

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-418

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

Patent and Exclusivity Search Results from query on Appl No 019304 Product 004 in the OB_Disc list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
019304	004	4895726	Jan 19, 2009				

Exclusivity Data

There is no unexpired exclusivity for this product.

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
2. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.

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FDA/Center for Drug Evaluation and Research

Office of Generic Drugs

Division of Labeling and Program Support

Update Frequency:

Orange Book Data - **Monthly**

Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through June, 2008

Patent and Generic Drug Product Data Last Updated: July 22, 2008

Patent and Exclusivity Search Results from query on Appl No 021203 Product 003 in the OB_Disc list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
021203	003	4895726	Jan 19, 2009				
021203	003	6074670	Jan 9, 2018	NOT ON OTHER LISTS			
021203	003	6277405	Jan 9, 2018				
021203	003	6589552	Jan 9, 2018	NOT ON OTHER LISTS			
021203	003	6652881	Jan 9, 2018		Y		
021203	003	7037529	Jan 9, 2018		Y		
021203	003	7041319	Jan 9, 2018		Y		

Exclusivity Data

There is no unexpired exclusivity for this product.

Additional information:

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2. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.

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Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through June, 2008

Patent and Generic Drug Product Data Last Updated: July 22, 2008

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

As required by 21 CFR §314.50(i)(1)(i)(A)(4), Mutual Pharmaceutical Company, Inc. hereby states that Mutual will comply with the requirements under 21 CFR §314.52(a) with the respect to providing a notice to the holder of the NDA No. 19-304 for Tricor® (discontinued) and each owner of U.S. Patent No 4,895,726 and with the requirements under 21 CFR §314.52(c) with respect to the content of the notice. The notice will be sent in compliance with the requirement under 21 CFR§314.52(b) by registered mail, return receipt requested.

Concurrently with sending the notice, Mutual Pharmaceutical Company, Inc. will, as required by 21 CFR 314.52(d), amend its NDA for Fenofibric Acid Tablets, 35mg and 105mg to include a statement certifying that the notice has been provided to each person identified under 21 CFR 314.52(a) and that the notice met the content requirements of 21 CFR 314.52(c).



E. Brendan Magrab
Executive Vice President of Commercial Operations, General Counsel

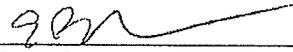
7/29/08

Date

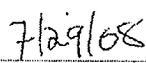
STATEMENT CONCERNING NOTICE TO PATENT AND NDA HOLDERS

As required by 21 CFR §314.50(i)(1)(i)(A)(4), Mutual Pharmaceutical Company, Inc. hereby states that Mutual will comply with the requirements under 21 CFR §314.52(a) with the respect to providing a notice to the holder of the NDA. 21-203 for Tricor® (discontinued) and each owner of U.S. Patent Nos. 4895726, 6074670, 6277405, 6589552, 6652881, 7037529, 7041319, and with the requirements under 21 CFR §314.52(c) with respect to the content of the notice. The notice will be sent in compliance with the requirement under 21 CFR §314.52(b) by registered mail, return receipt requested.

Concurrently with sending the notice, Mutual Pharmaceutical Company, Inc. will, as required by 21 CFR 314.52(d), amend its NDA for Fenofibric Acid Tablets, 35mg and 105mg to include a statement certifying that the notice has been provided to each person identified under 21 CFR 314.52(a) and that the notice met the content requirements of 21 CFR 314.52(c).



E. Brendan Magrab
Executive Vice President of Commercial Operations, General Counsel



Date

(48 mg)

Patent and Exclusivity Search Results from query on Appl No 021656 Product 001 in the OB_Rx list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
021656	001	5145684	✓Jan 25, 2011		Y	<u>U-615</u>	
021656	001	6277405	✓Jan 9, 2018	Y			
021656	001	6375986	✓Sep 21, 2020		Y	<u>U-615</u>	
021656	001	6652881	Jan 9, 2018	Y			
021656	001	7037529	✓Jan 9, 2018		Y		
021656	001	7041319	✓Jan 9, 2018		Y		
021656	001	7276249	✓Feb 21, 2023		Y		
021656	001	7320802	✓Feb 21, 2023			<u>U-847</u>	

Exclusivity Data**There is no unexpired exclusivity for this product.**

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
2. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.

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Update Frequency:

Orange Book Data - **Monthly**Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through December, 2008

Patent and Generic Drug Product Data Last Updated: February 09, 2009

(145 mg)

Patent and Exclusivity Search Results from query on Appl No 021656 Product 002 in the OB_Rx list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
021656	002	5145684 ✓	Jan 25, 2011		Y	U-615	
021656	002	6277405 ✓	Jan 9, 2018	Y			
021656	002	6375986 ✓	Sep 21, 2020		Y	U-615	
021656	002	6652881 ✓	Jan 9, 2018	Y			
021656	002	7037529 ✓	Jan 9, 2018		Y		
021656	002	7041319 ✓	Jan 9, 2018		Y		
021656	002	7276249 ✓	Feb 21, 2023		Y		
021656	002	7320802 ✓	Feb 21, 2023			U-847	

Exclusivity Data**There is no unexpired exclusivity for this product.**

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
2. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.

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Update Frequency:

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Orange Book Data Updated Through June, 2008

Patent and Generic Drug Product Data Last Updated: July 22, 2008

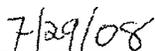
**STATEMENT CONCERNING NOTICE TO PATENT OWNER AND NDA
HOLDERS**

As required by 21 CFR §314.50(i)(1)(i)(A)(4), Mutual Pharmaceutical Company, Inc. hereby states that Mutual will comply with the requirements under 21 CFR §314.52(a) with the respect to providing a notice to the holder of the NDA Number 21-656 for Tricor® and each owner of U.S. Patent Nos. 5145684, 6277405, 6375986, 6632881, 7037529, 7041319, 7276249, 7320802, and with the requirements under 21 CFR §314.52(c) with respect to the content of the notice. The notice will be sent in compliance with the requirement under 21 CFR §314.52(b) by registered mail, return receipt requested.

Concurrently with sending the notice, Mutual Pharmaceutical Company, Inc. will, as required by 21 CFR 314.52(d), amend its NDA for Fenofibric Acid Tablets, 35mg and 105mg to include a statement certifying that the notice has been provided to each person identified under 21 CFR 314.52(a) and that the notice met the content requirements of 21 CFR 314.52(c).



E. Brendan Magrab
Executive Vice President of Commercial Operations, General Counsel



Date

Paragraph IV Certification

In accordance with the Federal Food, Drug, and Cosmetic Act, as amended September 24, 1984, Mutual Pharmaceutical Company, Inc., in its opinion and to the best of its knowledge, provides the following Patent Certification for our New Drug Application for Fenofibric Acid Tablets, 35mg and 105mg.

Mutual Pharmaceutical Company, Inc. certifies that U.S. Patent No. 4,895,726 is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of Mutual's Fenofibric Acid Tablets, 35mg and 105mg for which this application is submitted.

This certification is made in accordance with Section 505(b)(2)(A)(iv) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.50(i)(1)(i)(A)(4).



E. Brendan Magrab
Executive Vice President of Commercial Operations, General Counsel



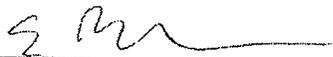
Date

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Mutual Pharmaceutical Company, Inc. certifies that the following U.S. Patents are invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of Mutual's Fenofibric Acid Tablets, 35mg and 105mg for which this application is submitted: 5145684, 6277405, 6375986, 6632881, 7037529, 7041319, 7276249, 7320802.

This certification is made in accordance with Section 505(b)(2)(A)(iv) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.50(i)(1)(i)(A)(4).



E. Brendan Magrab
Executive Vice President of Commercial Operations, General Counsel

7/29/08

Date

Paragraph IV Certification

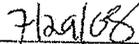
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Mutual Pharmaceutical Company, Inc. certifies that the following U.S. Patents are invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of Mutual's Fenofibric Acid Tablets, 35mg and 105mg for which this application is submitted: 4895726, 6074670, 6277405, 6589552, 6652881, 7037529, 7041319.

This certification is made in accordance with Section 505(b)(2)(A)(iv) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.50(i)(1)(i)(A)(4).



E. Brendan Magrab
Executive Vice President of Commercial Operations, General Counsel



Date

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**
*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

22-418

NAME OF APPLICANT / NDA HOLDER
Mutual Pharmaceutical Company, Inc.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)
Fenofibric Acid Tablets

ACTIVE INGREDIENT(S)
Fenofibric Acid

STRENGTH(S)
35mg and 105mg

DOSAGE FORM
Tablet

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

I. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
d. Name of Patent Owner	Address (of Patent Owner)	
	City/State	
	ZIP Code	FAX Number (if available)
	Telephone Number	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address (of agent or representative named in 1.e.)	
	City/State	
	ZIP Code	FAX Number (if available)
	Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? <input type="checkbox"/> Yes <input type="checkbox"/> No		
If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? <input type="checkbox"/> Yes <input type="checkbox"/> No		

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

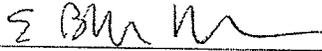
6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



7-28-08

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name
E. Brendan Magrab

Address
1100 Orthodox Street

City/State
Philadelphia

ZIP Code
19124

Telephone Number
215-288-6500

FAX Number (if available)

E-Mail Address (if available)

The public reporting burden for this collection of information has been estimated to average 20 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:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

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.

INFORMATION AND INSTRUCTIONS FOR FORM 3542a

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.

Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement (pending method of use).

- 4.2) For each pending method of use claimed by the patent, identify by number the claim(s) in the patent that claim the pending use of the drug. An applicant may list together multiple patent claim numbers and information for each pending method of use, if applicable. However, each pending method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

8/17/09

EXCLUSIVITY SUMMARY

NDA # 22-418

SUPPL #

HFD # 510

Trade Name Fibricor

Generic Name fenofibric acid

Applicant Name Mutual Pharmaceutical Corp., Inc.

Approval Date, If Known 814/09

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

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

YES NO

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

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

d) Did the applicant request exclusivity?

YES NO

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

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

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

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

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

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

NDA# 22224

Trilipx (fenofibric acid) Tablets

NDA#

NDA#

2. Combination product.

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

YES NO

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

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

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

summary for that investigation.

YES NO

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

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

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

Investigation #1 YES NO

Investigation #2 YES NO

Investigation #1
!
!
YES ! NO
Explain: ! Explain:

Investigation #2
!
!
YES ! NO
Explain: ! Explain:

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

YES NO

If yes, explain:

Name of person completing form: Kati Johnson
Title: Project Manager
Date: 8/17/09

Name of Office/Division Director signing form: Mary H. Parks, MD
Title: Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

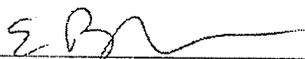
/s/

KATI JOHNSON
08/17/2009

MARY H PARKS
08/17/2009

EXCLUSIVITY STATEMENT

Mutual Pharmaceutical Company, Inc. certifies that, to the best of our knowledge, the listed drug is not entitled to a period of market exclusivity section 505(j)(4)(D) of the act. Please see the relevant page(s) from the Electronic Orange Book, which show the absence of exclusivity for Tricor®.



E. Brendan Magrab
Executive Vice President of Commercial Operations,
General Counsel

7/29/08

Date

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

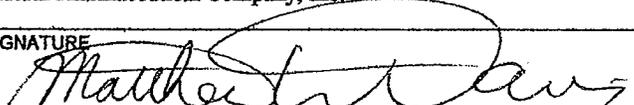
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the 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	See attached list	

- (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 Matthew W. Davis, M.D., RPh.	TITLE Vice President Branded Products and Medical Affairs
FIRM / ORGANIZATION Mutual Pharmaceutical Company, Inc.	
SIGNATURE 	DATE July 28, 2008

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

1 Page(s) Withheld

 ✓ § 552(b)(4) Trade Secret / Confidential

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

Johnson, Kati

From: Robert Dettery [RDettery@urlpharma.com]
Sent: Friday, August 14, 2009 2:09 PM
To: Johnson, Kati; Sherry Schultz
Subject: RE: Fibricor AP letter, NDA 22-418

I received the approval letter. Thank you for all your help and understanding.

Robert Dettery

Vice-President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.
AR Scientific, Inc.

From: Johnson, Kati [mailto:Kati.Johnson@fda.hhs.gov]
Sent: Friday, August 14, 2009 2:06 PM
To: Sherry Schultz
Cc: Robert Dettery
Subject: Fibricor AP letter, NDA 22-418

please confirm receipt
<<22418FINALsigned.pdf>>

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Phone-301-796-1234
Fax-301-796-9718
Kati.Johnson@fda.hhs.gov

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8/17/2009

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 22-418 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Fibracor Established/Proper Name: fenofibric acid Dosage Form: Tablets, 35 mg, 105 mg		Applicant: Mutual Pharmaceutical Co., Inc. Agent for Applicant (if applicable):
RPM: Kati Johnson		Division: Division of Metabolism and Endocrine Products
<p>NDA: NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>19-304: Tricor 67 mg, 134 mg, 200 mg 21-203: Tricor 54 mg, 160 mg 21-656: Tricor 48 mg, 145 mg</p> <p>Provide a brief explanation of how this product is different from the listed drug. Different strength</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.</p> <p style="text-align: center;">X No changes <input type="checkbox"/> Updated Date of check: 8/14/09</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p> <p>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</p>
❖ User Fee Goal Date Action Goal Date (if different)		6/15/09
❖ Actions		
• Proposed action		X AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions (specify type and date for each action taken)		X None

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

<p>❖ Promotional Materials (<i>accelerated approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance www.fda.gov/cder/guidance/2197df.pdf). If not submitted, explain _____</p>	<p><input type="checkbox"/> Received</p>
---	--

❖ Application ² Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC Comments: _____	
❖ Date reviewed by PeRC (<i>required for approvals only</i>) If PeRC review not necessary, explain: does not trigger PREA _____	
❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM (<i>approvals only</i>)	<input type="checkbox"/> Yes, date
❖ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (<i>approvals only</i>)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Press Office notified of action (by OEP)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Indicate what types (if any) of information dissemination are anticipated	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

² All questions in all sections pertain to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input type="checkbox"/> No <input checked="" type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date 10- year limitation expires:
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input checked="" type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (Summary Reviews)).</i> 	<input type="checkbox"/> N/A (no paragraph IV certification) <input checked="" type="checkbox"/> Verified

- [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for each paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
CONTENTS OF ACTION PACKAGE	
<p>❖ Copy of this Action Package Checklist³</p>	<p>X</p>
Officer/Employee List	
<p>❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)</p>	<p>X Included</p>
<p>Documentation of consent/non-consent by officers/employees</p>	<p><input type="checkbox"/> Included</p>
Action Letters	
<p>❖ Copies of all action letters (<i>including approval letter with final labeling</i>)</p>	<p>Action(s) and date(s) AP 8/14/09</p>
Labeling	
<p>❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)</p>	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	<p>X</p>
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
<p>❖ Medication Guide/Patient Package Insert/Instructions for Use (<i>write submission/communication date at upper right of first page of each piece</i>)</p>	<p><input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input checked="" type="checkbox"/> None</p>

³ Fill in blanks with dates of reviews, letters, etc.
Version: 9/5/08

<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date at upper right of first page of each submission</i>) 	
<ul style="list-style-type: none"> • Most-recent division proposal for (only if generated after latest applicant submission) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEDP 5/8/09 <input type="checkbox"/> DRISK <input type="checkbox"/> DDMAC <input type="checkbox"/> CSS <input checked="" type="checkbox"/> Other reviews SEALD 6/17/09
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Review(s) (<i>indicate date(s)</i>) • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) 	5/7/09 Acceptable 5/20/09
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	2/13/09
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents www.fda.gov/ora/compliance_ref/aip_page.html 	
<ul style="list-style-type: none"> • Applicant in on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatric Page (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input type="checkbox"/> Included N/A
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>) 	<input checked="" type="checkbox"/> Verified, statement is acceptable
<ul style="list-style-type: none"> ❖ Postmarketing Requirement (PMR) Studies 	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Outgoing communications (<i>if located elsewhere in package, state where located</i>) 	
<ul style="list-style-type: none"> • Incoming submissions/communications 	
<ul style="list-style-type: none"> ❖ Postmarketing Commitment (PMC) Studies 	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Outgoing Agency request for postmarketing commitments (<i>if located elsewhere in package, state where located</i>) 	

⁴ Filing reviews for other disciplines should be filed behind the discipline tab.
Version: 9/5/08

• Incoming submission documenting commitment	
❖ Outgoing communications (<i>letters (except previous action letters), emails, faxes, telecons</i>)	X
❖ Internal memoranda, telecons, etc.	N/A
❖ Minutes of Meetings	
• PeRC (<i>indicate date; approvals only</i>)	X Not applicable
• Pre-Approval Safety Conference (<i>indicate date; approvals only</i>)	X Not applicable
• Regulatory Briefing (<i>indicate date</i>)	X No mtg
• Pre-NDA/BLA meeting (<i>indicate date</i>)	X <input type="checkbox"/> No mtg Preliminary Responses to MR 1/5/08
• EOP2 meeting (<i>indicate date</i>)	X No mtg
• Other (e.g., EOP2a, CMC pilot programs)	
❖ Advisory Committee Meeting(s)	X No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	X None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 8/14/09
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None Same as DD summary memo above
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	8/14/09
• Clinical review(s) (<i>indicate date for each review</i>)	6/10/09
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	X None
❖ Safety update review(s) (<i>indicate location/date if incorporated into another review</i>)	Page 15 of 6/10/09 clinical review
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not	See page 18 of 6/10/09 clinical review
❖ Clinical reviews from other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	X None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	X Not needed
❖ Risk Management	X None
• Review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	
• REMS Memo (<i>indicate date</i>)	
• REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>)	
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested 5/15/09, 6/16/09
Clinical Microbiology <input type="checkbox"/> None	

⁵ Filing reviews should be filed with the discipline reviews.
Version: 9/5/08

❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	X None
Clinical Microbiology Review(s) (indicate date for each review)	X None
Biostatistics X None	
❖ Statistical Division Director Review(s) (indicate date for each review)	X None
Statistical Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	X None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	X None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 6/8/09
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	X None
• Supervisory Review(s) (indicate date for each review)	X None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 4/30/09
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	X None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	X No carc
❖ ECAC/CAC report/memo of meeting	X None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	X None requested
CMC/Quality <input type="checkbox"/> None	
❖ CMC/Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	X None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None 6/15/09
• CMC/product quality review(s) (indicate date for each review)	<input type="checkbox"/> None 5/18/09, 6/12/09
• BLAs only: Facility information review(s) (indicate dates)	X None
❖ Microbiology Reviews	
• NDAs: Microbiology reviews (sterility & pyrogenicity) (indicate date of each review)	X Not needed
• BLAs: Sterility assurance, product quality microbiology (indicate date of each review)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<input type="checkbox"/> None 5/13/09-Biopharm
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input type="checkbox"/> Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)	Page 59 of 5/18/09 CMC review
<input type="checkbox"/> Review & FONSI (indicate date of review)	

<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ NDAs: Methods Validation	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed
❖ Facilities Review/Inspection	
<ul style="list-style-type: none"> • NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) 	Date completed: 6/11/09 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> • BLAs: <ul style="list-style-type: none"> ○ TBP-EER ○ Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) (<i>date completed must be within 60 days prior to AP</i>) 	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation Date completed: <input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold

Appendix A to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
NDA 22418	ORIG 1	MUTUAL PHARM	FENOFIBRIC ACID TABS 35MG/105MG ORAL

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

/s/

KATI JOHNSON
08/17/2009

Johnson, Kati

From: Sherry Schultz [sschultz@urlpharma.com]
Sent: Tuesday, July 21, 2009 12:39 PM
To: Johnson, Kati
Subject: RE: NDA 22-418, Fibrivor, labeling comments

Hi Kati,

In response to your previous correspondence regarding the use of Child Resistant Closures (CRC) on 30, 60 and 90 count bottles, please note that it is Mutual's practice to package any size, under 100 fill, in a bottle with a Child Resistant Cap.

B. Child Resistant Closure

The bottle sizes of the 30, 60 and 90 count are considered unit of use based on the usual dosage of this product and could be dispensed directly to the patient. Therefore these product sizes should contain a Child Resistant Closure (CRC).

If you need any additional information regarding this matter, please feel free to contact me.

Thanks,

Sherry

From: Johnson, Kati [mailto:Kati.Johnson@fda.hhs.gov]
Sent: Tuesday, May 12, 2009 6:01 AM
To: Sherry Schultz
Subject: NDA 22-418, Fibrivor, labeling comments

Sherry,

Here are the labeling comments.

Please respond to them in an official submission. OK to e-mail it to me to speed up my final (I hope) review.

A. Container Labels (35 mg and 105 mg)

As currently presented, both labels look almost identical when compared side by side because the same colors used for the trade dress are also used to differentiate the two strengths.

This color scheme does not provide enough differentiation to distinguish between the two different strengths. Revise the labels to incorporate a more adequate means of differentiation (e.g., different contrast color schemes, boxing, etc.).

B. Child Resistant Closure

The bottle sizes of the 30, 60 and 90 count are considered unit of use based on the usual dosage of this product and could be dispensed directly to the patient. Therefore these product sizes should contain a Child Resistant Closure (CRC).

Let me know if you have any questions.

KJ

8/13/2009

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Phone-301-796-1234
Fax-301-796-9718
Kati.Johnson@fda.hhs.gov

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8/13/2009

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
NDA 22418	ORIG 1	MUTUAL PHARM	FENOFIBRIC ACID TABS 35MG/105MG ORAL

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

/s/

KATI JOHNSON

08/13/2009

In response to a comment in the 5/8/09 DMEPA review, the firm confirmed that package sizes under 100 count use child resistant caps.

URL MUTUAL

3 June 2009

United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street
Philadelphia, PA 19124

215-288-6500
www.urmutual.com

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

RECEIVED
JUN 03 2009
CDER CDR

**Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
Sequence No. 0010: Response to 21 May 2009 Request
for Information**

Dear Dr. Parks:

NB00-BTM

Please refer to NDA 22-418 for Fibracor™ (fenofibric acid), submitted 15 August 2008 and a request for information sent by Kati Johnson in an e-mail on 21 May 2009. The request pertained to study MPC-028-07-1007 which demonstrated the bioequivalence of the proposed new drug product, fenofibric acid 105 mg, and the reference listed drug, TriCor® (fenofibrate) 145 mg, when each was administered as a single dose under standard fasting conditions. The request is stated below in bold, verbatim:

According to the Division of Scientific Investigations, for study MPC-028-07-1007 the PRACS Institute-Cetero Research changed 50 of the 54 subjects' case report forms (CRFs) from meeting inclusion/exclusion criteria to not meeting inclusion/ exclusion criteria for medical history, physical examinations, clinical laboratory test results, vital sign measurements and ECG parameters 8 months after the completion of the study. The data from these 50 patients were included in the final study report.

Please provide the following to address this citing:
-tabulation of all deviations
-justification as to why patient data should be accepted.

Mutual Pharmaceutical Company, Inc. (Mutual) has reviewed the deviations and in doing so, has identified that the study report (Section 10.2 and Appendix 16.2.2) identified only 49 subjects of the 50 subjects with laboratory deviations. This response discusses all 50 subjects with laboratory deviations.

As background, PRACS Institute-Cetero Research (PRACS) directly transcribed the inclusion and exclusion criteria in the protocol to the Eligibility Checklist case report

form. The inclusion criterion that accounted for the protocol deviation affecting the 50 subjects noted above was stated as follows:

“Medically healthy on the basis of medical history, physical examination, clinical laboratory test results (especially tests for renal and hepatic function) within the normal range, and no clinically significant vital sign measurements and ECG parameters, as deemed by the Medical Investigator.”

During the conduct of the study, the clinical staff and Medical Investigator interpreted the above inclusion criterion as allowing the Medical Investigator to exercise clinical judgment as to the significance of any abnormality, including clinical laboratory test results. None of the values outside laboratory reference range were judged by the Medical Investigator as clinically significant and few warranted repeat. Thus, subjects with values outside reference range were enrolled as medically healthy with non-clinically significant laboratory values.

It was Mutual's intent that the phrase “as deemed by the Medical Investigator” applied only to the vital sign and ECG measurements. Therefore, laboratory deviations would need to be approved by Mutual. As Mutual was not consulted and, thus, did not approve these protocol deviations, the subjects with results outside laboratory reference range were identified in the clinical study report, as having violated the protocol. During study report preparation, these deviations were reviewed and it was concluded that these laboratory deviations did not affect the pharmacokinetics of fenofibric acid.

A total of 50 of the 54 subjects enrolled in study MPC-028-07-1007 was identified with one or more pre-treatment laboratory values outside the laboratory reference range. The majority of these laboratory values pertained to abnormalities in serum chemistry (elevated CPK or low total protein), urinalysis (primarily blood and/or white cells in the urine of women), and % white cell differentials outside the laboratory normal range.

Mutual has re-reviewed these laboratory results and concurs with the Medical Investigator's judgment. The subjects were healthy and the deviations were minor with no hepatic or renal dysfunction. None of the laboratory deviations presented a safety hazard and would not be expected to affect the pharmacokinetics of fenofibric acid.

A summary of the deviations and justification as to why the data should be accepted is provided in the **Attachment**. A listing of all clinical laboratory deviations at screening and check-in, organized by subject, is provided in **Appendix 1**. Should any additional tabulation be needed, Mutual will provide to the Division upon request.

Dr. Mary Parks
3 June 2009

Page 3

The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 3 June 2009. Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,

Robert Dettery auw

Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.



ORIGINAL

United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street
Philadelphia, PA 19124

215-288-6500
www.urlmutual.com

N-000-BC
ORIG AMENDMENT

29 May 2009

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

RECEIVED
MAY 29 2009
CDER CDR

**Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
Sequence No. 0009: Response to Discipline Review Letter**

Dear Dr. Parks:

In accordance with 21 CFR 314, Mutual Pharmaceutical Company, Inc., (Mutual) submitted a New Drug Application (NDA 22-418) for Fenofibric Acid Tablets, 35 mg and 105 mg for the treatment of hypercholesterolemia and hypertriglyceridemia on 15 August 2008

On 19 May 2009, the Division sent a Discipline Review Letter for the Chemistry, Manufacturing, and Controls section of NDA 22-418 with the following deficiencies identified (verbatim below in *italics*), followed by Mutual's responses.

+

7

b(4)

L

J

(2) As _____ cannot be formed during the manufacture of the drug product or by degradation during storage its acceptance criterion in the drug products should be NMT _____ instead of the proposed _____

b(4)

Further communication occurred on 26 May 2009 between the Division and Mutual regarding Item #2 of the Discipline Review Letter. An agreement was reached to omit the test and specification for _____ on the drug product specification analytical report given that the level of _____ is controlled in the drug substance at a limit of NMT _____. The revised test method and specification sheet, showing the elimination of the _____ specification and minor editorial changes, for the the drug product are

b(4)

located in Module 3.2.P.5.1 with justification of the change in Section 3.2.P.5.6.4. The drug substance test method and specification sheet, which includes the proposed specification of NMT _____ and some additional minor editorial changes, are provided in Module 3.2.S.4.1. b(4)

(3) *The dissolution method provided in your submission is acceptable* _____ b(4)

Mutual acknowledges the Division's request and commits _____ b(4)

(4) *Reference to the drug product in labels and labeling should read "Fibracor™ (fenofibric acid) Tablets" instead of " _____"*

The container labels have been revised to read "Fibracor™ (fenofibric acid) Tablets" in accordance with the Discipline Review Letter. In addition, Mutual has revised the color scheme on the principle display panel, to provide better differentiation of the two strengths, as requested in the 12 May 2009 email correspondence from the Division. The revised container labels are being provided in Module 1.14.1.1.

The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 29 May 2009. Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,

Robert Dettery cw
Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.

Johnson, Kati

From: Quaintance, Kim M
nt: Tuesday, May 26, 2009 3:37 PM
Johnson, Kati
cc: Duvall Miller, Beth A; Ripper, Leah W
Subject: NDA 22-418 for Fibracor (fenofibric acid)

Hi Kati,

We discussed your (b)(2) application today, and you are cleared for action! The only thing we ask is that your reviewers document somewhere that Tricor NDAs 19-304 and 21-203 were not discontinued for reasons due to safety or efficacy since Mutual has cited reliance on all of the Tricor applications.

Happy action!
Kim

Kim Quaintance
Associate Director for Regulatory Affairs
Office of New Drugs
CDER/FDA

301-796-0700 (OND IO main)

301-796-0140 (direct)

301-796-9856 (facsimile)

****Please note new email address****

k.quaintance@fda.hhs.gov



DEPARTMENT OF HEALTH & HUMAN SERVICES

5/20/09

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-418

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Mutual Pharmaceutical Company, Inc.
Attention: Robert Dettery
Vice President, Regulatory Affairs
1100 Orthodox Street
Philadelphia, PA 19124

Dear Mr. Dettery:

Please refer to your New Drug Application (NDA) dated August 15, 2008, received August 15, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for fenofibric acid tablets, 35 mg and 105 mg.

We also refer to your October 10, 2008, correspondence, received October 10, 2008, requesting review of your proposed proprietary name, Fibracor. We have completed our review of the proposed proprietary name, Fibracor and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your October 10, 2008 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Millie Wright, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-1027. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Kati Johnson at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, MD.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Eric Colman
5/20/2009 08:33:53 AM
Eric Colman for Mary Parks



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-418

DISCIPLINE REVIEW LETTER

Mutual Pharmaceutical Co., Inc.
Attention: Robert Dettery
Vice President, Regulatory Affairs
1100 Orthodox St.
Philadelphia, PA 19124

Dear Mr. Dettery:

Please refer to your August 15, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fibracor (fenofibric acid) Tablets, 35 mg, 105 mg.

Our review of the Chemistry, Manufacturing and Controls section of your submission is complete, and we have identified the following deficiencies:

- (1) [redacted] b(4)
- (2) As [redacted] cannot be formed during the manufacture of the drug product or by degradation during storage its acceptance criterion in the drug products should be NMT [redacted] % instead of the propose[redacted] b(4)
- (3) The dissolution method provided in your submission is acceptable [redacted] b(4)
- (4) Reference to the drug product in labels and labeling should read "Fibracor™ (fenofibric acid) Tablets" instead of "[redacted]" b(4)

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

NDA 22-418

Page 2

If you have any questions, call Kati Johnson, Project Manager, at (301) 796-1234.

Sincerely,

Ali Al-Hakim, Ph.D.
Chief, Branch II
Division of Pre-Marketing I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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

/s/

Ali Al-Hakim
5/19/2009 08:56:33 AM

Johnson, Kati

From: Griffis, Melina
Sent: Tuesday, May 19, 2009 7:38 AM
To: Johnson, Kati
Subject: RE: NDA 22-418, Fibracor, labeling comments

Hi Kati,

It looks like we are ok with these labels, Carol and Denise concur.

From: Johnson, Kati
Sent: Friday, May 15, 2009 3:55 PM
To: Griffis, Melina
Subject: RE: NDA 22-418, Fibracor, labeling comments

oops. my bad. let's try again

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Phone-301-796-1234
Fax-301-796-9718
Kati.Johnson@fda.hhs.gov

From: Griffis, Melina
Sent: Friday, May 15, 2009 3:54 PM
To: Johnson, Kati
Subject: RE: NDA 22-418, Fibracor, labeling comments

Hi Kati,

I don't see a file attached with the labels??? They are welcome to propose a total color change but I am doubtful it will matter, but you never know

From: Johnson, Kati
Sent: Friday, May 15, 2009 3:16 PM
To: Griffis, Melina
Subject: FW: NDA 22-418, Fibracor, labeling comments

5/19/2009

Hi melina,
I informed the sponsor of your concerns. Here is there counter proposal. I told them you weren't going to think this was any improvement, but said I would forward them anyway. See below for why they don't want to revise the fading bar color. This is fenofibrate #5 or 6, so I don't quite get why the appearance of the bottle means anything I guess I just don't have that marketing gene. thank goodness for that.
Kati

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Phone-301-796-1234
Fax-301-796-9718
Kati.Johnson@fda.hhs.gov

From: Sherry Schultz [mailto:sschultz@urlpharma.com]
Sent: Friday, May 15, 2009 1:28 PM
To: Johnson, Kati
Subject: RE: NDA 22-418, Fibracor, labeling comments

Hi Kati,

I think that we would benefit from totally changing the colors of the strengths instead, if that's okay. To change the fading bars would change the appearance from that of all of our currently marketed AR Scientific labeled products.

Attached are pdfs of the labels with the newly proposed colors. Hope they like them!

Thanks again for your assistance. Have a great weekend.

Sherry

From: Johnson, Kati [mailto:Kati.Johnson@fda.hhs.gov]
Sent: Friday, May 15, 2009 12:10 PM
To: Sherry Schultz
Subject: RE: NDA 22-418, Fibracor, labeling comments

Hi Sherry,
DMEPA says this is better, but they aren't completely satisfied. They indicated that if you changed the blue and red fading bars that are on the label such that one strength has 1 color and the other strength another color, then that would be OK. Can you send that to me and we will see what they say??

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products

5/19/2009

Office of Drug Evaluation II
Center for Drug Evaluation and Research
Phone-301-796-1234
Fax-301-796-9718
Kati.Johnson@fda.hhs.gov

From: Sherry Schultz [mailto:sschultz@urlpharma.com]
Sent: Wednesday, May 13, 2009 1:58 PM
To: Johnson, Kati
Subject: RE: NDA 22-418, Fibracor, labeling comments

Kati,

Thanks so much as always.

I have attached the different versions for your review.

1. The label pdf's attached, 1331010101 and 1331010201, contain the two labels where the only changes made from those previously submitted, are the knocked out strength box and the updated revision code.
2. The additional two pdf's attached, 15247 purifi label 35mg and purifi label 105mg, are the two that Marketing is proposing. The only reason I attached them is because the text proposed remains the same, other than the logo, and the labeling reviewers may actually prefer the layout of the front panel better.

You can disregard the two labels, 15247 purifi label 35mg and purifi label 105mg, proposed from the Marketing group if you feel that it will be cause for confusion or slow down the review process.

Thanks again and I am sure we will be talking soon.

Sherry

From: Johnson, Kati [mailto:Kati.Johnson@fda.hhs.gov]
Sent: Wednesday, May 13, 2009 11:36 AM
To: Sherry Schultz
Subject: RE: NDA 22-418, Fibracor, labeling comments

that would be fine. I am happy to chat with the DMEPA folks about your proposed revisions and see if they are OK with it.

KJ

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

5/19/2009

Phone-301-796-1234
Fax-301-796-9718
Kati.Johnson@fda.hhs.gov

From: Sherry Schultz [mailto:sschultz@urlpharma.com]
Sent: Wednesday, May 13, 2009 10:02 AM
To: Johnson, Kati
Subject: RE: NDA 22-418, Fibracor, labeling comments

Kati,

I had a quick question for you regarding the container labels. I had our labeling department create 1 label for each of the strengths with a color block knocked out strength box (if that makes any sense at all). I was wondering if I could send you the two examples to see if you believe that this will satisfy the request and adequately differentiate the strengths. I am asking only because I didn't want to update all 14 of the labels in an official submission and have it not satisfy the reviewer's request. If deemed satisfactory, I will then update all of the labels and include them in a formal submission along with the CRC information. I will not be incorporating any other changes to the labeling at this time. b(4)

Thanks so much.

Sherry

From: Johnson, Kati [mailto:Kati.Johnson@fda.hhs.gov]
Sent: Tuesday, May 12, 2009 6:01 AM
To: Sherry Schultz
Subject: NDA 22-418, Fibracor, labeling comments

Sherry,

Here are the labeling comments.

Please respond to them in an official submission. OK to e-mail it to me to speed up my final (I hope) review.

A. Container Labels (35 mg and 105 mg)

As currently presented, both labels look almost identical when compared side by side because

the same colors used for the trade dress are also used to differentiate the two strengths.

This color scheme does not provide enough differentiation to distinguish between the two

different strengths. Revise the labels to incorporate a more adequate means of differentiation

(e.g., different contrast color schemes, boxing, etc.).

B. Child Resistant Closure

The bottle sizes of the 30, 60 and 90 count are considered unit of use based on the usual dosage

of this product and could be dispensed directly to the patient. Therefore these product

sizes
should contain a Child Resistant Closure (CRC).

Let me know if you have any questions.
KJ

Kati Johnson
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Division of Metabolism and Endocrinology Products
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5/19/2009

2 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process



United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street
Philadelphia, PA 19124
215-288-6500
www.urlmutual.com

4 March 2009

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
Sequence No. 0008: Response to Request for Additional
Information (Dissolution Data);
Additional CMC Information (updated stability data, in-
process controls revision)

Dear Dr. Parks:

In accordance with 21 CFR 314, Mutual Pharmaceutical Company, Inc., (Mutual) submitted a New Drug Application (NDA 22-418) for Fenofibric Acid Tablets, 35 mg and 105 mg for the treatment of hypercholesterolemia and hypertriglyceridemia on 15 August 2008.

On 9 February 2009, the Division requested *via* email the following CMC information:

- Dissolution data in multiple media (3 media) for both strengths.
- Data comparing the similarity of dissolution profiles obtained of both strengths in all media tested.

Mutual is submitting the report containing the comparative dissolution data in Module 3.2.P.5.4. Sections 2.7.1.1.3 and 3.2.P.5.4 have been amended with this information.

Additionally, Mutual is submitting in this amendment the following CMC information:

- A revision to the proposed in-process controls of the 105 mg tablet (an extension of the range from _____ to _____, see Mutual's Summary Report for Tablet Hardness in Module 3. Sections 2.3.P.3 and 3.2.P.3.4 have been amended to reflect this change.
- 18-month long-term stability data for the three registration batches of 35-mg tablets (BB 787 0307, BB 787 0308, and BB 787 0309) in Module 3.2.P.8. Sections 3.2.P.8.1 and 3.2.P.8.3 have been amended to reflect this updated stability data.

b(4)

Dr. M. Parks
4 March 2009

Page 2 of 2

The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 3 March 2009. Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,

Robert Dettery

Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.

505(b)(2) ASSESSMENT

2/13/09

Application Information		
NDA # 22-418	NDA Supplement #:S-	Efficacy Supplement Type SE-
Proprietary Name: Pending(Proposed=Fibracor) Established/Proper Name: fenofibric acid Dosage Form: Tablets Strengths: 35 mg, 105 mg		
Applicant: Mutual Pharmaceutical Co.		
Date of Receipt: 8/15/08		
PDUFA Goal Date: 6/15/09		Action Goal Date (if different):
Proposed Indication(s): 1. Hypercholesterolemia or Mixed Dyslipidemia 2. Hypertriglyceridemia		

GENERAL INFORMATION

1. Is this application for a drug that is an "old" antibiotic as described in the Guidance to Industry, Repeal of Section 507 of the Federal Food, Drug and Cosmetic Act? (Certain antibiotics are not entitled to Hatch-Waxman patent listing and exclusivity benefits.)

YES NO

If "YES," proceed to question #3.

2. Is this application for a recombinant or biologically-derived product and/or protein or peptide product?

YES NO

If "YES" contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

**INFORMATION PROVIDED VIA RELIANCE
(LISTED DRUG OR LITERATURE)**

3. List the information essential to the approval of the proposed drug that is provided by reliance on our previous finding of safety and efficacy for a listed drug or by reliance on published literature. *(If not clearly identified by the applicant, this information can usually be derived from annotated labeling.)*

Source of information (e.g., published literature, name of referenced product)	Information provided (e.g., pharmacokinetic data, or specific sections of labeling)
NDA 21-656, Tricor (fenofibrate)	Indication, Dosage and Administration, Contraindications, Warnings and Precautions, Adverse Reactions, Drug Interactions, Use in Specific Populations, Clinical Pharmacology, Nonclinical toxicology, clinical studies

4. Reliance on information regarding another product (whether a previously approved product or from published literature) must be scientifically appropriate. An applicant needs to provide a scientific "bridge" to demonstrate the relationship of the referenced and proposed products. Describe how the applicant bridged the proposed product to the referenced product(s). (Example: BA/BE studies)

BE study

RELIANCE ON PUBLISHED LITERATURE

5. (a) Does the application rely on published literature to support the approval of the proposed drug product (i.e., the application *cannot* be approved without the published literature)?

YES NO

If "NO," proceed to question #6.

- (b) Does any of the published literature necessary to support approval identify a specific (e.g., brand name) *listed* drug product?

YES NO

If "NO", proceed to question #6

If "YES", list the listed drug(s) identified by name and answer question #5(c).

- (c) Are the drug product(s) listed in (b) identified by the applicant as the listed drug(s)?

YES NO

RELIANCE ON LISTED DRUG(S)

Reliance on published literature which identifies a specific approved (listed) drug constitutes reliance on that listed drug. Please answer questions #6-10 accordingly.

6. Regardless of whether the applicant has explicitly referenced the listed drug(s), does the application rely on the finding of safety and effectiveness for one or more listed drugs (approved drugs) to support the approval of the proposed drug product (i.e., the application cannot be approved without this reliance)?
- YES NO

If "NO," proceed to question #11.

7. Name of listed drug(s) relied upon, and the NDA/ANDA #(s). Please indicate if the applicant explicitly identified the product as being relied upon (see note below):

Name of Drug	NDA/ANDA #	Did applicant specify reliance on the product? (Y/N)
Tricor (fenofibrate) Tablets, 48mg, 145 mg.	NDA 21-656	Yes

Applicants should specify reliance on the 356h, in the cover letter, and/or with their patent certification/statement. If you believe there is reliance on a listed product that has not been explicitly identified as such by the applicant, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

8. If this is a supplement, does the supplement rely upon the same listed drug(s) as the original (b)(2) application?
- YES NO
- If "NO", please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

9. Were any of the listed drug(s) relied upon for this application:
- a. Approved in a 505(b)(2) application?
- YES NO
- If "YES", please list which drug(s).*

Name of drug(s) approved in a 505(b)(2) application:

- b. Approved by the DESI process?
- YES NO
- If "YES", please list which drug(s).*

Name of drug(s) approved via the DESI process:

- c. Described in a monograph?
- YES NO
- If "YES", please list which drug(s).*

Name of drug(s) described in a monograph:

d. Discontinued from marketing?

YES X NO

If "YES", please list which drug(s) and answer question d.1.

If "NO", proceed to question #10.

Name of drug(s) discontinued from marketing:

NDA 19-304, Tricor Capsules, 67 mg, 134 mg, 200 mg

NDA 21-203, Tricor Tablets 54 mg, 160 mg

1. Were the products discontinued for reasons related to safety or effectiveness?

YES NO X

(Information regarding whether a drug has been discontinued from marketing for reasons of safety or effectiveness may be available in the Orange Book. Refer to section 1.11 for an explanation, and section 6.1 for the list of discontinued drugs. If a determination of the reason for discontinuation has not been published in the Federal Register (and noted in the Orange Book), you will need to research the archive file and/or consult with the review team. Do not rely solely on any statements made by the sponsor.)

10. Describe the change from the listed drug(s) relied upon to support 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 capsule to solution").

Strength of tablets and change in dosage form:

Tricor, NDA 19-304-67 mg, 134 mg, 200 mg CAPSULES

Tricor NDA 21-203-54 mg, 160 mg TABLETS

Tricor, NDA 21-656-48 mg, 145 mg TABLETS

Fenofibric acid, NDA 22-418-35 mg, 105 mg.

The purpose of the following two questions is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.

11. (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved (via an NDA or ANDA)?

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical equivalent must also be a combination of the same drugs.

YES NO X

If "NO," to (a) proceed to question #12.

(b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval?

YES NO

(c) Is the listed drug(s) referenced by the application a pharmaceutical equivalent?

YES NO

If "YES" and there are no additional pharmaceutical equivalents listed, proceed to question #13.

If "NO" or if there are additional pharmaceutical equivalents that are not referenced by the application, list the NDA pharmaceutical equivalent(s); you do not have to individually list all of the products approved as ANDAs, but please note that there are approved generics listed in the Orange Book. Please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical equivalent(s):

12. (a) Is there a pharmaceutical alternative(s) already approved (via an NDA or ANDA)?

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical alternative must also be a combination of the same drugs.

YES X NO

If "NO", proceed to question #13.

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval?

YES X NO

(c) Is the approved pharmaceutical alternative(s) referenced as the listed drug(s)?

YES X NO

If "YES" and there are no additional pharmaceutical alternatives listed, proceed to question #13.

If "NO" or if there are additional pharmaceutical alternatives that are not referenced by the application, list the NDA pharmaceutical alternative(s); you do not have to individually list all of the products approved as ANDAs, but please note that there are approved generics listed in the Orange Book. Contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical alternative(s): approved generics and 5052 applications

PATENT CERTIFICATION/STATEMENTS

13. List the patent numbers of all patents listed in the Orange Book for the listed drug(s) for which our finding of safety and effectiveness is relied upon to support approval of the (b)(2) product.

Listed drug/Patent number(s):

<u>NDA 21-656</u>	<u>NDA 21-203</u>	<u>NDA 19-304</u>
5145684	4895726	4895726
6277405	6074670	
6375986	6277405	
6652881	6589552	
7037529	6652881	
7041319	7037529	
7276249	7041319	
7320802		

14. Did the applicant address (with an appropriate certification or statement) all of the patents listed in the Orange Book for the listed drug(s)?

YES X NO

If "NO", list which patents (and which listed drugs) were not addressed by the applicant.

Listed drug/Patent number(s):

15. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

- No patent certifications are required (e.g., because application solely based on published literature that does not cite a specific innovator product or for an "old antibiotic" (see question 1.))
- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
- 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
- Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
- Patent number(s):
- 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. (Paragraph IV certification)

Patent number(s): Same as under Question #13 response

If the application has been filed, did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]?

YES X NO

Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt.

YES X NO

Date Received:

Has the applicant been sued for patent infringement (within 45-days of receipt of the notification listed above)? Note: you may need to call the applicant to verify this information.

YES NO X

- 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).

Patent number(s):

If the application has been filed, did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]?

YES NO

Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt.

YES NO

Date Received:

Has the applicant been sued for patent infringement (within 45-days of receipt of the notification listed above)? Note: you may need to call the applicant to verify this information.

YES NO

- Written statement from patent owner that it consents to an immediate effective date of approval (applicant must also submit paragraph IV certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).

Patent number(s):

- 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 as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

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

/s/

Kati Johnson
2/13/2009 01:28:35 PM
CSO

2/13/09

NDA/BLA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

Application Information		
NDA # 22-418 BLA#	NDA Supplement #:S- BLA STN #	Efficacy Supplement Type SE-
Proprietary Name: TBD Established/Proper Name: Fenofibric acid Dosage Form: Tablets Strengths: 35 mg, 105 mg		
Applicant: Mutual Pharmaceutical Co., Inc. Agent for Applicant (if applicable): N/A		
Date of Application: 8/15/08 Date of Receipt: 8/15/08 Date clock started after UN: N/A		
PDUFA Goal Date: 6/15/09		Action Goal Date (if different):
Filing Date: 10/14/08 Date of Filing Meeting: 10/10/08		
Chemical Classification: (1,2,3 etc.) (original NDAs only) 5		
Proposed Indication(s): • as an adjunct to diet to reduce elevated total-C, LDL-C, triglycerides and apo B and to increase HDL-C in patients with primary hypercholesterolemia or mixed hyperlipidemia • as an adjunct to diet to treat patients with hypertriglyceridemia		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:		<input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
<i>Refer to Appendix A for further information.</i>		
Review Classification: <i>If the application includes a complete response to pediatric WR, review classification is Priority.</i> <i>If a tropical disease Priority review voucher was submitted, review classification defaults to Priority.</i>		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority <input type="checkbox"/> Tropical disease Priority review voucher submitted
Resubmission after withdrawal? N/A Resubmission after refuse to file? N/A		
Part 3 Combination Product? N/A	<input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Drug/Device <input type="checkbox"/> Biologic/Device	
<input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation <input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC	<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41)	

Other:	<input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)
Collaborative Review Division (if OTC product): N/A	
List referenced IND Number(s): 76,749	
PDUFA and Action Goal dates correct in tracking system? <i>If not, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	X YES <input type="checkbox"/> NO
Are the proprietary, established/proper, and applicant names correct in tracking system? <i>If not, ask the document room staff to make the corrections. Also, ask the document room staff to add the established name to the supporting IND(s) if not already entered into tracking system.</i>	X YES <input type="checkbox"/> NO
Are all classification codes/flags (e.g. orphan, OTC drug, pediatric data) entered into tracking system? <i>If not, ask the document room staff to make the appropriate entries.</i>	X YES <input type="checkbox"/> NO
Application Integrity Policy	
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at: http://www.fda.gov/ora/compliance_ref/aiplist.html</i> If yes, explain: If yes, has OC/DMPQ been notified of the submission? Comments:	<input type="checkbox"/> YES X NO <input type="checkbox"/> YES <input type="checkbox"/> NO
User Fees	
Form 3397 (User Fee Cover Sheet) submitted	X YES <input type="checkbox"/> NO
User Fee Status Comments:	X Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required
<i>Note: 505(b)(2) applications are no longer exempt from user fees pursuant to the passage of FDAAA. It is expected that all 505(b) applications, whether 505(b)(1) or 505(b)(2), will require user fees unless otherwise waived or exempted (e.g., business waiver, orphan exemption).</i>	
Exclusivity	

<p>Does another product have orphan exclusivity for the same indication? <i>Check the Electronic Orange Book at: http://www.fda.gov/cder/ob/default.htm</i></p> <p>If yes, is the product considered to be the same product according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?</p> <p><i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007)</i></p> <p>Comments:</p>	<p><input type="checkbox"/> YES X NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? (<i>NDAs/NDA efficacy supplements only</i>)</p> <p><i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i></p> <p>Comments:</p>	<p><input type="checkbox"/> YES # years requested: X NO</p>
<p>If the proposed product is a single enantiomer of a racemic drug previously approved for a different therapeutic use (<i>NDAs only</i>):</p> <p>Did the applicant (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b) request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?</p> <p><i>If yes, contact Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.</i></p>	<p>X Not applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>505(b)(2) (NDAs/NDA Efficacy Supplements only)</p>	
<p>1. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?</p> <p>2. Is the application for a duplicate of a listed drug whose only difference is that 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 21 CFR 314.54(b)(1)).</p> <p>3. Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug (see 21 CFR 314.54(b)(2))?</p>	<p><input type="checkbox"/> Not applicable</p> <p><input type="checkbox"/> YES X NO</p> <p><input type="checkbox"/> YES X NO</p> <p><input type="checkbox"/> YES X NO</p>

Note: If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9).

4. Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan or pediatric exclusivity)? *Check the Electronic Orange Book at: <http://www.fda.gov/cder/ob/default.htm>*

YES
 NO

If yes, please list below:

Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration

If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 108(b)(2). Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.

Format and Content

Do not check mixed submission if the only electronic component is the content of labeling (COL).

Comments:

All paper (except for COL)
 All electronic
 Mixed (paper/electronic)

CTD
 Non-CTD
 Mixed (CTD/non-CTD)

If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?

If electronic submission:
paper forms and certifications signed (non-CTD) or electronic forms and certifications signed (scanned or digital signature)(CTD)?

Forms include: 356h, patent information (3542a), financial disclosure (3454/3455), user fee cover sheet (3542a), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.

Comments:

YES
 NO

If electronic submission, does it follow the eCTD guidance?
(<http://www.fda.gov/cder/guidance/7087rev.pdf>)

YES
 NO

If not, explain (e.g., waiver granted):

<p>Form 356h: Is a signed form 356h included?</p> <p><i>If foreign applicant, both the applicant and the U.S. agent must sign the form.</i></p> <p>Are all establishments and their registration numbers listed on the form?</p> <p>Comments: in CMC section</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input checked="" type="checkbox"/> NO</p>
<p>Index: Does the submission contain an accurate comprehensive index?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including:</p> <p><input type="checkbox"/> legible <input type="checkbox"/> English (or translated into English) <input type="checkbox"/> pagination <input type="checkbox"/> navigable hyperlinks (electronic submissions only)</p> <p>If no, explain:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>Controlled substance/Product with abuse potential:</p> <p>Abuse Liability Assessment, including a proposal for scheduling, submitted?</p> <p>Consult sent to the Controlled Substance Staff?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>BLAs/BLA efficacy supplements only:</p> <p>Companion application received if a shared or divided manufacturing arrangement?</p> <p>If yes, BLA #</p>	<p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
Patent Information (NDAs/NDA efficacy supplements only)	
<p>Patent information submitted on form FDA 3542a?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
Debarment Certification	
<p>Correctly worded Debarment Certification with authorized signature?</p> <p><i>If foreign applicant, both the applicant and the U.S. Agent must</i></p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>

<p>sign the certification.</p> <p><i>Note: Debarment Certification should use wording in FD&C Act section 306(k)(l) i.e., "[Name of applicant] hereby certifies that it 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 this application." Applicant may not use wording such as, "To the best of my knowledge..."</i></p> <p>Comments:</p>	
<p>Field Copy Certification (NDAs/NDA efficacy supplements only)</p>	
<p>Field Copy Certification: that it is a true copy of the CMC technical section (<i>applies to paper submissions only</i>)</p> <p><i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i></p>	<p><input type="checkbox"/> Not Applicable (<i>electronic submission or no CMC technical section</i>)</p> <p>X YES</p> <p><input type="checkbox"/> NO</p>
<p>Financial Disclosure</p>	
<p>Financial Disclosure forms included with authorized signature?</p> <p><i>Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an Agent.</i></p> <p><i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i></p> <p>Comments:</p>	<p>X YES</p> <p><input type="checkbox"/> NO</p>
<p>Pediatrics</p>	
<p>PREA</p> <p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PerC prior to approval of the application/supplement.</i></p>	
<p>Are the required pediatric assessment studies or a full waiver of pediatric studies included?</p> <p>If no, is a request for full waiver of pediatric studies OR a request for partial waiver/deferral and a pediatric plan included?</p> <ul style="list-style-type: none"> <i>If no, request in 74-day letter.</i> If yes, does the application contain the certification(s) required under 21 CFR 314.55(b)(1), (c)(2), (c)(3)/21 CFR 601.27(b)(1), (c)(2), (c)(3) <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable</p> <p>X YES</p> <p><input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p> <p>XYES</p> <p><input type="checkbox"/> NO</p>

BPCA (NDAs/NDA efficacy supplements only):	
Is this submission a complete response to a pediatric Written Request? <i>If yes, contact PMHS (pediatric exclusivity determination by the Pediatric Exclusivity Board is needed).</i>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
Comments:	
Prescription Labeling	
Check all types of labeling submitted.	<input type="checkbox"/> Not applicable <input checked="" type="checkbox"/> Package Insert (PI) <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use <input type="checkbox"/> MedGuide <input type="checkbox"/> Carton labels <input checked="" type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)
Comments:	
Is electronic Content of Labeling submitted in SPL format? <i>If no, request in 74-day letter.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
Package insert (PI) submitted in PLR format? <i>If no, was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request? If no, request in 74-day letter.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Comments: PI not submitted because we have a template PI for fenofibrates/fenofibric acid	
MedGuide or PPI (plus PI) consulted to OSE/DRISK? (<i>send WORD version if available</i>)	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
REMS consulted to OSE/DRISK?	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
Carton and immediate container labels, PI, PPI, and proprietary name (if any) sent to OSE/DMEDP?	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	

OTC Labeling	
<p>Check all types of labeling submitted.</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> Outer carton label</p> <p><input type="checkbox"/> Immediate container label</p> <p><input type="checkbox"/> Blister card</p> <p><input type="checkbox"/> Blister backing label</p> <p><input type="checkbox"/> Consumer Information Leaflet (CIL)</p> <p><input type="checkbox"/> Physician sample</p> <p><input type="checkbox"/> Consumer sample</p> <p><input type="checkbox"/> Other (specify)</p>
<p>Is electronic content of labeling submitted?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p>Are annotated specifications submitted for all stock keeping units (SKUs)?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p>If representative labeling is submitted, are all represented SKUs defined?</p> <p><i>If no, request in 74-day letter.</i></p> <p>Comments:</p>	<p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p>Proprietary name, all labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEDP?</p> <p>Comments:</p>	<p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
Meeting Minutes/SPA Agreements	
<p>End-of Phase 2 meeting(s)?</p> <p><i>If yes, distribute minutes before filing meeting.</i></p> <p>Comments:</p>	<p><input type="checkbox"/> YES</p> <p>Date(s):</p> <p><input checked="" type="checkbox"/> NO</p>
<p>Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)?</p> <p><i>If yes, distribute minutes before filing meeting.</i></p> <p>Comments: written comments sent 1/18/08 following denial of meeting request</p>	<p><input type="checkbox"/> YES</p> <p>Date(s):</p> <p><input checked="" type="checkbox"/> NO</p>
<p>Any Special Protocol Assessment (SPA) agreements?</p> <p><i>If yes, distribute letter and/or relevant minutes before filing meeting.</i></p>	<p><input type="checkbox"/> YES</p> <p>Date(s):</p> <p><input checked="" type="checkbox"/> NO</p>

Comments:	
------------------	--

ATTACHMENT

MEMO OF FILING MEETING

DATE: 10/10/08

NDA/BLA #: 22-418

PROPRIETARY/ESTABLISHED NAMES: fenofibric acid tablets

APPLICANT: Mutual Pharmaceutical

BACKGROUND: This is a 505(b)(2) application with Tricor (NDA 21-656) as the reference product. Fenofibric acid is the active metabolite of fenofibrate, for which there are multiple approved 505B2 applications.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Kati Johnson	Y
	CPMS/TL:	Enid Galliers	N
Cross-Discipline Team Leader (CDTL)	Eric Colman		N
Clinical	Reviewer:	Iffat Chowdhury	Y
	TL:	Eric Colman	N
Social Scientist Review (for OTC products)	Reviewer:	N/A	
	TL:		
Labeling Review (for OTC products)	Reviewer:	N/A	
	TL:		
OSE	Reviewer:	TBD	
	TL:		
Clinical Microbiology (for antimicrobial products)	Reviewer:	N/A	

	TL:		
--	-----	--	--

Clinical Pharmacology	Reviewer:	Jaya Vaidyanathan	Y
	TL:	Sally Choe	Y
Biostatistics	Reviewer:	N/A	
	TL:		
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Lee Elmore	Y
	TL:	Karen Davis Bruno	Y
Statistics, carcinogenicity	Reviewer:	Min Min	N
	TL:	Karl Lin	N
Product Quality (CMC)	Reviewer:	Yvonne Yang	Y
	TL:	Su Tran	Y
Facility (for BLAs/BLA supplements)	Reviewer:	N/A	
	TL:		
Microbiology, sterility (for NDAs/NDA efficacy supplements)	Reviewer:	N/A	
	TL:		
Bioresearch Monitoring (DSI)	Reviewer:	TBD	
	TL:		
Other reviewers			

OTHER ATTENDEES:

505(b)(2) filing issues? If yes, list issues:	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
Per reviewers, are all parts in English or English translation? If no, explain:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

<p>Electronic Submission comments</p> <p>List comments:</p>	<input type="checkbox"/> Not Applicable
<p>CLINICAL</p> <p>Comments: labeling only</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical study site(s) inspections(s) needed? <p>If no, explain: no clinical studies</p>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<ul style="list-style-type: none"> Advisory Committee Meeting needed? <p>Comments:</p> <p><i>If no, for an original NME or BLA application, include the reason. For example:</i></p> <ul style="list-style-type: none"> <i>this drug/biologic is not the first in its class</i> <i>the clinical study design was acceptable</i> <i>the application did not raise significant safety or efficacy issues</i> <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i> 	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason: this drug is not the first in its class
<ul style="list-style-type: none"> 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? <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>CLINICAL MICROBIOLOGY</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>CLINICAL PHARMACOLOGY</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE

Comments:	<input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical pharmacology study site(s) inspections(s) needed? 	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
BIOSTATISTICS	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE
Comments:	<input type="checkbox"/> Review issues for 74-day letter
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE
Comments:	<input type="checkbox"/> Review issues for 74-day letter
PRODUCT QUALITY (CMC)	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE
Comments:	<input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Categorical exclusion for environmental assessment (EA) requested? <p>If no, was a complete EA submitted?</p> <p>If EA submitted, consulted to EA officer (OPS)?</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Establishment(s) ready for inspection? <ul style="list-style-type: none"> Establishment Evaluation Request (EER/TBP-EER) submitted to DMPQ? <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Sterile product? 	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO

<p>If yes, was Microbiology Team consulted for validation of sterilization? (NDAs/NDA supplements only)</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<p>FACILITY (BLAs only)</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
REGULATORY PROJECT MANAGEMENT	
<p>Signatory Authority: Division/Mary Parks, MD</p> <p>GRMP Timeline Milestones:</p> <p>Comments:</p>	
REGULATORY CONCLUSIONS/DEFICIENCIES	
<input type="checkbox"/>	<p>The application is unsuitable for filing. Explain why:</p>
<input checked="" type="checkbox"/>	<p>The application, on its face, appears to be suitable for filing.</p> <p><input type="checkbox"/> No review issues have been identified for the 74-day letter.</p> <p><input checked="" type="checkbox"/> Review issues have been identified for the 74-day letter. List (optional):</p> <p><input type="checkbox"/> Standard Review</p> <p><input type="checkbox"/> Priority Review</p>
ACTIONS ITEMS	
<input checked="" type="checkbox"/>	<p>Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into tracking system.</p>
<input type="checkbox"/>	<p>If RTF action, notify everybody who already received a consult request, OSE PM., and Product Quality PM. Cancel EER/TBP-EER.</p>
<input type="checkbox"/>	<p>If filed and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.</p>
<input type="checkbox"/>	<p>If BLA or priority review NDA, send 60-day letter.</p>
<input checked="" type="checkbox"/>	<p>Send review issues/no review issues by day 74</p>
<input type="checkbox"/>	<p>Other</p>

Appendix A (NDA and NDA Supplements only)

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original application is likely to be a 505(b)(2) application if:

- (1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
- (2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),
- (2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and
- (3) All other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely

for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),
- (2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or
- (3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your OND ADRA or OND IO.

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

/s/

Kati Johnson
2/13/2009 12:22:52 PM
CSO



United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street
Philadelphia, PA 19124

215-288-6500
www.urlmutual.com

15 January 2009

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
Sequence No. 0007: Updated Stability Data

Dear Dr. Parks:

In accordance with 21 CFR 314, Mutual Pharmaceutical Company, Inc., (Mutual) submitted a New Drug Application (NDA 22-418) for Fenofibric Acid Tablets, 35 mg and 105 mg for the treatment of hypercholesterolemia and hypertriglyceridemia on 15 August 2008.

Mutual is submitting this amendment to NDA 22-418 to provide for the following Chemistry, Manufacturing, and Controls stability updates submitted in Module 3.2.P.8.3:

- o 18-month long-term supportive stability data for the 30-mg bracketing tablet strength batch (NB 1396 26);
- o 24-month long-term supportive stability data for the 50-mg, 90-mg, and 130-mg bracketing tablet strength batches (BB 790 0205, BB 792 0208, BB 793 0209, respectively).

The electronic files submitted for this application have been scanned for viruses with AVG Antivirus; using virus definitions of 15 January 2009. Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,

Robert Dettery ew

Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.



7 January 2009

United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street
Philadelphia, PA 19124
215-288-6500
www.urlmutual.com

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
Serial No. 0006: Patent Amendment – Delivery
of Notice Letter and Legal Status

Dear Dr. Parks:

This Patent Amendment is to inform you that no legal action has been taken against Mutual by the NDA holder or patent owners for the patents covered by our Paragraph IV Certifications in NDA 22-418.

Mutual provided proper notice under 21 CFR §314.52(a) and no legal action for patent infringement was filed within 45 days of receipt of the notices of certification, making immediate approval upon completion of the agency's review of NDA 22-418 permissible under 21 CFR §314.107(f)(2).

- On October 30, 2008, Mutual sent its Notice Letter via registered certified mail, return receipt requested to the individuals representing patent owners and the NDA holder (collectively the "Notice Letter Recipients"), as identified in the document included in this submission, titled "Fenofibric Acid Notice Letter Receipts". The U.S. Postal Service has returned receipts from nine recipients, copies of which are included with this submission. Mutual received the return receipts for all Notice Letter Recipients except for Fournier Laboratories Ireland Ltd. The latest date of the postal delivery receipts was November 7, 2008.
- On October 30, 2008, Mutual also sent its Notice Letter to the Notice Letter Recipients by FedEx and received confirmation that all Notice Letter Recipients had received notice by this method by November 3, 2008. Therefore, notice was clearly received by all Notice Letter recipients by this date.
- On November 7, 2008, Counsel for Fournier Ireland (with copies to counsel for the remaining Notice Letter Recipients), acknowledged receipt of Mutual's Notice letter. Therefore, notice was clearly received by all Notice Letter recipients by this date. A copy of this letter is included with this submission.
- On November 13, 2008 all Notice Letter Recipients further confirmed that they had received notice because all had contacted Mutual and signed a Confidential

Disclosure Agreement for access to NDA 22-418. These signed Disclosure Agreements are included in this submission.

21 CFR 314.52(e) provides that documentation of notice can be shown by return receipt or other similar evidence. The evidence shows that all Notice Letter Recipients must have received the Notice Letter no later than November 13, 2008, and in view of the foregoing, November 14, 2008 counts as the latest possible first day of the 45-day statutory period, pursuant to 21 CFR §314.52(f). Relying on this time frame, the 45-day period ended December 29, 2008.

Please feel free to contact me if you require additional information.

Sincerely,



Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.



DEPARTMENT OF HEALTH & HUMAN SERVICES

12/15/08

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 22-418

**PROPRIETARY NAME REQUEST
ADVICE/ACKNOWLEDGMENT**

Mutual Pharmaceutical Company, Inc
Attention: Robert Dettery
Vice President, Regulatory Affairs
1100 Orthodox Street,
Philadelphia, Pennsylvania 19124

Dear Mr. Dettery:

Please refer to your New Drug Application (NDA) dated August 15, 2008, received August 15, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fenofibric Acid Tablets 35 mg and 105 mg.

We also refer to your October 10, 2008, correspondence, received October 10, 2008, requesting a review of your proposed proprietary name, FIBRICOR™.

We note that you have also included an alternate proposed proprietary name, _____, in your submission. We will not initiate review of this alternate name as part of this review cycle. If the proposed proprietary name, FIBRICOR, is denied, we will notify you of this decision. At that time you must submit a new complete request for review of the alternate name.

b(4)

If you have any questions regarding the contents of this letter or any other aspect of the proprietary name review process, call Cheryl Campbell, Regulatory Project Manager in the Office of Surveillance and Epidemiology (OSE), at (301) 796-0723. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager.

Sincerely,

{See appended electronic signature page}

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products
Office of New Drugs
Center for Drug Evaluation and Research

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

/s/

Kati Johnson
12/15/2008 05:37:52 AM



United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.
1100 Orthodox Street
Philadelphia, PA 19124
215-288-6500
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15 December 2008

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
Sequence No. 0005: 120-Day Safety Update

Dear Dr. Parks:

In accordance with 21 CFR 314, Mutual Pharmaceutical Company, Inc., (Mutual) submitted a New Drug Application (NDA 22-418) for Fenofibric Acid Tablets, 35 mg and 105 mg for the treatment of hypercholesterolemia and hypertriglyceridemia on 15 August 2008. In this submission, Mutual is submitting the 120-Day Safety Update for this pending NDA.

The safety information provided in this 120-Day Safety Update to NDA 22-418 has been derived from three sources. A 4-week toxicokinetic study, sponsored by Mutual, has been completed subsequent to NDA submission; this is a report of a study that was included in the original NDA. The other information is publicly available, *i.e.*, published literature and postmarketing safety reports. This information has been updated with a cut-off date of 18 November 2008.

Tables summarizing all sections added or amended in this 120-Day Safety Update (by module) are provided below. No new safety concerns have been identified that warrant revision of the proposed label for fenofibric acid.

NONCLINICAL MODULES

Module	Sections	Comment
Module 2.4 Nonclinical Overview	2.4.4.4 Carcinogenicity	Amended with new exposure data
Module 2.6.1 Nonclinical Introduction	2.6.1.1 Sources of Information	Amended with updated literature search summaries
Module 2.6.2 Pharmacology Written Summary	2.6.2.7 References	Amended with link to correct publication (<i>Gonzalez and Shah, 2008</i>)
Module 2.6.4 Pharmacokinetics Written Summary	2.6.4.2.1.1.4 Partial Validation in Beagle Dog (FA and RFA) and Wistar Han Rat with Matrix Equivalence to Sprague-Dawley Rat and Dutch Belted Rabbit (FA Only) - Long-term Matrix Stability subsection	Amended with new data
Module 2.6.6 Toxicology Written Summary	2.6.6.5.2.1 Wistar Rats	Amended with new data
Module 2.6.7 Toxicology Tabulated Summary	2.6.7.2 Toxicokinetics: Overview of Toxicokinetics Studies 2.6.7.3.A Mean Steady-State (28-Day Repeated-Dose) Pharmacokinetic Parameters of Fenofibric Acid in Male Animal Plasma Following Oral Administration of Fenofibrate 2.6.7.3.B Accumulation Ratio (R) of Fenofibric Acid in Male Animal Plasma Following Oral Administration of Fenofibrate 2.6.7.3.D Mean Pharmacokinetic Profile of Fenofibric Acid in Male Rat Plasma Following Repeated Oral Administration of Fenofibrate for 28 Days (Study No. MPC-028-08-0002)* 2.6.7.3.E Mean Pharmacokinetic Profile of Fenofibric Acid in Male Wistar Han Rat Plasma Following Repeated Oral Administration of Fenofibrate for 28 Days (Study No. MPC-028-08-0006)	Amended with new data
Module 4.2 Study Reports	4.2.2.1 Analytical Methods and Validation Reports 4.2.2.7 Other Pharmacokinetic Studies	New and amended reports
Module 4.3 Literature References	--	Added correct publication (<i>Gonzalez and Shah, 2008-missing from original application</i>)

CLINICAL MODULES

Module	Sections	Comment
Module 2.7.2 Summary of Clinical Pharmacology Studies	2.7.2.1.2 Literature Search Strategies	Amended with updated literature search summaries
Module 2.7.4 Summary of Clinical Safety	2.7.4 Summary of Clinical Safety (<i>Introduction</i>) 2.7.4.1.1 Overall Safety Evaluation Plan and Available Safety Data 2.7.4.1.1.2.2 Published Literature 2.7.4.1.1.2.3 Postmarketing Safety Data 2.7.4.2.1.2.2.2 Musculoskeletal System 2.7.4.2.1.2.2.4 Cardiovascular System 2.7.4.3.2.3 Serum Creatinine 2.7.4.5.6 HMG-CoA Reductase Inhibitors 2.7.4.5.12 Aliskiren 2.7.4.6 Postmarketing Safety Data	Amended with new postmarketing data and safety publications
Module 2.7.5 Literature References	2.7.5.4 Safety	Amended with new publications
Module 5.3.5.3 Integrated Summary of Safety	1. Introduction 4.2 Available Safety Data 4.1.2.2 Published Literature 4.1.2.3 Postmarketing Safety Data 5.1.2.2.2 Musculoskeletal System 5.1.2.2.4 Cardiovascular System 5.1.2.3 Postmarketing Safety Data 6.2.2 Serum Creatinine 6.3 Postmarketing Safety Data 7.1.3 Postmarketing Safety Data 7.2.3 Postmarketing Safety Data 8.3 HMG-CoA Reductase Inhibitors 8.9 Aliskiren 12.2. Published Literature	Amended with new postmarketing data and safety publications
Module 5.3.6 Reports of Postmarketing Experience	--	New postmarketing reports from FDA and WHO
Module 5.4 Literature References	--	New publications

The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 15 December 2008. Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,

Robert Dettery *aw*

Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.



United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.
1100 Orthodox Street
Philadelphia, PA 19124
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14 November 2008

Mary Parks, MD., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

**Re: NDA 22-418
Fenofibric Acid Tablets, 35mg and 105mg
Serial No. 0004: Response to Filing Communication –
Chemistry and Clinical Pharmacology**

Dear Dr. Parks:

Please refer to the filing communication for NDA 22-418, received by Mutual Pharmaceutical Company, Inc. (Mutual) on 27 October 2008, in which the Division identified some potential review issues. In this submission, Mutual is responding to these potential issues (provided verbatim below in **bold**, followed immediately by Mutual's response).

Chemistry

- 1. Confirm that the manufacturing and testing facilities listed in Tables 2.3.S.4 and 2.3.P.7 are all the facilities involved in the manufacture and testing of the commercial drug substance and drug product.**

Mutual confirms that the manufacturing facilities listed for the drug substance and drug product in Table 2.3.S.4 and Table 2.3.P.7 are indeed all the facilities involved in the manufacture and testing of the commercial drug substance and drug product. These tables were directly extracted from the corresponding sections in Module 3. Note that "alternate testing facility" means a possible site that was used in the release/stability testing of the registration batches of drug substance, drug product, or excipients; or an additional facility qualified by Mutual to be used as alternate testing site in the event that our analytical laboratory is over-burdened.

- 2. Provide the physical dimension of the finished tablets.**

The physical dimensions of the finished tablets are as follows (as found in the executed batch records):

- 35 mg – Size: _____; Thickness: _____
- 105 mg – Size: _____ Modified Oval; Thickness: _____

b(4)

3. Provide information on the physicochemical properties of the _____ of fenofibric acid and the impact of the _____ on the performance of the drug product. The information should cover aspects such as solubility, stability, dissolution, _____, Ratio, and effects on safety and efficacy.

b(4)

Please refer to the Comprehensive _____ Screen of Fenofibric Acid Report, conducted by _____ in Section S.2.S.4.5.3 of the original application for the requested information. Table 1 on Page 10 of this report contains the physical properties of the _____. In addition, the report includes pages of comparative characterization and spectral data for the _____. Based on the results and conclusions contained in this report, Mutual had concluded that _____ has no effect on the safety and/or efficacy of the proposed drug substance or drug product.

b(4)

b(4)

b(4)

4. Provide references to the 21 CFR food additive regulations for the drug-contact components of the container closure systems used to package the drug substance and drug product.

In the NDA, Mutual cross references a number of Drug Master Files (DMF) for full description of the drug substance as well as of container closure systems of the drug product. Please refer to these DMFs for the information requested. In addition, for your convenience, Mutual has asked each of the relevant DMF holders to amend their DMF(s) to provide a general statement of compliance with 21 CFR food additive regulations and/or indicate the location of these statements in the DMF(s).

Clinical Pharmacology

We could not locate the SAS transport files for the BE study MPC-028-07-1007. Either notify us where in the application this information can be found or submit it.

The SAS transport files for BE study MPC-028-07-1007 can be located in the m5/datasets/mpc-028-07-1007/tabulations folder in the original NDA application.

Mutual is submitting this application in electronic Common Technical Document (eCTD) format. The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 14 November 2008.

Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500/(800) 523-3684.

Sincerely,

Robert Dettery cw
Robert Dettery
Vice-President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.

REQUEST FOR CONSULTATION

TO (Division/Office):

CDER OSE CONSULTS

FROM: Kati Johnson, PM, DMEP

DATE
10/30/08

IND NO.

NDA NO.
22-418

TYPE OF DOCUMENT

DATE OF DOCUMENT
9/30 and 10/10/08

NAME OF DRUG
fenofibric acid 35mg, 105
mg

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
4/1/09

NAME OF FIRM: Mutual Pharmaceuticals, Inc.

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|---|
| <input type="checkbox"/> NEW PROTOCOL
<input type="checkbox"/> PROGRESS REPORT
<input type="checkbox"/> NEW CORRESPONDENCE
<input type="checkbox"/> DRUG ADVERTISING
<input type="checkbox"/> ADVERSE REACTION REPORT
<input type="checkbox"/> MANUFACTURING CHANGE/ADDITION
<input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> PRE-NDA MEETING
<input type="checkbox"/> END OF PHASE II MEETING
<input type="checkbox"/> RESUBMISSION
<input type="checkbox"/> SAFETY/EFFICACY
<input type="checkbox"/> PAPER NDA
<input type="checkbox"/> CONTROL SUPPLEMENT | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER
<input type="checkbox"/> FINAL PRINTED LABELING
<input type="checkbox"/> LABELING REVISION
<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE
<input type="checkbox"/> FORMULATIVE REVIEW
<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/SPECIAL INSTRUCTIONS: The firm is proposing to market this drug for dyslipidemia. It is a 505B2 application referencing Tricor (NDA 21-656). They are proposing to market 35 mg and 105 mg tablets in 30,60, 90, 100, 250, 500 and 1000-count bottles. They have proposed 2 tradenames in descending order of preference:
-FIBRICOR

In the 9/30/08 submission (\\CDSESUB1\EVSPROD\NDA022418\0002) they have provided mock-ups of the bottle labels as well as the proposed PI. In the subfolder labeled "promotional material" they have included their research of the tradename FIBRICOR. When I suggested that they send in a second name, they submitted _____ in a 10/10/08 submission.
 This NDA is in the EDR.

PDUFA DATE: 6/15/09

b(4)
b(4)

ATTACHMENTS: Draft Package Insert, Container and Carton Labels

CC: Archival IND/NDA

HFD- /Division File

HFD- /RPM

HFD- /Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER

Kati Johnson, 6-1234

METHOD OF DELIVERY (Check one)

DFS ONLY

MAIL

HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

5/28/05

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

/s/

Kati Johnson

10/30/2008 03:04:31 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

10/27/08

FILING COMMUNICATION

NDA 22-418

Mutual Pharmaceutical Company, Inc.
Attention: Robert Dettory
VP, Regulatory Affairs
1100 Orthodox Street
Philadelphia, PA 19124

Dear Mr. Dettory:

Please refer to your new drug application (NDA) dated August 15, 2008, received August 15, 2008, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Fenofibric Acid Tablets, 35 mg, 105 mg.

We also refer to your submissions dated September 18 and 30, and October 10, 2008.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is June 15, 2009.

During our filing review of your application, we identified the following potential review issues:

Chemistry

1. Confirm that the manufacturing and testing facilities listed in Tables 2.3.S.4 and 2.3.P.7 are all the facilities involved in the manufacture and testing of the commercial drug substance and drug product.
2. Provide the physical dimension of the finished tablets.
3. Provide information on the physicochemical properties of the _____ of fenofibric acid and the impact of the _____ on the performance of the drug product. The information should cover aspects such as solubility, stability, dissolution, _____ ratio, and effects on safety and efficacy.
4. Provide references to the 21 CFR food additive regulations for the drug-contact components of the container closure systems used to package the drug substance and drug product.

b(4)

Clinical Pharmacology

We could not locate the SAS transport data files for the BE study MPC-028-07-1007. Either notify us where in the application this information can be found or submit it.

We are providing the above comments to give you preliminary notice of potential 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. Issues may be added, deleted, expanded upon, or modified as we review the application.

If you have not already done so, you must submit the content of labeling [21 CFR 314.50(1)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>. The content of labeling must be in the Prescribing Information (physician labeling rule) format.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a waiver of pediatric studies for this application for all pediatric patients.

If you have any questions, call Kati Johnson, Regulatory Project Manager, at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, MD
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Kati Johnson
10/27/2008 06:15:30 AM
signing for Mary Parks, MD



United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.
1100 Orthodox Street
Philadelphia, PA 19124
215-288-6500
www.urlmutual.com

10 October 2008

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
Serial No. 0003: Request for Proprietary Name Review

Dear Dr. Parks:

In accordance with provisions of 21 CFR 314, Mutual Pharmaceutical Company, Inc., (Mutual) of Philadelphia, Pennsylvania submitted a New Drug Application (NDA) for Fenofibric Acid Tablets, 35 mg and 105 mg for the treatment of hypercholesterolemia and hypertriglyceridemia on 15 August 2008. This NDA was submitted under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act as amended and as such, reliance is on the Agency's prior judgment of the safety and efficacy of TriCor[®], the chosen reference listed drug (RLD).

Mutual is submitting this amendment to request a proprietary name review for fenofibric acid tablets, 35 mg and 105 mg. