DUPLICATE

cipher
PHARMACEUTICALS LTD

409 Matheson Blvd. E. Mississauga, ON Canada L4Z 2H2
tel: (905) 602 5840
fax: (905) 602 0628
www.cipherpharma.com

September 9, 2005

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research
5600 Fisher's Lane
Rockville, MD 20857

N000 C
NEW CORRESP

Re: **NDA 21-612**
CIP-FENOFIBRATE (fenofibrate capsules) 50 mg, 100 mg, 150 mg [redacted] b(4)

Dear Dr. Orloff:

Reference is made to Cipher Pharmaceuticals' New Drug Application (NDA) dated December 24, 2002 and received by FDA on February 26, 2003. Reference is also made to submissions made to the NDA since that time, and to the FDA's tentative approval letter dated July 15, 2004. Further reference is made to the amendment to the tentatively approved NDA submitted November 30, 2004, and the revised amendment to the tentatively approved NDA dated July 4, 2005.

In relation to Cipher's revised amendment to the tentatively approved NDA, a teleconference took place with the Agency on September 6, 2005. As per the request of Margaret Simoneau during that discussion, please find enclosed a revised FDA form 356h for the July 4, 2005 revised amendment to the tentatively approved NDA. As requested, the form has been signed by Arthur Deboeck (VP and General Manager of Galephar PR Inc., Cipher US Agent) as well as Larry Andrews (President of Cipher Pharmaceuticals Ltd.), both individuals named on the form.

One original and two (2) copies of this correspondence are provided.

If you have any questions or comments, please do not hesitate to call me at 905 602 5840 x 24, or you may contact [redacted] b(4)

[redacted] regarding this b(4)
correspondence, or on other related matters.

Yours sincerely,

Larry Andrews

Larry Andrews
President
Cipher Pharmaceuticals Ltd.

CC: Arthur DeBoeck, Galephar PR Inc.

b(4)

Appears This Way
On Original

Simoneau, Margaret A

From: Larry Andrews [landrews@cipherpharma.com]
Sent: Tuesday, September 06, 2005 11:50 AM
To: simoneaum@cder.fda.gov
Subject: Cipher conference call

The number is 18663686248 code # is 1516347

Larry

Larry Andrews
President
Cipher Pharmaceuticals Ltd.
409 Matheson Blvd. E.
Mississauga, ON
L4Z 2H2
Office: 905 602 5840 ext 24
Cell: 416 434 1132
landrews@cipherpharma.com

Simoneau, Margaret A

Subject:	NDA 21-612 Cip-Fenofibrate/Sponsor T-con Tradename (Lipofen)
Location:	CDER 510 Calendar; Dr. Park's Office
art:	Tue 9/6/2005 11:30 AM
End:	Tue 9/6/2005 12:00 PM
Recurrence:	(none)
Meeting Status:	Meeting organizer
Required Attendees:	Simoneau, Margaret A; Parks, Mary H
Resources:	CDER 510 Calendar

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-612

Cipher Pharmaceuticals Ltd.
Galephar PR Inc., Agent for Cipher Pharmaceuticals Ltd.
Road 198 No. 100 km 14.7
Juncos Industrial Park
Juncos, Puerto Rico 00777-3873

Attention: Arthur Deboeck
Vice President and General Manager

Dear Mr. Deboeck:

We acknowledge receipt on July 11, 2005, of your July 4, 2005, resubmission to your new drug application for Cip-Fenofibrate (fenofibrate capsules) 50, 100, 150 [redacted] mg. b(4

We consider this a complete, class 2 response to our July 15, 2004, action letter. Therefore, the user fee goal date is January 11, 2006.

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. We note that you have not fulfilled the requirement. We are waiving the requirement for pediatric studies for this application.

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

Sincerely,

{See appended electronic signature page}

Appears This Way
On Original

Margaret Simoneau, M.S., R.Ph.
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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
8/5/05 11:04:32 AM

Appears This Way
On Original

Simoneau, Margaret A

From: Colangelo, Kim M
Sent: Friday, July 29, 2005 10:01 AM
To: Simoneau, Margaret A
Cc: Peat, Raquel; Chen, Andrea
Subject: RE: COMIS 6966 - Cipher Pharmaceuticals LTD, Cip-Fenofibrate caps, 505(b)(2)

Margaret,

Thanks for the information! It is good to let us know when a resubmission to an TA/AE/NA letter is received as we need to obtain ORP/OCC clearance for any (b)(2) approval. In your case, however, you will be getting clearance from OCC as per your consult. Please keep us in the loop regardless of their response, your plans, etc. I know we have played phone tag as well - please let me know if you still wish to speak with me (otherwise I'll consider this matter taken care of!)

Have a great weekend!
Kim

Andrea - Please update the spreadsheet with this information - thanks!

Kim Colangelo
Associate Director for Regulatory Affairs
Office of New Drugs
CDER/FDA
301-443-5374
301-480-8329 (f)

-----Original Message-----
From: Simoneau, Margaret A
Sent: Friday, July 29, 2005 7:31 AM
To: Colangelo, Kim M
Subject: FW: COMIS 6966 - Cipher Pharmaceuticals LTD, Cip-Fenofibrate caps, 505(b)(2)

Hi Kim,
Just FYI. This is a re-submission on a Tentative Approval of a 505(b)(2) application. If you don't need to be notified of this type submission, please let me know.

Thanks.
Margaret

-----Original Message-----
From: Jordan, Kathleen M
Sent: Thursday, July 28, 2005 3:21 PM
To: Guido, Mirna; Anselmo, Rita
Cc: Fain, Kevin; Ray, Seth; Vaid, Sonal; Thakur, Emily; Schwemer, Tawni B; Simoneau, Margaret A; Dickinson, Elizabeth
Subject: COMIS 6966 - Cipher Pharmaceuticals LTD, Cip-Fenofibrate caps, 505(b)(2)

Hi. Attached is the OCC consult request for COMIS 6966 - Cipher Pharmaceuticals LTD, Cip-Fenofibrate caps, 505(b)(2). This is a 60 day request. The GC goal date is 9/28/05. Supporting documents are attached. Liz Dickinson has been involved with this project.

<< File: 21612OCC.pdf >> << File: 6966.pdf >>
Kathy

Kathleen Jordan

Division of Regulatory Policy II
Office of Regulatory Policy
Center for Drug Evaluation and Research
Food and Drug Administration
Jordank@cder.fda.gov
(301) 443-5539
RKW2 RM1125, HFD-007
5515 Security Lane

Appears This Way
On Original

Simoneau, Margaret A

From: Jordan, Kathleen M
Sent: Thursday, July 28, 2005 3:21 PM
To: Guido, Mirna; Anselmo, Rita
Cc: Fain, Kevin; Ray, Seth; Vaid, Sonal; Thakur, Emily; Schwemer, Tawni B; Simoneau, Margaret A; Dickinson, Elizabeth
Subject: COMIS 6966 - Cipher Pharmaceuticals LTD, Cip-Fenofibrate caps, 505(b)(2)

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21612OCC.pdf (342 KB)


6966.pdf (518 KB)

Kathy

Kathleen Jordan
Division of Regulatory Policy II
Office of Regulatory Policy
Center for Drug Evaluation and Research
Food and Drug Administration
Jordank@cder.fda.gov
(301) 443-5539
RKW2 RM1125, HFD-007
515 Security Lane

CENTER FOR DRUG EVALUATION AND RESEARCH
OCC TRACKING INFORMATION FORM

TRACKING NUMBERS

COMIS NO. 6966 FRDTS NO. (If applicable) CATEGORY NO. 4

PROJECT INFORMATION

CDER CONTACT PERSON	PHONE NO.	FAX NO.
Margaret Simoneau/HFD-510	301-827-6411	301-443-9282

DATE SENT TO OCC July 28, 2005 9/28/05

GOAL DATE _____2 Weeks _____30 days __X__60 days _____Ongoing Advice

Note: All standard requests should have a 60-day goal date. Those requesting a 2 week or 30-day goal date, must get prior approval through Jane Axelrad (E-mail Axelradj and cc: Bricet) prior to submitting a request to OCC. Refer to MAPP 4140.5. Please fill in the actual goal date on the appropriate line above.

PROJECT NAME
Cipher Pharmaceuticals LTD, Cip-Fenofibrate capsules, 50, 100, 150 [redacted] mg, NDA 21-612 b(4)

PROJECT DESCRIPTION
An amendment to a Tenatively Approved NDA was submitted to the Division on July 4, 2005. Please verify that the three attached "Final Judgments" are sufficient to permit final approval of the NDA. Request final clearance to approve this Tenatively Approved (letter attached) NDA, which is a 505b2 submission. Division will take an action in early December 2005.

PROJECT TYPE

_____Federal Register	_____Guidance	_____Question/Opinion
_____Citizen Petition	_____Letter	_____Ongoing Advice
_____Suitability Petition	_____Memo	_____Other

REQUESTED ACTION

_____Meeting Request	_____Concurrent Clearance	_____Other
_____Review and Comment	__X__Final Clearance	

OFFICE/DIVISION DIRECTOR'S SIGNATURE

OCC INFORMATION

DATE RECEIVED DATE COMPLETED

ASSIGNED ATTORNEY ACTION TAKEN BY OCC

OCC SIGNATURE _____Cleared _____Comments

_____Not Cleared _____Other

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF PUERTO RICO

ABBOTT LABORATORIES, et al.,
Plaintiffs

v.

CIVIL NO. 03-1421, 03-2067, AND 04-1089(DRD)(Consolidated)

CIPHER PHARMACEUTICALS, LTD.,
Defendant

AMENDED J U D G M E N T

The court, having approved on this same date parties' joint motion requesting dismissal, hereby **ENTERS** Judgment dismissing this action against all Defendants **WITH PREJUDICE** and without imposition of costs, expenses or attorneys' fees. **All Claims and non-infringement counterclaims are hereby DISMISSED WITH PREJUDICE.** Likewise, the parties have agreed to dismiss all invalidity counterclaims **WITHOUT PREJUDICE. CASES 03-1421, 03-2067, AND 04-1089(DRD) ARE CLOSED FOR ALL STATISTICAL PURPOSES.**

IT IS SO ORDERED.
In San Juan, Puerto Rico this 27th day of May 2005.

S/DANIEL R. DOMINGUEZ
DANIEL R. DOMINGUEZ
U.S. DISTRICT JUDGE

Appears This Way
On Original

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF PUERTO RICO

ABBOTT LABORATORIES, et al.,
Plaintiffs

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In San Juan, Puerto Rico this 27th day of May 2005.

S/DANIEL R. DOMINGUEZ
DANIEL R. DOMINGUEZ
U.S. DISTRICT JUDGE

Appears This Way
On Original

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FOR THE DISTRICT OF PUERTO RICO

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IT IS SO ORDERED.
In San Juan, Puerto Rico this 27th day of May 2005.

S/DANIEL R. DOMINGUEZ
DANIEL R. DOMINGUEZ
U.S. DISTRICT JUDGE

Appears This Way
On Original

Simoneau, Margaret A

From: Qiu, Wei
Sent: Thursday, July 28, 2005 2:27 PM
To: Simoneau, Margaret A
Cc: Galliers, Enid M; Ahn, Hae Young; Malinowski, Henry J
Subject: RE: NDA 21-612 Cip-Fenofibrate DSI consult

Peggy,

The compositions of the finished products are proportional among strengths. As you mentioned, a DSI biopharm inspection of two biopharm studies with [redacted]CIP-Fenofibrate capsules was done in 2003. Since the two new biopharm studies with 150 mg CIP-Fenofibrate capsules were conducted in the same clinical and analytical sites, no DSI audit is necessary.

b(4

Thanks,

Wei

-----Original Message-----
From: Simoneau, Margaret A
Sent: Tuesday, July 26, 2005 3:14 PM
To: Qiu, Wei
Cc: Galliers, Enid M
Subject: NDA 21-612 Cip-Fenofibrate DSI consult

Wei,
Do we need a consult on this re-submission? There was a DSI biopharm audit done on this NDA back in October 2003. Please let me know as soon as possible so that I can get a consult into DFS if we plan to take an action sometime in December.

Thanks.
Peggy

Appears This Way
On Original

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Director, Division of Medication Errors and Technical Support (DMETS), HFD-420
PKLN Rm. 6-34

FROM: Division of Metabolic and Endocrine Drug Products, HFD-510, PKLN, 14B45

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 27,2005		21-612	Resubmission of a Tentative Approval Letter	July 4, 2005 (in EDR)

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Cip-Fenofibrate capsules	High (6 month clock)	lipid altering	28 November 2005

NAME OF FIRM: Cipher Pharmaceuticals Ltd.

REASON 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)*: **Trade name 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
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: Review of Tradenames: Lipofen [redacted] b(4)

PDUFA DATE:
ATTACHMENTS: Draft Package Insert, Container and Carton Labels
CC: Archival IND/NDA 21-612
HFD-510/Division File
HFD-510/RPM
HFD-510/Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER	METHOD OF DELIVERY (Check one)
Margaret Simoneau/301-827-6411	☒ DFS ONLY ☐ MAIL ☐ HAND
GNATURE OF RECEIVER	SIGNATURE OF DELIVERER

5/28/05

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
7/27/05 10:13:25 AM

Simoneau, Margaret A

Subject:	NDA 21-612 Cip-Fenofibrate (Cipher); Internal Status Mtg regarding Resubmission
ocation:	CDER PKLN 14B39 Conf Room -AR; CDER 510 Calendar
rt:	Fri 7/22/2005 11:30 AM
End:	Fri 7/22/2005 12:00 PM
Recurrence:	(none)
Meeting Status:	Meeting organizer
Required Attendees:	Simoneau, Margaret A; Parks, Mary H; Ahn, Hae Young; Qiu, Wei; Adams, William M
Optional Attendees:	Galliers, Enid M
Resources:	CDER PKLN 14B39 Conf Room -AR; CDER 510 Calendar

cipher PHARMACEUTICALS LTD

409 Matheson Blvd. E. Mississauga, ON Canada L4Z 2H2
tel: (905) 602 5840
fax: (905) 602 0628

www.cipherpharma.com

ORIGINAL

RECEIVED
JUL 12 2005
FDR/CDER

ORIG AMENDMENT
N-000-BZ

July 4, 2005

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research
5600 Fisher's Lane
Rockville, MD 20857

RECEIVED
JUL 11 2005
CDR / CDER

Re: **NDA 21-612**
CIP-FENOFIBRATE (fenofibrate capsules) 50 mg, 100 mg, 150 mg [redacted] b(4)
Amendment to Tentatively Approved NDA

Dear Dr. Orloff:

Reference is made to Cipher Pharmaceuticals' New Drug Application (NDA) dated December 24, 2002 and received by FDA on February 26, 2003. Reference is also made to the submissions dated January 10, March 24, April 21, May 6, October 15, 23, November 7, December 2 and 8, 2003, and January 7, 25, February 3, 9, 16, March 30, May 5, 14, 21, June 1 and 4, 2004. Further reference is made to the FDA's tentative approval letter dated July 15, 2004, and the amendment to the tentatively approved NDA submitted November 30, 2004.

The November 30, 2004 amendment to the tentatively approved NDA was submitted as per the July 15, 2004 tentative approval letter, and it provided updated information primarily to accommodate changes relating to [redacted] b(4)

Due to events following the November 30, 2004 submission, however, [redacted] will no longer be acting as a [redacted] As a result b(4) the information provided in the November 30, 2004 amendment is no longer valid, and we wish to withdraw this amendment, effective immediately. We had previously been advised that review of this amendment would not commence until we had advised the FDA that any outstanding legal matters had been resolved, and we trust that withdrawal of this amendment has not caused any undue inconvenience.

Please find enclosed a revised amendment submitted in place of the November 30, 2004 amendment. As per the July 15, 2004 tentative approval letter, we are submitting copies of the final judgment order for each of the outstanding patent litigation cases, in order to terminate the relevant 30-month stays. We are also amending the NDA by providing updated information relating to chemistry, manufacturing and controls data, and other changes in the information previously outlined in NDA 21-612.

Galephar Pharmaceuticals Research Inc. (Cipher's U.S. Agent) will continue to be responsible for all activities related to Cipher's fenofibrate product in the USA, until further notice. b(4)
will remain as with a new address within
indicated on the Establishment Information (attched to the 356h Form). With b(4)
the brand name will no longer be
used for the product, and hence the name appears on the enclosed b(4)
documentation. Cipher would like to propose two new brand names for consideration by the Agency, which are listed below in order of preference:

- LIPOFEN
-

Please find enclosed one original and two (2) copies of this submission. The amendment consists of eight (8) volumes, and the proposed changes to the NDA are as follows:

- Package Insert and Bottle Labels (updated and provided in paper and electronic format)
  - The main change indicated in the package insert is reference to the 150 mg strength so that now the proposed strengths are 50, 100 and 150 mg. In discussions between and Dr. Mary Parks (May 25 and June 1, 2004), it was suggested that Cipher choose either the 150 Since that time, two comparative bioavailability studies have been performed using the 150 mg strength of CIP-FENOFIBRATE and 160 mg strength of Tricor®, demonstrating bioequivalence, and as a result, the changes noted above have been proposed. The studies are as follows, and the reports are provided (including one copy of the electronic datasets in SAS System XPORT Transport Format, in the original copy):
    - FENPK.04.01 (2004-813) – A Single-Dose, Comparative Bioavailability Study of Two Formulations of Fenofibrate Given with a High Fat Breakfast
    - FENPK.04.02 (2004-814) – A Single-Dose, Comparative Bioavailability Study of Two Formulations of Fenofibrate Given with a Low Fat Breakfast
- Chemistry, Manufacturing and Controls (CMC) changes:
  - Capsule Shell (markings)
  - Dissolution Specification (sampling time updated to 120 minutes, as per FDA's request)
  - Batch Records (additional batch sizes and other minor changes)
  - Package (change to child resistant caps)
  - Expiry (extension of commercial product expiry to 36 months)

It should be noted that while the strength of CIP-FENOFIBRATE has been removed from the package insert, CMC documentation has been provided for all strengths (50, 100, 150 mg) in the event that the proposed 150 mg claims are not approved by the Agency. b(4)

If you have any questions or comments, please do not hesitate to call me at 905 602 5840 x 24, or you can contact b(4)

[redacted] regarding b(4)
this submission, or on other related matters.

Yours sincerely,

Larry Andrews

Larry Andrews
President
Cipher Pharmaceuticals Ltd.

CC: Arthur DeBoeck, Galephar PR Inc.
[redacted] b(4)

Appears This Way
On Original

Galliers, Enid M

From: Targoff, Carol
Sent: Friday, February 18, 2005 1:57 PM
To: Jones, Michael D; Friedman, Beverly J; Schwemer, Tawni B; Jordan, Kathleen M; Weitzman, Mitchell; Vincent, Carla; Galliers, Enid M; Forfa, Tracey; Newkirk, David R
Subject: Cipher Pharmaceuticals Ltd.

Cipher Pharmaceuticals Ltd. - Request for Partial Refund of Fiscal Year 2003 Application Fee for NDA 21-612, Luxacor Capsules - is denied. No hard copy to follow.

Cipher
naceuticals Ltd

Appears This Way
On Original

Department of Health and Human Services Public Health Service

Food and Drug Administration
Rockville, MD 20857

FEB 1 8 2005

Larry Andrews
President
Cipher Pharmaceuticals Ltd.
409 Matheson Blvd. East
Mississauga, Ontario L4Z 2H2
CANADA

RE: Request for Partial Refund of Fiscal Year 2003 Application Fee for NDA 21-612, Luxacor Capsules

Dear Mr. Andrews:

This responds to your September 20, 2004, letter to Beverly Friedman of my staff, requesting a partial refund of the fiscal year (FY) 2003 application fee (User Fee ID (UFID) 4494) paid under the user fee provisions of the Federal Food, Drug, and Cosmetic Act (the Act)[1] for new drug application (NDA) 21-612 for Luxacor[2] (fenofibrate) Capsules. For the reasons described below, the Food and Drug Administration (FDA) denies your request for a refund of one-half the FY 2003 application fee paid by Cipher Pharmaceuticals Ltd. (Cipher) for NDA 21-612, Luxacor Capsules.

I. Cipher's Request

You request that FDA refund one-half of the FY 2003 application fee that Cipher paid for NDA 21-612, Luxacor Capsules ($533,400, UFID 4494), which was accepted for filing on February 26, 2003.

In your letter, you state the following:

- NDA 21-612 was submitted on December 24, 2002.
- In January 2003, Dr. Ian French, then Chairman and Chief Scientific Officer of Cipher, spoke with Ms. Friedman regarding Cipher's position that NDA 21-612 is a 505(b)(2) application that meets the statutory exclusion criteria for application fees because the product is not a new molecular entity and the application does not seek approval for a new indication for use.

[1] Sections 735 and 736 of the Act (21 U.S.C. 379(g) and 379(h)).
[2] When Cipher originally submitted the NDA, the product trade name was CIP-Fenofibrate.

- You also note that the Agency considers a change in dosage strength to be a new "indication for a use" for purposes of assessing a fee.
- You are not aware of any support for the "expansive interpretation of an indication for use" and you maintain that the application meets the statutory exclusion from application fees.
- You state that clinical data, as defined by the Agency for purposes of assessing user fees,[3] were neither included nor required as a condition of approval, and only bioavailability and bioequivalence studies were submitted with NDA 21-612.
- In acquiescence to the Agency's demands, and in order to start the review process, Cipher submitted the full $533,400 application fee under protest on January 14, 2003.
- The user fee cover sheet that you submitted with the application clearly indicated that no clinical data were required for approval and that this was a 505(b)(2) application that did not require a fee.
- After receiving notice (in a letter dated March 10, 2003) that FDA had accepted NDA 21-612 for filing on February 26, 2003, Cipher contacted the Agency to secure return of at least one-half the user fee on the basis that no clinical data were required for approval.
- You claim your records show that Mr. Arthur Deboeck, Cipher's designated U.S. Agent, "on or about" March 17, 2003, spoke with personnel in the Division of Metabolic and Endocrine Drug Products who informed him that one-half of the application fee would be returned to Cipher and no further action was required on Cipher's part.[4] At this point, Cipher decided to settle for the one-half fee refund.
- You did not follow up on the status of the refund until recently due to transition of personnel at Cipher.

II. Refund Request

A. What is the statutory requirement for a request for a refund?

Under section 736(i) of the Act, to qualify for consideration of a waiver, reduction, or refund of a fee, an applicant must submit a written request no later than 180 days after such fee is due.

---

[3] FDA's Guidance for Industry: *Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees* (bundling guidance), available on the Internet at www.fda.gov/cder/pdufa/default.htm under Guidance.

[4] We note that you did not provide the names of the FDA personnel with whom Mr. Deboeck allegedly spoke.

B. When was a request for a refund of the application fee due?

plication fee for NDA 21-612 was due when the application was received, ıber 26, 2002. On January 8, 2003, Cipher was notified that its application was not ed for filing because an application fee had not been submitted.[5] Cipher then tted a full application fee with a check dated January 15, 2003. Processing was ed because Cipher's check was drawn on a Canadian bank. FDA was notified on ıary 26, 2003, that the full application fee, in U.S. funds, was received. A timely, en, refund request for the application fee paid by Cipher was due by the close of ıess, August 25, 2003 (180 days after the receipt of the application including full nent of the application fee).

C. Did Cipher submit a timely request for a refund of the application fe

cording to FDA records, Dr. French of Cipher and Ms. Friedman of my staff ımmunicated on January 9, 10, and 13, 2003, regarding the user fee eligibility of the 5(b)(2) application and the reasons FDA believed the application was fee eligible.[6] s. Friedman reminded Dr. French that requests for user fee waivers or refunds must b ıbmitted within 180 days of the date the fee is due. On January 13, 2003, Dr. French s e was having an attorney look over the law and he would get back with FDA if the ttorney could come up with some reasonable method for appeal of FDA's decision.

ater, on January 13, 2003, FDA received a call from Natasha Leskovsek of Heller Ehrman representing Cipher Pharmaceuticals. She requested information about the u fee eligibility of a 505(b)(2) application. She also requested information about FDA' refusal to accept an application from an applicant for non-payment of user fees, how remove an application from that status, and fees-exceed-the-costs waivers.

You state that your written request was timely and made on the January 15, 2003, ir form of the User Fee Cover Sheet, Form 3397 (cover sheet). FDA notes that your "request" on the cover sheet, dated January 14, 2003, states:

---

[5] Further information regarding the refusal to accept for filing can be found in the Center for Drug Evaluation and Research's (CDER's) Manual of Policies and Procedures (MAPP) 6050.1, *Refusal Application for Filing from Applicants in Arrears*, available on the Internet at www.fda.gov/cder/r

[6] You were directed to submit the full fee for a user fee eligible application that requires clinical d approval based on e-mails and conversations between Dr. French and Ms. Friedman. It appeared available dosage ranges and dosing levels proposed in Cipher's application were not the same as t approved in the innovator's product. Although Cipher did not perform any new clinical trials to s these changes, Dr. French indicated that there was a literature review of relevant clinical trials. A the Bundling Guidance, study reports or literature reports can be considered clinical data.

