CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: 019304/S001

Trade Name: LIPIDIL MICRO (micronized)

Generic Name: FENFIBRATE CAPSULES

Sponsor: FOURNIER RESEARCH, INC.

Approval Date: 02/09/98

Indication(s): AS AN ADJUNCTIVE THERAPY TO DIET FOR THE TREATMENT OF ADULT PATIENTS WITH VERY HIGH ELEVATIONS OF SERUM TRIGLYCERIDE LEVELS (TYPES IV AND V HYPERLIPIDEMIA) WHO ARE AT RISK OF PANCREATITIS AND WHO DO NOT RESPOND ADEQUATELY TO A DETERMINED DIETARY EFFORT TO CONTROL THEM.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: 019304/S001

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	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tenative Approval Letter				X
Approvable Letter	X			
Final Printed Labeling		X		
Medical Review(s)				X
Chemistry Review(s)	X			
EA/FONSI				X
Pharmacology Review(s)				X
Statistical Review(s)				X
Microbiology Review(s)				X
Clinical Pharmacology Biopharmaceutics Review(s)				X
Bioequivalence Review(s)				X
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CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: 019304/S001

APPROVAL LETTER

NDA 19-304/S-001

Fournier Research Inc.
Attention: Mr. R. Lance Boyett
Director, Clinical Development
9 Law Drive
Fairfield, New Jersey 07004

FEB 9 1998

APPEARS THIS WAY
ON ORIGINAL

Dear Mr. Boyett:

Please refer to your supplemental new drug application dated June 20, 1997, received June 25, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lipidil Micro (fenofibrate capsules), micronized. We also refer to your January 9, 1998, submission, received January 12, 1998, in response to our approvable letter dated December 23, 1997 and additionally requesting a change in the Tradename for the product (from Lipidil Micro to Tricor). We also refer to your submissions of January 8 (fax), 9 (fax), 29 (fax), 30 (fax), February 2 (fax) and 6, 1998 (fax).

The User Fee goal date for this application is July 12, 1998.

APPEARS THIS WAY
ON ORIGINAL

The supplemental application provides for:

1. A change in the formulation of the drug product to a micronized version of fenofibrate.

2. A change in the strength of the drug product from 100 mg to 67 mg of micronized formulation.

3. Revisions in the labeling for the drug product which includes:

   a. A revision in the trade name and established name for the drug product to read Tricor (fenofibrate capsules), micronized per the February 2, 1998, FAX communication with revised draft labeling.

   b. Revisions in the DESCRIPTION, CLINICAL PHARMACOLOGY, INDICATIONS AND USAGE, WARNINGS, PRECAUTIONS, OVERDOSAGE, ADVERSE REACTIONS, DOSAGE AND ADMINISTRATION, HOW SUPPLIED AND STORAGE sections of the package insert.

APPEARS THIS WAY
ON ORIGINAL

We have completed the review of this supplemental application, including the submitted draft labeling, and have concluded that adequate information has been presented to demonstrate that

the drug product is safe and effective for use as recommended in the draft labeling in the submission dated February 2, 1998 (FAX). Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the draft labeling submitted on February 2, 1998 Edition date: January 29, 1998 (FAX).

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved supplemental NDA 19-304/S-001. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to the Division of Metabolic and Endocrine Drug Products and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications, HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Should a letter communicating important information about this drug product (i.e., a "Dear Doctor" letter) be issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20852-9787

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

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

Sincerely yours,

/S/ 9/99

Solomon Sobel, M.D.
Director
Division of Metabolic
and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

cc:
Original NDA 19-304
HFD-510/Div. files
HFD-510/CSO/M. Simoneau
HFD-510/SMoore/CNiu/EBarbehenn/RSteigerwalt/DOrloff
DISTRICT OFFICE
HF-2/Medwatch (with labeling + labeling reviews)
HFD-92/DDM-DIAB (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-735/DPE (with labeling) - for all NDAs and supplements for adverse reaction changes.
HFD-560/OTC (with labeling - for OTC Drug Products Only)
HFI-20/Press Office (with labeling)

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

Drafted by: Mas/February 5, 1998/wpf19304.1
Initialed
by:D.Orloff2.9.98/C.Niu2.5.98/S.Moore2.5.98/E.Barbehenn2.6.98/R.Steigerwalt2.6.98/H.Ahn2.9.98/E.Galliers2.9.98
final: Mas2.9.98

APPROVAL (AP)

APPEARS THIS WAY
ON ORIGINAL

FINAL PRINTED LABELING HAS NOT BEEN SUBMITTED TO THE FDA.

DRAFT LABELING IS NO LONGER BEING SUPPLIED SO AS TO ENSURE ONLY CORRECT AND CURRENT INFORMATION IS DISSEMINATED TO THE PUBLIC.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 019304/S001

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-304/S-001

Fournier Research Inc.
Attention: Mr. R. Lance Boyett
Director, Clinical Development
9 Law Drive
Fairfield, New Jersey 07004

DEC 2 3 1997

Dear Mr. Boyett:

Please refer to your supplemental new drug application dated June 20, 1997, received June 25, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for LIPIDIL Micro® (fenofibrate capsules), micronized.

We acknowledge receipt of your submissions dated August 29, October 24 and 31, November 24, December 4, 8, 12 (fax), 15, and 19 (fax), 1997. The User Fee goal date for this application is December 25, 1997.

APPEARS THIS WAY
ON ORIGINAL

The supplemental application provides for:

1. A change in the formulation of the drug product to the use of a micronized version of fenofibrate.

2. A change in the strength of the drug product from 100 mgm to 67 mgm of micronized formulation.

3. Revisions in the labeling for the drug product which includes:

   a. A revision in the trade name and established name for the drug product to read LIPIDIL Micro® (fenofibrate capsules), micronized

   b. Revisions in the DESCRIPTION, CLINICAL PHARMACOLOGY, INDICATIONS AND USAGE, WARNINGS, PRECAUTIONS, OVERDOSAGE, ADVERSE REACTIONS, DOSAGE AND ADMINISTRATION, HOW SUPPLIED and STORAGE sections of the package insert.

APPEARS THIS WAY
ON ORIGINAL

We have completed the review of this supplemental application as submitted with draft labeling dated December 19, 1997 (fax), and it is approvable. Before this application can be approved, however, it will be necessary for you to submit draft labeling revised as follows:

1. Under Clinical Pharmacology, **Pharmacokinetics** subsection:

   a. Information/data should be presented as appropriate under the subheadings of Absorption, Distribution, Metabolism, and Excretion.

   b. A section with the heading Special Populations and Pharmacokinetic Information/Data should be included under subheadings Geriatric, Pediatric, Gender, Race, Renal Insufficiency, Hepatic Insufficiency and Drug-Drug Interactions.

2. A table with pharmacokinetic parameters to include Absolute Bioavailability, Tmax, Clearance, Volume of Distribution, Half-Life (including effective half life) and Renal Clearance for normals and each special population, including the drug's targeted population (and where numbers of subjects/patients are indicated) should be prepared. Mean values (with the coefficients of variation) and 95% C.I. values should be provided.

3. Information about the food effect should be included in the labeling.

In addition, we have the following comments and recommendations:

1. Regarding your proposed dissolution specification for the new formulation we have the following comments/recommendations:

   a.

   b.

c.

d.

e.

f.

