

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

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

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

**APPLICANT INFORMATION**

NAME OF APPLICANT Cipher Pharmaceuticals Ltd	DATE OF SUBMISSION 2/9/04
TELEPHONE NO. (Include Area Code) 905 696 9380	FACSIMILE (FAX) Number (Include Area Code) 905 602 0628
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Suite 201 Lauriston, Collymore Rock St. Michael, Barbados	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE 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) Fenofibrate	PROPRIETARY NAME (trade name) IF ANY Luxacor	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)	CODE NAME (If any)	
DOSAGE FORM: Capsules	STRENGTHS: 50, 100, 150 mg	ROUTE OF ADMINISTRATION: Oral

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

**APPLICATION DESCRIPTION**

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 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) <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input checked="" type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)
REASON FOR SUBMISSION Request for clarification of questions in FDA letter December 18, 2003
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>N/A</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> 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)

<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling (check one) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input checked="" type="checkbox"/>	20. OTHER (Specify) Letter

**CERTIFICATION**

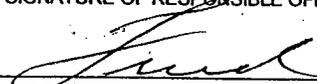
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. 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 Ian W. French, CSO Arthur M Deboeck, VP & General Manager	DATE: 9/2/04
ADDRESS (Street, City, State, and ZIP Code) US Agent, Galephar PR Inc., Juncos, Puerto Rico, 00777-3873		Telephone Number ( 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  
401 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.

***cipher***  
**Pharmaceuticals Limited**

No Cover Letter  
2-3-04  
Submission

ORIGINAL

XP

RECEIVED

FEB 12 2004

FDR/CDER

**PATENT CERTIFICATION**

**Paragraph IV Certification**  
**U.S. Patent No. 6,652,881 B2**

In accordance with the Federal Food, Drug and Cosmetic Act, as amended by Title XI of the Medicare Prescription Drug, Improvement and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003), 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. 6,652,881 B2 ("the '881 patent") is hereby provided for our New Drug Application ("NDA") ~~No. 21-612~~ for Fenofibrate Capsules 50, 100, 150 \_\_\_\_\_ 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 '881 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 \_\_\_\_\_ mg for which Cipher's application has been submitted, and/or that the '881 patent is invalid.

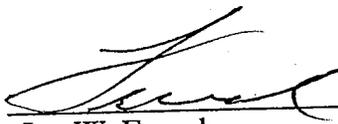
b(4)

**STATEMENT CONCERNING NOTICE TO  
PATENT OWNER AND NDA HOLDER**

As required by Section 505(b)(3)(B) of the Federal Food, Drug and Cosmetic Act, as amended by Title XI of the Medicare Prescription Drug, Improvement and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003), Cipher hereby states that the notice required by Section 505(b)(3) and 21 C.F.R. § 314.52 has been concurrently sent to Abbott Laboratories Inc., as the holder of approved NDA No. 21-203 for Tricor<sup>®</sup> (fenofibrate) 54 mg and 160 mg tablets and the exclusive licensee of U.S. Patent No. 6,652,881 B2, and to Laboratories Fournier S.A., as the record owner of U.S. Patent No. 6,652,881 B2.

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

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



---

Ian W. French  
Chief Scientific Officer  
Cipher Pharmaceuticals Ltd.

Feb 3, 2004  
Date

Appears This Way  
On Original

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
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FOR FDA USE ONLY

APPLICATION NUMBER

**APPLICANT INFORMATION**

NAME OF APPLICANT Cipher Pharmaceuticals Ltd.	DATE OF SUBMISSION 2/3/04
TELEPHONE NO. (Include Area Code) Contact 905-696-938	FACSIMILE (FAX) Number (Include Area Code) 246-228-8329
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Suite 201 Lauriston, Collymore Rock ST. Michaels Barbados	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Arthur M. Deboeck Galephar P.R. Inc. Road 198 No. 100 km 14/7 Juncos Industrial Park Juncos, Puerto Rico 00777-3873 Tel: 787-713-0340 Fax: 787-713-0344

**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) Fenofibrate	PROPRIETARY NAME (trade name) IF ANY CIP-Fenofibrate	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)	CODE NAME (If any)	
DOSAGE FORM: Capsules	STRENGTHS: 50, 100, 150 _____ mg	ROUTE OF ADMINISTRATION: Oral
(PROPOSED) INDICATION(S) FOR USE: Hypercholesterolemia, mixed dyslipidemia and hypertriglyceridemia		

**PRODUCT DESCRIPTION**

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 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 <u>Tricor Tablets</u> Holder of Approved Application <u>Abbott Laboratories</u>
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)
REASON FOR SUBMISSION Paragraph IV Certification - a new US patent # 6,652,881 was listed in the Orange Book
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC

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See original NDA for establishment information

**Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)**  
IND 62,780; DMFs: \_\_\_\_\_

This application contains the following items: (Check all that apply)

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<input type="checkbox"/>	2. Labeling (check one) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
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<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
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<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
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<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input checked="" type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input type="checkbox"/>	20. OTHER (Specify)

**CERTIFICATION**

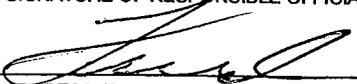
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. 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:

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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 Ian W. French, Ph.D., Chief Scientific Officer Arthur M. Deboeck, VP and General Manager	DATE: 2/3/04
ADDRESS (Street, City, State, and ZIP Code) , Arthur M. Deboeck, Galephar P. R. Inc. See original NDA for contact information		Telephone Number ( ) Cipher: 905-696-9380 Galephar: 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:

(XP) Stamp date  
Jan 28, 2004

***cipher***  
***Pharmaceuticals Limited***

January 25, 2004

Ms. V. Jimenez  
Food and Drug Administration  
Division of Metabolic and Endocrine Drug Products  
HFD-510  
Center for Drug Evaluation and Research  
Office of Drug Evaluation II  
5600 Fisher Lane  
Rockville, MD 20857

Fax 301-443-9282

Dear Ms. Jimenez:

Cipher Pharmaceuticals Ltd. should have submitted amendment to NDA 21-612 for the US # 6,589,552 patent to Notice of Patent Infringement Action. Abbott and Fournier sued Cipher Pharmaceuticals Ltd. in October, 2003.

I am attaching the 356h form and the letter of Filing of Patent Infringement Action. Cipher will send the original by courier.

Yours sincerely,



Ian W. French, Ph. D.  
Chief Scientific Officer

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

<p><b>DEPARTMENT OF HEALTH AND HUMAN SERVICES</b>  <b>FOOD AND DRUG ADMINISTRATION</b></p> <p><b>APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,  OR AN ANTIBIOTIC DRUG FOR HUMAN USE</b>  <i>(Title 21, Code of Federal Regulations, Parts 314 &amp; 601)</i></p>	<p><i>Form Approved: OMB No. 0910-0338  Expiration Date: August 31, 2005  See OMB Statement on page 2.</i></p>
<p><b>FOR FDA USE ONLY</b></p>	
<p>APPLICATION NUMBER</p>	

<b>APPLICANT INFORMATION</b>	
<p>NAME OF APPLICANT  <b>Cipher Pharmaceuticals Ltd.</b></p>	<p>DATE OF SUBMISSION  <b>1/25/04</b></p>
<p>TELEPHONE NO. <i>(Include Area Code)</i>  <b>Contact 905-696-938</b></p>	<p>FACSIMILE (FAX) Number <i>(Include Area Code)</i>  <b>905-602-0628</b></p>
<p>APPLICANT ADDRESS <i>(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):</i>  <b>Suite 201  Lauriston, Collymore Rock  ST. Michaels  Barbados</b></p>	<p>AUTHORIZED U.S. AGENT NAME &amp; ADDRESS <i>(Number, Street, City, State, ZIP Code, telephone &amp; FAX number) IF APPLICABLE</i>  <b>Arthur M. Deboeck  Galephar P.R. Inc.  Road 198 No. 100 km 14/7  Juncos Industrial Park  Juncos, Puerto Rico 00777-3873</b>      <b>Tel: 787-713-0340  Fax: 787-713-0344</b></p>

<b>PRODUCT DESCRIPTION</b>		
<p>NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER <i>(if previously issued)</i> <b>21-612</b></p>		
<p>ESTABLISHED NAME <i>(e.g., Proper name, USP/USAN name)</i>  <b>Fenofibrate</b></p>	<p>PROPRIETARY NAME <i>(trade name) IF ANY</i>  <b>CIP-Fenofibrate</b></p>	
<p>CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME <i>(if any)</i></p>		<p>CODE NAME <i>(if any)</i></p>
<p>DOSAGE FORM:  <b>Capsules</b></p>	<p>STRENGTHS:  <b>50, 100, 150 _____ng</b></p>	<p>ROUTE OF ADMINISTRATION:  <b>Oral</b></p>
<p>(PROPOSED) INDICATION(S) FOR USE:  <b>Hypercholesterolemia, mixed dyslipidemia and hypertriglyceridemia</b></p>		

<b>PRODUCT DESCRIPTION</b>		
<p>APPLICATION TYPE <i>(check one)</i></p> <p> <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50)      <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)  <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601) </p>		

<p>IF AN NDA, IDENTIFY THE APPROPRIATE TYPE      <input type="checkbox"/> 505 (b)(1)      <input checked="" type="checkbox"/> 505 (b)(2)</p>
<p>IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION</p> <p>Name of Drug    <u><b>Tricor Tablets</b></u>      Holder of Approved Application    <u><b>Abbott Laboratories</b></u></p>

<p>TYPE OF SUBMISSION <i>(check one)</i></p> <p> <input type="checkbox"/> ORIGINAL APPLICATION      <input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION      <input type="checkbox"/> RESUBMISSION  <input type="checkbox"/> PRESUBMISSION      <input type="checkbox"/> ANNUAL REPORT      <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT      <input type="checkbox"/> EFFICACY SUPPLEMENT  <input type="checkbox"/> LABELING SUPPLEMENT      <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT      <input type="checkbox"/> OTHER </p>
---

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  
**Notice of Filing of Patent Infringement Action**

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

NUMBER OF VOLUMES SUBMITTED      **1**        THIS APPLICATION IS   
 PAPER   
 PAPER AND ELECTRONIC   
 ELECTRONIC

**ESTABLISHMENT INFORMATION** *(Full establishment information should be provided in the body of the Application.)*  
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IND 62,780; DMFs: \_\_\_\_\_

b(4)

**This application contains the following items: (Check all that apply)**

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

**CERTIFICATION**

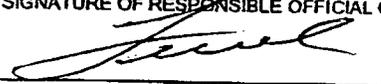
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. 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 Ian W. French, Ph.D., Chief Scientific Officer Arthur M. Deboeck, VP and General Manager	DATE: 1/25/04
ADDRESS (Street, City, State, and ZIP Code) U.S. Agent, Arthur M. Deboeck, Galephar P. R. Inc. See original NDA for contact information		Telephone Number ( ) Cipher: 905-696-9380 Galephar: 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:



**NOTICE OF FILING OF PATENT INFRINGEMENT ACTION**  
21 C.F.R. § 314.107(f)(2)

**CIP-Fenofibrate 50, 100, 150 \_\_\_\_\_ mg Capsules**  
**NDA # 21-612**

b(4)

The undersigned hereby certifies, pursuant to 21 C.F.R. § 314.107(f)(2), that on October 2, 2003, an action for patent infringement was filed by Abbott Laboratories ("Abbott"), and \_\_\_\_\_ and \_\_\_\_\_ (collectively \_\_\_\_\_), against Cipher Pharmaceuticals Limited ("Cipher") in the United States District Court for the District of Puerto Rico. Civil Action No. 03-2067 (DRD). The complaint in this action alleges infringement of only one of the three patents for which Cipher filed a Paragraph IV Certification, specifically, U.S. Patent No. 6,589,552

b(4)

b(4)

Dated: January 25, 2004

Ian W. French, Ph.D.  
Chief Scientific Officer

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Jan 7, 2004

# ***cipher*** ***Pharmaceuticals Limited***

January 7, 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 Fishers Lane  
Rockville, MD 20857

Re: **NDA 21-612**  
Luxacor (fenofibrate) Capsules 50 mg, 100 mg, 150 mg, \_\_\_\_\_ **b(4)**

Dear Dr. Orloff:

We refer to your letter of December 18, 2003 which was received by fax in our Canadian office earlier today. We understand that this was previously sent to our US Agent, Galephar P.R. Inc., in Puerto Rico on December 18, 2003. However, as discussed between Ms. Valerie Jimenez and Dr. Arshi Kizilbash today, the mailed copy was not received by Galephar until today.

At this time, we wish to notify you of our intent to file an amendment for this application to address the deficiencies noted in your letter of December 18, 2003, and to request that the submission should not be withdrawn because the 10 day timeframe in your letter of December 18, 2003 has been exceeded.

If you have any questions or comments, please do not hesitate to contact me at 905 696 9380 x 24, or you can contact \_\_\_\_\_

\_\_\_\_\_ regarding this submission, or on other related matters.

Yours sincerely,



Larry Andrews  
President  
Cipher Pharmaceuticals Ltd.

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Cc: FDA Central Document Room  
Arthur DeBoeck, Galephar PR Inc.