> A user fee is being submitted with this 505(b)(2) NDA at the direction of FDA's Ms. B. Friedman. Cipher Pharmaceuticals believes this application is exempt from the user fee requirement, and Cipher *intends* to appeal the imposition of the fee. The fee is being submitted at this time in order to expedite the filing of the NDA pending resolution of the user fee status. (emphasis added)

Although your notation on the user fee cover sheet announces Cipher's intention to appeal the imposition of a fee, it was not and cannot reasonably be construed as a written request for a refund of the fee as required under section 736(i) of the Act.[7]

On September 7, 2004, Dr. Larry Gontovnick of Cipher called FDA to ask about the status of the 50 percent refund of the application fee for NDA 21-612 submitted in early January 2003. In his conversation with Ms. Friedman, Dr. Gontovnick stated that Dr. French had halted the refund letter originally prepared by Cipher because he believed FDA was already working on the refund. Unfortunately, your follow-up letter dated September 20, 2004, requesting a refund of the application fee, was received well after the 180-day due date. Therefore, FDA does not have the authority to grant your request for a refund of the FY 2003 application fee, and your request is denied.

If you have any further questions regarding this matter or other user fee questions, please contact Beverly Friedman or Michael Jones at 301-594-2041.

Sincerely,

Jane A. Axelrad

Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research

Appears This Way
On Original

[7] In other words, an intent to request a refund is not a request for a refund.

bcc:

M. Jones, HFD-5
T. Schwemer/K. Jordan, HFD-7
User Fee File, HFD-5
Chron file
B. Friedman, HFD-7
M. Weitzman HFD-7
C. Vincent, HFM-51
E. Galliers, HFD-510
T. Forfa, HFV-3
D. Newkirk HFV-100

J:\USERFEE\LETTERS\cipher_refund_deniedv3.doc

Drafted: B. Friedman 1/10/05, 1/19/05
Reviewed: M. Jones 1/16/05, 1/26/05
Edited: O. Pritzlaff 2/11/05
Reviewed: J. Axelrad

USER FEE PAYMENT & PDUFA/FDAMA VALIDATION SHEET

Must be completed for ALL original NDAs, efficacy supplements and initial rolling review submissions

NDA # 21-612 SUPP TYPE & #_____ Division 510 UFID #_____

Applicant Name: Cipher Pharmaceuticals Inc. Drug Name: Lukacor (fenofibrate) Capsules

For assistance in filling out this form see the Document Processing Manual for complete instructions and examples.

1. **Was a Cover Sheet submitted?**
   ☒ Yes ☐ No

2. **Firm in Arrears?**
   ☐ Yes ☒ No

3. **Bundling Policy Applied Appropriately? Refer to Draft "Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees" http://www.fda.gov/cder/guidance**
   ☑ Yes ☐ No (explain in comments)

4. **Administrative Split? (list all NDA#s and Divisions)**

NDA #/Doc Type	Div.	Fee? (Y/N)

5. **Type 6?**
   ☐ Yes ☑ No

   Type 6 to which other application?

   NDA #_____ Supp Type &#_____

6. **Clinical Data Required for Approval? (Check one)**
   ☐ Yes*

   ☒ Yes, by reference to another application

   NDA #~~21-203~~ Supp Type & #_____

   ☒ No

   *** Yes if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., adding an adverse reaction, contraindication or warning to the labeling).**

7. **505(b)(2) application? (NDA original applications only) Refer to Draft "Guidance for Industry Applications Covered by Section 505(b)(2)" http://www.fda.gov/cder/guidance** Ref. NDA 21-203
   ☒ Yes ☐ No ☐ To be determined

8. **Subpart H (Accelerated Approval/Restricted Distribution)?**
   ☐ Yes ☒ No ☐ To be determined

9. **Exclusion from fees? (Circle the appropriate exclusion. For questions, contact User Fee staff)** N/A

   List of exclusions:

   2 – No fee - administrative split
   4 – No fee - 505b2
   7 – Supplement fee - administrative split
   9 – No fee Subpart H supplement– confirmatory study
   11 – No fee Orphan Exception
   13 – No fee State/Federal exemption from fees

10. **Waiver Granted?**
    ☐ Yes (letter enclosed) ☒ No

    Select Waiver Type below: Letter Date: _____

    ☐ Small Business ☐ Barrier-to-Innovation
    ☐ Public Health ☐ Other (explain)

11. **If required, was the appropriate fee paid?**
    ☒ Yes ☐ No

12. **Application Review Priority**
    ☐ Priority ☒ Standard ☐ To be determined

13. **Fast Track/Rolling Review Presubmission?**
    ☐ Yes ☒ No

Comments

Valerii Jimenez 11/14/03
PM Signature/Date

This form is the initial data extraction of information for both User Fee payment and PDUFA/FDAMA data elements. The information entered may be subject to change due to communication with the User Fee staff. This form will not reflect those changes. Please return this form to your document room for processing.

CC: original archival file
HFD-007

Processor Name & Date _____

QC Name & Date _____

(8/18/03)

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

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

Cipher Pharmaceuticals Limited

Suite 201
Lauriston, Collymore Rock
St. Michael, BARBADOS

2. TELEPHONE NUMBER *(Include Area Code)*

(905) 696-9380

3. PRODUCT NAME

CIP-Fenofibrate (Fenofibrate capsules)

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

NDA # 21-612

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☐ YES ☒ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

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

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

4494

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)*

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☒ NO

(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

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.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
[signature]	Chairman and Chief Scientific Officer	March 24, 2003

FORM FDA 3397 (4/01)

Created by: PSC Media Arts (301) 443-2454 EF

PM: Jimenez, V

2/26/03
paid $533,400.00

USER FEE VALIDATION SHEET

NDA # 21-612 Supp. Type & # N-000 UFID # 4494
(e.g., N000, SLR001, SE1001, etc.)

1. (YES) NO User Fee Cover Sheet Validated? MIS_Elements Screen Change(s):

2. (YES) NO **APPLICATION CONTAINS CLINICAL DATA?**
(Circle YES if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).

lmw 5/28/04

REF **IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION.**

3. YES (NO) **SMALL BUSINESS EXEMPTION**

4. YES (NO) **WAIVER GRANTED**

5. YES (NO) **NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (other then bundling).**
If YES, list all NDA #s, review division(s) and those for which an application fee applies.

NDA #	Division			
N_____	HFD-_____	Fee	No Fee	N
N_____	HFD-_____	Fee	No Fee	N

6. (YES) NO **BUNDLING POLICY APPLIED CORRECTLY? No Data Entry Required**
(Circle YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Circle NO if application should be split into more than one application or be submitted as an original instead of a supplement. If NO, list resulting NDA #s and review division(s).

NDA #	Division	NDA #	Division
N_____	HFD-_____	N_____	HFD-_____

7. P (S) **PRIORITY or STANDARD APPLICATION?**

Valerie Jimenez
PM Signature / Date

2/27/03
CPMS Concurrence Signature / Date

2/14/00

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

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

Cipher Pharmaceuticals Limited

Suite 201
Lauriston, Collymore Rock
St. Michael, BARBADOS

2. TELEPHONE NUMBER *(Include Area Code)*

(905) 696-9380

3. PRODUCT NAME

CIP-Fenofibrate (Fenofibrate capsules)

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

NA

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

[X] YES [ ] NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

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

[X] THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

[ ] THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

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)

[X] 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)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

[ ] YES [X] NO

(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

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.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
[signature]	Chairman and Chief Scientific Officer	Dec 18/02

FORM FDA 3397 (4/01)

Created by: PSC Media Arts (301) 443-2454 EF

cipher
PHARMACEUTICALS LTD

DUPLICATE

409 Matheson Blvd. E. Mississauga, ON Canada L4Z 2H2
tel: (905) 602 5840
fax: (905) 602 0628
www.cipherpharma.com

September 20, 2004

RECEIVED
SEP 21 2004
CDR / CDER

RECEIVED
SEP 22 2004
FDR/CDER

Ms. Beverly Friedman
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Regulatory Policy, HFD-5
5600 Fishers Lane
Rockville, MD 20857

Re: **NDA 21-612**
Luxacor (fenofibrate) Capsules 50 mg, 100 mg, 150 mg, ——— b(4)
User Fee I.D. 4494, Cipher Pharmaceuticals Ltd.
Confidential Correspondence Not for Disclosure Under FOIA

Dear Ms. Friedman:

As we recently discussed, it has come to my attention that the return of one-half the above referenced application fee to Cipher Pharmaceuticals (Cipher), to which your office committed in March 2003, has yet to occur. I write today to again request the prompt refund of the monies that the Agency has received in connection with the above application under the Prescription Drug User Fee Act (PDUFA).

Application and User Fee History for NDA 21-612

Cipher's 505(b)(2) New Drug Application (NDA) for CIP-fenofibrate was originally submitted to the Agency on December 24, 2002. The NDA was not accepted for filing because in a letter dated January 8, 2004, FDA contended that the payment of an application User Fee was required.[1] Dr. Ian French, then Chairman and Chief Scientific Officer of Cipher Pharmaceuticals, spoke and corresponded with you during January 2003 regarding Cipher's position that, as a 505(b)(2) application, this NDA met the statutory exclusion criteria for application fees.[2] Specifically, CIP-fenofibrate is not a new molecular entity (NME) and the application does not seek approval for a new indication for use.[3] Although your office had informed us that the Agency considers a change in dosage strength to be a new "indication for a use" for purposes of assessing a fee under 21 U.S.C. § 379g(1)(B)(ii), we are not aware of any support for this expansive interpretation of an indication for use, and believe that this application met the statutory exclusion from PDUFA application fees. Moreover, 'clinical data', as defined by the Agency for purposes of assessing user fees,[4] were neither included nor required as a

[1] FDA's letter of January 8, 2003 is provided in Attachment A.
[2] Copies of relevant email correspondence dated January 10, 2003 and January 13, 2003, are provided in Attachment B.
[3] 21 U.S.C. § 379g(1); *See also* Instructions for Completing User Fee Cover Sheet Form FDA 3397, at Item 7 ("Exclusions: Section 505(b)(2) applications, as defined by the Federal Food, Drug, and Cosmetic (FD&C) Act, are excluded from application fees if: they are NOT for a new molecular entity which is an active ingredient (including any salt or ester of an active ingredient); and NOT a new indication for a use.")
[4] Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees (Revision 1, December 2000) at page 7.

condition of approval for NDA 21-612; only bioavailability and bioequivalence studies were submitted with NDA 21-612.[5]

Despite Cipher's objections, we were informed by you that until a *full* user fee was received, substantive review of the NDA could not begin under 21 U.S.C. § 379h(e) and a determination could therefore not be made as to whether or not this application was for an NME or new indication requiring the review of clinical data.

In acquiescence to the Agency's demands, and in order to begin the review process, Cipher submitted the full $533,400 user fee under protest on January 14, 2003.[6] The User Fee Cover Sheet (see Attachment D), clearly indicated that no clinical data were required for approval (box 5) and that this was a 505(b)(2) application that did not require a fee (box 7).

Cipher received notice of the acceptance for filing of NDA 21-612 on February 26, 2003, in a letter dated March 10, 2003. Immediately after receipt of the March 10, 2003 letter, Cipher was once again in contact with the Agency in order to secure return of *at least* one half the user fee, as substantive review would certainly confirm that this 505(b)(2) met the exclusion criteria and did not require review of clinical data. Our records indicate that on or about Monday March 17, 2003, Arthur Deboeck, Cipher's designated U.S. Agent, spoke with personnel in the Division of Metabolic and Endocrine Drug Products, who informed him that one half of the user fee would be returned to Cipher at that time and that no further action was required on Cipher's part. Cipher relied on the Agency's assurance in this matter, and having been previously informed that the review division kept in close contact with the User Fee Office on this matter, reasonably expected that determination -- i.e., that this application in fact contained no "clinical" data -- to be communicated to your office and a refund promptly paid. Importantly, Cipher decided at that point to settle for the promised half-refund, despite never having received clear legal authority of the Agency's right to request a user fee on this application at all.

Due to a subsequent transition in personnel at Cipher Pharmaceuticals, follow-up on actual receipt of the promised refund of one-half of the user fee ($266,700) did not occur until Dr. French recently inquired as to whether the funds had in fact ever been received. This explains the delay in our inquiry.