2.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of such action FDA may take action to withdraw this application.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

If you have any questions, please contact Ms. Margaret Simoneau, Project Manager, at (301) 827-6418.

Sincerely yours,

/S/

Solomon Sobel, M.D.
Director
Division of Metabolic
and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 019304/S001

CHEMISTRY REVIEW(S)

ORIGINAL

FEB - 6 1998

CHEMIST'S REVIEW	1. ORGANIZATION DMEDP, HFD-510	2. NDA NUMBER 19-304
3. NAME AND ADDRESS OF APPLICANT Laboratoires Fournier 50, rue de Dijon 21121 Daix- France		4. SUPPLEMENT NUMBER, DATE Supplement SCF-001 6/20/97
5. NAME OF THE DRUG Lipidil Micro	6. NONPROPRIETARY NAME Fenofibrate	8. AMENDMENT DATE 1/9/98 1/30/98
7. SUPPLEMENT PROVIDES FOR: A change in the new dosage formulation of the drug product utilizing a micronized version of fenofibrate.		
9. PHARMACOLOGICAL CATEGORY Lipid-lowering agent	10. HOW DISPENSED RX	RELATED IND/NDA/DMF
12. DOSAGE FORM Capsule	13. POTENCY 65 mg	

14. CHEMICAL NAME AND STRUCTURE

15. COMMENTS

On 1/9/98, a telephone call was placed to Ms. Margaret Simoneau, Project Manager, by Mr. Lance Boyett (Director, Clinical Development, Fournier Research, Inc.). During the telephone conversation, Mr. Boyett requested that the tradename of "Lipidil Micro" be changed to "Tricor" due to legal issues and possible confusion of another tradename "Lipitor". In the 1/9/98 amendment, the sponsor requested a change in the tradename for the product from Lipidil Micro to Tricor. On 1/13/98, this new tradename "Tricor" was submitted to Labeling and Nomenclature Committee for their review.

16. CONCLUSIONS AND RECOMMENDATIONS

The sponsor has properly responded the concern of the Nomenclature Committee about the conflict with other tradenames, including Trikort and Zocor. Thus there are no other outstanding issues in terms of chemistry, manufacturing and controls of the drug product. Therefore, the supplement can be approved from chemistry viewpoint

17. NAME	REVIEWER SIGNATURE	DATE COMPLETED
Chien-Hua Niu, Ph.D.	/S/	2/2/98

DISTRIBUTION: ORIGINAL JACKET REVIEWER DIVISION FILE

R/D initialed by:

Disc Supplement #3: NDA19304.S1B

/S/ 2/6/98

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 019304/S001

ADMINISTRATIVE DOCUMENTS/CORRESPONDENCE

ORIGINAL

LABORATOIRES
FOURNIER

February 2, 1998

Dr. Solomon Sobel
Director, Division of Metabolism
& Endocrine Drug Products
Food and Drug Administration, HFD-510
Room 14 B 03
5600 Fishers Lane
Rockville, MD 20857 U.S.A.

Noted
Acc. Chem. Rev. for
S-001 /S/
2/4/98

Re : NDA # 19-304/S-01 - (fenofibrate capsules), micronized
Final Draft Labeling - January 29, 1998

Noted
/S/
2-12-98

Dear Dr. Sobel,

We reference our teleconference with the Division on January 29, 1998 at which time Dr. Niu indicated that the changes to page 14 of the labeling, faxed to the Division earlier that same day, were acceptable from the chemistry perspective. Those changes include :

"How Supplied" Section :
APPEARS THIS WAY
ON ORIGINAL
"(micronized fenofibrate), capsules" *changed to* "(fenofibrate capsules), micronized"
[the established name had not been modified in this particular section and therefore, was not consistent with the wording requested by the Division], and

"Storage" Section :
APPEARS THIS WAY
ON ORIGINAL
"Distributed by Abbott Laboratories . . ." *changed to* "Manufactured for Abbott Laboratories . . . by Laboratoires Fournier . . . "

APPEARS THIS WAY
ON ORIGINAL
Ms. Simoneau further stated that all other aspects were acceptable. The only outstanding issue is the trade name. In this regard, we reference a letter submitted to the Agency on January 30, 1998 in which an explanation is provided for why we wish to retain the trade name TRICOR™.

APPEARS THIS WAY
ON ORIGINAL
In closing, the final draft labeling dated January 29, 1998 is submitted herewith in triplicate. If you require additional information regarding this correspondence, please contact Laboratoires Fournier's US agent, Mr. R. Lance Boyett at (973) 575-1010.

Sincerely,

L. Ospital
Regulatory Affairs Project Manager

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

Noted
/S/
2/17/98

cc: A. Munoz (LF), L. Boyett, J. Mohr (FRI), M.L. Reed (Abbott)

ORIGINAL

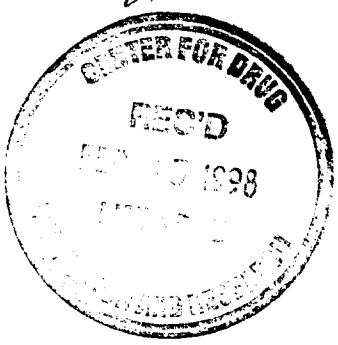
LABORATOIRES
FOURNIER

NDA SUPPLEMENT

January 30, 1998

Noted
/S/ 2/11/98
(See clin Rev. for S-001)

Dr. Solomon Sobel
Director, Division of Metabolism
& Endocrine Drug Products
Food and Drug Administration, HFD-510
Room 14 B 03
5600 Fishers Lane
Rockville, MD 20857 U.S.A.



Re : NDA # 19-304/S-01 - (fenofibrate capsules), micronized

Dear Dr. Sobel,

We reference our teleconference with the Division on January 29, 1998 at which time Dr. Niu discussed the recommendations of the Nomenclature Committee regarding the tradename TRICOR™ proposed for the above-mentioned product. We understand that the Committee indicated that TRICOR™ was possibly in conflict with the trademark TRIKORT, and possibly too similar to ZOCOR.

APPEARS THIS WAY
ON ORIGINAL

Laboratoires Fournier and Abbott Laboratories wish to retain the trade name for fenofibrate capsules, micronized as TRICOR™. This name has been tested in market research and did not cause any confusion with the physician groups who were part of the test group. In addition, Fournier and Abbott voluntarily offered to change the trade name from LIPIDIL Micro® to avoid confusion with another trade name LIPITOR to assist the Agency and prevent confusion and prescription errors.

APPEARS THIS WAY
ON ORIGINAL

The prefix "TRI" is no closer to Zocor than Mevacor, Posicor, Helicore, Thelicor, Maxicor Tambocor, Inocor, Memcor, Stedicor, Omacor, Gemcor, Vitacor, Natrecor, Bradycor, Dilacor, Carnicor, Primacor, Topocor, Symcor, Bepricor and Vascor all of which have been approved. Challenges by Merck to date have only included trade names such as Zocin, Zinecor and Zemcor which are not close to TRICOR.