Suite 201, Lauriston, Collymore Rock  
St. Michael, Barbados  
Tel: (246) 228-9863 Fax: (246) 228-8329

***A Drug Development Company***

***cipher***  
*Pharmaceuticals Limited*

Suite 201, Lauriston, Collymore Rock,  
Saint Michael, Barbados  
Tel: (246) 288-9663 Fax: (246) 288-8329

# Fax

<b>To:</b> Valerie Jimenez	<b>From:</b> Larry Andrews
<b>Fax:</b> (301) 443-9282	<b>Pages:</b> 2 (including cover)
<b>Company:</b> FDA	<b>Date:</b> Jan 7, 2004
<b>Re:</b> NDA 21,612	<b>CC:</b>

**Urgent**     **For Review**     **Please Comment**     **Please Reply**     **Please Recycle**

If you do not receive a complete transmission, please call: (905) 602-0628

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12/17/03

**MEMO TO FILE**

**FROM:** WEI QIU, Ph.D.  
**TO:** NDA 21-612  
**SUBMISSION DATE:** Dec. 24, 2002 and Jan 10, 2003  
**SUBJECT:** Labeling comments

The following labeling text should be deleted:

Under CLINICAL PHARMACOLOGY Section Pharmacokinetics/Metabolism Subsection:

---

Hae-Young Ahn, Team Leader

---

Wei Qiu, Biopharm Reviewer

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/s/

-----  
Wei Qiu  
12/17/03 04:07:55 PM  
BIOPHARMACEUTICS

Hae-Young Ahn  
12/17/03 05:05:54 PM  
BIOPHARMACEUTICS

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12/17/03

**DIVISION OF METABOLIC AND ENDOCRINE DRUG PRODUCTS**

**PROJECT MANAGER LABELING REVIEW**

**Application:** NDA 21-612 Luxacor (fenofibrate) Capsules, 50 mg, 100 mg, 150 mg, \_\_\_\_\_

b(4)

**Submission Date:** December 24, 2002; Receipt date December 26, 2002.

**Material reviewed:**

The draft labeling for this 505(b)(2) NDA was compared to the September 4, 2001, approved labeling text for the reference listed drug, Tricor Tablets, 54 and 160 mg, NDA 21-203.

**Background**

This drug is proposed to be indicated as adjunctive therapy to diet to reduce elevated LDL-C, Total-C, Triglycerides and Apo B, and to increase HDL-C in adult patients with primary hypercholesterolemia or mixed dyslipidemia (Fredrickson Types IIa and IIb. It is also indicated as adjunctive therapy to diet for the treatment of adult patients with hypertriglyceridemia (Fredrickson Types IV and V hyperlipidemia). The drug is supplied in 90-count bottles for each of the four strengths.

**Review**

1. Name change → "Tricor" has been changed to "CIP-Fenofibrate" throughout the labeling.

DMETS found this name unacceptable. The firm submitted the name "Luxacor" subsequently and it was approved by DMETS and DDMAC. DMEDP concurs. The firm should replace "CIP-FENOFIBRATE" with "Luxacor".

**PACKAGE INSERT (PI)**

2. Under the **DESCRIPTION** section

- The text "hard gelatin capsules" replaces "tablets" in the Tricor label.
- The dosage is changed to 50, 100, 150, a \_\_\_\_\_ mg from 54 and 160mg in the Tricor Tablets label.
- The inactive ingredients differ.

b(4)

The chemistry review requires that the sponsor replace " \_\_\_\_\_ " with "Gelucire 44/14 (lauryoyl macrogol glycerides type 1500)" as described in the application; replace " \_\_\_\_\_ " with "polyethylene glycol 20,000" and "polyethylene glycol 8000" which are specific materials; and include "gelatin and titanium dioxide."

b(4)

3. Under the **CLINICAL PHARMACOLOGY** section

- **Pharmacokinetics/Metabolism** subsection, the Tricor label was changed from "Plasma concentrations of fenofibric acid after administration of 54 mg and 160 mg tablets are equivalent under fed conditions to 67 and 200 mg capsules, respectively" to \_\_\_\_\_

b(4)

# 3 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

These changes are acceptable according to the chemistry reviewer and if the proprietary name is changed to \_\_\_\_\_

b(4)

7. The Storage section says "\_\_\_\_\_ although the bottle labels state "Protect from moisture and light."

b(4)

The chemistry review requires that the package insert be revised to use the same statement as on the bottle labels.

8. The pharmacology review requires replacement of the "\_\_\_\_\_ and \_\_\_\_\_ subsections. (Note: The usual title for the former subsection is "Carcinogenesis, Mutagenesis, and Impairment of Fertility." Some information regarding female fertility is included in the "Teratogenic Effects" section.)

b(4)

**BOTTLE LABELS**

9. The \_\_\_\_\_ bottle labels add the term "\_\_\_\_\_ to the label.

b(4)

This is unacceptable and must be removed.

**RECOMMENDATIONS:**

Draft an approvable (AE) letter that includes the CMC deficiencies and the labeling changes recommended above plus the revisions to two subsections of the PRECAUTIONS section recommended by Dr. Antonipillai.

Reviewed by: {See attached electronic signature page.}

\_\_\_\_\_  
Enid Galliers  
CPMS, DMEDP

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/s/

-----  
Enid Galliers  
12/17/03 12:51:21 PM  
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**NDA REGULATORY FILING REVIEW**  
**(Including Memo of Filing Meeting)**

NDA # 21-612

Supplement # N/A

Trade Name: **Luxacor** (fenofibrate) Capsules

(DMETS approved trade name 11/06/03)

Generic Name: Fenofibrate Capsules

Strengths: 50, 100, 150, ~~200~~ mg **b(4)**

Applicant: Cipher Pharmaceuticals, Limited

U.S. Agent: Galephar

Date of Application: December 24, 2003

Date of Receipt: December 26, 2003

Date clock started after UN: February 26, 2003

Date of Filing Meeting: April 15, 2003

Filing Date: April 27, 2003

74-Day letter issue date: May 7, 2003

Action Goal Date (optional): December 17, 2003

User Fee Goal Date: December 26, 2003

Indication(s) requested: Reduction of LDL-C, Total-C, TG, Apo-B, and increase HDL-C in adults with primary hypercholesterolemia (IIA & IIB) and adults with hypertriglyceridemia (Type IV & V).

Type of Application: Original (b)(1) NDA \_\_\_\_\_ Original (b)(2) NDA   X    
(b)(1) Supplement \_\_\_\_\_ (b)(2) Supplement \_\_\_\_\_  
[If the Original NDA was a (b)(2), all supplements are (b)(2)s; if the Original NDA was a (b)(1), the supplement can be either a (b)(1) or a (b)(2).]

NOTE: If the application is a 505(b)(2) application, complete the 505(b)(2) section at the end of this summary.

Therapeutic Classification: S   X   P \_\_\_\_\_  
Resubmission after a withdrawal?   No   Resubmission after a refuse to file?   No    
Chemical Classification: (1,2,3 etc.)   3    
Other (orphan, OTC, etc.)   N/A  

User Fee Status: Paid   X   Waived (e.g., small business, public health) \_\_\_\_\_  
Exempt (orphan, government) \_\_\_\_\_

Form 3397 (User Fee Cover Sheet) submitted:   YES  

User Fee ID # **4494**

Clinical data? YES \_\_\_\_\_ **NO**, Referenced to NDA #   21-203  

Is there any 5-year or 3-year exclusivity on this active moiety in either a (b)(1) or a (b)(2) application?  
(Note: The 3-year exclusivity for Fredericksons Iia + Iib (indication) expired April 24, 2003.)

**NO**

If yes, explain:

Does another drug have orphan drug exclusivity for the same indication?

**NO**

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?

N/A

Is the application affected by the Application Integrity Policy (AIP)?  
If yes, explain.

NO

If yes, has OC/DMPQ been notified of the submission?

YES

• Does the submission contain an accurate comprehensive index?

YES

• Was form 356h included with an authorized signature?

NO

**If foreign applicant, both the applicant and the U.S. agent must sign.**

**Eventually FDA received 356h forms signed by either the applicant or the agent, not by both.**

• Submission complete as required under 21 CFR 314.50?

YES

If no, explain: (Note: A comprehensive index and various required forms were submitted as amendments.)

• If an electronic NDA, does it follow the Guidance?

NO

**If an electronic NDA, all certifications must be in paper and require a signature. YES**

Which parts of the application were submitted in electronic format?

Partially electronic submission of biopharmaceutics data sets. Some parts were not readable, but were corrected.

• If in Common Technical Document format, does it follow the guidance?

YES

When submitted in paper, it did not contain an comprehensive table of contents (TOC) with unique identifiers that corresponded with the CDR volume numbering system. A revised TOC was submitted as an amendment.

• Is it an electronic CTD?

NO

**If an electronic CTD, all certifications must be in paper and require a signature.**

Which parts of the application were submitted in electronic format?

• Patent information included with authorized signature?

YES

• Exclusivity requested?

NO

Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

• Correctly worded Debarment Certification included with authorized signature?

YES (applicant)

NO (agent)

**The certification submitted by the agent, Mr. Deboeck, included "to the best of my knowledge."**

**If foreign applicant, both the applicant and the U.S. Agent must sign the certification.**

**-Certifications signed by the applicant and the agent were submitted separately.**

**NOTE:** Debarment Certification must have correct wording, e.g.: "I, the undersigned, hereby certify that \_\_\_\_\_ Co. did not and will not use in any capacity the services of any person debarred under

section 306 of the Federal Food, Drug and Cosmetic Act in connection with the studies listed in Appendix \_\_\_\_.” Applicant may not use wording such as “To the best of my knowledge . . . .”

- Financial Disclosure information included with authorized signature? YES  
(Forms 3454 and/or 3455 must be used and must be signed by the APPLICANT.)  
Individual investigator forms were submitted, but the applicant did not submit either form.
- Field Copy Certification (that it is a true copy of the CMC technical section)? YES

**Refer to 21 CFR 314.101(d) for Filing Requirements**

- PDUFA and Action Goal dates correct in COMIS? YES  
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name/Applicant name correct in COMIS? If not, have the Document Room make the corrections.
- List referenced IND numbers: IND 62,780
- End-of-Phase 2 Meeting(s)? Date(s) \_\_\_\_\_ NO  
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) 7/23/02 YES  
If yes, distribute minutes before filing meeting.

**Project Management**

- Package insert consulted to DDMAC? YES
- Trade name (plus PI and all labels and labeling) consulted to ODS/Div. of Medication Errors and Technical Support? YES
- MedGuide and/or PPI (plus PI) consulted to ODS/Div. of Surveillance, Research and Communication Support? N/A
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A

**If Rx-to-OTC Switch application:**

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/ Div. of Surveillance, Research and Communication Support? N/A
- Has DOTCDP been notified of the OTC switch application? N/A

**Clinical**

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? N/A

**Chemistry**

- Did applicant request categorical exclusion for environmental assessment? YES  
If no, did applicant submit a complete environmental assessment? N/A  
If EA submitted, consulted to Nancy Sager (HFD-357)? N/A
- Establishment Evaluation Request (EER) submitted to DMPQ? YES
- If parenteral product, consulted to Microbiology Team (HFD-805)? N/A

**If 505(b)(2) application, complete the following section:**

- Name of listed drug(s) and NDA/ANDA #: **NDA 21-203 Tricor Tablets, 54 mg, 160 mg (cited in 356h);**  
(Relevant but not cited by applicant: NDA 19-304 Tricor Capsules, 67 mg, 134 mg, 200 mg)
- Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").  
**This application provides for a capsule dosage form with strengths different from NDA 19-304, which is not marketed. One of the — Luxacor capsule strengths is the same as one of the two marketed Tricor Tablet strengths.** **b(4)**
- Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs.) NO
- Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 314.101(d)(9). NO
- **Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD? (See 314.54(b)(2)). If yes, the application should be refused for filing under 314.101(d)(9).** NO
- Which of the following patent certifications does the application contain? Note that a patent certification must contain an authorized signature.
  - \_\_\_ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA.
  - \_\_\_ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired.
  - \_\_\_ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire.
  - X  21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted.

*IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must submit a signed certification that the patent holder was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].*

- **The applicant submitted proof of notification and notification that the patent holder, Abbott Labs, had filed suit to contest this patent issue.**

\_\_\_ 21 CFR 314.50(i)(1)(ii): No relevant patents.

\_\_\_ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications.

\_\_\_ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)

\_\_\_ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

- Did the applicant:
  - Identify which parts of the application rely on information the applicant does not own or to which the applicant does not have a right of reference?
 

	YES	NO
--	-----	----
  - Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?
 

	YES	
--	-----	--
  - Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?
 

	YES	
--	-----	--
  - Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?
 

		NO
--	--	----
- If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):
 

	N/A	
--	-----	--

  - Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).
 

	YES	NO
--	-----	----
  - A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.
 

	YES	NO
--	-----	----
  - EITHER  
 The number of the applicant's IND under which the studies essential to approval were conducted.

YES, IND # \_\_\_\_\_ NO

OR

A certification that it provided substantial support of the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

N/A YES NO

- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?