The Administrative Record Reflects that Cipher's Refund Request Was Timely Made

Cipher met the statutory exclusion criteria for application User Fees at the time it submitted NDA 21-612. NDA 21-612 is a 505(b)(2) application for CIP-fenofibrate for the indications of hypercholesterolemia and hypertriglyceridemia. Thus, it is neither a new molecular entity nor for new indications of use, and therefore does not meet the PDUFA definition of a fee-bearing "human drug application." 21 U.S.C. § 379g(1)(B). Cipher agreed to submit the full application fee with the understanding that *at least* half would be returned since the reviewing division did not require clinical data to support approval of the NDA. Although Cipher acquiesced to the Agency's original demand and paid the full fee in order to start the review, that action should not

[5] Changing the minimum dose and range for dosing of the drug are not changes in the indication for use, as the IND consultation documents confirm that review of clinical data was not required for this purpose (see Attachment C for the FDA Pre-IND meeting minutes dated February 7, 2001, for comment at question 7 that approval for the nonexclusive indications of the RLD could be obtained without submission of a clinical trial; also attached are FDA's pre-NDA meeting minutes dated August 23, 2002, concluding with action items for sponsor that specifically refer to these as bioequivalence and dosage form equivalence studies.). Tentative approval to NDA 21-612 was granted by FDA on July 15, 2004.

[6] 67 Fed. Reg. 50448 at 50450 (August 2, 2002).

be perceived by the Agency as Cipher's acceptance that imposition of the fee was correct and acceptable. Indeed, Cipher paid the fee under protest and requested a refund in compliance with the procedural preferences expressed by FDA in its website Question and Answer on this subject (there being no formal procedural requirements described in the statute, regulations or current final guidance pertaining to refund requests). Specifically, all of the necessary details for refunding the fee or portion thereof were submitted to your office and to the reviewing division with the User Fee Cover Sheet, Form 3397, on January 14, 2003, and were reiterated in correspondence and telephone contact between Dr. French and your office.

Cipher's written request was timely made on January 15, 2003 in the form of the User Fee Cover Sheet, which included:

-name and address of entity and contact person
-identification of the specific fee for which refund was requested
-the application number for which the refund or reduction was requested, the date it was submitted, and whether the application required clinical data for approval
-the date on which payment was made.

Cipher is committed to obtaining the refund of *at least* half the application User Fee, to which it is entitled, and as was promised by your office. If you have any questions whatsoever, or foresee any delay in processing this refund, please contact me immediately, at (905) 602-5840 ext. 24. Please make the refund check payable to Cipher Pharmaceuticals Ltd. and return it to my attention at the letterhead address.

Sincerely,

Larry Andrews
President
Cipher Pharmaceuticals Ltd.

cc: Valerie Jimenez, Division of Metabolic and Endocrine Drug Products, FDA
James N. Czaban, Esq., Heller Ehrman White & McAuliffe LLP
Arthur DeBoeck, Galephar PR Inc.

b(4)

Appears This Way
On Original

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-612

Cipher Pharmaceuticals Ltd.
Galephar PR Inc., Agent for Cipher Pharmaceuticals Ltd.
Road 198 No. 100 km 14.7
Juncos Industrial Park
Juncos, Puerto Rico 00777-3873

Attention: Arthur Deboeck
Vice President and General Manager

Dear Mr. Deboeck:

Please refer to your new drug application (NDA) dated December 24, 2002, received February 26, 2003, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Luxacor (fenofibrate capsules) 50 mg, 100 mg, 150 mg, [redacted] b(4)

We acknowledge receipt of your submissions dated June 1 and 4, 2004. Your submission of June 4, 2004, constituted a complete response to our June 2, 2004, action letter.

This NDA provides for the use of Luxacor (fenofibrate capsules) as adjunctive therapy to diet to reduce elevated LDL-C, Total-C, Triglycerides, Apo B, and to increase HDL-C in patients with primary hypercholesterolemia or mixed dyslipidemia (Frederickson Type IIa, IIb) in addition to the treatment of adult patients with hypertriglyceridemia (Frederickson Types IV and V hyperlipidemia).

We have completed our review of this application, as amended, and have determined that based upon the information you have presented to date, the drug product is safe and effective for use as recommended in the agreed-upon enclosed labeling (package insert and immediate container labels, submitted June 4, 2004). Accordingly, this application is **tentatively approved** under 21 CFR 105. This determination is contingent upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing practices of the facilities used in manufacturing and testing of the drug product) and is, therefore, subject to change on the basis of any new information that may come to our attention.

The reference listed drug (RLD) product referenced in your application, Tricor Tablets of Abbott Laboratories, is subject to periods of patent protection which expire on January 19, 2009, (U.S. Patent No. 4,895,726 [the '726 patent]), and on January 9, 2018 (U.S. Patent No. 6,074,670 [the '670 patent]), (U.S. Patent No. 6,277,405 [the '405 patent]), (U.S. Patent No. 6,589,552 [the '552 patent]), and (U.S. Patent No. 6,652,881 [the '881 patent]). Your application contains a paragraph IV certification to each of these patents under section 505(b)(2)(A)(iv) of the Act.

These certifications state that the above listed patents are invalid, unenforceable or would not be infringed by your manufacture, use, offer for sale, or sale of this drug product.

Section 505(c)(3)(C) of the Act governs the timing of approval of applications submitted pursuant to section 505(b)(2) that contain a paragraph IV certification. Congress recently amended this section. See Title XI ("Access to Affordable Pharmaceuticals") of the Medicare Prescription Drug, Improvement, and Modernization Act (MMA), Pub. L. No. 108-173, 117 Stat. 2066 (Dec. 8, 2003). To determine the effect of these amendments on the timing of approval of a 505(b)(2) application, the relevant consideration is the date of submission to the FDA of the patent to which the paragraph IV certification was made. Patents submitted to FDA before August 18, 2003, are governed by the unamended section 505(c)(3)(C). Patents submitted to FDA on or after August 18, 2003, are governed by section 505(c)(3)(C) as amended by the MMA. Four of the five listed patents for Tricor were submitted before August 18, 2003. Only the '881 patent was submitted to FDA on or after August 18, 2003. Thus, only the '881 patent is governed by the amended provision.

The effects of section 505(c)(3)(C) are generally as follows:

(1) For patents that were submitted to FDA before August 18, 2003: Under section 505(c)(3)(C) before amendment by the MMA, the approval of a new drug application submitted pursuant to section 505(b)(2) of the Act shall be made effective immediately, unless an action is brought for infringement of any listed patent that is the subject of a paragraph IV certification. This action must be taken before the expiration of 45 days from the date the notice provided under section 505(b)(3)(A) is received by both the holder of the new drug application (NDA) and the patent owner. If patent infringement litigation is brought within the 45-day period, approval cannot be granted until, with respect to each patent, one of the following has occurred:

(a) expiration of the 30-month period provided for in section 505(c)(3)(C) beginning on the date of receipt of the 45-day notice required under section 505(b)(3)(A), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action; or

(b) the date described in section 505(c)(3)(C)(i), (ii), (iii), or (iv); or

(c) the patent has expired.

Section 505(c)(3)(C) (as amended).

(2) For patents that were submitted to FDA on or after August 18, 2003: Under section 505(c)(3)(C) as amended by the MMA, the approval of a new drug application submitted pursuant to section 505(b)(2) of the Act shall be made effective immediately, unless an action is brought for infringement of a patent that is the subject of a paragraph IV certification and for which information was submitted to FDA before the date on which the 505(b)(2) NDA was submitted to FDA. This action must be taken before the expiration of 45 days from the date the notice provided under section 505(b)(3)(A) is received by both the holder of the new drug application (NDA) and the patent owner. If patent infringement litigation is brought within the

45- day period, approval cannot be granted until, with respect to each patent, one of the following has occurred:

(a) expiration of the 30-month period provided for in section 505(c)(3)(C) beginning on the date of receipt of the 45-day notice required under section 505(b)(3)(A), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action; or

(b) the date described in section 505(c)(3)(C)(i), (ii), (iii), or (iv); or

(c) the patent has expired.

Section 505(c)(3)(C) (as amended). Under this new approach, then, if an NDA holder or patent owner sues the 505(b)(2) applicant within 45 days of receipt of notice of a paragraph IV certification to a patent (submitted to FDA on or after August 18, 2003) that had not been submitted to FDA before the date the 505(b)(2) NDA was submitted, there will be no 30-month stay on approval as a result of that litigation.

You have notified the Agency that Cipher Pharmaceuticals Ltd. (Cipher) has complied with the requirements for providing notice under sections 505(b)(3) and (c)(3)(C). In addition, you have notified the Agency that the patent owner and the NDA holder initiated patent infringement suits against Cipher with respect to the '405, '552, and '881 patents in the United States District Court for the District of Puerto Rico (Abbott Laboratories, an Illinois corporation, Fournier Industrie et Santé, a French corporation, and Laboratoires Fournier S.A., a French corporation, vs. Cipher Pharmaceuticals Ltd, a Barbados corporation, Case Nos. 03-1421, 03-2067, and 04-1089, respectively). As described above, there is now a 30-month stay in effect as a result of the patent infringement litigation regarding the '405 and '552 patents because these patents were submitted to FDA before August 18, 2003. This stay will be terminated by one of the events described at (1)(a)-(c) above. There is no 30-month stay in effect as a result of litigation regarding the '881 patent, because that patent was submitted to FDA after August 18, 2003 and after your 505(b)(2) application was submitted to FDA.

Final approval, therefore, cannot be granted until the 30-month stay relating to the '405 and '552 patents has been terminated and the Agency is assured there is no new information that would affect whether final approval should be granted.

Because the Agency is granting a tentative approval for this application, when you believe that your application may be considered for final approval, you must amend your application to notify the Agency whether circumstances have or have not arisen that may affect the final approval. This amendment must provide the following information:

1. Please include updated information related to labeling or chemistry, manufacturing, and controls data, or any other change in the conditions outlined in your application.

2. Please submit a copy of a final order or judgement or a settlement agreement between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information.

An amendment should be submitted even if no changes were made to the application since the date of this tentative approval. In addition to this amendment, the Agency may request at any time prior to the date of final approval that you submit an additional amendment containing the information described above. Failure to submit either or, if requested, both amendments, may result in rescission of the tentative approval status of your application, or result in a delay in the issuance of the final approval letter.

We additionally have the following comments pertaining to this application.

Labeling
We refer to your June 4, 2004, labeling submission, which contains the agreed upon labeling text attached to this letter (enclosure). Please note that the labeling may need to be updated as labeling changes are made to the RLD, Tricor Tablets, prior to final approval of this application.

Tradename
Your proposed tradename of Luxacor has been found to be acceptable. This is considered a tentative decision and the tradename will need to be re-evaluated approximately 90 days prior to the expected final approval of this application.

Dissolution Specification
We note your agreement to adopt the following dissolution method and specification for all strengths (50 mg, 100 mg, 150 mg, [redacted] of Luxacor (fenofibrate capsules): b(4)

Apparatus:	USP Apparatus II (Paddles)
Medium:	2% Tween 80, 0.1% Pancreatin @pH 6.8
Volume:	900 mL
Temperature:	37° ± 0.5 °C
Rotation Speed:	75 rpm
Sampling Time:	120 minutes
Specification:	[redacted] (Q) b(4)

Methods Validation
It is the policy of the Center not to withhold approval while the analytical methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified during the process.

Promotional Material
In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert(s) directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Other
Any significant change in the conditions outlined in this NDA requires our review before final approval may be granted.

The drug product that is the subject of this new drug application may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the effective final approval date is prohibited under section 501 of the Act. Also, until the Agency issues the final approval letter, the drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book") published by the Agency.

The drug product may not be legally marketed until you have been notified in writing that the application is finally approved.

If you have any questions, call Valerie Jimenez, Regulatory Project Manager, at (301) 827-9090.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES

21 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

✓ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

David Orloff
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MEMO TO THE FILE

NDA 21-612 Luxacor (fenofibrate capsules) 50 mg, 100 mg, 150 mg, [redacted] b(4)

Cipher Ltd. submitted a 505(b)(2) NDA, **NDA 21-612**, for **fenofibrate capsules** in [redacted] strengths, 50 mg, 100 mg, 150 mg, [redacted] The application referenced NDA 21-203 Tricor (fenofibrate tablets); which is approved in 54 and 160 mg strengths. The only relevant listed drug product is the 160 mg tablet, and five patents are listed in the Orange Book for that product. b(4)

Abbott also owns approved, but "discontinued," NDA 19-304 for Tricor (fenofibrate micronized capsules), 67 mg, 134 mg, 200 mg. The Cipher product, now named **"Luxacor", appropriately referenced NDA 21-**203 for fenofibrate tablets although the dosage forms are different, because the bioavailability of the 160 mg strength capsule [redacted] the same as the Tricor 160 mg tablet and that provides the link to the safety and efficacy information supporting NDA 21-203. Also, NDA 19-304 is approved for a micronized formulation of fenofibrate, but neither NDA 21-203 (fenofibrate tablets) nor NDA 21-612 (fenofibrate capsules) uses a micronized formulation. b(4)

Cipher appropriately submitted the "Luxacor" application as a 505(b)(2) rather than a 505(j) application, because acceptance of a suitability petition would be required to accept a change in dosage form in a 505j application, and the Agency cannot require submission of a suitability petition.

Cipher Ltd. has sent paragraph 4 certification notifications to Abbott Laboratories, the applicant for the referenced NDA 21-203, and to Fournier Laboratoires, which owns the patents associated with the listed drug. The proofs of receipt by Abbott and Fournier have been submitted. Abbott and Fournier are suing Cipher for patent infringement for three of the five patents listed for NDA 21-203. All three of those patents expire on January 9, 2018. The date of the latest receipt of notification is February 11, 2004, and the civil suit was filed timely. The next day, February 12, 2004, is the first day of the 30-month stay of approval. In April 2004 the District Court consolidated all the suits into one. (Refer to **21 CFR 314.107** for the regulations concerning determination of the effective date of approval for a 505b2 application.)

See the attached chart for patent numbers and other information pertaining to the notifications and the dates the suits were filed.

Listed Drug NDA # Product #	Patent Number	Patent Expiration Date	Type of Patent Certification	Para 4 Notification Received	Date Suit Filed or No Suit	Location Where Suit Filed	Civil Action Number
21-203 003	4,895,726	Jan. 19, 2009	Para 4	3/14/03; 3/17/03	NO	N/A	N/A
21-203 003	6,074,670	Jan. 9, 2018	Para 4	3/14/03; 3/17/03	NO	N/A	N/A
21-203 003	6,277,405	Jan. 9, 2018	Para 4	3/14/03; 3/17/03	April 21, 2003	District Court for District of Puerto Rico	03-1421
21-203 003	6,589,552	Jan. 9, 2018	Para 4	9/2/2003; 9/3/2003	Oct. 2, 2003	District Court for District of Puerto Rico	03-2067
21-203 003	6,652,881	Jan. 9, 2018	Para 4	2/9/2004; 2/11/2004	Feb. 5, 2004	District Court for District of Puerto Rico	04-1089

Drafted: E.Galliers/6.16.2004/

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/s/

Enid Galliers
6/28/04 02:44:14 PM
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6/22/04

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-612

Galephar PR Inc., Agent for
Cipher Pharmaceuticals Ltd.
Attention: Arthur M. Deboeck
Vice President and General Manager
Road 198 No. 100 km 14.7, Juncos Industrial Park
Juncos, PR 00777-3873

Dear Mr. Deboeck:

We acknowledge receipt on June 7, 2004, of your June 4, 2004, resubmission to your new drug application for Luxacor (fenofibrate capsules), 50 mg, 100 mg, 150 mg. [redacted] b(4)

We consider this a complete, class 1 response to our June 2, 2004, action letter. Therefore, the user fee goal date is August 7, 2004.

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. We note that you have not fulfilled the requirement. We are waiving the requirement for pediatric studies for this application.

If you have any question, call me at (301) 827-9090.

Sincerely,

{See appended electronic signature page}

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Valerie Jimenez
Regulatory Project Manager
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Valerie Jimenez
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06/22/04

Division of Metabolic & Endocrine Drug Products

PROJECT MANAGER LABELING REVIEW #3

Application Number: NDA 21-612

Name of Drug: Luxacor™ (fenofibrate capsules), 50 mg, 100 mg, 150 mg, [redacted] b(4)

Sponsor: Cipher Pharmaceuticals, Inc.

Materials Reviewed:

Submission Date(s): Draft Labeling: Package Insert (PI), container labels, and physician sample labels, June 4, 2004; received June 7, 2004.

Background and Summary

The revised draft labeling was submitted on June 4, 2004, in response to an approvable letter issued on June 2, 2004. Luxacor, a 505(b) (2) application, is indicated as adjunctive therapy to diet to reduce elevated LDL-C, Total-C, Triglycerides, Apo B, and to increase HDL-C in patients with primary hypercholesterolemia or mixed dyslipidemia (Fredrickson Type IIa, IIb) in addition to the treatment of adult patients with hypertriglyceridemia (Fredrickson Types IV and V hyperlipidemia). The reference listed drug is Tricor Tablets, 54 mg and 160 mg strengths for Luxacor Capsules, 50 mg, 100 mg, 150 mg. [redacted] strengths. b(4)

Review

Package Insert

The revised labeling (June 4, 2004) was compared to the March 30, 2004, labeling with the labeling revisions specified in the June 2, 2004, approvable letter. The following revisions have been made:

- The trade mark symbol "™" has been added throughout the package insert.

This an acceptable editorial change.

1. Under **Pharmacokinetics/Metabolism** section, Absorption subsection, has been revised as follows:

   "Absorption

   The absolute bioavailability of fenofibrate cannot be determined as the compound is virtually insoluble in aqueous media suitable for injection. However, fenofibrate is well absorbed from the gastrointestinal tract. Following oral administration in healthy volunteers, approximately 60% of a single dose of radiolabelled fenofibrate appeared in urine, primarily as fenofibric acid and its glucuronate conjugate, and 25% was excreted in the feces.

   The absorption of fenofibrate is increased when administered with food.

b(4)

2. The "Metabolism" subsection of **Pharmacokinetics/Metabolism** in the CLINICAL PHARMACOLOGY section of the package insert has been revised as follows:

   "Metabolism

   Following oral administration, fenofibrate is rapidly hydrolyzed by esterases to the active metabolite, fenofibric acid; unchanged fenofibrate is detected at low concentrations in plasma compared to fenofibric acid over most of the single dose and multiple dosing periods.

   Fenofibric acid is primarily conjugated with glucuronic acid and then excreted in urine. A small amount of fenofibric acid is reduced at the carbonyl moiety to a benzhydrol metabolite which is, in turn, conjugated with glucuronic acid and excreted in urine.

   In vivo metabolism data indicate that neither fenofibrate nor fenofibric acid undergo oxidative metabolism (e.g., cytochrome P450) to a significant extent."

These are acceptable revisions as requested in the June 4, 2004, action letter.

Container Labels

The draft bottle labels submitted on December 24, 2002, were compared to the submitted draft labels (June 4, 2004). The following changes were made to the 50 mg, 100 mg, 150 mg, [redacted] trade (30 and 90 count bottles) and [redacted]

b(4)

- The established name, fenofibrate capsules, has been revised to meet the requirement that it be at least one-half the height of the proprietary name, Luxacor™.

This change is acceptable per 21 CFR 201.10(g)(2).

Carton Labels

Note: The firm communicated that it did not intend to use cartons.

Conclusion

The Biopharmaceutics and Chemistry items listed in the June 2, 2004, action letter have been addressed in the June 4, 2004, resubmission. The requested patent notification information was submitted. A Tentative Approval (TA) letter should be drafted because approval is contingent on the resolution of a pending patent infringement suit.

Valerie Jimenez
Regulatory Project Manager, HFD-510

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/s/

Valerie Jimenez
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CSO

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NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST #3

Application Information			
NDA 21-612	Efficacy Supplement Type SE-	Supplement Number	
Drug: Luxacor (fenofibrate capsules)		Applicant: Cipher Pharmaceuticals Limited	
RPM: Valerie Jimenez		HFD-510	Phone # (301) 827-9090
Application Type: ( ) 505(b)(1) (X) 505(b)(2)		Reference Listed Drug (NDA #, Drug name): NDA 21-203 Tricor Tablets 54 mg and 160 mg	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	3
• Other (e.g., orphan, OTC)	N/A
❖ User Fee Goal Dates	August 7, 2004
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) (X) I ( ) II (X) III (X) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	(X) Verified 4,895,226, 6,074,670 and 6,277,405 B1 6,652,881 B2 expires January 9, 2018, Paragraph IV, no proof of notification 6,589,552 no Cipher certification or

	proof of notification submitted
Exclusivity Summary (approvals only)	N/A
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	PM: 12/12/03, 05/30/04
General Information	
❖ Actions	
• Proposed action	( ) AP (X) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	AE:12/18/03, AE:6/2/04
• Status of advertising (approvals only)	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling	12/26/02, 3/30/04, 6/4/04
• Original applicant-proposed labeling	12/26/02
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	8/4/03, 12/17/03, 4/28/04 PM: 12/17/03, 6/2/04, 6/22/04
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	Tricor Capsules, NDA 21-203
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	N/A
• Reviews	12/12/03
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	
❖ Memoranda and Telecons 12/17/03, 4/17/03, 4/18/03, 4/23/04, 7/18/03, 8/7/03, 8/18/03,	5/28/04
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	7/23/02
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	N/A
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A

Clinical and Summary Information	
Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	
❖ Clinical review(s) *(indicate date for each review)*	12/15/03
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	N/A
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	N/A No Clinical S & E done
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	N/A
❖ Statistical review(s) *(indicate date for each review)*	N/A
❖ Biopharmaceutical review(s) *(indicate date for each review)*	11/12/03, 4/17/03, 5/13/04
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	10/20/03
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	12/2/03, 5/21/04
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	12/2/03
• Review & FONSI *(indicate date of review)*	N/A
• Review & Environmental Impact Statement *(indicate date of each review)*	N/A
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report)	Date completed: 10/22/03 and 11/25/03 (X) Acceptable ( ) Withhold recommendation
❖ Methods validation Methods validation package not submitted	( ) Completed N/A ( ) Requested (X) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	04/17/03, 10/07/03
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	N/A

5/30/04

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST #2

Application Information		
NDA 21-612	Efficacy Supplement Type SE-	Supplement Number
Drug: Luxacor (fenofibrate capsules)	Applicant: Cipher Pharmaceuticals Limited	
RPM: Valerie Jimenez	HFD-510	Phone # (301) 827-9090
Application Type: ( ) 505(b)(1) (X) 505(b)(2)	Reference Listed Drug (NDA #, Drug name): NDA 21-203 Tricor Tablets 54 mg and 160 mg	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	3
• Other (e.g., orphan, OTC)	N/A
❖ User Fee Goal Dates	December 26, 2003
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) (X) I ( ) II (X) III (X) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	(X) Verified 4,895,226, 6,074,670 and 6,277,405 B1 6,652,881 B2 expires January 9, 2018, Paragraph IV, no proof of notification 6,589,552 no Cipher certification or

	proof of notification submitted
Exclusivity Summary (approvals only)	N/A
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	PM: 12/12/03, 05/30/04
General Information	
❖ Actions	
• Proposed action	( ) AP ( ) TA (X) AE ( ) NA
• Previous actions (specify type and date for each action taken)	N/A
• Status of advertising (approvals only)	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	N/A; Changes to biopharm section
• Most recent applicant-proposed labeling	12/26/02, 3/30/04
• Original applicant-proposed labeling	12/26/02
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	8/4/03, 12/17/03, 4/28/04 PM: 12/17/03, 6/2/04
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	Tricor Capsules, NDA 21-203
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	N/A
• Reviews	12/12/03
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	
❖ Memoranda and Telecons 12/17/03, 4/17/03, 4/18/03, 4/23/04, 7/18/03, 8/7/03, 8/18/03,	5/28/04, 6/8/04, 5/13/04
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	7/23/02
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	N/A
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A

Clinical and Summary Information	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	
❖ Clinical review(s) *(indicate date for each review)*	12/15/03
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	N/A
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	N/A No Clinical S &E done
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	N/A
❖ Statistical review(s) *(indicate date for each review)*	N/A
❖ Biopharmaceutical review(s) *(indicate date for each review)*	11/12/03, 4/17/03, 5/13/04
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	10/20/03
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	12/2/03, 5/21/04
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	12/2/03
• Review & FONSI *(indicate date of review)*	N/A
• Review & Environmental Impact Statement *(indicate date of each review)*	N/A
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report)	Date completed: 10/22/03 and 11/25/03 (X) Acceptable ( ) Withhold recommendation
❖ Methods validation Methods validation package not submitted	( ) Completed N/A ( ) Requested (X) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	04/17/03, 10/07/03, 6/3/04
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	N/A