Regarding possible confusion with the name Trikort, we have discovered the following information. This name was used by Keene Pharmaceuticals for an injectable form of triamcinolone. In contacting Keene, they have stated they no longer use this trade name and have not used it in years. Further search of an on-line data base for pharmaceuticals in use does not show any product with the name Trikort or Tri-Kort in use. In addition, a search of the IMS database does not show any recorded sales of any product with that name. Regarding a topical cream with the Trikort or Tri-Kort trade name, we cannot find a listing of such a product in the Physician's Desk Reference, OTC Physician's Desk Reference, or Facts and

Comparisons. If in fact such a product exists, the availability of it would be so insignificant that there should not exist any confusion in the market. Also considering that one product is in the over-the-counter market and TRICOR™ is in the prescription market, any confusion would be further reduced.

In summary, we believe the objection to the trade name TRICOR™ is without merit and would request that the Nomenclature Committee review the acceptability of the name in light of the foregoing information.

Lastly, subsequent to Dr. Niu's confirmation that the following modifications to the labelling were acceptable from his perspective :

"How Supplied" Section :
"(micronized fenofibrate), capsules" changed to "(fenofibrate capsules), micronized" and

"Storage" Section :
"Distributed by Abbott Laboratories . . ." changed to "Manufactured for Abbott Laboratories . . . by Laboratoires Fournier . . . "

the final draft labeling dated January 29, 1998 will be submitted, under separate cover, in triplicate.

If you require additional information regarding this correspondence, please contact Laboratoires Fournier's US agent, Mr. R. Lance Boyett at (973) 575-1010.

Sincerely,

L. Ospital
Regulatory Affairs Project Manager

REVIEWS COMPLETED

CSO ACTION:
☒ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

APPEARS THIS WAY
ON ORIGINAL

cc: A. Munoz (LF), L. Boyett, J. Mohr (FRI), M.L. Reed (Abbott)

APPEARS THIS WAY
ON ORIGINAL

ORIGINAL

JAN 29 1998

RECORD OF TELEPHONE CONVERSATION/MEETING	**Date:** January 29, 1998
Telephone Conference Time: 09:30AM Place: Parklawn 1456 FDA: Chien-Hua Niu Margaret Simoneau Fournier: Lance Boyette Liz Ospital Discussion: 1. Enclosure (1) fax dated January 29, 1998 regarding page 14 of labeling was accepted by chemistry. 2. "Tricor" tradename nominclature committee recommendations were conveyed to the company. Specifically, the possibility that "Tricor" is too close to Tri-Kort (a topical) product and Zocor (another lipid altering agent). These two examples of look and/or sound alikes were presented to Mr. Boyett in addition to two options. The first option was to present another name besides "Tricor" and the second option was to sent the Division an explanation as to why they request to keep "Tricor". Dr. Niu also brought up the concern of the name similarities with problems that arose in Canada with Lipidil, which was why they requested a name change (see January 9, 1998 fax, first paragraph, second sentence). 3. Results were: Lance Boyett will discuss with Abbott Company BUT does not want to change the name from "Tricor" and will fax a justification letter today. cc:Original NDA Div file /S/ --------- **Name: Margaret Simoneau**	**NDA#:** 19-304/S-001 **Telecon/Meeting initiated by:** O Applicant/Sponsor **By:** Telephone **Product Name:** Fenofibrate Capsules, micronized **Firm Name: Fournier** Research, Inc **Phone:** 9-011-333-80447765

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

ORIGINAL

FOURNIER
RESEARCH INC.

JAN 8 1998

To: **Margaret Simoneau (CSO)** Date: January 8, 1998
FDA Div. of Endo. and Metab. Drug Products

From: R. Lance Boyett Fax: (1) (973) 575 75 95, Tel: (1) (973) 575 10 10 ext. 108

CC: A. Munoz (Laboratoires Fournier)
M. Reed (Abbott)

Pages: 1 of 4

REF: NDA 19-304/S-001 [Lipidil Micro (fenofibrate capsules), micronized]
Background information for Teleconference

Following is a DRAFT proposal for revision of the Clinical Pharmacology section of the label We wish to discuss the following proposals:

1. For the most part, the rewrite of the section is limited to reformatting information that was already included in the label. We believe that this is in keeping with the goal of this supplemental application. However, new information that was submitted pursuant to this supplement, for example the effects of food on absorption, has been included in the labeling as requested. This new information is underscored in the current proposal, and will be cross-referenced to facilitate verification by the reviewer(s).

2. We have excluded the requested table of pharmacokinetic parameters in the various subpopulations, as we believe the information is adequately described in the paragraphs of the section, and will not contribute additional information that is important to the safe prescription of the medication.

3. Finally, we have deleted the table in the Clinical Pharmacology section that describes the lipid responses from a subgroup of one of the US studies. The reference to the table has also been deleted from the text. We believe that this change brings the description of the pharmacological activities of the fenofibrate labeling in line with the format of labeling for other drugs in the fibrate class, e.g. gemfibrozil, and provides adequate information for prescription of the medication.

In closing, we wish to inform the Division that Laboratoires Fournier will be licensing the product to Abbott Laboratories for marketing in the US. In view of this, one or more members of the Abbott regulatory department will sit in on the teleconference. As a further consequence, we will be requesting a change in the Tradename for the product.

Please see that this information is distributed to the representatives of the Division who will be involved in this teleconference. You can feel free to contact the undersigned if you have any questions or require additional information.

R. Lance Boyett
Director, Clinical Development
Fournier Research, Inc.
(US Agent for Laboratoires Fournier, S.A.)

C. Original NDA 19-304/S-001
Div File

DEC 2 3 1997

LABEL REVIEW

Application Number: 19-304/S-001

Name of Drug: LIPIDIL Micro (fenfibrate capsules), micronized

Sponsor: Laboratories Fournier

Material Reviewed: December 19, 1997 draft labeling

APPEARS THIS WAY
ON ORIGINAL

Submission Date(s): December 19, 1997 draft Labeling

Receipt Date(s): December 19, 1997 draft labeling

Background and Summary Description: This submission included revised draft labeling in response to a December 18, 1997 telephone conversation with the Division and the firm. The telecommunication dealt with revisions to the package insert as submitted in the original submission dated June 20, 1997.

Review

APPEARS THIS WAY
ON ORIGINAL

The revised draft labeling dated December 19, 1997, was compared with the currently approved labeling and the draft labeling dated June 20, 1997. The following changes were noted:

1. **TRADE NAME:**

APPEARS THIS WAY
ON ORIGINAL

The name "LIPIDIL® (Fenofibrate Capsules)" has been changed

to "LIPIDIL Micro® (fenofibrate capsules), micronized."

Reviewer comment: The firm proposed in this supplement that the new trade and established name should be LIPIDIL Micro® (micronized fenofibrate capsules). A FAX communication dated November 24, 1997, was sent to the firm indicating the Labeling and Nomenclature recommendations for revisions. The final revised trade name and established name as stated above was agreed upon in a December 19, 1997, telephone conversation with Dr. Stephen Moore, Chemistry Team leader, and Lance Boyett of Fournier.