YES

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ATTACHMENT

MEMO OF FILING MEETING

DATE: April 15, 2003

BACKGROUND: This is a 505(b)(2) NDA for fenofibrate capsules in \_\_\_\_\_ strengths, 50 mg, 100 mg, 150 mg. \_\_\_\_\_ The innovator, Abbott Labs, is not marketing its approved 67 mg, 134 mg, or 200 mg capsules (NDA 19-304). However, Abbott is marketing tablets approved in 54 mg and 160 mg strengths (NDA 21-203).

b(4)  
b(4)

(Provide a brief background of the drug, e.g., it was already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES:

ASSIGNED REVIEWERS:

**Discipline**

**Reviewer**

Medical:	Mary Parks, M.D.
Secondary Medical:	N/A
Statistical:	J. Todd Sahlroot, Ph.D.
Pharmacology:	Indra Antonipillai, Ph.D.
Statistical Pharmacology:	N/A
Chemist:	William Adams, Ph.D.
Environmental Assessment (if needed):	
Biopharmaceutical:	Wei Qiu, Ph.D.
Microbiology, sterility:	N/A
Microbiology, clinical (for antimicrobial products only):	N/A
DSI:	
Regulatory Project Manager:	Bill Koch (subsequently re-assigned to Valerie Jimenez)
Other Consults:	N/A

Per reviewers, are all parts in English or English translation? YES  
If no, explain:

CLINICAL FILE  X  REFUSE TO FILE \_\_\_\_\_

- Clinical site inspection needed: NO
- Advisory Committee Meeting needed? NO
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

N/A

CLINICAL MICROBIOLOGY		N/A	
STATISTICS	FILE _____	REFUSE TO FILE _____	N/A
BIOPHARMACEUTICS	FILE <u> X </u>	REFUSE TO FILE _____	
	• Biopharm. inspection needed:		YES
PHARMACOLOGY	FILE <u> X </u>	REFUSE TO FILE _____	
	• GLP inspection needed:		NO
CHEMISTRY	FILE <u> X </u>	REFUSE TO FILE _____	
	• Establishment(s) ready for inspection?		YES
	• Microbiology		NO

**ELECTRONIC SUBMISSION:**

Any comments: Some of the electronic documents cannot be opened.

**REGULATORY CONCLUSIONS/DEFICIENCIES:**

\_\_\_\_\_ The application is unsuitable for filing. Explain why:

X  The application, on its face, appears to be well organized and indexed. The application appears to be suitable for filing.

X  No filing issues have been identified.

\_\_\_\_\_ Filing issues to be communicated by Day 74. List (optional):

**ACTION ITEMS:**

1. Document filing issues/no filing issues conveyed to applicant by Day 74.

*{See attached electronic signature page.}*

\_\_\_\_\_  
Enid Galliers on behalf of William Koch (for meeting minutes)  
and on behalf of Valerie Jimenez (for PM administrative review)  
Regulatory Project Manager, HFD-510

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/s/

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Enid Galliers  
12/12/03 07:40:47 PM  
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Suite 201, Lauriston, Collymore Rock,  
Saint Michael, Barbados  
Tel: (246) 288-9663 Fax: (246) 288-8329

# Fax

**To:** Valerie Jimenez  
Division of Metabolic and Endocrine  
Drug Products  
FDA  
**From:** Ian W. French

**Fax:** (301) 443-9282 **Pages:** 5 (including cover)

**Phone:** **Date:** Dec 08, 2003

**Re:** NDA # 21,612 **CC:**

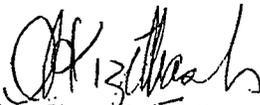
- Urgent     For Review     Please Comment     Please Reply     Please Recycle

If you do not receive a complete transmission, please call: (905) 602-0628, x23

Dear Ms Jimenez,

Please find attached a letter and corrected form FDA 356h related to proposed indication for Fenofibrate capsules.

Thank you.

  
Ian French, PhD  
Chief Scientific Officer

This fax transmission is privileged and contains confidential information intended only for the person(s) named above. Any other distribution, copying or disclosure is strictly prohibited. If you have received this fax transmission in error, please notify the sender immediately and destroy these pages promptly. We thank you for your cooperation.

# ***cipher***

***Pharmaceuticals Limited***

December 08, 2003

Valerie Jimenez  
Regulatory Project Manager  
Division of Metabolic and Endocrine Drug Products (HFD-510)  
Parklawn Building  
5600 Fishers Lane  
Rockville  
MD 20857-1706

Fax No: (301) 443-9282

**Re: NDA # 21,612**  
CIP-Fenofibrate (fenofibrate capsules)  
Proposed Indications for Use

Dear Ms Jimenez,

We refer to NDA # 21,612 which is currently under review, and a telephone conversation between you and Dr. Arshi Kizilbash of Cipher Canada Inc. on December 01, 2003.

In September, 2003, we received a copy of the Establishment Inspection Report for Galephar PR Inc., where the fenofibrate capsules that are the subject of this NDA are manufactured. On review of this document, we noted that the proposed indications for use were listed as "FFB is indicated for patients with Type IV & V hypercholesterolemia and hyperlipidemia". On further review of our own files, we realized that the original Form FDA 356h that was submitted with the NDA identified the proposed indications as "For Type IV and V hypercholesterolemia", while the draft labelling submitted with the NDA proposes that the indications include the following (bolding added here for clarity):

"CIP-Fenofibrate is indicated as adjunct therapy to diet to reduce elevated LDL-C, Total-C, Triglycerides and Apo B, and to increase HDL-C in adult patients with primary hypercholesterolemia or mixed dislipidemia (**Fredrickson Type IIa and IIb**)"

and

"CIP\_Fenofibrate is also indicated as adjunct therapy to diet for the treatment of adult patients with Hypertriglyceridemia (**Fredrickson Type IV and V hyperlipidemia**)".

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

*A Drug Development Company*

At this time, we would like to provide a revised Form FDA 356h that correctly reflects the proposed indications for use. A copy of the revised Form FDA 356h is attached for your files. We apologize for any inconvenience that Cipher's administrative error has caused.

If you have any questions, please do not hesitate to call me at (905) 602-0628 —

**b(4)**

Yours sincerely,



† Ian W. French, PhD  
Chief Scientific Officer

cc: Central Document Room

Appears This Way  
On Original

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

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

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,  
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**  
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

**APPLICANT INFORMATION**

NAME OF APPLICANT Cipher Pharmaceuticals Limited	DATE OF SUBMISSION 12/8/03
TELEPHONE NO. (Include Area Code) Contact # (905) 696-9380	FACSIMILE (FAX) Number (Include Area Code) (905) 602-0628
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Suite 201 Lauriston, Collymore Rock St. Michael, Barbados	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Arthur M. Deboeck Galephar PR Inc. Road 198 No. 100 km 14.7 Juncos Industrial Park, Juncos 00777-3873 Puerto Rico

**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) Fenofibrate	PROPRIETARY NAME (trade name) IF ANY Luxacor	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)	CODE NAME (If any)	
DOSAGE FORM: Capsules	STRENGTHS: 50, 100, 150 mg	ROUTE OF ADMINISTRATION: Oral
(PROPOSED) INDICATION(S) FOR USE: For Type IIa, IIb, IV and V dyslipidemia		

b(4)

**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 PENDING 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  
Correction of information related to proposed indications as submitted with original Form FDA 356h dated December 24, 2002

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

NUMBER OF VOLUMES SUBMITTED NA 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) Letter and corrected Form FDA 356h

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 Ian W. French, CSO Arthur M. Deboeck, VP & General Manager	DATE: 12/8/03
ADDRESS (Street, City, State, and ZIP Code) US Agent, Galephar PR Inc.		Telephone Number ( 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  
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.

***cipher***  
Pharmaceuticals Limited

N 000 C  
NEW CORRESP

ORIGINAL RECEIVED  
DEC 09 2003  
CDR/CDER

December 8, 2003

Central Document Room  
Food and Drug Administration  
12229 Wilkins Avenue  
Rockville, Maryland  
20852

RECEIVED  
DEC 10 2003  
FDR/CDER

Re: NDA # 21,612  
CIP-Fenofibrate Capsules  
Proposed Indications For Use

Dear Sir/Madam,

Please find enclosed an archival copy of the cover letter and corrected FDA Form 356h from Cipher Pharmaceuticals Limited regarding the proposed indications for the CIP-Fenofibrate (Luxacor) capsules.

A copy of the letter and FDA Form 356h has already been faxed to Ms. Valerie Jimenez, Project Manager, Division of Metabolic and Endocrine Drug Products.

Thank you.

  
Ian W. French, PhD  
Chief Scientific Officer

Appears This Way  
On Original

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

*A Drug Development Company*

# ***cipher*** **Pharmaceuticals Limited**

**RECEIVED**  
DEC 04 2003  
FDR/CDER

December 02, 2003

Ms. Valerie Jimenez  
Regulatory Project Manager  
Food and Drug Administration  
Division of Metabolic and Endocrine Drug Products  
Parklawn Building  
5600 Fishers Lane  
Rockville, MD 20857-1706

Via Fax: (301) 443-9282

**Re: Cipher Regulatory Contact**  
**IND # 62,780; NDA # 21,612 (Cipher Fenofibrate Capsules)**

Dear Ms. Jimenez,

Please be advised that Cipher Pharmaceuticals Limited has contracted the services of a regulatory consulting company. \_\_\_\_\_

b(4)

In addition to our US agent, Galephar PR Inc., \_\_\_\_\_

b(4)

b(4)

The fax number for all official correspondence to Cipher remains (905) 602-0628. A list of relevant Cipher contacts is attached with this letter.

Please feel free to contact me if you have any questions.

Thank you,

*Larry Andrews*

Larry Andrews  
President  
Cipher Pharmaceuticals Ltd.

cc.: FDA Central Document Room b(4)

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

***cipher***  
Pharmaceuticals Limited

November 7, 2003

ORIGINAL

RECEIVED  
NOV 12 2003  
FDR/CDER

Ms. V. Jimenez  
Regulatory Project Manager  
Division of Metabolic and Endocrine Drug Products  
Office Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Room 845  
5600 Fishers Lane  
Rockville, MD 20857

ORIG AMENDMENT  
N000BB

Dear Ms. Jimenez:

Enclosed, find 3 copies of biopharmaceutical study (PMRI No. 2003-647: CIPHER No. FENPK.03.01) that we conducted after we sent the NDA 21-612 into the FDA. This single dose study was compared to Tricor Tablets 160 mg and CIPHER Capsules — and both products were administered with a low fat breakfast. CIPHER product is bioequivalent with Tricor Tablets under these conditions.

b(4)

I indicated on each volume (5 volumes in total) original (copy 1), copy 2, and copy 3. There is SAS disk in copy 1 (original) and copy 2. I have also enclosed a CD-ROM with the entire 2003-647 study on it and the SAS files, as well.

I have filled out a FDA 356 Form as required, and that is in the 1<sup>st</sup> volume of copy 1, 2 and 3. This cover is letter is volume 1 of each copy.

If you need an more information call me or Arthur Deboeck at Galephar P.R. Inc. in Puerto Rico. The numbers are on the form 356.

Yours sincerely,



Ian W. French, Ph. D.  
Chief Scientific Officer

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

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

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,  
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**  
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

**APPLICANT INFORMATION**

NAME OF APPLICANT CIPHER PHARMACEUTICALS LTD.	DATE OF SUBMISSION 11/7/03
TELEPHONE NO. (Include Area Code) Contact 905-696-9380	FACSIMILE (FAX) Number (Include Area Code) 246-228-8319
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Suite 201 Lauriston, Collymore Rock St. Michaels, BARBADOS	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Arthur M. DeBoeck Galephar P. R. Inc. Road 198 No. 100 km 14.7 Juncos Industrial Park Juncos, Puerto Rico 00777-3873 Tel: 787-713-0340 Fax: 787-713-0344

**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) FENOFIBRATE	PROPRIETARY NAME (trade name) IF ANY N/A	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) FENOFIBRATE	CODE NAME (If any)	
DOSAGE FORM: Capsules	STRENGTHS: 50, 100, 150 mg	ROUTE OF ADMINISTRATION: Oral
(PROPOSED) INDICATION(S) FOR USE: Hypercholesterolemia, mixed dyslipidemia and hypertriglyceridemia		

**APPLICATION DESCRIPTION**

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 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 <u>Tricor Tablets</u> Holder of Approved Application <u>Abbott Laboratories Inc.</u>
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO APENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)

**REASON FOR SUBMISSION**

Additional Biopharmaceutics Study Under Low Fat Meal Study No. 2003-647 (FENPK-03.01)

PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>5 (3 copies)</u> THIS APPLICATION IS <input type="checkbox"/> PAPER <input checked="" type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> 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.

See original NDA for establishment information

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

IND 62,780,; DMFs \_\_\_\_\_ **b(4)**

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

**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 Ian W. French, Ph. D., Chief Scientific Officer (Cipher Pharmaceuticals Ltd.) Arthur M. DeBoeck, VP & Heneral Manager (Galephar P. R. Inc.)	DATE: 10/25/03
---	--	-------------------

ADDRESS <i>(Street, City, State, and ZIP Code)</i> U. S. Agent: Arthur M. DeBoeck, Galephar P. R. Inc. See above and original NDA for contact information.	Telephone Number ( 905 ) 686-9380 (Cipher) Galephar 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:

1   Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)



October 15, 2003

Ms. Valerié Jimenez  
Regulatory Project Manager  
Division of Metabolic and Endocrine Drug Products (HFD-510)  
Parklawn Building  
5600 Fishers Lane  
Rockville,  
MD 20857-1706

Fax: (301) 443-9282

**Re: NDA 21-612; FDA Request for CIP-Fenofibrate Name Change**

Dear Ms. Jimenez:

With reference to your telephone call to Cipher on August 7, 2003 and the advice of the Division to propose another name for CIP-Fenofibrate as presented in the NDA #21-612, Cipher recommends the name **LUXACOR** for the fenofibrate product.

Thank you.

Sincerely,

A handwritten signature in black ink, appearing to read "Arshi Kizilbash".

Arshi Kizilbash, MD  
Director, Medical Affairs

Appears This Way  
On Original

**Cipher Canada Inc.**

6560 Kennedy Road  
Mississauga, Ontario  
L5T 2X4  
Tel. (905) 696-9380  
Fax (905) 602-0628

**Fax**

<b>To:</b> Ms. Valerie Jimenez	<b>From:</b> Arshi Kizilbash, M.D.
<b>Fax:</b> (301) 443-9282	<b>Pages:</b> 2 (including cover page)
<b>Company:</b> Div of Metabolic and Endocrine Drug Products (HFD-510)/FDA	<b>Date:</b> October 15, 2003
<b>Re:</b> NDA # 21-612	<b>CC:</b>

**If you do not receive a complete transmission, please call: (905) 696-9380**

**• Comments:**

This fax transmission is privileged and contains confidential information intended only for the person(s) named above. Any other distribution, copying or disclosure is strictly prohibited. If you have received this fax transmission in error, please notify the sender immediately and destroy these pages promptly. We thank you for your cooperation.

***cipher***  
**Pharmaceuticals Limited**

RECEIVED  
MAY 08 2003  
FDR/CDER

May 6, 2003

Ms. Valerie Jimenez  
Regulatory Project Manager  
Division of Metabolic and Endocrine Drug Products (HFD-510)  
Parklawn Building  
5600 Fishers Lane  
Rockville, MD 20857-1706

NEW CORRESP

ORIGINAL

N-000-C

**Re: NDA 21-612; Notice of Filing of Patent Infringement Action**

Dear Ms. Jimenez:

Enclosed is one volume containing the notice of filing of patent infringement action.

If you require any further information or clarification, please do not hesitate to contact me at 905-696-9380 \_\_\_\_\_ or our U.S. agent in Puerto Rico, Mr. Arthur Deboeck at 787-713-0340 (adeboeck@galephar.com).

b(4)

Yours sincerely,



Ian W. French, Ph.D.  
Chairman & Chief  
Scientific Officer

Appears This Way  
On Original

March 24, 2003

Ms. Valerie Jimenez  
Regulatory Project Manager  
Division of Metabolic and Endocrine Drug Products (HFD-510)  
Parklawn Building  
5600 Fishers Lane  
Rockville, MD 20857-1706

NOV 27 2003  
NEW CORRESP

**Re: NDA 21-612; Cipher Fenofibrate Capsules; Request for Additional Information**

Dear Ms. Jimenez:

Enclosed is one volume of additional information in response to your request by facsimile of March 17, 2003.

Enclosed in this volume is:

1. Completed and signed form FDA 356h.
2. Revised completed and signed User Fee Cover Sheet (form FDA 3397).
3. Debarment certification for Galephar PR Inc.
4. Completed and signed form FDA 3454.
5. Statement of notice of paragraph IV patent certification, and letter acknowledging receipt of notice.
6. Eight (8) copies of the revised table of contents with the requested FDA volume numbering alongside the original Cipher volume numbering.

If you require any further information or clarification, please do not hesitate to contact me at 905-696-9380 \_\_\_\_\_ or our U.S. agent in Puerto Rico, Mr. Arthur Deboeck at 787-713-0340 (adeboeck@galephar.com).

Yours sincerely,



Ian W. French, Ph.D.  
Chairman & Chief  
Scientific Officer

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

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

Cipher Pharmaceuticals Limited

DATE OF SUBMISSION

March 24, 2003

TELEPHONE NO. (Include Area Code)

NA Contact 905-696-9380

FACSIMILE (FAX) Number (Include Area Code)

246-228-8329

APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):

Suite 201  
Lauriston, Collymore Rock  
St. Michael, BARBADOS

AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE

Arthur M. Deboeck  
Galephar PR Inc.  
Road 198 No. 100 km 14.7  
Juncos Industrial Park  
Juncos 00777-3873  
Puerto Rico

Tel: (787) 713-0340

Fax: (787) 713-0344

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)

Fenofibrate

PROPRIETARY NAME (trade name) IF ANY

CIP-Fenofibrate

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)

CODE NAME (If any)

DOSAGE FORM:

Capsules

STRENGTHS:

50, 100, 150 mg

ROUTE OF ADMINISTRATION:

Oral

(PROPOSED) INDICATION(S) FOR USE:

Hypercholesterolemia, Mixed Dyslipidemia and Hypertriglyceridemia

APPLICATION INFORMATION

APPLICATION TYPE

(check one)

NEW DRUG APPLICATION (21 CFR 314.50)

ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)

BIOLOGICS LICENSE APPLICATION (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 Tricor Tablets

Holder of Approved Application

Abbott Laboratories

TYPE OF SUBMISSION (check one)

ORIGINAL APPLICATION

AMENDMENT TO A PENDING 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

Response to request for additional information

PROPOSED MARKETING STATUS (check one)

PRESCRIPTION PRODUCT (Rx)

OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED

1

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.

See attached sheet for Establishment Information.

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

ID 62,780, DMFs:

b(4)

This application contains the following items: (Check all that apply)

<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling (check one) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input checked="" type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input checked="" type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input checked="" type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input checked="" type="checkbox"/>	20. OTHER (Specify) Revised Table of Contents, Form 3454

**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 Dr. I. W. French, President and COO Arthur M. Deboeck, Vice President & General Manager	DATE: March 24, 2003
ADDRESS (Street, City, State, and ZIP Code) U.S. Agent, Galephar P.R. Inc. See attachment for address & contact numbers		Telephone Number Cipher: (905)696-9380 Galephar: (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.

***cipher***

***Canada Inc.***

N-000-C  
NEW CORRESP

ORIGINAL

January 10, 2003

RECEIVED

JAN 13 2003

CDR/CDER

Central Document Room (HFD-94)  
Center for Drug Evaluation and Research  
Food and Drug Administration  
12229 Wilkins Avenue  
Rockville, MD 20852

RECEIVED

JAN 14 2003

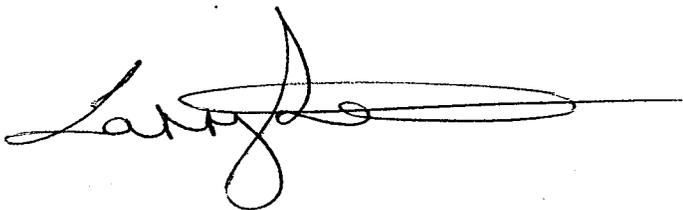
FDR/CDER

**Re: Cipher Oral Fenofibrate Capsules NDA (Application N 21612)  
Resubmission of Electronic Files**

Please find enclosed 2 binders of electronic files in response to your facsimile of December 24, 2002; one binder containing the electronic files for the Clinical-Pharmacokinetics and Bioavailability review copy of the NDA and one binder containing the electronic files for the archival copy of the NDA. The resubmitted electronic files are in the required format specified in the electronic NDA guidance.

I trust that the electronic media submission is now acceptable and review of this application can begin.

Yours sincerely,



Appears This Way  
On Original

Larry S. Gontovnick, Ph.D.  
Vice-President, Clinical Development and Regulatory Affairs

No Cover Letter

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
Expiration Date: April 30, 2000  
See OMB Statement on page 2.

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

21-612

APPLICANT INFORMATION

NAME OF APPLICANT  
Cipher Pharmaceuticals Limited

DATE OF SUBMISSION  
December 24, 2002

TELEPHONE NO. (Include Area Code)  
NA Contact 905-696-9380

FACSIMILE (FAX) Number (Include Area Code)  
246-228-8329

APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):

Suite 201  
Lauriston, Collymore Rock  
St. Michael, BARBADOS

RECEIVED  
DEC 26 2002

AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code telephone & FAX number) IF APPLICABLE

Arthur M. Deboeck  
Galephar PR Inc.  
Road 198 No. 100 km 14.7  
Juncos Industrial Park  
Juncos 00777-3873  
Puerto Rico

Tel: (787) 713-0340  
Fax: (787) 713-0344

PRODUCT DESCRIPTION

CDR/CDER

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) NA

ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Fenofibrate

PROPRIETARY NAME (trade name) IF ANY CIP-Fenofibrate

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)

CODE NAME (If any)

DOSAGE FORM: Capsules

STRENGTHS: 50, 100, 150 mg

ROUTE OF ADMINISTRATION: Oral

(PROPOSED) INDICATION(S) FOR USE: For Type IV and V hypercholesterolemia.

b(4)

APPLICATION INFORMATION

APPLICATION TYPE  
(check one)

NEW DRUG APPLICATION (21 CFR 314.50)

ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 31.94)

BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE

505 (b) (1)

505 (b) (2)

507

IF AN ANDA, OR AADA, 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 A PENDING APPLICATION

RESUBMISSION

PRESUBMISSION

ANNUAL REPORT

ESTABLISHMENT DESCRIPTION SUPPLEMENT

SUPAC SUPPLEMENT

EFFICACY SUPPLEMENT

LABELING SUPPLEMENT

CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT

OTHER

REASON FOR SUBMISSION This is for a 505(b)(2) filing for this formulation of fenofibrate and for an indication for Type IV and IV hypercholesterolemia with supporting literature evidence.

PROPOSED MARKETING STATUS (check one)

PRESCRIPTION PRODUCT (Rx)

OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 44

THIS APPLICATION IS

PAPER

PAPER AND ELECTRONIC

ELECTRONIC

ESTABLISHMENT INFORMATION

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.

See attached sheet for Establishment Information.

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

62,780, DMFs: \_\_\_\_\_

b(4)

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

**CERTIFICATION**

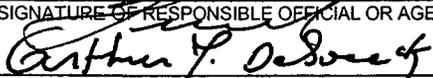
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. 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 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 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 202.
5. Regulations on making changes in application in 21 CFR 314.70, 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 review 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 Dr. I. W. French, President and COO Arthur M. Deboeck, Vice President & General Manager	DATE
--	--	------

ADDRESS (Street, City, State, and ZIP Code) U.S. Agent, Galephar P.R. Inc. See attachment for address & contact numbers	Telephone Number Cipher: (905)696-9380 Galephar: (787) 713-0340
---	---

**Public reporting burden for this collection of information** is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing 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:

DHHS, Reports Clearance Officer  
Paperwork Reduction Project (0910-0338)  
Robert H. Humphrey Building, Room 531-H  
Independence Avenue, S.W.  
Washington, DC 20201

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.

Please **DO NOT RETURN** this form to this address.

## MODULE 1 - TABLE OF CONTENTS

## 1.0 MODULE 1 - ADMINISTRATIVE AND PRESCRIBING INFORMATION

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1.3.1 Administrative Documents	1 of 1	1.3.1
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1.3.1.3 Debarment Certification	1 of 1	<del>1.3.1.3</del>
1.3.1.4 Field Copy Certification	1 of 1	1.3.1.4
1.3.1.5 User Fee Cover Sheet	1 of 1	1.3.1.5
1.3.1.6 Financial Disclosure Information	1 of 1	1.3.1.6
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1.3.1.9 Request for Categorical Exclusion	1 of 1	1.3.1.9
1.3.1.10 Statements of Claimed Exclusivity and Associated Certificates	1 of 1	1.3.1.10
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1.3.2.1 CIP-Fenofibrate Capsules Prescribing Information	1 of 1	1.3.2.1
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Appears This Way  
On Original

**NDA REGULATORY FILING REVIEW**  
**(Including Memo of Filing Meeting)**

NDA # 21-612

Supplement # N/A

Trade Name: **Luxacor** (fenofibrate) Capsules

(DMETS approved trade name 11/06/03)

Generic Name: Fenofibrate Capsules

Strengths: 50, 100, 150 ~~mg~~ **b(4)**

Applicant: Cipher Pharmaceuticals, Limited

U.S. Agent: Galephar

Date of Application: December 24, 2003

Date of Receipt: December 26, 2003

Date clock started after UN: February 26, 2003

Date of Filing Meeting: April 15, 2003

Filing Date: April 27, 2003

74-Day letter issue date: May 7, 2003

Action Goal Date (optional): December 17, 2003

User Fee Goal Date: December 26, 2003

Indication(s) requested: Reduction of LDL-C, Total-C, TG, Apo-B, and increase HDL-C in adults with primary hypercholesterolemia (IIA & IIB) and adults with hypertriglyceridemia (Type IV & V).

Type of Application: Original (b)(1) NDA \_\_\_\_\_ Original (b)(2) NDA   X    
(b)(1) Supplement \_\_\_\_\_ (b)(2) Supplement \_\_\_\_\_  
[If the Original NDA was a (b)(2), all supplements are (b)(2)s; if the Original NDA was a (b)(1), the supplement can be either a (b)(1) or a (b)(2).]

NOTE: If the application is a 505(b)(2) application, complete the 505(b)(2) section at the end of this summary.

Therapeutic Classification: S   X   P \_\_\_\_\_  
Resubmission after a withdrawal?   No   Resubmission after a refuse to file?   No    
Chemical Classification: (1,2,3 etc.)   3    
Other (orphan, OTC, etc.)   N/A  

User Fee Status: Paid   X   Waived (e.g., small business, public health) \_\_\_\_\_  
Exempt (orphan, government) \_\_\_\_\_

Form 3397 (User Fee Cover Sheet) submitted:   YES  

User Fee ID # **4494**

Clinical data? YES \_\_\_\_\_   NO  , Referenced to NDA #   21-203  

Is there any 5-year or 3-year exclusivity on this active moiety in either a (b)(1) or a (b)(2) application?  
(Note: The 3-year exclusivity for Fredericksons IIA + IIB (indication) expired April 24, 2003.)