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-612	Efficacy Supplement Type SE-	Supplement Number
Drug: Luxacor (fenofibrate) Capsules, 50, 100, 150, ~~mg~~		Applicant: Cipher Pharmaceuticals Limited
RPM: Valerie Jimenez	HFD-510	Phone # (301) 827-9090
Application Type: ( ) 505(b)(1) (X) 505(b)(2)	Reference Listed Drug (NDA #, Drug name): NDA 21-203, Tricor 54mg, 160mg Tablets	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	3
• Other (e.g., orphan, OTC)	—
❖ User Fee Goal Dates AGD = NLT 12.19.03	December 26, 2003
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(X) Verified — Applicant & Agent Deficient - Agent - Galephar Submitted March 30, 2004
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(i)(A) ( ) I ( ) II ( ) III (X) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	X Verified
❖ Exclusivity Summary (approvals only)	N/A
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	PM: 12.12.03

General Information	
❖ Actions	
• Proposed action	( ) AP ( ) TA (X) AE ( ) NA
• Previous actions (specify type and date for each action taken)	N/A
• Status of advertising (approvals only)	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	N/A; Changes to several sections
• Most recent applicant-proposed labeling	12/26/02
• Original applicant-proposed labeling	12/26/02
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	DMETS 8/4/03, 11/6/03 PM: 12/17/03
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	Tricor N 21-203
Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	12/26/02
• Reviews	N/A
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	✓
❖ Memoranda and Telecons 4/17/03; 8/7/03;	✓ 4/18/03; 8/18/03; 12/12/03
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date) 7/23/02	✓
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	N/A
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A

Clinical and Summary Information	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	T/L Review = M.O.R.
❖ Clinical review(s) *(indicate date for each review)*	12/15/03
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	N/A
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	N/A No clin. SAE were done
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	N/A
❖ Statistical review(s) *(indicate date for each review)*	N/A
❖ Biopharmaceutical review(s) *(indicate date for each review)*	11/12/03; 4/17/03, 5/13/04
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	10/20/03
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	12/02/03
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	12/02/03
• Review & FONSI *(indicate date of review)*	N/A
• Review & Environmental Impact Statement *(indicate date of each review)*	N/A
Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report)	Date completed: 10/22/03 11/25/03 (X) Acceptable ( ) Withhold recommendation
❖ Methods validation MV pkg not submitted	( ) Completed ( ) Requested (X) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	04/17/03, 10/07/03
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	N/A

acg 12/ /03

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On Original

cipher
PHARMACEUTICALS LTD

409 Matheson Blvd. E. Mississauga, ON Canada L4Z 2H2
tel: (905) 602 5840
fax: (905) 602 0628
www.cipherpharma.com

DUPLICATE

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JUN 0 9 2004
FDR/CDER

RECEIVED
JUN 0 7 2004
CDR / CDER

June 4, 2004

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research
5600 Fisher's Lane
Rockville, MD 20857

N 000 BZ
ORIG AMENDMENT

Re: **NDA 21-612**
Luxacor (fenofibrate) Capsules 50 mg, 100 mg, 150 mg, [redacted] b(4)
Complete Response to FDA letter of June 2, 2004

Dear Dr. Orloff:

We refer to our new drug application (NDA) dated December 24, 2002 and received by FDA on February 26, 2003. We also refer to our submissions dated January 10, March 24, May 6, October 15, November 7, December 2 and 8, 2003, and January 7, 18, 25, February 3, 9, 16, March 30, May 5, 14, and 21 2004.

Please find enclosed a complete response to your letter of June 2, 2004. This response consists of 1 volume of original information, and two copies of the same. This submission includes revised draft labeling (clean and marked-up versions), one copy in paper format, and one copy in electronic format, as requested.

If you have any questions or comments, please do not hesitate to call me at 905 602 5840 x 24, or you can contact [redacted] b(4) regarding this submission, or on other related matters.

Yours sincerely,

Larry Andrews

Appears This Way
On Original

Larry Andrews
President
Cipher Pharmaceuticals Ltd.

CC: Arthur DeBoeck, Galephar PR Inc.
[redacted] b(4)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Cipher Pharmaceuticals Ltd.	6/4/04
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE** *(FAX)* **Number** *(Include Area Code)*
905 602 5840	905 602 0628
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* **IF APPLICABLE**
Suite 201 Lauriston, Collymore Rock St. Michael, Barbados	Arthur M. Deboeck Galephar PR Inc. Road 198 No. 100 km 14.7 Juncos Industrial Park, Juncos 00777-3873

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 21,612

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Fenofibrate	Luxacor

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*

CODE NAME *(If any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION
Capsules	50, 100, 150 [redacted]	Oral

RECEIVED
JUN 07 2004
CDR / CDER

b(4

(PROPOSED) INDICATION(S) FOR USE:
For Type IIa, IIb, IV and V dyslipidemia

APPLICATION DESCRIPTION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (CDA, 21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b)(1) ☒ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug _____ Holder of Approved Application _____

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO APENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION
Complete response to FDA letter June 2, 2004

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 (in triplicate) THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Please refer to original NDA # 21,612 for Establishment Information

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

NDA # 21,612

This application contains the following items: *(Check all that apply)*	
☒	1. Index
☐	2. Labeling *(check one)* ☒ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50 (c))
☐	4. Chemistry section
☐	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306 (k)(1))
☐	17. Field copy certification (21 CFR 314.50 (l)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial Information (21 CFR Part 54)
☒	20. OTHER *(Specify)* Notice of Filing of Patent Infringement Action, resubmission of Paragraph IV Certification

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE:
	Jan W. French, CSO Arthur M Deboeck, VP & General Manager	6/4/04

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
US Agent, Galephar PR Inc., Juncos, Puerto Rico, 00777-3873	(787) 713 0340

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CDER, HFD-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

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.

INSTRUCTIONS FOR FILLING OUT FORM FDA 356h

APPLICANT INFORMATION This section should include the name, street address, telephone and facsimile numbers of the legal person or entity submitting the application in the appropriate areas. Note that, in the case of biological products, this is the name of the legal entity or person to whom the license will be issued. The name, street address and telephone number of the legal person or entity authorized to represent a non-U.S. applicant should be entered in the indicated area. Only one person should sign the form.

PRODUCT DESCRIPTION This section should include all of the information necessary to identify the product that is the subject of this submission. For new applications, the proposed indication should be given. For supplements to an approved application, please give the approved indications for use.

APPLICATION INFORMATION If this submission is an ANDA or 505(b)(2), this section should include the name of the approved drug that is the basis of the application and identify the holder of the approved application in the indicated areas.

TYPE OF SUBMISSION should be indicated by checking the appropriate box:

Original Application = a complete new application that has never before been submitted;

Amendment to a Pending Application = all submissions to pending original applications, or pending supplements to approved applications, including responses to Information Request Letters;

Resubmission = a complete response to an action letter, or submission of an application that has been the subject of a withdrawal or a refusal to file action;

Presubmission = information submitted prior to the submission of a complete new application;

Annual Report = periodic reports for licensed biological products (for NDAs Form FDA-2252 should be used as required in 21 CFR 314.81 (b)(2));

Establishment Description Supplement = supplements to the information contained in the Establishment Description section (#15) for biological products;

Efficacy Supplement = submissions for such changes as a new indication or dosage regimen for an approved product, a comparative efficacy claim naming another product, or a significant alteration in the patient population; e.g., prescription to Over-The-Counter switch;

Labeling Supplement = all label change supplements required under 21 CFR 314.70 and 21 CFR 601.12 that do not qualify as efficacy supplements;

Chemistry, Manufacturing, and Controls Supplement = manufacturing change supplement submissions as provided in 21 CFR 314.70, 21 CFR 314.71, 21 CFR 314.72 and 21 CFR 601.12;

Other = any submission that does not fit in one of the other categories (e.g., Phase IV response). If this box is checked the type of submission can be explained in the **REASON FOR SUBMISSION** block.

Submission of Partial Application Letter date of agreement to partial submission should be provided. Also, provide copy of scheduled plan.

CBE "Supplement-Changes Being Effected" supplement submission for certain moderate changes for which distribution can occur when FDA receives the supplement as provided in 21 CFR 314.70 and 21 CFR 601.12.

CBE-30 "Supplement-Changes Being Effected in 30 Days" supplement submission for certain moderate changes for which FDA receives at least 30 days before the distribution of the product made using the change as provided in 21 CFR 314.70 and 21 CFR 601.12.

Prior Approval (PA) "Prior Approval Supplements" supplement submission for a major change for which distribution of the product made using the change cannot occur prior to FDA approval as provided in 21 CFR 314.70 and 21 CFR 601.12.

REASON FOR SUBMISSION This section should contain a brief explanation of the submission, e.g., "manufacturing change from roller bottle to cell factory" or "response to Information Request Letter of 1/9/97" or "Pediatric exclusivity determination request" or "to satisfy a subpart H postmarketing commitment".

NUMBER OF VOLUMES SUBMITTED Please enter the number of volumes, including and identifying electronic media, contained in the archival copy of this submission.

This application is
☐ Paper ☐ Paper and Electronic ☐ Electronic
Please check the appropriate box to indicate whether this submission contains only paper, both paper and electronic media, or only electronic media.

ESTABLISHMENT INFORMATION This section should include information on the locations of all manufacturing, packaging and control sites for both drug substance and drug product. If continuation sheets are used, please indicate where in the submission they may be found. For each site please include the name, address, telephone number, registration number (Central File Number), Drug Master File (DMF) number, and the name of a contact at the site. The manufacturing steps and/or type of testing (e.g. final dosage form, stability testing) conducted at the site should also be included. Please indicate whether the site is ready for inspection or, if not, when it will be ready. Please note that, when applicable, the complete establishment description is requested under item 15.

CROSS REFERENCES This section should contain a list of all License Applications, Investigational New Drug Applications (INDs), NDAs, Premarket Approval Applications (PMAs), Premarket Notifications (510(k)s), Investigational Device Exemptions (IDEs), Biological Master Files (BMFs) and DMFs that are referenced in the current application.

Items 1 through 20 on the reverse side of the form constitute a check list that should be used to indicate the types of information contained within a particular submission. Please check all that apply. The numbering of the items on the checklist is not intended to specify a particular order for the inclusion of those sections into the submission. The applicant may include sections in any order, but the location of those sections within the submission should be clearly indicated in the Index. It is therefore recommended that, particularly for large submissions, the Index immediately follows the Form FDA 356h and, if applicable, the User Fee Cover Sheet (Form FDA 3397).

The CFR references are provided for most items in order to indicate what type of information should be submitted in each section. For further information, the applicant may consult the guidance documents that are available from the Agency.

Signature The form must be signed and dated. Ordinarily only one person should sign the form, i.e., the applicant, or the applicant's attorney, agent, or other authorized official. However, if the person signing the application does not reside or have a place of business within the United States, the application should be countersigned by an attorney, agent, or other authorized official who resides or maintains a place of business within the United States.

TABLE OF CONTENTS

Questions and comments from the Agency are presented below in bolded text, and Cipher Pharmaceuticals Inc.'s responses are provided in italicized text.

REGULATORY

1. **Submit a patent certification for patent 6,589,552**

   Our records indicate that a paragraph IV certification, pursuant to 21 U.S.C. § 355(b)(2)(A)(iv), for U.S. Patent No. 6,589,552 B2 was originally submitted by Cipher Pharmaceuticals Ltd. ("Cipher") on or about August 18, 2003. At that same time, Cipher notified the patent owner (Laboratoires Fournier S.A.) and the holder of the new drug application (NDA) No. 21-203 for fenofibrate tablets (Abbott Laboratories) of the basis for this paragraph IV certification, pursuant to 21 U.S.C. § 355(b)(3). Proof of receipt of this notification is hereby attached to this response, as discussed further in response to question no. 2, below. Since it appears from your correspondence of June 2, 2004 that FDA is unable to readily access this original certification, please find enclosed a replacement paragraph IV certification, pursuant to 21 U.S.C. § 355(b)(2)(A)(iv), for U.S. Patent No. 6,589,552 B2, included as Attachment 1.