APPEARS THIS WAY
ON ORIGINAL

2. **DESCRIPTION** section:

a. Paragraph 1, line 1, "*LIPIDIL® (fenofibrate capsules) . . .* " has been revised to read, *"LIPIDIL Micro® (fenofibrate capsules), micronized . . ."*

b. Paragraph 1, line 2, *"Each capsule contains 100 mg of fenofibrate."*, has been revised to read, *"Each capsule contains 67 mg of micronized fenofibrate."*

c. Paragraph 1, line 2 and 3 *"Each capsule also contains lactose, NF; pregelatinized starch, NF; and pre gelatinized starch, NF."* has been revised to read, *"Each capsule also contains lactose, NF; sodium lauryl sulfate, NF; and magnesium stearate, NF."*

d. Paragraph 1, line 4, *"The chemical name is . . ."* has been revised to read, *"The chemical name for fenofibrate is . . .".*

e. Paragraph 1, line 6, *"The empirical formula is . . .and the molecular wight is 360.84; . . . The melting point is 77-82° C."* has been revised to read, *"The empirical formula is . . .and the molecular wight is 360.83 . . . The melting point is 79-82° C."*

APPEARS ON OBS

3. **CLINICAL PHARMACOLOGY**

a. Paragraph 1, line 1, *"The effects of LIPIDIL Micro® . . .",* has been revised to read, *"The effects of fenfibrate . . ."*

b. Paragraph 1, line 6 ". . . treatment with LIPIDIL . . . ", has been revised to read, ". . . treatment with fenofibrate at dosages equivalent to 3 capsules of 67 mg Lipidil Micro® per day . . . "

c. Paragraph 2, line 1, *"The mechanism of action of LIPIDIL . . . "*, has been revised to read, *"The mechanism of action of LIPIDIL Micro® . . . "*

d. Paragraph 2, line 4, *"LIPIDIL also reduces serum uric acid . . . "* has been revised to read, *"Fenofibrate also reduces serum uric acid . . . "*

e. Paragraph 3, line 3, ". . . *60% of a single radiolabeled 300 mg dose of fenofibrate,"* has been revised to read, ". . . *60% of a single dose of fenofibrate,"*

f. Paragraph 3, line 5, the following was added after *". . . the compound was eliminated with a half-life of 20 hours."* as follows, *". . . allowing once daily administration in a clinical setting."*

g. Paragraph 4, line 4, *". . . within 5 days of dosing with 100 mg/day . . . "*, has been revised to read *"within 5 days of dosing with single oral doses equivalent to 67 mg LIPIDIL Micro®. . ."*

h. Paragraph 4, line 8, *". . . following a single oral dose of 100 mg . . . " has been revised to read, ". . . following a single dose of fenofibrate . . . "*

I. Paragraph 5, line 8, " . . . "Therefore, the dosage of LIPIDIL should be reduced . . . ", should be revised to read "Therefore, the dosage of LIPIDIL Micro® should be minimized . . . "

4. **INDICATIONS AND USAGE**

APPEARS THIS WAY
ON ORIGINAL

a. Paragraph 1, line 1, *"LIPIDIL (fenofibrate capsules) . . ."* has been revised to read, *"LIPIDIL Micro® (fenofibrate capsules, micronized) . . . "* .

b. Paragraph 1, line 9, *"LIPIDIL . . . "* has been revised to read, *"LIPIDIL Micro®. . ."*

c. Paragraph 1, line 14, *". . . but the influence of LIPIDIL . . ."* has been revised to read, *"LIPIDIL Micro®. . . "*

d. Paragraph 4, line 1, *"Because of the benefit/risk ratio of LIPIDIL fenofibrate . . . LIPIDIL is not indicated for such use."*, has been revised to read, *"Because of the benefit/risk ratio of LIPIDIL Micro®. . . LIPIDIL Micro® is not indicated for such use."*

5. **WARNINGS**

APPEARS THIS WAY
ON ORIGINAL

a. Paragraph 1, line 1, *". . . LIPIDIL (fenofibrate) . . . "* has been revised to read, *". . LIPIDIL Micro® (micronized fenofibrate)."*

b. Paragraph 1, line 4, ". . . LIPIDIL. ", has been revised to read, *"LIPIDIL Micro®"*

c. Paragraph 4, line 1., "Liver function: Fenofibrate use at doses of 200 to 300 mg/day . . . " has been revised to read "Fenofibrate used at doses equivalent to 2 to 3 capsules of 67 mg LIPIDIL Micro® per day . . . "

d .Paragraph 4, line 6, ". . . LIPIDIL treated patients taking 200 to 300 mg/day . . . " has been revised to read . . . feonfibrate at doses equivalent to 2 to 3 capsules of 67 mg LIPIDIL Micro® per day . . ."

e. Table "Patients with AST or ALT.3x the Upper Normal Limits in Controlled Clinical Trials vs Fenofibrate', the following has been after the table, *"* Dosages equivalent to 2 to 3 capsules of 67 mg LIPIDIL Micro® per day."*

f. Paragraph 5, line 10, *". . . patients receiving 100 or 50 mg/day or placebo. Both hepatocellar and cholestatic hepatitis have been reported. In literature reports, hepatitis associated with fenofibrate has occurred after exposures of weeks to several years."*, has been revised to read, *". . . patients receiving dosages equivalent to 2 to 3 capsules per day and was 0% in those receiving dosages equivalent to one or ½ capsule per day, or placebo. Hepatocellar, chronic active and cholestatic hepatitis associated with fenofibrate therapy have been reported after exposures of weeks to several years. In extremely rare cases cirrhosis has been reported in association with chronic active hepatitis."*

g. In paragraph 6, line 2, *". . . LIPIDIL . . ." has been revised to read, " . . . LIPIDIL Micro®. . .".*

h. In paragraph 7, paragraph 8, paragraph 9, and paragraph 10, *". . . LIPIDIL . . ."* has been revised to read, *" . . . LIPIDIL Micro®. . .".*

6. **PRECAUTIONS**

APPEARS THIS WAY ON ORIGINAL

a. Paragraph 1, line 3, *". . . LIPIDIL . . ."* has been revised to read, *" . . . LIPIDIL Micro®. . .".*

b. Paragraph 2, line 4, *". . . LIPIDIL . . ."* has been revised to read, *" . . . LIPIDIL Micro®. . .".*

c. Paragraph 2, line 7, *". . . 300 mg/day"* has been revised to read, *" . . . 3 capsules per day(201 mg)."*

d. Paragraph 4, line 5, *". . . treatment with LIPIDIL. " has been revised to read, ". . . treatment with fenofibrate. "*

e. Paragraph 5, line 4, *". . . LIPIDIL therapy."*, has been revised to read, *". . . fenofibrate therapy."*

f. Paragraph 5, line 10, ". . . LIPIDIL administration." , has been revised to read, LIPIDIL Micro® administration.

g. Under Skeletal Muscle, line 2, *". . . LIPIDIL"* has been revised to read, *". . . LIPIDIL Micro®."*

I. Under **Drug Interactions, Oral Anticoagulants**, line 4, *". . . LIPIDIL"* has been revised to read, *". . . LIPIDIL Micro®."*

j. Under HMD-CoA reductase inhibitors, line 8, *". . . LIPIDIL"* has been revised to read, *". . . LIPIDIL Micro®."*

k. Under Resins, line 3, *". . . LIPIDIL"* has been revised to read, *". . . LIPIDIL*

Micro®."

l. Under Cyclosporin, line 2, *". . . nephrotoxicity with decrease . . . ",* has been revised to read, *". . . nephrotoxicity with decrease . . . ".*

m. Under Cyclosporin, line 6 and 8, *". . . LIPIDIL"* has been revised to read, *". . LIPIDIL Micro®."*

o. Under **Carcinogenesis, Mutagenesis, Impairment of Fertility**, a new paragraph has been added after paragraph 3, as follows:

"Electron microscopy studies have demonstrated peroxisomal proliferation following fenofibrate administration to the rat. An adequate study to test for peroxisome proliferation in humans has not been done, but changes in perisome morphology and numbers have been observed in humans after treatment with other members of the fibrate class when liver biopsies were compared before and after treatment in the same individual."