  NO  

If yes, explain:

Does another drug have orphan drug exclusivity for the same indication?

  NO

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?

N/A

Is the application affected by the Application Integrity Policy (AIP)?  
If yes, explain.

NO

If yes, has OC/DMPQ been notified of the submission?

YES

• Does the submission contain an accurate comprehensive index?

YES

• Was form 356h included with an authorized signature?

NO

**If foreign applicant, both the applicant and the U.S. agent must sign.**

**Eventually FDA received 356h forms signed by either the applicant or the agent, not by both.**

• Submission complete as required under 21 CFR 314.50?

YES

If no, explain: (Note: A comprehensive index and various required forms were submitted as amendments.)

• If an electronic NDA, does it follow the Guidance?

NO

**If an electronic NDA, all certifications must be in paper and require a signature. YES**

Which parts of the application were submitted in electronic format?

Partially electronic submission of biopharmaceutics data sets. Some parts were not readable, but were corrected.

• If in Common Technical Document format, does it follow the guidance?

YES

When submitted in paper, it did not contain an comprehensive table of contents (TOC) with unique identifiers that corresponded with the CDR volume numbering system. A revised TOC was submitted as an amendment.

• Is it an electronic CTD?

NO

**If an electronic CTD, all certifications must be in paper and require a signature.**

Which parts of the application were submitted in electronic format?

• Patent information included with authorized signature?

YES

• Exclusivity requested?

NO

Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

• Correctly worded Debarment Certification included with authorized signature?

YES (applicant)

NO (agent) Yes, 3/30/04

**The certification submitted by the agent, Mr. Deboeck, included "to the best of my knowledge."**

*The certification has been resubmitted and states "did not and will not use,..."*

**If foreign applicant, both the applicant and the U.S. Agent must sign the certification.**

**-Certifications signed by the applicant and the agent were submitted separately.**

**NOTE:** Debarment Certification must have correct wording, e.g.: "I, the undersigned, hereby certify that \_\_\_\_\_ Co. did not and will not use in any capacity the services of any person debarred under

section 306 of the Federal Food, Drug and Cosmetic Act in connection with the studies listed in Appendix \_\_\_\_." Applicant may not use wording such as "To the best of my knowledge . . . ."

- Financial Disclosure information included with authorized signature? YES  
**(Forms 3454 and/or 3455 must be used and must be signed by the APPLICANT.)**  
Individual investigator forms were submitted, but the applicant did not submit either form.
- Field Copy Certification (that it is a true copy of the CMC technical section)? YES

**Refer to 21 CFR 314.101(d) for Filing Requirements**

- PDUFA and Action Goal dates correct in COMIS? YES  
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name/Applicant name correct in COMIS? If not, have the Document Room make the corrections.
- List referenced IND numbers: IND 62,780
- End-of-Phase 2 Meeting(s)? Date(s) \_\_\_\_\_ NO  
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) 7/23/02 YES  
If yes, distribute minutes before filing meeting.

**Project Management**

- Package insert consulted to DDMAC? YES
- Trade name (plus PI and all labels and labeling) consulted to ODS/Div. of Medication Errors and Technical Support? YES
- MedGuide and/or PPI (plus PI) consulted to ODS/Div. of Surveillance, Research and Communication Support? N/A
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A

**If Rx-to-OTC Switch application:**

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/ Div. of Surveillance, Research and Communication Support? N/A
- Has DOTCDP been notified of the OTC switch application? N/A

**Clinical**

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? N/A

**Chemistry**

- Did applicant request categorical exclusion for environmental assessment? YES  
If no, did applicant submit a complete environmental assessment? N/A  
If EA submitted, consulted to Nancy Sager (HFD-357)? N/A
- Establishment Evaluation Request (EER) submitted to DMPQ? YES
- If parenteral product, consulted to Microbiology Team (HFD-805)? N/A

**If 505(b)(2) application, complete the following section:**

- Name of listed drug(s) and NDA/ANDA #: **NDA 21-203 Tricor Tablets, 54 mg, 160 mg (cited in 356h);**  
(Relevant but not cited by applicant: NDA 19-304 Tricor Capsules, 67 mg, 134 mg, 200 mg)
- Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").  
**This application provides for a capsule dosage form with strengths different from NDA 19-304, which is not marketed. One of the four \_\_\_\_\_ capsule strengths is \_\_\_\_\_ marketed Tricor Tablet strengths.** **b(4)**
- Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs.) NO
- Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 314.101(d)(9). NO
- Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD? (See 314.54(b)(2)). If yes, the application should be refused for filing under 314.101(d)(9). NO
- Which of the following patent certifications does the application contain? Note that a patent certification must contain an authorized signature.
  - \_\_\_\_ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA.
  - \_\_\_\_ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired.
  - \_\_\_\_ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire.
  - X   21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted.

*IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must submit a signed certification that the patent holder was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].*

- **The applicant submitted proof of notification and notification that the patent holder, Abbott Labs, had filed suit to contest this patent issue.**

\_\_\_ 21 CFR 314.50(i)(1)(ii): No relevant patents.

\_\_\_ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications.

\_\_\_ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)

\_\_\_ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

- Did the applicant:

- Identify which parts of the application rely on information the applicant does not own or to which the applicant does not have a right of reference?  
YES NO

- Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?  
YES

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?  
YES

- Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?  
NO

- If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):  
N/A

- Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).  
YES NO

- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.  
YES NO

- EITHER  
The number of the applicant's IND under which the studies essential to approval were conducted.

YES, IND # \_\_\_\_\_ NO

OR

A certification that it provided substantial support of the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

N/A YES NO

- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?

YES

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ATTACHMENT

MEMO OF FILING MEETING

DATE: April 15, 2003

BACKGROUND: This is a 505(b)(2) NDA for fenofibrate capsules in ~~\_\_\_\_\_~~ strengths, 50 mg, 100 mg, 150 mg, ~~\_\_\_\_\_~~. The innovator, Abbott Labs, is not marketing its approved 67 mg, 134 mg, or 200 mg capsules (NDA 19-304). However, Abbott is marketing tablets approved in 54 mg and 160 mg strengths (NDA 21-203).

b(4)  
b(4)

(Provide a brief background of the drug, e.g., it was already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES:

ASSIGNED REVIEWERS:

<u>Discipline</u>	<u>Reviewer</u>
Medical:	Mary Parks, M.D.
Secondary Medical:	N/A
Statistical:	J. Todd Sahlroot, Ph.D.
Pharmacology:	Indra Antonipillai, Ph.D.
Statistical Pharmacology:	N/A
Chemist:	William Adams, Ph.D.
Environmental Assessment (if needed):	
Biopharmaceutical:	Wei Qiu, Ph.D.
Microbiology, sterility:	N/A
Microbiology, clinical (for antimicrobial products only):	N/A
DSI:	
Regulatory Project Manager:	Bill Koch (subsequently re-assigned to Valerie Jimenez)
Other Consults:	N/A

Per reviewers, are all parts in English or English translation? YES  
If no, explain:

CLINICAL FILE  X  REFUSE TO FILE \_\_\_\_\_

- Clinical site inspection needed: NO
- Advisory Committee Meeting needed? NO

- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

N/A

CLINICAL MICROBIOLOGY

N/A

STATISTICS

FILE \_\_\_\_\_

REFUSE TO FILE \_\_\_\_\_

N/A

BIOPHARMACEUTICS

FILE  X

REFUSE TO FILE \_\_\_\_\_

- Biopharm. inspection needed:

YES

PHARMACOLOGY

FILE  X

REFUSE TO FILE \_\_\_\_\_

- GLP inspection needed:

NO

CHEMISTRY

FILE  X

REFUSE TO FILE \_\_\_\_\_

- Establishment(s) ready for inspection?
- Microbiology

YES

NO

**ELECTRONIC SUBMISSION:**

Any comments: Some of the electronic documents cannot be opened.

**REGULATORY CONCLUSIONS/DEFICIENCIES:**

\_\_\_\_\_ The application is unsuitable for filing. Explain why:

X  The application, on its face, appears to be well organized and indexed. The application appears to be suitable for filing.

X  No filing issues have been identified.

\_\_\_\_\_ Filing issues to be communicated by Day 74. List (optional):

**ACTION ITEMS:**

1. Document filing issues/no filing issues conveyed to applicant by Day 74.

*{See attached electronic signature page.}*

\_\_\_\_\_  
Enid Galliers on behalf of William Koch (for meeting minutes)  
and on behalf of Valerie Jimenez (for PM administrative review)  
Regulatory Project Manager, HFD-510

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/s/

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Enid Galliers  
12/12/03 07:40:47 PM  
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## REQUEST FOR CONSULTATION

TO (Division/Office):

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

FROM: Valerie Jimenez, HFD-510  
(301) 827-9090

DATE  
October 15, 2003

IND NO.

NDA NO.  
21-612

TYPE OF DOCUMENT  
New NDA

DATE OF DOCUMENT  
October 15, 2003

NAME OF DRUG  
CIP/Fenofibrate Capsules

PRIORITY CONSIDERATION  
Standard

CLASSIFICATION OF DRUG  
Lipid Altering (5)

DESIRED COMPLETION DATE  
November 7, 2003

NAME OF FIRM:

### REASON FOR REQUEST

#### I. GENERAL

- |  |  |  |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL<br><input type="checkbox"/> PROGRESS REPORT<br><input type="checkbox"/> NEW CORRESPONDENCE<br><input type="checkbox"/> DRUG ADVERTISING<br><input type="checkbox"/> ADVERSE REACTION REPORT<br><input type="checkbox"/> MANUFACTURING CHANGE/ADDITION<br><input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> PRE-NDA MEETING<br><input type="checkbox"/> END OF PHASE II MEETING<br><input type="checkbox"/> RESUBMISSION<br><input type="checkbox"/> SAFETY/EFFICACY<br><input type="checkbox"/> PAPER NDA<br><input type="checkbox"/> CONTROL SUPPLEMENT | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER<br><input type="checkbox"/> FINAL PRINTED LABELING<br><input type="checkbox"/> LABELING REVISION<br><input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE<br><input type="checkbox"/> FORMULATIVE REVIEW<br><input checked="" type="checkbox"/> 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
- 
- 
- BIOAVAILABILITY 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, CONCERNS, and/or SPECIAL INSTRUCTIONS:

Because this is a 505(b)(2) NDA which references NDA 19-304, the package insert will need to follow that of the innovator. Therefore, we are requesting your comments only **on the proposed proprietary name, "LUXACOR."** Please call if you need anything, Valerie Jimenez, Regulatory Project Manager, (301) 827-9090.

Attachment: Proposed PI

SIGNATURE OF REQUESTER

METHOD OF DELIVERY (Check one)  
x MAIL  HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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/s/

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Valerie Jimenez  
10/16/03 08:15:14 AM

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## MEMORANDUM OF TELECON

DATE: August 7, 2003

APPLICATION NUMBER: NDA 21-612, CIP-Fenofibrate (fenofibrate) 50 mg, 100 mg, 150 mg, \_\_\_\_\_ Tablets **b(4)**

BETWEEN:

Name: Archie Kizilbash, M.D., Director Medical Affairs  
Ian French, M.D., Chief Scientific Officer  
Larry Andrews, President, Cipher Pharmaceuticals Limited

Phone: (905) 696-9380

Representing: Cipher Pharmaceuticals Limited

AND

Name: Mary Parks, M.D., Deputy Director and Medical Team Leader  
Enid Galliers, Chief, Project Management Staff  
Valerie Jimenez, Regulatory Project Manager  
Division of Metabolic and Endocrine Drug Products, HFD-510

SUBJECT: Proprietary Name Review

BACKGROUND: Cipher Pharmaceuticals Limited submitted a new drug application (NDA) on February 23, 2003, for the proposed indication of Type IV and Type V Hypercholesterolemia. A consult for the proprietary name, CIP-Fenofibrate, was submitted for review.

- The firm was notified that the proprietary name, CIP-Fenofibrate, was unacceptable.
- Reason specified: Nonproprietary names are not subject to proprietary trademark rights, but are entirely in the public domain.
- The firm also wanted to know if the resubmission of the names would affect the time of application review.
- The firm was advised to submit several names indicating the order of preference by early to mid September as the Division of Medication Errors and Technical Support reviews proposed proprietary names 90 days before the action goal date.
- In addition, the firm was informed that the timeframe for proprietary name review would be approximately ninety days.

---

Valerie Jimenez  
Regulatory Project Manager

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/s/

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Valerie Jimenez  
8/18/03 09:19:16 AM  
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**Office of Drug Safety**

# Memo

**To:** David Orloff, M.D.  
Division of Metabolic and Endocrine Drug Products  
HFD-510

**From:** Charlie Hoppes, R.Ph., M.P.H.  
Safety Evaluator, Division of Medication Errors and Technical Support  
Office of Drug Safety, HFD-420

**Through:** Alina Mahmud, R.Ph.  
Team Leader, Division of Medication Errors and Technical Support  
Office of Drug Safety, HFD-420

Carol Holquist, R.Ph.  
Deputy Director, Division of Medication Errors and Technical Support  
Office of Drug Safety, HFD-420

Jerry Phillips, R.Ph.  
Associate Director  
Office of Drug Safety, HFD-400

**CC:** Valerie Jimenez  
Project Manager  
HFD-510

**Date:** July 25, 2003

**Re:** DMETS Consult 03-0162; CIP-Fenofibrate (Fenofibrate Capsules); NDA 21-612

---

This memorandum is in response to a May 5, 2003, request from your Division for a review of the proprietary name, CIP-Fenofibrate. The usual proprietary name review was not conducted for this name because it contains the established name and is therefore unacceptable.

