at an early age (1). However, other epidemiological studies have shown that there is no direct correlation between hyperlipidemia in childhood and hyperlipidemia in adulthood (2, 3). Therefore while it is clear that atherosclerotic disease may have its beginnings in childhood, not all children with elevated lipids will develop cardiovascular disease, thus providing no clear target population for intervention among the general pediatric population.

For those children with homozygous familial hypercholesterolemia who are at high risk for sever premature atherosclerosis, HMG coA reductase inhibitors have come to be considered the standard of care, since these compounds provide the greatest degree of cholesterol reduction among the currently available compounds.

Clinical Data

Reduction of serum cholesterol in children has been the subject of three small studies conducted by Groupe Fournier, the developer of fenofibrate (4-6). Each of those studies demonstrated that both total cholesterol and LDL cholesterol is reduced following pharmacologic intervention with fenofibrate. The dose of fenofibrate used was 5 mg/kg of the standard formulation. This is equivalent to 350 mg/kg (for the average 70 kg adult) of the standard formulation or 230 mg/kg of the currently marketed micronized formulation.

One study (4) examined the effect of fenofibrate in 30 patients aged 7-19 years with severe familial Type II hyperlipidemia. Following 3-12 months of therapy, total

cholesterol and triglyceride levels were reduced by 27-31% and 20-25% respectively as compared with baseline levels achieved following 6 months of dietary therapy.

A second study (5) evaluating 17 patients aged 4-19 years demonstrated a reduction in total cholesterol of 22%, and a reduction in triglycerides of 39% at three months. In addition it was noted that uric acid levels were reduced 20% ($p<0.001$) and bilirubin was decreased by 19% ($p<0.05$). For those subjects who were followed for at least 6 months ($n=9$), the changes noted at three months were still evident. In terms of safety, it was noted that 4 of the 17 subjects had ALT (SGPT) elevations of at least 100% and AST (SGOT) elevations of at least 80%. The maximum ALT observed was 109 U/L. Elevated values persisted during treatment and decreased following discontinuation of therapy.

The third study (6), examined 12 children with Type IIa hyperlipidemia. Assessment of total cholesterol and apoprotein B after 6 months of therapy demonstrated a reduction of 20% and 26% respectively ($p<0.01$). A 10% increase in Apoprotein A, (p=NS) was also observed.

These three studies have shown that some reduction of total cholesterol and triglycerides is achievable with the use of fenofibrate, and that fenofibrate treatment is safe and well tolerated. However, the magnitude of this reduction does not reach that reported with the most potent of the HMG coA reductase inhibitors.

Conclusion

Based on the above information, it does not appear likely that the use of fenofibrate tablets would offer a meaningful therapeutic benefit over existing treatments for pediatric patients who require very aggressive cholesterol lowering to prevent severe premature atherosclerosis. In addition, the necessary studies are highly impractical because the number of such patients is relatively small.

There are no recommendations for the treatment of "low" HDL-C for the general pediatric population (1).

References

1) Berenson GS, Srinivasan SR, Bao W, Newman WP, Tracy RE and Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. New England Journal of Medicine, V338 (23):1650-1656, 1998

2) Genest JJ, Martin-Munley SS, McNamara JR, Ordovas JM, Jenner J, Myers RH, Silberman SR, Wilson PWF, Salem DN and Schaefer EJ. Familial lipoprotein disorders in patients with premature coronary artery disease. Circulation V85:2025-2033, 1992

3) Porkka KVK, Viikari JSA, Taimela S, Dahl M and Akerblom HK. Tracking and predictiveness of serum lipid and lipoprotein measurements in childhood: A 12 year follow-up: The cardiovascular risk in young Finns study. American Journal of Epidemiology V140(12):1096-1110, 1994

4) Drouin P, Sauvanet JP, Mejean L, Pointel JP and Debry G. Effect of procetofen in young patients affected by severe familial Type IIa HLP. International Conference on Atherosclerosis, Milan (Italy) Nov 9-11, 1977 Abstract (p. 226)

5) Steinmetz J, Morin C, Panek E, Siest G and Drouin P. Biological variations in hyperlipidemic children and adolescents treated with fenofibrate. Clinica Chemica Acta 112: 43-53, 1981

6) Chicaud P, Demange J, Drouin P and Debry G. Action of fenofibrate in hypercholesterolemic children: 18 month follow-up. La Presse Medicale V13(7): 417-419, 1984

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 # 21-203 Supplement # _____ Circle one SE1 SE2 SE3 SE4 SE5 SE6 3S

CDER Trade and generic names/dosage form: Tricor Tablets Action: AP (AE) NA

Applicant Abbott Therapeutic Class Lipid Altering

Indication(s) previously approved New fix tablet formulation

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

Proposed indication in this application _____

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) __Adolecents(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 /S/ (e.g., medical review, medical officer, team leader)

/S/ Medical Officer 9-7-00

Signature of Preparer and Title Date

cc: Orig NDA/BLA # _____

HFD-_____/Div File

NDA/BLA Action Package

HFD-006/ KRoberts

FOR QUESTIONS OR COMPLETING THIS PAGE

(revised 10/20/97)

Electronic Mail Message

Date: **September 5, 2001**
From: William C. Koch, R.Ph., Regulatory Project Manager
To: APPROVALS
Subject: NDA 21-203

Original submission date: November 10, 1999

Approval date: September 5, 2001

NDA 21-203

Trade name: Tricor Tablets

Generic Name: fenofibrate tablets

Applicant's name: Abbott Laboratories

Dosage form: tablet, 54 mg and 160 mg

Route of Administration: oral

Drug class: Lipid lowering agent

Application legend: Rx only

Indication(s): Type II, IV and V hyperlipidemia

Review priority: Standard