APPEARS THIS WAY
ON ORIGINAL

7. **ADVERSE REACTIONS**

A. Under CLINICAL, line 2, 6 and 8, *"LIPIDIL"* has been replaced with *"fenofibrate".*

B. Under LABORATORY, paragraph 1, line 4, *" . . . Lipidil at doses of 300 mg/day. ",* has been revised to read, *". . . Fenofibrate ate doses equivalent to three capsules of 67 mg LIPIDIL Micro®, per day."*

8. **OVERDOSAGE**

APPEARS THIS WAY
ON ORIGINAL

The section has been revised to read as follows and place before the **DOSAGE AND ADMINISTRATION** section as follows:

"Because fenofibrate is highly bound to plasma proteins, hemodialysis should not be considered.

While there has been no reported cases of overdosages, symptomatic supportive measures should be taken should it occur."

9. **DOSAGE AND ADMINISTRATION**

a. Paragraph 1, line 2 and 3, paragraph 2 line 1, and paragraph 3 line 2, ". . . LIPIDIL . . ." Has been revised to read, *". . . LIPIDIL Micro® . . ."*

b. Paragraph 2, line 2, Paragraph 3, line 2 and 6, *"100 mg/day"* should now read *"67 mg/day."*

c. Paragraph 2, lin 8 which reads, *"The maximum dose is 300 mg/day,"*, should now read, *"The maximum dose is 3 capsules per day (201 mg)."*

10. **HOW SUPPLIED**

APPEARS THIS WAY
ON ORIGINAL

The section has been revised to read,

"LIPIDIL Micro® (micronized fenofibrate) is available as yellow opaque, hard gelatin capsules. Each capsule containers 67 mg of micronized fenofibrate. Each capsule is printed with "LIPIDIL 67". LIPIDIL Micro® is available in bottles of 90 and bottles of 1000."

11. **STORAGE**

APPEARS THIS WAY
ON ORIGINAL

This section has been revised to read,

"Store at controlled room temperature, 15-30° C (59-86° F). Keep out of reach of children. Protect from moisture."

Distributed by

FOURNIER RESEARCH INC.
9 Law Drive
Fairfield, NJ. 07004

APPEARS THIS WAY
ON ORIGINAL

CONCLUSIONS:

All changes requested by the Division per the December 18, 1997, meeting and FAX have been made as requested.

However the following recommendations have been made to the labeling by the biopharmaceutics reviewer/team leader, Dr. Hae Young Ahn as follows:

1. Under Clinical Pharmacology, **Pharmacokinetics** subsection:

   a. Information/data should be presented as appropriate under the subheadings of Absorption, Distribution, Metabolism, and Excretion.

   b. A section with the heading Special Populations and pharmacokinetic Information/Data should be included under subheadings geriatric, Pediatric, Gender, Race, Renal Insufficiency, Hepatic Insufficiency and Drug-Drug Interactions.

2. A table with pharmcokinetic parameters to include Absolute bioavailability, Tmax, Clearance, Volume of Distribution, Half-Life (including effective half life) and Renal

2. A table with pharmcokinetic parameters to include Absolute bioavailability, Tmax, Clearance, Volume of Distribution, Half-Life (including effective half life) and Renal Clearance for normals and each special population, including the drug's's targeted population (and where numbers of subjects/patients are indicated) should be prepared. Mean values (with the coefficients of variation) and 95% C.I. values should be provided.

3. Information about the food effect should be included in the labeling.

RECOMMENDATION:

APPEARS THIS WAY
ON ORIGINAL

With the concurrence of the reviewing group, the revised labeling dated December 19, 1997, is approved with the following above labeling recommendations.

/S/ 12.23.97
Project Manager

/S/ 12/23/97
Pharmacology Supervisor

/S/ 12/23/97
Chemistry Reviewer

/S/ 12/23/97
Pharmacology Reviewer

/S/ 12/23/97
Chemistry Team Leader

/S/ 12/23/97
Biopharmaceutics Team Leader

/S/ 12-23-97
Medical Team Leader

APPEARS THIS WAY
ON ORIGINAL

cc:
NDA 19-304/S-001
HFD-510/Div. Files
HFD-510/MSimoneau/DOrloff/SMoore/CNiu//RSteigerwalt/EBarbehenn / mcw
HFD-510/Solomon Sobel, M.D.

LABEL REVIEW

APPEARS THIS WAY
ON ORIGINAL

LABEL REVIEW

Application Number: 19-304/S-001

Name of Drug: Lipidil Micro (fenofibrate capsules), micronized → Tricor

Sponsor: Laboratories Fournier

Materials Reviewed: February 2, 1998 (FAX) Final Draft Labeling-January 29, 1998

Background and Summary Description: This submission included revised draft labeling in response to a December 23, 1998 "Approvable Letter" and to faxes dated January 8, 9, 29, 30 and February 2 and 6, 1998.

1. Trade Name
   The name "Lipidil (Fenofibrate capsules) has been changed to Tricor (Fenofibrate capsules), micronized.
Reviewer comments: See chemistry review dated February 6, 1998 by Dr. Niu, approved by Dr. Steve Moore.

2. Pharmacokinetics/ Metabolism
   Referenced to the "Approvable Letter" from the Division dated 12/23/97 and a fax dated January 8, 1998 , the revised draft labeling of February 2, 1998 (Edition date: January 29, 1998) was acceptable by Dr. Hae-Young Ahn and Dr. David Orloff.

3. Storage
   "Manufactured for Abbott Laboratories, North Chicago, IL 60064 U.S.A. by Laboratories Fournier, S.A., 21300 Chenova, France" was added to the section.

4. Clinical Pharmacology
   Paragraph 1, second sentence, ..."and the other TG levels of 350 to 500 mg/dL".
Label reviewer comment: Change noted from the original submission from 250mg.
February 6, 1998 (fax) explanation justification.

RECOMMENDATION:

Label review was completed on 12/23/97 by Mr. Steve McCort from the original submission dated June 20, 1997. The above noted corrections were in response to the 12/23/98 approvable letter. With the concurrence of the reviewing group, the revised labeling dated February 2, 1998 (Edition date: January 29, 1998) is approved.

Medical Team Leader /S/ 2-6-98

Chemistry Reviewer /S/

Chemistry Team Leader /S/ 2/6/98

Biopharmaceutics Team Leader /S/ 2/9/98

Pharmacology Reviewer /S/ 2/9/98

Pharmacology Team Leader /S/ 2/9/98

Project Manager /S/

APPEARS THIS WAY
ON ORIGINAL

cc: NDA 19-304/S-001
Div File

LABEL REVIEW

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

FOURNIER
RESEARCH INC.

To: **Margaret Simoneau** Date: January 9, 1998

From: R. Lance Boyett Fax: (1) (973) 575 75 95, Tel: (1) (973) 575 10 10 ext. 108

CC: Marilou Reed (Abbott)
Alain Munoz, Liz Ospital (Laboratoires Fournier)

Pages: 1 of 1

REF: NDA 19-304/S-001

We reference our teleconference this morning, which was held in response to the Approvable Letter from the Division, dated December 23, 1997. During that teleconference, we mentioned that we would need to change the tradename of "Lipidil Micro" due to legal issues and possible confusion of the tradename with another lipid lowering agent. We are proposing the tradename be changed to "Tricor".