2. **Submit proof of receipt by the patent holder and applicant for the listed drug of your Paragraph 4 Patent Certification notification for patent 6,589,552 and patent 6,652,881.**

   Please find enclosed, as Attachment 2, proof of receipt of the required notification, pursuant to 21 U.S.C § 355(b)(3), of the basis for Cipher's paragraph IV certifications relating to U.S. Patent Nos. 6,589,552 B2 and 6,652,881 B2 by the patent owner (Laboratoires Fournier S.A.) and the holder of NDA 21-203 for fenofibrate tablets (Abbott Laboratories). Cipher's notice of certification for U.S. Patent No. 6,589,552 B2 was received by Laboratoires Fournier S.A. on September 2, 2003 and by Abbott Laboratories on September 3, 2003. Cipher's notice of certification for U.S. Patent No. 6,652,881 B2 was received by Laboratoires Fournier S.A. on February 11, 2004 and by Abbott Laboratories on February 9, 2004.

3. **Submit a statement whether the patent holder or applicant (for the listed drug) has filed any suit against your firm with respect to patent 6,652,881.**

   As the enclosed Statement of Notice of Litigation indicates, in Attachment 3, Laboratoires Fournier S.A. (owner of U.S. Patent No. 6,652,881 B2) and Fournier Industrie Et Santé (collectively Fournier), and Abbott Laboratories (holder of NDA No. 21-203 for fenofibrate tablets) initiated a lawsuit on February 5, 2004 in the United States District Court for the District of Puerto Rico against Cipher with respect to U.S. Patent No. 6,652,881 B2.

4. **Submit a statement regarding the status or final disposition of each patent infringement suit filed against Cipher Pharmaceuticals with respect to this application.**

   Fournier and Abbott Laboratories have initiated three lawsuits in the United States District Court for the District of Puerto Rico relating to the NDA No. 21-612 filed by Cipher for fenofibrate capsules. Specifically, on April 21, 2003, Fournier and Abbott filed suit against Cipher (Civil No. 03-1421) alleging infringement of U.S. Patent No. 6,277,405 B1, under 35 U.S.C. § 271(e)(2)(A). On October 2, 2003, Fournier and Abbott filed suit against Cipher (Civil No. 03-2067) alleging infringement of U.S. Patent No. 6,589,552 B2, under 35 U.S.C. § 271(e)(2)(A). And, finally, on February 5, 2004, Fournier and Abbott filed suit against Cipher (Civil No. 04-1089) alleging infringement of U.S. Patent No. 6,652,881 B2, under 35 U.S.C. § 271(e)(2)(A). On April 21, 2004, all three of these cases were consolidated by the Court. These matters are all still pending.

LABELLING

5. **In addition, it will be necessary for you to submit draft with the following revisions to the labeling you submitted March 30, 2004:**

   a. **Revise the "Absorption" subsection of Pharmacokinetics/Metabolism in the CLINICAL PHARMACOLOGY section of the package insert as follows (additions are underlined and deletions are noted in the margin):**

   Absorption

   The absolute bioavailability of fenofibrate cannot be determined as the compound is virtually insoluble in aqueous media suitable for injection. However, fenofibrate is well absorbed from the gastrointestinal tract. Following oral administration in healthy volunteers, approximately 60% of a single dose of radiolabeled fenofibrate appeared in urine, primarily as fenofibric acid and its glucuronate conjugate, and 25% was excreted in the feces.

   The absorption of fenofibrate is increased when administered with food.

b(4

b(4)

b(4)

The extent of absorption of [redacted] in terms of AUC value of fenofibric acid increased in a less than proportional manner while the rate of absorption in terms of C_{max} value of fenofibric acid increased proportionally related to dose.

The package insert has been revised as requested, and a clean copy is included in Attachment 4, and a marked-up copy in Attachment 5.

b. Revise the "Metabolism" subsection of Pharmacokinetics/Metabolism in the CLINICAL PHARMACOLOGY section of the package insert as follows:

Metabolism

Fenofibric acid is primarily conjugated with glucuronic acid and then excreted in urine. A small amount of fenofibric acid is reduced at the carbonyl moiety to a benzhydrol metabolite which is, in turn, conjugated with glucuronic acid and excreted in urine.

In vivo metabolism data indicate that neither fenofibrate nor fenofibric acid undergo oxidative metabolism (e.g., cytochrome P450) to a significant degree.

The package insert has been revised as requested, and a clean copy is included in Attachment 4, and a marked-up copy in Attachment 5.

6. Revise the mock-ups of the bottle labels submitted March 30, 2004, to comply with 21 CFR 201.10(g)(2). In your March 30, 2004 submission, the size of the established name is too small with respect to the proprietary name. The established name must be no less than one half the height of the proprietary name.

The mock-ups of the bottle labels have been revised so that the established name is in 12 pt font, and the proprietary name is in 18 pt font. These are included as Attachment 6.

The mock-ups of the bottle labels are also provided electronically, along with the clean and marked up versions of the package insert, in Attachment 7 of this response.

cipher
Pharmaceuticals Limited

PATENT CERTIFICATION

Paragraph IV Certification
U.S. Patent No. 6,589,552 B2

In accordance with the Federal Food, Drug and Cosmetic Act and 21 C.F.R. § 314.50(i)(1)(i)(A)(4), a Patent Certification, and in particular a Paragraph IV Certification pursuant to 21 U.S.C. § 355(b)(2)(A)(iv), as to U.S. Patent No. 6,589,552 B2 ("the '552 patent") is hereby provided for our New Drug Application ("NDA") No. 21-612 for Fenofibrate Capsules 50, 100, 150, [redacted] mg. b(4)

Cipher Pharmaceuticals hereby certifies, pursuant to 21 U.S.C. § 355(b)(2)(A)(iv), that, in its opinion and to the best of its knowledge, the '552 patent, expiring on or about January 9, 2018, will not be infringed upon by the manufacture, use, sale, offer for sale or importation by Cipher Pharmaceuticals of Fenofibrate Capsules 50, 100, 150, [redacted] mg for which Cipher's application has been submitted, and/or that the '552 patent is invalid. b(4)

STATEMENT CONCERNING NOTICE TO PATENT OWNER AND NDA HOLDER

As required by Section 505(b)(3)(A) of the Federal Food, Drug and Cosmetic Act, Cipher hereby states that the notice required by Section 505(b)(3) and 21 C.F.R. § 314.52 was sent to Abbott Laboratories Inc., as the holder of approved NDA No. 21-203 for Tricor® (fenofibrate) 54 mg and 160 mg tablets and the exclusive licensee of U.S. Patent No. 6,589,552 B2, and to Laboratories Fournier S.A., as the record owner of U.S. Patent No. 6,589,552 B2.

This notice to Abbott Laboratories Inc. and Laboratories Fournier S.A., was sent by certified mail, return receipt requested, as required by 21 C.F.R. § 314.52(a).

Ian W. French
Chief Scientific Officer
Cipher Pharmaceuticals Ltd.

Date: Jan 3/04

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax: (246) 228-8329

Proof of receipt of notice of Cipher's certification to U.S. Patent No. 6,589,552 B2

Appears This Way
On Original

Postal administration of origin

ADVICE of receipt/of delivery/of payment/of entry

CN 07 (old C 5)

Office of posting	Date
GPO # 37375	21/08/2003

Addressee of the item GENERAL COUNSEL,

On postal service

Stamp of the office returning the advice

DIJON PROVIDENCE CCTI 12 - CÔTE D'OR 2-9 2003

Priority/
By airmail

b(4,

Nature of the item

☑ Priority/ Letter	☐ Non-priority/ Printed paper	☐ Parcel	☐
☑ Registered No. of item	☐ Recorded delivery	☐ Insured Amount	
☐ Ordinary money order ☐ Inpayment money ord	☐ Outpayment ☐ Cheque	Amount	

To be completed at the point of destination

The item mentioned above has been duly
☐ delivered ☐ paid ☑ credited to giro account

Date and Signature* 21/08/03

* This advice may be signed by the addressee or, if the regulations of the country of destination so provide, by another authorized person or by the official of the office of destination.

To be filled in by the sender

Return to

Name
CIPHER PHARMACEUTICALS LTD.
Street and No.
SUITE 201 LAURISTON, COLLYMORE ROCK,
Locality and country
ST. MICHAEL, BARBADOS

Parcels, Seoul 1994, art RE 1501.2 – Size 210 x 105 mm, with a tolerance of 2mm, colour light red

Postal administration of origin

ADVICE of receipt/of delivery/of payment/of entry

CN 07 (old C 5)

Office of posting	Date
GPO # 37376	21/08/2003

Addressee of the item GENERAL COUNSEL, ABBOTT LABORATORIES INC. PHARMACEUTICAL PRODUCTS DIVISION, 100 ABBOTT PARK RD, ABBOTT PARK, IL 60064-6400, U.S.A.

On postal service

Stamp of the office returning the advice

Priority/
By airmail

Nature of the item

☑ Priority/ Letter	☐ Non-priority/ Printed paper	☐ Parcel	☐
☑ Registered No. of item	☐ Recorded delivery	☐ Insured Amount	
☐ Ordinary money order ☐ Inpayment money ord	☐ Outpayment ☐ Cheque	Amount	

To be completed at the point of destination

The item mentioned above has been duly
☐ delivered ☐ paid ☐ credited to giro account

Date and Signature* 9/3/3

To be filled in by the sender

Return to

Name
CIPHER PHARMACEUTICALS LTD.
Street and No.
SUITE 201 LAURISTON, COLLYMORE RK,
Locality and country
ST. MICHAEL, BARBADOS

Proof of receipt of notice of Cipher's certification to U.S. Patent No. 6,652,881 B2

Appears This Way
On Original

CANADA POST / POSTES CANADA

Advice of Receipt
Registered International

Avis de réception
Recommandé international

CN07

Office of Posting / Bureau de dépôt	Date
Orangeville	Feb 03/04

Addressee / Destinataire: Gen. Counsel

Stamp of returning office / Timbre du bureau de renvoi

ON POSTAL SERVICE / SERVICE DES POSTES
AIRMAIL / PAR AVION

ORANGEVILLE ON CAPNORD 19 FEB -2 2004 POSTE-POST

b(4)

Item Identifier No. / N° de l'envoi: R RT 743 721 790 CA

Item was delivered on: / L'envoi a été livré le: Date

Printed Name of Signator / Nom du signataire (lettres moulées)

Signature

33-086-587 (96-10)

Return to / Nom

Name: Dr. Ian W. French

Street and Number / Rue et numéro: 6905 Hwy 9. RR#1

City / Province / Postal Code / Ville / Province / Code postal: Caledon, East, Ont

CANADA L0N 1E0

Appears This Way
On Original

CANADA POSTES CANADA POST

Advice of Receipt
Registered International

Avis de réception
Recommandé International

CN07

Office of Posting / Bureau de dépôt: Orangeville

Date: Feb 03/04

Addressee / Destinataire:
GENERAL COUNSEL
ABBOTT LABORATORIES INC
PHARMACEUTICAL PRODUCTS DIV
100 ABBOTT PARK DR.
ABBOTT PARK, IL 60064-6400

Stamp of returning office / Timbre du bureau de renvoi

ON POSTAL SERVICE / SERVICE DES POSTES
AIRMAIL / PAR AVION

Item Identifier No / N° de l'envoi: RT 743 721 786 CA

Item was delivered on: / L'envoi a été livré le: Date

Printed Name of Signator / Nom du signataire(lettres moulées): J. Durden

Signature: J Durden 2/9/04

93-086-587 (98-10)

Return to / Renvoyer à

Name / Nom: IAN W. FRENCH

Street and Number / Rue et numéro: 6905 HWY 9

City / Province/ Postal Code / Ville / Province/ Code postal: CALEDON EAST ON L0N 1E0

CANADA

Appears This Way
On Original

cipher
Pharmaceuticals Limited

STATEMENT OF NOTICE OF LITIGATION

Cipher Pharmaceuticals Ltd. hereby submits Notice of Litigation in relation to U.S. Patent No. 6,652,881 B2. An infringement suit was filed against Cipher on February 5, 2004 in the United States District Court for the District of Puerto Rico by [redacted] (owner of U.S. Patent No. 6,652,881 B2), and Abbott Laboratories (holder of new drug application No. 21-203 for fenofibrate tablets). A copy of the complaint in this matter is attached. b(4)

Ian W. French
Chief Scientific Officer
Cipher Pharmaceuticals Ltd.

June 3/04
Date

Appears This Way
On Original

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax: (246) 228-8329

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF PUERTO RICO

ABBOTT LABORATORIES, an Illinois corporation, [redacted] a French corporation, and [redacted] a French corporation,

Plaintiffs,

vs.

CIPHER PHARMACEUTICALS LTD., a Barbados corporation,

Defendant.

b(4)

04-1089(SEF)

Civil Action No.

COMPLAINT

Plaintiffs, Abbott Laboratories, [redacted] and [redacted] for their complaint allege against Defendant, Cipher Pharmaceuticals Ltd., as follows:

b(4)

THE PARTIES

1. Plaintiff Abbott Laboratories ("Abbott") is a corporation organized under the laws of the State of Illinois, having its headquarters and principal place of business at Abbott Park, Illinois 60064.

2. Plaintiffs [redacted] formerly known as [redacted] and [redacted] (collectively [redacted] are [redacted] corporations having their principal place of business at [redacted]

b(4)

b(4)

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3. Defendant Cipher Pharmaceuticals Ltd. ("Cipher") is an alien, organized and existing under the laws of Barbados and having its principal place of business at Lauriston, Collymore Rock, St. Michael, Barbados.

JURISDICTION AND VENUE

4. This Complaint is an action for patent infringement arising under the patent laws of the United States, Title 35, United States Code, §§ 1 et seq. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. § 1338(a).

5. Venue properly exists in this judicial district pursuant to 28 U.S.C. § 1391 and § 1400(b).

6. This Court has personal jurisdiction over Defendant under 32 L.P.R.A. App. III, Rule 4.7(a) or, in the alternative, Fed. R. Civ. P. 4(k)(2).

FACTUAL BACKGROUND

7. Fournier is the owner by assignment of U.S. Patent No. 6,652,881, entitled "Fenofibrate Pharmaceutical Composition Having High Bioavailability" (the '881 patent) (attached hereto as Exhibit 1).

8. Abbott is the exclusive licensee of the '881 patent.

9. The '881 patent, which issued on November 25, 2003, claims a novel fenofibrate composition that exhibits a particular dissolution profile. The '881 patent expires on January 9, 2018.

10. Fenofibrate is useful as a lipid and cholesterol lowering agent for treatment of adults with increased triglyceride levels.

11. Abbott has approval from the United States Food and Drug Administration ("FDA") to market fenofibrate tablets under the name TRICOR®.

12. TRICOR® (fenofibrate) is included in the FDA's list of "Approved Drug Products With Therapeutic Equivalence Evaluations" also known as the "Orange Book." Approved drugs may be used as the basis of a later applicant's New Drug Application ("NDA") to obtain approval of the NDA applicant's drug product under provisions of 21 U.S.C. § 355(b)(2).

13. The FDA's "Orange Book" also lists patents associated with approved drugs. The '881 patent is listed in the "Orange Book" in association with TRICOR® (fenofibrate).

14. Abbott and Fournier received a letter from Cipher, stating that Cipher had filed an NDA, designated as No. 21-612, requesting FDA approval to market a capsule fenofibrate drug product in 50mg, 100mg, 150mg b(4) dosages before the expiration of the '881 patent. The letter contends that Cipher's proposed product will not infringe the '881 patent. The letter indicated that Cipher's United States agent for its NDA is Arthur M. Deboeck, Galephar P.R. Inc., Road 198 No. 100 km 14.7, Juncos Industrial Park, Juncos, Puerto Rico 00777-3873.

INFRINGEMENT

15. 35 U.S.C. § 271(e)(2) provides that the submission of an application under 21 U.S.C. § 355(b)(2) for a drug claimed in a patent or for a drug use claimed in a patent is an act of infringement if the applicant seeks FDA marketing approval effective prior to the expiration of the patent. Cipher's

submission of an NDA for approval to sell fenofibrate capsules 50mg, 100mg, 150mg [redacted] dosages prior to the expiration of the '881 patent constitutes an act of infringement of one or more claims of the '881 patent under 35 U.S.C. § 271(e)(2). In addition, Cipher's generic version of TRICOR® (fenofibrate) infringes one or more claims of the '881 patent.

b(4

16. Plaintiffs have no adequate remedy at law to redress Cipher's infringement.

PRAYER

WHEREFORE, Plaintiffs pray for relief and judgment as follows:

(a) a judgment that the '881 patent remains valid and enforceable, and is infringed under 35 U.S.C. § 271(e)(2) by Cipher's filing of its NDA No. 21-612;

(b) an order that the effective date of the approval of NDA No. 21-612 be subsequent to the expiration date of the '881 patent;

(c) an injunction prohibiting Cipher from commercially manufacturing, selling, using, or importing the fenofibrate compositions claimed in the '881 patent or otherwise infringing one or more claims of said patent;

(d) damages and/or other monetary relief pursuant to 35 U.S.C. § 284 for any commercial manufacture, use or sale of fenofibrate compositions falling within the scope of one or more claims of the '881 patent by Cipher;

(e) a judgment that Cipher willfully infringed the '881 patent;

(f) an award of Plaintiffs' interest, costs, reasonable attorneys' fees and such other relief as the Court deems just and proper pursuant to 35 U.S.C. § 271(e)(4) and 35 U.S.C. § 285; and,

(g) such other and further relief as this Court may deem just and proper.

Respectfully submitted in San Juan, Puerto Rico, this 5th day of February, 2004.

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US006652881B2

(12) **United States Patent**
Stamm et al.

(10) Patent No.: US 6,652,881 B2
(45) Date of Patent: Nov. 25, 2003

EXHIBIT 1

(54) **FENOFIBRATE PHARMACEUTICAL COMPOSITION HAVING HIGH BIOAVAILABILITY**

(75) Inventors: André Stamm, Griesheim (FR); Pawan Seth, Irvine, CA (US)

(73) Assignee: Laboratories Fournier, S.A., Dijon (FR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 10/288,425

(22) Filed: Nov. 6, 2002

(65) Prior Publication Data

US 2003/0104051 A1 Jun. 5, 2003

Related U.S. Application Data

(63) Continuation of application No. 10/126,875, filed on Apr. 22, 2002, which is a continuation of application No. 10/078,500, filed on Feb. 21, 2002, which is a continuation of application No. 09/899,026, filed on Jul. 6, 2001, which is a continuation of application No. 09/572,330, filed on May 18, 2000, now Pat. No. 6,277,405, which is a continuation of application No. 09/005,128, filed on Jan. 9, 1998, now Pat. No. 6,074,670.

(30) Foreign Application Priority Data

Jan. 17, 1997 (FR) 97 00479

(51) Int. Cl.[7] A61K 9/58; A61K 9/48; A61K 9/20; A61K 9/14; A61K 9/54

(52) U.S. Cl. 424/462; 424/451; 424/452; 424/456; 424/458; 424/459; 424/464; 424/465; 424/489; 424/490; 424/492; 424/494; 427/213

(58) Field of Search 424/451, 452, 424/456, 458, 459, 462, 489, 490, 492, 494, 464, 465; 427/213

(56) References Cited

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4,800,079	A	*	1/1989	Boyer
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EP	0 793 958	9/1997
FP	0 256 933	2/1998
WO	WO 82/01649	5/1982
WO	WO 98/31361	7/1998

OTHER PUBLICATIONS

Temeljotov et al, Acta Pharm., 46:131–136 (1996).

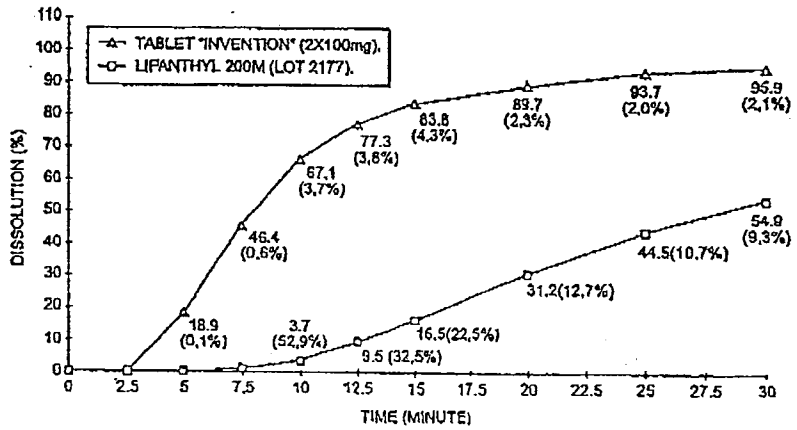
* cited by examiner

Primary Examiner—Thurman K. Page
Assistant Examiner—Humera N. Sheikh
(74) *Attorney, Agent, or Firm*—Hale and Dorr LLP

(57) **ABSTRACT**

The invention provides compositions comprising micronized fenofibrate, where the compositions have a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia, in a dissolution medium constituted by water with 2% by weight polysorbate 80 or 0.025 M sodium lauryl sulfate.

41 Claims, 2 Drawing Sheets



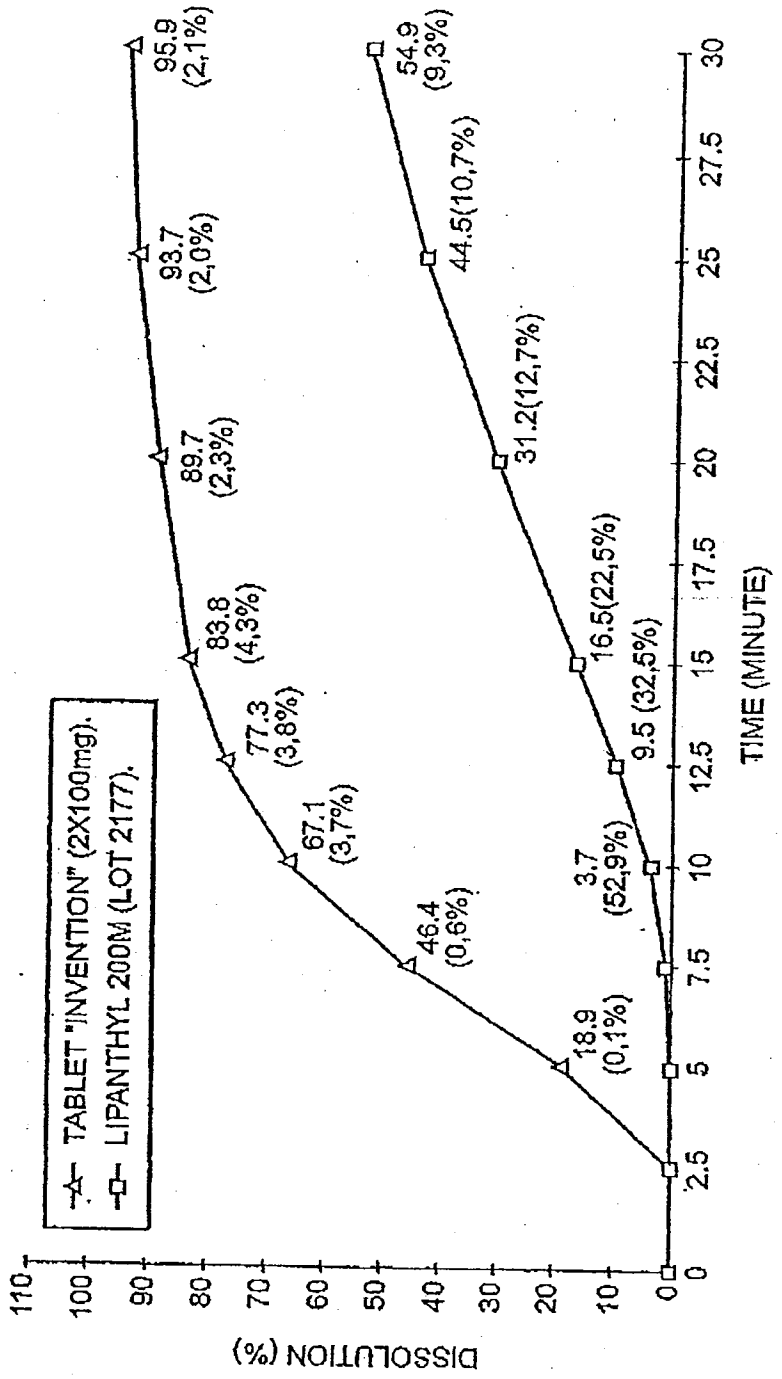

TABLET "INVENTION" (2X100mg).
LIPANTHYL 200M (LOT 2177).
DISSOLUTION (%)
TIME (MINUTE)
95.9 (2,1%)
93.7 (2,0%)
89.7 (2,3%)
83.8 (4,3%)
77.3 (3,8%)
67.1 (3,7%)
46.4 (0,6%)
18.9 (0,1%)
54.9 (9,3%)
44.5(10,7%)
31.2(12,7%)
16.5(22,5%)
9.5 (32,5%)
3.7 (52,9%)

FIG. 1