We note that the prefix, "CIP" is derived from the name of the sponsor, Cipher Pharmaceuticals, Ltd. Fenofibrate is listed in the Dictionary as a USAN (United States Adopted Name). As described in 21 CFR 299.4(d), the Agency supports the Guiding Principles for Coining United States Adopted Names for Drugs published in the USP Dictionary of USAN and International Drug Names. The "Guiding Principles" state that a "USAN is a nonproprietary name selected by the USAN Council" and "By definition, nonproprietary names are not subject to proprietary trademark rights, but are entirely in the public domain.". Therefore, based on this regulation, the use of "fenofibrate" in the proposed proprietary name, "CIP-Fenofibrate" is unacceptable.

In addition, DMETS has safety concerns regarding the use of the prefix "CIP". DMETS questions whether the sponsor intends to utilize the prefix "CIP" in conjunction with other names with subsequent applications. Post-marketing experience has shown confusion and resulting medication errors due to proliferation of names with a common prefix. One example of such confusion has been seen with products having the prefix "APO", manufactured in Canada by Apotex (see Appendix 1 for list of names with prefix "APO"). Consequently, DMETS has objected to inclusion of the prefix "APO" for proprietary names proposed in this country since this practice may result in the introduction of numerous sound-alike/look-alike names. DMETS continues to object to proposals which would lead to a proliferation of products with commonalities in nomenclature. DMETS believes that the entrance in the marketplace of different products which include common lettering, "CIP", would lead to confusion and result in medication errors.

Furthermore, the prefix CIP may look very much like the medical abbreviation "QID", meaning four times daily (see writing sample below). A misinterpretation of the prefix CIP could result in a four-fold overdose of fenofibrate.

<i>Continue</i>	<i>Continue</i>
<i>CIP Fenofibrate</i>	<i>QID Fenofibrate</i>

Similarly, the prefix CIP could look like the medical abbreviations "QD" (once daily) or "UD" (as directed), as seen in the writing samples below.

CIP vs. QD

<i>CIP</i>	<i>QD</i>
------------	-----------

CIP vs. UD

<i>CIP</i>	<i>UD</i>
------------	-----------

In summary, DMETS does not recommend the use of the proprietary name, CIP-Fenofibrate.

If you have any questions or need clarification, please contact Sammie Beam at 301-827-3242.

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/s/  
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Charles Hoppes  
8/1/03 02:46:38 PM  
PHARMACIST

Alina Mahmud  
8/1/03 02:48:00 PM  
PHARMACIST

Carol Holquist  
8/1/03 03:00:12 PM  
PHARMACIST

Jerry Phillips  
8/4/03 08:10:46 AM  
DIRECTOR

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07.18.03

NDA 21-612

INFORMATION REQUEST LETTER

Galephar PR Inc.  
Attention: Authur M. Deboeck  
U.S. Agent for Cipher Pharmaceuticals Inc.  
Road 198 No. 100 km 14.7  
Juncos Industrial Park  
Juncos, PR 00777-3873

Dear Mr. Deboeck:

Please refer to your December 24, 2002 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cip-Fenofibrate 50 mg, 100 mg, 150 mg, \_\_\_\_\_ Capsules.

b(4)

We are reviewing the Biopharmaceutical section of your submission, and we have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

The \_\_\_\_\_ paddle speed is not acceptable. It is recommended to investigate a lower paddle speed(s) and other USP apparatus such as basket. In order to obtain an appropriate dissolution method and specification for this product and to be granted biowaivers for strengths lower than \_\_\_\_\_ please submit dissolution profiles for the 50 mg, 100 mg, and 150 mg capsules from \_\_\_\_\_ batches under three different conditions.

b(4)

b(4)

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

Sincerely,

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

-----  
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/s/

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Mary Parks  
7/18/03 12:20:06 PM  
for Dr. Orloff

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DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

## FILING REVIEW LETTER

NDA 21-612

Galephar PR. Inc.  
Attention: Arthur Deboeck  
U.S. Agent for Cipher Pharmaceuticals, Limited  
Road 198 Km. 14.7  
No. 100 Juncos Industrial Park  
Juncos, PR 00777-3873

Dear Mr. Deboeck:

Please refer to your February 26, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CIP-Fenofibrate, 50 mg, 100 mg, 150 mg, \_\_\_\_\_ Tablets. **b(4)**

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on April 27, 2003 in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

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 New Drug II  
Center for Drug Evaluation and Research

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/s/

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David Orloff  
5/7/03 06:40:45 PM

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***cipher***  
*Pharmaceuticals Limited*

RECEIVED  
MAY 08 2003  
FDR/CDER

May 6, 2003

Ms. Valerie Jimenez  
Regulatory Project Manager  
Division of Metabolic and Endocrine Drug Products (HFD-510)  
Parklawn Building  
5600 Fishers Lane  
Rockville, MD 20857-1706

NEW CORRESP

ORIGINAL

N-000-C

**Re: NDA 21-612; Notice of Filing of Patent Infringement Action**

Dear Ms. Jimenez:

Enclosed is one volume containing the notice of filing of patent infringement action.

If you require any further information or clarification, please do not hesitate to contact me at 905-696-9380 ( \_\_\_\_\_ ) or our U.S. agent in Puerto Rico, Mr. Arthur Deboeck at 787-713-0340 (adeboeck@galephar.com).

b(4)

Yours sincerely,



Ian W. French, Ph.D.  
Chairman & Chief  
Scientific Officer

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

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

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,  
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**  
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

**APPLICANT INFORMATION**

NAME OF APPLICANT <b>Cipher Pharmaceuticals Limited</b>	DATE OF SUBMISSION <b>May 6, 2003</b>
TELEPHONE NO. (Include Area Code) <b>NA Contact 905-696-9380</b>	FACSIMILE (FAX) Number (Include Area Code) <b>246-228-8329</b>
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): <b>Suite 201 Lauriston, Collymore Rock St. Michael, BARBADOS</b>	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE <b>Arthur M. Deboeck Galephar PR Inc. Road 198 No. 100 km 14.7 Juncos Industrial Park Juncos 00777-3873 Puerto Rico</b> <b>Tel: (787) 713-0340 Fax: (787) 713-0344</b>

**PRODUCT DESCRIPTION**

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) <b>21-612</b>		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) <b>Fenofibrate</b>	PROPRIETARY NAME (trade name) IF ANY <b>CIP-Fenofibrate</b>	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)	CODE NAME (If any)	
DOSAGE FORM: <b>Capsules</b>	STRENGTHS: <b>50, 100, 150 mg</b>	ROUTE OF ADMINISTRATION: <b>Oral</b>
(PROPOSED) INDICATION(S) FOR USE: <b>Hypercholesterolemia, Mixed Dyslipidemia and Hypertriglyceridemia</b>		

**APPLICATION INFORMATION**

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)		
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 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 <u>Tricor Tablets</u> Holder of Approved Application <u>Abbott Laboratories</u>		
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO A PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER		
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____		
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)		
REASON FOR SUBMISSION <b>Response to request for additional information</b>		
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)		
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> 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. <b>See attached sheet for Establishment Information.</b>		

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

62,780, DMFs:

**b(4)**

This application contains the following items: (Check all that apply)

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

**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 <b>Dr. I. W. French, President and COO</b> <b>Arthur M. Deboeck, Vice President &amp; General Manager</b>	DATE: <b>May 6, 2003</b>
ADDRESS (Street, City, State, and ZIP Code) <b>U.S. Agent, Galephar P.R. Inc.</b> <b>See attachment for address &amp; contact numbers</b>	Telephone Number <b>Cipher: (905)696-9380</b> <b>Galephar: (787) 713-0340</b>	

**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.



**NOTICE OF FILING OF PATENT INFRINGEMENT ACTION**  
21 C.F.R. § 314.107(f)(2)

**CIP-Fenofibrate 50, 100, 150 mg Capsules**  
**NDA # 21-612**

b(4)

The undersigned hereby certifies, pursuant to 21 C.F.R. § 314.107(f)(2), that on October 2, 2003, an action for patent infringement was filed by Abbott Laboratories ("Abbott"), and \_\_\_\_\_ and \_\_\_\_\_ (collectively \_\_\_\_\_) against Cipher Pharmaceuticals Limited ("Cipher") in the United States District Court for the District of Puerto Rico. Civil Action No. 03-2067 (DRD). The complaint in this action alleges infringement of only one of the three patents for which Cipher filed a Paragraph IV Certification, specifically, U.S. Patent No. 6,589,552

b(4)

Dated: January 25, 2004

Ian W. French, Ph.D.  
Chief Scientific Officer

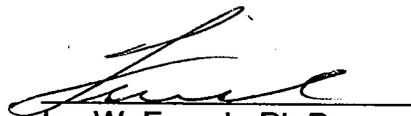
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**NOTICE OF FILING OF PATENT INFRINGEMENT ACTION**  
21 C.F.R. § 314.107(f)(2)

**Cip-Fenofibrate 50, 100, 150 \_\_\_\_\_mg Capsules      b(4)**  
**NDA # 21-612**

The undersigned hereby certifies, pursuant to 21 C.F.R. § 314.107(f)(2), that on April 21, 2003, an action for patent infringement was filed by Abbott Laboratories ("Abbott"), and \_\_\_\_\_ and \_\_\_\_\_ (collectively \_\_\_\_\_), against CIPHER Pharmaceuticals Limited ("CIPHER") in the United States District Court for the District of Puerto Rico. Civil Action No. 03-1421 (DRD). The complaint in this action alleges infringement of only one of the three patents for which CIPHER filed a Paragraph IV Certification, specifically, U.S. Patent No. 6,277,405.      b(4)

Dated: May 6, 2003



Ian W. French, Ph.D.  
Chairman & Chief Scientific Officer

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STATEMENT OF NOTICE OF PARAGRAPH IV PATENT CERTIFICATION  
Cip-Fenofibrate 50, 100, 150 ~~mg~~ mg Capsules  
NDA # 21-612

b(4)

I certify that the notice of certification of invalidity or noninfringement of U.S. Patent Nos. 4,895,726 ("the 726 patent"), 6,074,670 ("the '670 patent"), and 6,277,405 ("the '405 patent") has been provided to Abbott Laboratories. ~~\_\_\_\_\_~~ and ~~\_\_\_\_\_~~ on March 5, 2003.

b(4)

I also certify that the notice met the content requirement under paragraph (c) of 21CFR314.52.

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\_\_\_\_\_  
Dr. Ian W. French Ph.D.  
Chairman and Chief Scientific Officer

March 25/03  
Date

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Office of posting <i>V.P.O</i>	Date <i>03-03-07</i>
Addressee of the item <i>GENERAL COUNCIL</i>	

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Stamp of the office returning the advice

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<input checked="" type="checkbox"/> Registered No. of item <i>12025</i>	<input type="checkbox"/> Recorded delivery	<input type="checkbox"/> Insured Amount	
<input type="checkbox"/> Ordinary money order Inpayment money ord	<input type="checkbox"/> Outpayment Cheque	Amount	

To be filled in by the sender

Return to

Name <i>CIPHER Pharmaceuticals</i>
Street and No. <i>201 Lauriston, Cullymore Park</i>
Locality and country <i>St. Michael</i>
<i>BARBADOS</i>

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Date and Signature* <i>11/03/07</i>			

\* 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.

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

Office of posting <i>V.P.O</i>	Date <i>03-03-07</i>
Addressee of the item <i>GENERAL COUNCIL Abbott Laboratories Inc. - Phar 100 Abbott Park Road Abbott Park, IL-60064-6400</i>	

On postal service

Stamp of the office returning the advice

Priority/  
By airmail



To be filled in by the sender

Return to

Name <i>CIPHER Pharmaceuticals</i>
Street and No. <i>201 Lauriston, Cullymore Park</i>
Locality and country <i>St. Michael</i>
<i>BARBADOS</i>

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Date and Signature* <i>Linda Cozzino</i>			

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**JONES DAY**

77 WEST WACKER

CHICAGO, ILLINOIS 60601-1692

TELEPHONE: 312-782-3939 • FACSIMILE: 312-782-8585

WRITER'S DIRECT NUMBER:

(312) 289-4067

tjheverin@jonesday.com

March 18, 2003

VIA FACSIMILE AND FEDERAL EXPRESS

Ian W. French, Ph.D.  
Chairman & Scientific Officer  
Cipher Pharmaceuticals Ltd.  
Suite 201, Lauriston, Collymore Rock  
St Michael, Barbados

Re: Cipher Pharmaceuticals Ltd., Fenofibrate Capsule NDA 21-612

Dear Dr. French:

We represent Abbott Laboratories. Fournier is represented by Arnold & Porter, who has authorized me to send this letter on Fournier's behalf as well. This letter responds to your March 5, 2003 letter. In your letter you state that Cipher Pharmaceuticals has filed an NDA for 50 mg, 100 mg, 150 mg ~~fenofibrate~~ fenofibrate capsules and has certified that Cipher's proposed products do not infringe U.S. Patent Nos. 4,895,726 ("the '726 patent"), 6,074,670 ("the '670 patent"), or 6,277,405 ("the '405 patent").

b(4)

To evaluate Cipher's claim of non-infringement, Abbott and Fournier need certain data and product samples, which will be reviewed by in-house counsel and by one or more scientists and laboratory technicians. Accordingly, so that Abbott and Fournier may fully evaluate their positions within the time allowed under the relevant statutes and regulations, Abbott and Fournier request that Cipher provide the following samples and information for its 50 mg, 100 mg, 150 mg ~~fenofibrate~~ fenofibrate capsules (the "products"):

b(4)

1. 100 capsules from each lot of the products manufactured to date;
2. 50 grams of each initial ingredient, including excipients, active and inactive ingredients used to manufacture each lot referenced above;
3. all analytical data which were used to characterize the products as non-infringing; and
4. documents detailing the ingredients in the products and Cipher's manufacturing process, including, without limitation, manufacturing work orders, protocols and batch records from each lot manufactured to date (expressly including batch records for lots utilized in bioequivalence testing), any particle size data for any

CHI-1346331v1

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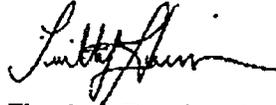
JONES DAY

Ian W. French, Ph.D.  
March 18, 2003  
Page 2

ingredients in the products, and including all portions of NDA 21-612 relating to manufacturing processes or ingredients.

Please send these samples and this information to Chuck Ossola's and my attention no later than March 24, 2003. Mr. Ossola's address is: Arnold & Porter, Thurman Arnold Building, 555 Twelfth Street, N.W., Washington, D.C. 20004-1202. I have enclosed a confidentiality agreement regarding the protection of Cipher's confidential materials. If the agreement is acceptable to you, please execute and return it to me. Thank you for your cooperation in this matter.

Very truly yours,



Timothy J. Heverin

Enclosure

cc: Charles D. Ossola

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### 1.3.1 Patent Information

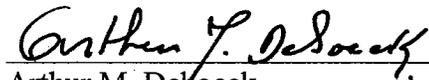
This section complies with 21 CRF 314.53.

Patent No.: 5,545,628  
Date Issued: Aug. 13, 1996  
Date of Expiry: Aug. 13, 2016  
Type of patent: Formulation patent  
Patent Owner: Galephar P.R. Inc, Puerto Rico  
Road 198, No. 100 km 14.7  
Juncos Industrial Park,  
Juncos 00777-3873  
Puerto Rico

#### Original Declaration of Use under 314.53(c)(2)(i)

The undersigned declares that Patent No. 5,545,628 covers the formulation, composition or method of use of CIP-FENOFIBRATE 50, 100, 150, ~~200~~ Capsules. This product is the subject of this application for which approval is being sought

b(4)



Arthur M. Deboeck  
Galephar P.R. Inc.

### 1.3.2 Patent Certification

There is one (1) listed patent in the Orange Book for Tricor (micronized) Capsules which were approved on February 9, 1998 for a 67 mg strength and on June 30, 1999 for strengths of 134 and 200 mg Capsules. Tricor Tablets were approved on September 4, 2001 for strengths of 54 and 160 mg Tablets and there are three (3) listed patents in the Orange Book for this product. All of the above approvals were granted to Abbott Laboratories.

**Tricor Capsules** has a patent # 4,895,726, issued on Jan.23, 1990, expiring Jan. 19, 2009 listed in the Orange Book. Although this product remains listed in the Orange Book, Cipher Pharmaceuticals Ltd, could find no product on the market. Abbott Laboratories are advising patients that Tricor Tablets 54, and 160 mg are equivalent to Tricor Capsules 67 mg and 200 mg, respectively.

Cipher Pharmaceuticals Ltd. does not infringe patent # 4,895,726 for the following reasons:

1. The primary claim for patent # 4,895,726 states "a therapeutic composition, which is presented in the form of gelatin capsules and which is useful

especially in the treatment of hyperlipidemia and hypercholesterolemia, said composition containing a co-micronized mixture of particles of fenofibrate and a solid surfactant, wherein the mean particle size of said co-micronized mixture is less than 15  $\mu\text{m}$ ."

Claims 2, 3, 4, 5, 6, 7, and 8 are dependent claims to claim 1.

Claim 8, which describes the method of manufacture as "a method for the manufacture of a therapeutic composition according to claim\_1, which comprises;

- (i) intimately mixing and then co-micronizing the fenofibrate and a solid surfactant.
- (ii) adding lactose and starch to the mixture obtained,
- (iii) converting the whole granules in the presence of water,
- (iv) drying the granules until they contain no more than 1% water,
- (v) grading the granules,
- (vi) adding polyvinylpyrrolidone and magnesium stearate, and
- (vii) filling gelatin capsules."

Claim 9 is dependent on claim 8, and states that the co-micronized fenofibrate and sodium lauryl-sulfate is less than 15  $\mu\text{m}$ .

Claim 10 claims "a method of improving the bioavailability of fenofibrate in vivo, which comprises co-micronization of the fenofibrate and a solid surfactant, the said co-micronization being carried out by micronization of a fenofibrate/solid surfactant mixture until the particle size of the powder obtained in less than 15  $\mu\text{m}$ ."

Claim 11 states "a method for treatment of hyperlipidemia or hypercholesterolemia comprising orally administering the therapeutic composition of claim 6 to a patient."

Claim 12, the last claim in this patent, states "the method of treatment of claim 11, wherein said particles size is less than or equal to 5  $\mu\text{m}$ ."

**CIP-FENOFIBRATE** does not infringe the above patent claims because:

1.
2.
3.
4.
5.

b(4)

**Tricor Tablets** have three (3) patents listed in the Orange Book, # 4,895,726 (issued on Jan. 23, 1990 and expiring Jan. 19, 2009), # 6,074,670 (issued on Jun. 13, 2000, and expiring Jan. 09, 2018) and # 6,277,405 (issued on Aug. 21, 2001 and expiring on Jan 09, 2018).

Cipher Pharmaceuticals Ltd. has access to patent # 5,545,628 by a licensing agreement with Galephar P.R. Inc., the owner of record of patent # 5, 545,628, issued on Aug. 13, 1996, for a product containing the same active drug as Tricor Capsules and Tablets, fenofibrate.

Cipher Pharmaceuticals Ltd., claims that patent # 4,895,726 is listed in the Orange Book for an inappropriate product. This patent claims ONLY capsules, and the product is a tablet.

Galephar P.R. Inc, was assigned a patent # 5,545,628 on Aug. 13, 1996 so this patent does not infringe patents # 6,074,670, issued on Jun. 13, 2000, and patent # 6,277,405 B1 issued on Aug. 21, 2001, because these patents were issued later than Galephar P.R. Inc. patent # 5,545,628.

In addition, Galephar patent # 5,545,628 does not infringe these listed patents on other grounds, such as;

1. Patent # 6,074,670 primary claim is "an immediate-release fenofibrate composition comprising;  
(a) an inert hydrosoluble carrier covered with at least one layer containing fenofibrate in a micronized form having a size less than 20  $\mu$ m, a hydrophilic polymer and a surfactant; and  
(b) optionally one or several outer phase(s) or layer(s), wherein, based on the weight of (a), said inert hydrosoluble carrier makes up from 20-59% by weight, said fenofibrate makes up from 20-45% by weight, said hydrophilic polymer makes up 20-45% by weight, and said surfactant makes up 0.1 to 3% by weight.

All of the other claims, except claim 12, are dependent claims.

Claim 12 is essentially the same as claim 1, but claim 12 states specifically the inert hydrosoluble carrier is polyvinylpyrrolidone.

Patent # 6,277,405 B1 primary claim is "a composition comprising a hydrosoluble carrier and micronized fenofibrate having a dissolution of at least 10% in 5 minutes, 20% in 30 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 with 0.025M sodium lauryl sulfate.

All of the other claims in patent # 6,277,405 B1 are dependent claims.

Cipher Pharmaceuticals Ltd, relies on the same arguments and claims listed under Tricor Capsules (patent # 4,895,726) (see above).

Also, CIP-FENOFIBRATE has different dissolution characteristics than stated in patent # 6,277,405 B1.

Also, in the "file wrapper" (Application No. 09/005,128) for Stamm and Seth issued Patent # 6,074,670, the examiner rejected some claims because "Deboeck teaches fenofibrate formulations with improved dissolution with high amounts of surfactants and distintegrating agents such as polyols and poloxamers". The response to the comment was filed on January 9, 1998, "Deboeck requires a molten solution of fenofibrate in glycerides. This necessarily excludes the micronized form of fenofibrate recited in claim 1. In fact, Deboeck teaches that: [A] need to exists for a fenofibrate formulation that avoids the use of co-micronization....

***"Consequently, Deboeck specifically teaches away from the presently claimed invention." (emphasis by Cipher)***

#### **Other Patents Not Listed in the Orange Book**

On a search of the U.S. Patent Office, Cipher Pharmaceuticals Ltd. found a few other patents for fenofibrate dosage forms:

Patent # 6,180,138 B1 issued on Jan. 30, 2001 assigned to Abbott Laboratories. This patent teaches preparing a solid formulation of a lipid-regulating agent, wherein such lipid-regulating agent is a fibrate, comprising suspending said lipid-regulating agent with a surfactant solution in the presence or absence of an electrolyte; drying the mixture; granulating the mixture optionally in the presence of one or more excipients, and optionally forming a finished dosage form. All other claims are dependent claims.

Galephar P.R. Inc. patent 5,545,628 was issued on Aug. 13, 1996, over 4 years earlier than patent # 6,180,138 B1, so we cannot infringe this patent. CIP-FENOFIBRATE also does not infringe this patent on other grounds, as CIP-FENOFIBRATE is not a solid dosage form and the manufacture of CIP-FENOFIBRATE does not use a ~~process~~ process.

**b(4)**

**Paragraph IV Certification In Compliance With 21 CFR 314.50**

Cipher Pharmaceuticals Ltd., certifies that Patents No. 4,895,726, 6,074,670 and 6,277,405 B1 will not be infringed by the manufacture, use or sale of CIP-FENOFIBRATE for which this application is submitted.

Cipher Pharmaceuticals Ltd., will comply with 21 CFR 314.52 (a) with respect to notifying Abbott Laboratories, the holders of the patents listed in the Orange Book for Tricor Tablets and Tricor Capsules, the reference listed products.

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4/18/03

## MEMORANDUM OF TELECON

DATE: April 17, 2003

APPLICATION NUMBER: NDA 21-612, CIP/Fenofibrate (CIP/Fenofibrate) 50 mg, 100 mg,  
150 mg, \_\_\_\_\_ Tablets

**b(4)**

BETWEEN:

Name: Mr. Arthur Deboeck,  
Phone: (787) 713-0340  
Representing: Galaphar P.R., Inc./Cipher Pharmaceuticals, Limited

AND

Name: Valerie Jimenez, Regulatory Project Manager  
Division of Metabolic and Endocrine Drug Products, HFD-510

SUBJECT: Request for additional information

We refer to the telephone conversation on April 17, 2003, requesting the submission of additional information regarding the histocompatibility summary table with severity scores on a 13-week toxicity study in dogs. We have not received this information as of yet.

We also refer to your submission on March 24, 2003. The debarment certification for Galaphar P.R., Inc. needs to be resubmitted using the standard language defined in the Federal Food, Drug, and Cosmetic Act.

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Valerie Jimenez  
Regulatory Project Manager

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this page is the manifestation of the electronic signature.**  
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/s/

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Valerie Jimenez  
4/18/03 10:53:52 AM  
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Food and Drug Administration  
 Division of Metabolic and Endocrine  
 Drug Products, HFD-510  
 Center for Drug Evaluation and Research  
 Office of Drug Evaluation II

**FACSIMILE TRANSMITTAL SHEET**

DATE: 3/17/03

To: Arthur Deboeck	From: Valerie Jimenez
Company: Galephar PR Inc.	Division of Metabolic and Endocrine Drug Products
Fax number: (787) 713-0344	Fax number: (301) 443-9282
Phone number: (787) 713-0340	Phone number: (301) 827-9090
Subject: Additional info required	

Total no. of pages including cover:

Comments: Revised Table of contents = 8 copies  
 Corrected User fee Cover sheet  
 Debarment and Forms 3454 and 3455

Document to be mailed:  YES  NO

Thank You

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

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FDA  
Volume

Module

Cipher Module  
Numbering

1.1	1	1 of 1
1.1A	2	1 of 1
1.1B	3	1.1
1.2	3	1.2
1.3	3	1.3
1.4	3	1.4
1.5	3	1.5
1.1C	4	1.1
1.6	4	1.2
1.7	4	1.3
1.1D	5	1 of 34
1.8	5	2 of 34
1.9	5	3 of 34
1.10	5	4
1.11	5	5
1.12	6	6
1.13	7	7
1.14	8	8
1.15	9	9
1.16	10	10
1.17	11	11
1.18	12	12
1.19	13	13
1.20	14	14
1.21	15	15
1.22	16	16
1.23	17	17
1.24	18	18

FDA  
ref. no.

Module

Cipher  
No.

1.25	5	19
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1.32		26
1.33		27
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## DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning \_\_\_\_\_, who participated as a clinical investigator in the submitted study \_\_\_\_\_, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

*Name of clinical investigator*

*Name of clinical study*

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation, in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
FIRM/ORGANIZATION	
SIGNATURE	DATE

### Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services  
Food and Drug Administration  
5600 Fishers Lane, Room 14-72  
Rockville, MD 20857

# CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

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

Please mark the applicable checkbox.

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

Clinical Investigators		

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

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

NAME	TITLE
FIRM/ORGANIZATION	
SIGNATURE	DATE

### Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

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



DEPARTMENT OF HEALTH & HUMAN SERVICES

03.10.03

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-612

Cipher Pharmaceuticals Limited  
Attention: Authur M. Deboeck  
U.S. Agent, Galephar PR Inc.  
Road 198 No. 100 km 14.7  
Juncos Industrial Park  
Juncos, PR 00777-3873

Dear Mr. Deboeck:

Please refer to your December 24, 2002, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for CIP-fenofibrate (fenofibrate) capsules, 50, 100, 150, \_\_\_\_\_ **b(4)**

We note that the date of your application is actually December 24, 2002, although our initial correspondence cited it as December 23, 2002.

You were notified in our letter dated January 8, 2003, that your application was not accepted for filing due to non-payment of fees. This is to notify you that the Agency has received all fees owed and your application has been accepted as of February 26, 2003.

The review priority classification for this application is standard(s).

Unless we notify you within 60 days of the above date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on April 27, 2003, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be December 26, 2003.

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

U.S. Postal Service/Courier/Overnight Mail:  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolic and Endocrine Drug Products, HFD-510  
Attention: Fishers Document Room, 8B-45  
5600 Fishers Lane  
Rockville, Maryland 20857

NDA 21-612

Page 2

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

Sincerely,

*{See appended electronic signature page}*

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

01.08.03

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-612

Galephar PR, Inc., U.S. Agent for  
Cipher Canada Inc.  
Attention: Authur M. Deboeck  
Road 198 No. 100 km 14.7  
Juncos Industrial Park  
Juncos, PR 00777-3873

Dear Mr. Deboeck:

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

Name of Drug Product: CIP-Fenofibrate (fenofibrate) Capsules, 50 mg, 100 mg, 150 mg ~~\_\_\_\_\_~~ **b(4)**  
Date of Application: December 23, 2002  
Date of Receipt: December 26, 2002  
Our Reference Number: NDA 21-612

We have not received the appropriate user fee for this application. An application is considered incomplete and cannot be accepted for filing until all fees owed have been paid. Therefore, this application is not accepted for filing. We will not begin a review of this application's adequacy for filing until FDA has been notified that the appropriate fee has been paid. Payment should be submitted to the following address:

Food and Drug Administration  
P.O. Box 360909  
Pittsburgh, PA 15251-6909

Checks sent by a courier should be addressed to:

Food and Drug Administration (360909)  
Mellon Client Service Center, Room 670  
500 Ross Street  
Pittsburgh, PA 15262-0001

**NOTE: This address is for courier delivery only. Make sure the FDA Post Office Box Number (P.O. Box 360909) and user fee identification number are on the enclosed check.**

The receipt date for this submission (which begins the review for filability) will be the date the review division is notified that payment has been received by the bank.

In addition, we note that the original electronic media submission was not acceptable as per the Guidance for Industry titled "*Providing Regulatory Submissions in Electronic Format – NDAs*". The review of this application cannot begin until this information is available.

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

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

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Metabolic and Endocrine Drug Products, HFD-510  
Attention: Fishers Document Room, 8B-45  
5600 Fishers Lane  
Rockville, Maryland 20857

If you have any questions, call William C. Koch, R.Ph., Regulatory Project Manager, at (301) 827-6412.

Sincerely,

*{See appended electronic signature page}*

Mary H. Parks, M.D.  
Deputy Director  
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/

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Mary Parks  
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ENVIRONMENTAL IMPACT ANALYSIS STATEMENT

Name of applicant/petitioner:  
Cipher Pharmaceuticals Limited  
Suite 201  
Lauriston, Collymore Rock  
St. Michael, Barbados

The applicant/petitioner requests a Categorical Exclusion (21 CFR §25.24 (C) (1)) in that this drug product will not be administered at higher dosage levels, for longer duration, or for different indications than were previously in effect; and if data available to the agency do not establish that, at the expected level of exposure, the substance may be toxic to organisms in the environment.

The procedures proposed in this application will comply with all Federal laws, state, and local laws.

The undersigned certifies that the above-mentioned information is true, accurate, and complete to the best of his knowledge.

A handwritten signature in cursive script, appearing to read "Ian W. French", is written over a horizontal line.

Ian W. French, Ph.D.  
Chairman and Chief Scientific Officer

A handwritten date "Dec 18/02" is written over a horizontal line.

Date

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

8/22/02

Meeting Date: July 23, 2002 Time: 1:30 PM Location: PKLN 3<sup>rd</sup> Flr "POTOMAC"

IND 62,780

CIP-Fenofibrate (fenofibrate) Capsules

Type of Meeting:

Pre-NDA

External Participant:

Cipher Pharmaceuticals LTD.

Meeting Chair:

David G. Orloff, M.D., Director

External Participant Lead:

Ian W. French, Ph.D. Chairman and Chief Scientific Officer, Cipher Canada, Inc.

Meeting Recorder:

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

FDA Attendees and titles:

Robert J. Meyer, M.D., Director, Office of Drug Evaluation II

David G. Orloff, M.D., Director, Division of Metabolic and Endocrine Drug Products (DMEDP), ODEII

Mary H. Parks, M.D., Deputy Director, DMEDP

Karen Davis-Bruno, Ph.D., Supervisory Pharmacologist, DMEDP

Shiao-Wei Shen, M.D., Clinical Reviewer, DMEDP

Stephen Moore, Ph.D., Chemistry Team Leader, Division of New Drug Chemistry II, ONDC @ DMEDP

Hae-Young Ahn, Ph.D., Team Leader, Division of Pharmaceutical Evaluation II, OCPB @ DMEDP

Wei Qiu, Ph.D., Reviewer, Division of Pharmaceutical Evaluation II, OCPB @ DMEDP

William M. Adams, Ph.D., Chemistry Reviewer, Division of New Drug Chemistry II, ONDC @ DMEDP

Enid Galliers, Chief, Project Management Staff

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

Donald Hare, Special Assistant to the Director, Office of Generic Drugs

External participant Attendees and titles:

Ian W. French, Ph.D. Chairman and Chief Scientific Officer, Cipher Canada, Inc.

Arthur Deboeck, President, Galephar Pharmaceutical Research, Inc.

Meeting Objectives:

To provide guidance on the proposed Phase 3 development program for a 505(b)(2) NDA.

Discussion Points and Questions Submitted by Industry:

**Table of Contents (Tab 2)**

Are there any issues or deficiencies that need to be addresses prior to filing the NDA?

The Division stated that the proposed TOC's are acceptable and added the following recommendations:

1. Immediately after the Form FDA 356h in Volume 1, attach a complete list of all manufacturing sites, their functions, and when they will be ready for inspection.
2. Place all administrative forms, declarations, certifications, etc. in first volume.
3. Place all labeling in first volume including color mock-ups of the immediate container and carton labels, and the annotated package insert.
4. Provide a duplicate copy of the first volume for the project manager.
5. Number volumes from 1 to X (where X represents the number of the last volume), do not use 1.1 to X.1 numbering.
6. The Guidance for Industry provides for an MS Word version of the draft package insert to be submitted to the original submission accompanying the pdf version of the labeling. We encourage the establishment of a secure e-mail certificate with the project manager for the expedient exchange of package insert drafts during labeling negotiations.
7. Indicate whether or not the application will be submitted in the common technical document (CTD) format?

The sponsor indicated that the NDA will be submitted in the CTD format

**Package Insert (Tab 3)**

Is it acceptable to follow the Tricor Tablet Package Insert, with appropriate changes specific for the Cipher product?

The Division stated that the Reference Listed Product package insert may be followed in the Cipher Package Insert with disclaimers including a statement in the **CLINICAL TRIALS** section that no clinical trials were performed with CIP-Fenofibrate.

**Biopharmaceutics (Tab 4)**

Are there any biopharmaceutics issues or deficiencies in the submission that need to be addressed prior to filing the NDA?

The Division stated that the reason for not demonstrating dose proportionality is unclear since different strengths were used in the study.

The Division stated that there was no data on the pharmacokinetics of CIP-Fenofibrate compared to the reference listed product under low-fat or fasting conditions. Therefore, a bioequivalence study under fasting conditions comparing \_\_\_\_\_ dose of CIP-Fenofibrate with the 160-mg dose of Tricor tablet is recommended.

b(4)

The sponsor asked if the bioequivalence data could be submitted after the NDA is submitted.

The Division responded that the NDA would have to be complete for filing.

The Division requested a dosage form equivalence study comparing the pharmacokinetics of four of the 50 mg capsules with one of the 200 mg capsules under low-fat conditions.

The Division stated that there was no discussion of dissolution in the pre-meeting package. The Division recommended completion of the solubility profile first. The Division recommends conducting dissolution tests under 3 different conditions and using as little surfactant as possible to reach sink conditions. Completion of the dissolution testing as soon as possible would allow for an agreement on the conditions before stability studies are started for the NDA.

The sponsor stated that the stability studies were already started.

The Division emphasized the importance of conducting dissolution tests. If the Division does not agree with the sponsor's current dissolution conditions, the sponsor will need to conduct a bridging study.

#### **Pre-Clinical Toxicology (Tab 5)**

Does the FDA agree that Cipher has addressed all the toxicology issues, as requested (at the Pre-IND meeting and in the July 27, 2001, comments from the Pharmacology/Toxicology reviewer)?

The Division responded that the 3-month dog toxicity study provided in response to question 1 of the July 27, 2001, comments was missing histopathology, ECG and AUC data and a complete draft report has not been submitted. Exposures based upon AUC were also requested. Safety margins based upon AUC or  $\text{mg}/\text{m}^2$  are acceptable, however, multiples based upon  $\text{mg}/\text{kg}$  comparisons are not.

The Division asked the sponsor to provide the cause of death in the *in vivo* micronucleus assay.

The Division stated that a full translation from the Japanese toxicology for the drug substance would not be required.

#### **Chemistry, Manufacturing, Control (Tab 6)**

Are there any CMC issues or deficiencies in the submission that need to be addressed prior to filing the NDA?

The Division requested a minimum of 12 months stability data in the NDA submission.

The sponsor stated that 18 months of stability will be available at submission of the NDA.

The Division asked if the to-be-marketed formulation would be the same as the trial formulation submitted in the IND.

The sponsor responded that the trial formulation would also be submitted in the NDA.

The Division requested data on the thermal stability of the drug substance and the excipients.

The sponsor stated that testing performed has not revealed any degradation.

The Division requested the test reports.

The Division asked if the ingredients are \_\_\_\_\_

b(4)

The sponsor stated that the ingredients are \_\_\_\_\_ and that supporting data would be provided.

b(4)

### Regulatory (Tab7)

1. How was the exclusivity from the Tricor Capsules transferred to the Tricor Tablet formulation? (This question was paraphrased by the Division.)

The Division responded that it is standard procedure to transfer the remainder of any exclusivity from one dosage form to another with the same active ingredient.

2. Is a review and analysis of the published fenofibrate literature sufficient to support a maximum dose of \_\_\_\_\_ for Ciper CIP-Fenofibrate Capsules?

b(4)

The Division responded that the concept is acceptable, but a determination would have to wait for the full review. The Division added that a large safety exposure is desirable and that the study in the published article is of short duration and relatively few patients.

- 3a. Is the toxicology and published clinical trial information adequate to administer up to \_\_\_\_\_ of CIP-Fenofibrate in a clinical trial?

b(4)

The Division stated that a clinical study would be needed to determine the safety of a 250 mg dose in addition to all published data supporting high-doses. The Division recommended submitting \_\_\_\_\_ as the highest dose in the NDA \_\_\_\_\_

b(4)

- 3b. Will the FDA suggest a patient population that they would like to see clinical trial data generated at a dose of \_\_\_\_\_ of CIP-Fenofibrate?

b(4)

Refer to discussion of question 3a.

3. Is that (the safety margin generated by the 3-month dog toxicity study) acceptable to the FDA.

The Division stated that exposures based on a mg/kg dosing were not acceptable. The Division requires AUC or mg/m<sup>2</sup> (true exposures) otherwise we cannot comment on the safety margins generated by the 3-month study.

The sponsor asked if a waiver of pediatric studies should be requested in the NDA submission.

The Division advised the sponsor to request a waiver because typically fenofibrate is not beneficial until patients reach maturity.

Unresolved or Issues Requiring Further Discussion:

- None

Action Items:

For the sponsor:

Complete a bioequivalence study with CIP-Fenofibrate compared to the reference listed product under fasting conditions.

Complete a dosage form equivalence study comparing the pharmacokinetics of four of the 50 mg capsules with one of the 200 mg capsules under low-fat conditions.

Conduct dissolution testing under 3 different conditions, avoiding acidic medium, and using as little surfactant as possible to reach in-sink conditions.

Provide the cause of death in the *in vivo* micronucleus assay.

Provide missing histopathology and a complete draft report from the 3 month dog toxicity study.

Provide test reports on the thermal stability of the drug substance and the excipients.

Request a waiver of pediatric studies in the NDA.

Prepared by: *{See appended electronic signature page}*, Meeting Recorder  
William C. Koch, R.Ph. date  
Regulatory Project Manager

Concurrence: *{See appended electronic signature page}*, Meeting Chair  
David G. Orloff, M.D. date  
Director

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/s/

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