This topic was also discussed by telephone with Dr. Dan Bohring of the Nomenclature Committee, who indicated that due to the anticipated timing of the Approval Letter, he would be willing to expedite the review of this proposed name. He explained that the request for expedited review should be submitted by the Division.

Accordingly, we respectfully request that the Division ask for an expedited review of the proposed tradename "Tricor".

Please note that this change in name will be formally submitted along with the other changes to the labeling for the product, which were agreed to by teleconference today.

We sincerely appreciate your efforts in this regard.

Lance Boyett
Director, Clinical Development
Fournier Research, Inc.
(US Agent for Laboratoires Fournier)

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

Two telephone conversations took place January 28, 1998.
#1. At 10:45AM
FDA-Margaret Simoneau
Fournier-Lance Boyett
Issues:
1. W/R to status of nomenclature committee decision.
The January 27 meeting has been reschuled to February 10.

But at this time, no recommendation has been submitted to Dr. Niu.
2. W/R to chemistry review of the January 9th submission:
Two recommendations on page 14:
a. Under HOW SUPPLIED section , after the word TRICOR, (micronized fenofibrate) needs to come in conformity with (fenofibrate capsules), micronized.
b. Under STORAGE section, "Made in France" needs to be modified to come in compliance with 21 CFR Ch. 1(4-1-97 Edition), p. 10, a copy will be faxed to him in France. Mr. Boyett said this was a custom requirement and needed to be there. I told him I would speak with both Drs Niu & Steve Moore and call back.

#2. At 11:00AM after faxing (enclosure 1) and consult with both chemists.
FDA: Margaret Simoneau
Fournier: Liz Ospital, Regulatory Affairs Project Manager
F/U issue:
Need add "manufactured by " company name, address, France in addition to "Distributed by:" in the STORAGE section.

APPEARS THIS WAY
ON ORIGINAL

/S/
Margaret Simoneau, Project Manager

APPEARS THIS WAY
ON ORIGINAL

cc: Original NDA 19-304/S-001
Div file

NDA#:19-304/S-001

Telecon/Meeting initiated by:

○ Applicant/Sponsor
● FDA
By: Telephone

Product Name: Fenofibrate Capsules, micronized
Firm Name: Fournier Research, Inc
Phone:
9-011-333-80447765

APPEARS THIS WAY
ON ORIGINAL

ORIGINAL

DEC 23 1997

MEMORANDUM

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

DATE: December 23, 1997

FROM: Steve McCort
Project Manager, HFD-510

SUBJECT: Resolution of Review Chemistry Comments

TO: NDA 19-304/S-001

The following deficiency was addressed in Dr. Chien-Hua Niu, reviewing chemist, in his December 18, 1997 review as follows:

> The proprietary name "LIPIDIL Micro" should be converted to Lipidil when the non-micronized formulation of fenofibrate is no longer distributed.

In a December 19, 1997, telephone conversation, with Dr. Stephen Moore, Chemistry Team Leader, and Lance Boyett of Fournier, a final revised trade name and established name was agreed upon, as follows:

> LIPIDIL Micro® (fenofibrate capsules), micronized

Therefore the deficiency addressed in Dr. Niu's December 18, 1997 review is no longer applicable.

/S/ 12/23/97
Steve Moore, Ph.D.
Chemistry Team Leader

APPEARS THIS WAY
ON ORIGINAL

/S/
Chien-Hua Niu, Ph.D.
Reviewing Chemist

/S/ 12-23-97
Steve McCort
Project Manager

APPEARS THIS WAY
ON ORIGINAL

cc: NDA 19-304/S-001
Div File
HFD-510/Simoneau/Niu
HFD-510/Moore

ORIGINAL

LABORATOIRES
FOURNIER

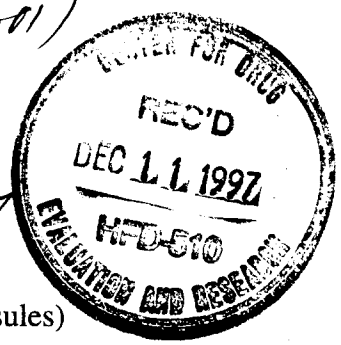
NDA SUPPL AMENDMENT

Dated
Review completed
(Elec clin Rev. #2)
for S-001)
/S/
12/10/97

December 8, 1997

Dr. Stephen K. Moore
Chemistry Team Leader
Division of Metabolism
& Endocrine Drug Products
Food & Drug Administration, HFD-510
Room 14 B 03, 5600 Fishers Lane
Rockville, MD 20857

APPEARS THIS WAY
ON ORIGINAL



Re : NDA 19-304/S-001 Lipidil Micro® (micronized fenofibrate capsules)

Dear Dr. Moore,

We reference the Division's telefax dated November 24, 1997. We also reference a telefax to the Division dated December 4, 1997 following a teleconference discussion with Dr. Nui on December 1, 1997.

For ease of reference, the Division's questions/recommendations of November 24 are reproduced in ***bold italics*** below.

APPEARS THIS WAY
ON ORIGINAL

A. ***Regarding tests and specifications:***

B. Regarding Labeling:

(1) It is recommended that the word "Micro" in the proposed proprietary name "LIPIDIL Micro" is unnecessary because the drug is a micronized substance. Moreover, the established name for this product should be changed to (fenofibrate capsules) micronized. Thus the original proprietary name "LIPIDIL" should be used in all labeling, including the package insert and bottle labels.

We thank you for this recommendation.

The recommendation regarding the "established" name, is acceptable.

(2) It is recommended that National Drug Code (NDC) numbers be added to "How Supplied"section of the package insert.

We thank you for this recommendation. National Drug Codes will be incorporated into the "How Supplied" Section of the package insert as they are assigned.

Please address any questions and your comments on the above to our authorized US Agent, at (973) 575-1010. We appreciate your continued review of our sNDA.

Sincerely,

Liz Ospital

Liz Ospital
Regulatory Affairs Project Manager
Laboratoires Fournier

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

APPEARS THIS WAY
ON ORIGINAL

cc Dr. Chin-Hua Niu (Chemistry Reviewer, FDA)
Margaret. Simoneau (CSO)
R. Lance Boyett (Fournier Research, Inc., Applicant's authorized US agent)
Ph. Reginault (Laboratoires Fournier, Director of Pharmaceutical Development)
M. Forest (LF, Quality Assurance)
S. Lagneau (LF, Registration & Regulatory Affairs)
Dr. Alain Munoz (Vice President, R&D Groupe Fournier)

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

NDA SUPPLAMENDMENT ORIGINAL

LABORATOIRES
FOURNIER

December 4, 1997

Noted
Review completed
(Lee Claudius
for S-001)
/S/
12/18/97

CENTER FOR DRUG
REC'D
DEC 09 1997
HFD-510
EVALUATION AND RESEARCH

Dr. Stephen K. Moore
Chemistry Team Leader
Division of Metabolism
& Endocrine Drug Products
Food & Drug Administration, HFD-510
Room 14 B 03
5600 Fishers Lane
Rockville, MD 20857

Re : NDA 19-304/S-001 Lipidil Micro® (micronized fenofibrate capsules)

Dear Dr. Moore,

We refer to a teleconference discussion held with Dr. Chin-Hua Niu on December 1, 1997 as well as the Division's fax addressed to our Authorized Agent, Mr. R. Lance Boyett, on November 24, 1997. Laboratoires Fournier personnel participating in the conference call were the undersigned as well as Dr. Philippe Reginault (Director of Pharmaceutical Development).

Following the teleconference, we understand that Dr. Niu has requested that the following tests be included in the release specifications (acceptance criteria) and Certificate of Analysis :

Impurities
Microbial Limits
Disintegration
Loss-On-Drying

We also understand that these would be acceptable to include in the release specifications for the bulk drug product and not the packaged product.

We agree to include impurities testing, microbial limits, and disintegration testing in the bulk drug product's release. Accordingly, the specifications for final release of the bulk drug product will incorporate these tests.

Concerning the "loss-on-drying" analysis

We understand that it is not necessary to provide specifications at this time since we have few data to date to establish a specification (three batches on stability) and that it would suffice to provide the available information in order for Dr. Niu to obtain a general idea of what the specification could be.

Sincerely,

APPEARS THIS WAY
ON ORIGINAL

Liz Ospital
Regulatory Affairs Project Manager
Laboratoires Fournier

cc Dr. Chin-Hua Niu (Chemistry Reviewer, FDA)
Margaret. Simoneau (CSO)
R. Lance Boyett (Fournier Research, Inc., Applicant's authorized US agent)
Ph. Reginault (Laboratoires Fournier, Director of Pharmaceutical Development)
Dr. Alain Munoz (Vice President, R&D Groupe Fournier)

NDA SUPPL AMENDMENT

ORIGINAL

FOURNIER
RESEARCH INC.

November 24, 1997

Dr. Solomon Sobel
Director, Division of Metabolism
& Endocrine Drug Products
Food And Drug Administration, HFD-510
Room 14 B 03
5600 Fishers Lane
Rockville, MD 20857

RE: NDA #19,304, S-001: LIPIDIL® Micro (micronized fenofibrate)

Dear Dr. Sobel:

We reference the telephone call from Dr. Hua-Young Ahn to the undersigned on November 18, 1997. During this telephone call, Dr. Ahn asked for a description of the metabolic pathway for fenofibrate, and specifically

Enclosed is a copy of the response from the Department of Metabolism and Pharmacokinetics of Laboratoires Fournier. This answer was provided to Dr. Ahn by telefax on November 21, 1997.

Please address any questions or comments regarding this correspondence to the undersigned.

Sincerely yours,

R. Lance Boyett
Director,
Clinical Development

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO
/S/ 1/16/98
CSO INITIALS DATE

Enclosure: 1 page answer (in duplicate)

/S/
12-10-97

Voted /S/ 12/11/97

Voted /S/ 1/16/98

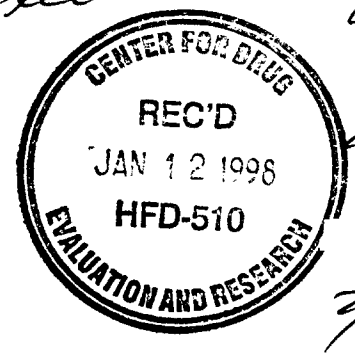
9 LAW DRIVE • FAIRFIELD, NJ 07004
TEL 973 575-1010 • FAX 973 575-7595

GROUPE FOURNIER

FOURNIER
RESEARCH INC.

Noted
Revised/updated
Label elec. Rec. for the
1/9/98
amendment.
/S/
2/4/98.

January 9, 1998



Dr. Solomon Sobel
Director, Division of Metabolism
& Endocrine Drug Products
Food And Drug Administration, HFD-510
Room 14 B 03
5600 Fishers Lane
Rockville, MD 20857

RE: NDA #19-304/S-001: (fenofibrate capsules), micronized

Dear Dr. Sobel:

APPEARS THIS WAY
ON ORIGINAL

We reference the "Approvable Letter" from the Division dated December 23, 1997, and our teleconference of January 9, 1998 at which the requested revisions to the Draft Labeling for fenofibrate were discussed. We further reference our telefax of January 9, 1998, in which we informed the Division that we are amending the Supplemental application referenced above in order to incorporate the changes agreed to during the teleconference, and to request a change in the Tradename for the product (from Lipidil Micro® to Tricor™). We also reference our submission of December 31, 1997, which included our telefax of December 30, 1997 to Mr. Steven McCort of the Division, indicating the intent of Laboratoires Fournier to address the issues in the Approvable Letter.

Enclosed herewith are the following:

APPEARS THIS WAY
ON ORIGINAL

- Revised draft labeling for the product, dated January 9, 1998: The changes which were discussed at the above referenced teleconference have been incorporated. In addition, the tradename of Lipidil Micro® has been replaced throughout by Tricor™. Further, the identification markings on the capsules as noted in the "HOW SUPPLIED" section of the labeling have been changed pursuant to the change of name, and Abbott Laboraties, North Chicago, IL, has been added as a distributor.

- Annotation of the changes to the Clinical Pharmacology portions of the labeling: Only the information that has been added subsequent to the Approvable letter is annotated herein. All other portions of the labeling submitted on December 19, 1997 remain the same except as noted above.

- A brief summary of the pharmcokinetic information related to "Gender" is also included.

9 LAW DRIVE • FAIRFIELD, NJ 07004
TEL 973 575-1010 • FAX 973 575-7595

GROUPE FOURNIER

Please address any questions or comments regarding this correspondence to the undersigned.

Sincerely yours,

R. Lance Boyett
Director, Clinical Development
Fournier Research, Inc.
(US Agent for Laboratoires Fournier)

REVIEWS COMPLETED

CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO

/S/ 2/9/98
CSO INITIALS DATE

Enclosure: 1 volume, in triplicate

/S/

APPEARS THIS WAY
ON ORIGINAL

ORIGINAL

FOURNIER
RESEARCH INC.

Noted /S/ 1/15/98

December 31, 1997

Dr. Solomon Sobel
Director, Division of Metabolism
& Endocrine Drug Products
Food And Drug Administration, HFD-510
Room 14 B 03
5600 Fishers Lane
Rockville, MD 20857

RE: NDA #19,304, S-001: LIPIDIL® Micro (fenofibrate capsules), micronized

Dear Dr. Sobel:

We reference the telephone conversation between Mr. Steven McCord of the Division and the undersigned on December 30, 1997, and the telefax of the same date from the undersigned to Mr. McCord, indicating the intent of Laboratoires Fournier to address the issues in the "Approvable Letter" sent by telefax to the undersigned on December 23, 1997.

Per instructions of Mr. McCord, a copy of this telefax is being submitted to the SNDA file herewith.

Please address any questions or comments regarding this correspondence to the undersigned.

Sincerely yours,

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☒ N.A.I. ☐ MEMO
/S/ 1/6/98
CSO INITIALS DATE

R. Lance Boyett
Director,
Clinical Development

Noted /S/ 1-14-98

noted /S/ 1/16/98

/S/ noted 1/16/98

Enclosure: 1 page answer (in duplicate)

9 LAW DRIVE • FAIRFIELD, NJ 07004
TEL 973 575-1010 • FAX 973 575-7595

GROUPE FOURNIER

FOURNIER
RESEARCH INC.

To: Mr. Steven McCort (Project Manager) Date: December 30, 1997
FDA Div. of Metab. and Endo. Drug Products.
From: R. Lance Boyett Fax: (1) (973) 575 75 95, Tel: (1) (973) 575 10 10 ext. 108
CC: Ms. Margaret Simoneau (FDA Project Manager)
A. Munoz, S. Lagneau, J.P. Guichard (Laboratoires Fournier)
Pages: 1 of 1
REF: NDA 19-304/S-001
Lipidil Micro (fenofibrate capsules), micronized

APPEARS THIS WAY
ON ORIGINAL

We refer to the "Approvable Letter" for the above cited Supplement, sent to us via telefax on December 23, 1997. In the absence of Ms. Margaret Simoneau, we wish to communicate the following to the Division:

3. Finally, Laboratoires Fournier intends to submit revised draft labeling to include a Pharmacokinetics Subsection under the Clinical Pharmacology Section.

All of the above will be conveyed in formal correspondence.

In order to facilitate and expedite the final review and approval process, Laboratoires Fournier wishes to briefly discuss the requested content of the Pharmacokinetics subsection by telephone as soon as possible, prior to submission of the revised draft labeling. We anticipate requesting this teleconference early next week.

Thank you for your help in this matter. Please contact the undersigned if you have any questions regarding this communication.

Sincerely,

APPEARS THIS WAY
ON ORIGINAL

R. Lance Boyett
Director, Clinical Development
Fournier Research, Inc
(US Agent for Laboratoires Fournier, S.A.)

ORIGINAL

LABORATOIRES
FOURNIER

FAX

December 12, 1997

/S/
1/15/98.

Dr. Stephen K. Moore
Chemistry Team Leader
Division of Metabolism
& Endocrine Drug Products
Food & Drug Administration, HFD-510
Room 14 B 03, 5600 Fishers Lane
Rockville, MD 20857

Re : NDA 19-304/S-001 Lipidil Micro® (micronized fenofibrate capsules)
Response following telephone call from Dr. Niu on December 10, 1997

Dear Dr. Moore,

We reference a telephone call from Dr. Niu on December 10, 1997.
we agree

We also confirm your acceptance that as more data become available on this test, and the data demonstrate

A hard copy (in triplicate) of this letter will be submitted to the Division under separate cover. Please address any questions or comments on the above to our authorized US Agent, at (973) 575-1010. We appreciate your continued review of our sNDA.

Sincerely,

Liz Ospital
Regulatory Affairs Project Manager
Laboratoires Fournier

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO
/S/ 1/16/98
CSO INITIALS DATE

/S/
1-16-98

/S/

cc Dr. Chin-Hua Niu (Chemistry Reviewer, FDA)
R. Lance Boyett (Fournier Research, Inc., Applicant's authorized US agent)
Ph. Reginault (Laboratoires Fournier, Director of Pharmaceutical Development)
M. Forest (LF, Quality Assurance)
S. Lagneau (LF, Registration & Regulatory Affairs)
Dr. Alain Munoz (Vice President, R&D Groupe Fournier)

ORIGINAL

T-Con requested by Fournier
Date: January 9, 1998
Time: 0:930-10:00AM
Place:PKLN 1456

FDA Representation:
Dr. Orloff
Hae-Young Ahn
Margaret Simoneau

Fournier Research, Inc.
(Three representatives from Abbott)
1. Marilou Reed
2. Roland Catherall, Director Regulatory
3. Bruce Wallin, Div. V.P.
(Four representatives from France)
1. Dr. Alan Munoz
2. Jean-Pierre Guichard
3. Liz Ospital
4. Sylvia Lagneau
And Lance Boyett

Discussion:
1. Enclosure (1), Fax of January 8, 1998 addressed the "Approvable Letter" of December 23, 1997.
2. #1 comments discussed, and accepted by Fournier are highlighted in Enclosure (1).
3. #2 was accepted by H. Ahn (that there was no need for the table).
4. #3 was accepted by Dr. Orloff. He also reminded Fournier that promotional information needs to be submitted to DDMAC.
5. Major focus was on the paragraph about "licensing the product to Abbott Laboratories" and requesting a change in the Tradename for the product. FDA asked the proposed Tradename request , and "Tricor" was submitted. Secondly, FDA asked if Abbott would be distributing the product or was the intent to transfer NDA ownership. Mr. Boyett said the NDA would be transferred to Abbott. Request was made by Marilou Reed, of Abbott, to get the new name approval with this supplement. Further information would be needed before this question was completely answered.
cc:Original NDA 19-304/S-001
D. File

NDA#:19-304/S-001
AE Letter
Telecon/Meeting initiated by:

○ Applicant/Sponsor
● FDA
By: Telephone

Product Name: Lipidil

Firm Name: Fournier

Name and Title of Person with whom conversation was held:

Phone: 1-973-575-1010
Ext 108

ORIGINAL

DEC 19 1997

Three T-cons:
1. On 12/18/97 at 1045AM with R. Lance Boyett, Dr. Niu and M. Simoneau.
Discussion: 12/15/97 fax outlining problems
Outcome: Dr. Niu requested a written commitment from Synkem to provide

Fenofibrate Drug This needs to include

2. Second T-Con took place on 12/18/97 at 345PM with R. Lance Boyett, Dr. Ahn, Dr. Orloff, and M. Simoneau.
Discussion: Biopharm issues and proposed labeling
Outcome: Dr. Orloff discussed that there was a problem with the proposed labeling that could be misleading by inserting "micro" in the label. Two places presented the problem: 2-6 in the Clin Pharm Section and 2-7 (last sentence). Dr. Orloff suggested that LIPIDIL Micro be changed to fenofibrate in both places. Dr. Orloff explained this was due to no efficacy data on the population recorded in the label for the indication. Secondly, Dr. Ahn discussed the food effect. All clinical trials were conducted with food. Micronized fenofibrate given without food is only about half as available when compared to it given with a meal. Dr. Orloff gave the option to add the "Take with food" to the labeling or statement to the effect that if food is not taken, effects are not known.
Decision: Mr. Boyett will discuss with other members of Fournier and will respond.

3. Third T-Con took place at 11AM on 12/19/97 with R. Lance Boyett, Dr. Orloff, Dr. Munoz of Fournier Laboratories, and M. Simoneau.
Discussion: Follow up from the 12/18/ 97 T-Con w/r to proposed labeling. Also the established name, trade name, and the request of Dr. Niu to add micronized to the proposed labeling were discussed but deferred because neither Dr. Niu nor Dr. Steve Moore were present.
Outcome: Accepted were the Lipidil Micro to fenofibrate in the two places suggested by Dr. Orloff in the 18th T-con. Also accepted in the Clin Pharm section the addition of "at doses equiv to 3 capsules of 67mg Lipidil Micro per day"

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Phone: 973-575-7595

after "fenofibrate" in the third sentence. Also agreed upon, under the Dosage and Administration section, second paragraph, after the word meals, "thereby optimizing the bioavailability of the medication" may be added.
Results: Require another T-Con with either Dr. Niu or Dr. Moore to discuss the micronized aspect of the proposed labeling.
Attached is the proposed labeling discussed with the company in the above telephone conversations.

/S/

M. Simoneau

cc:Original NDA 19-304/S-001
Div File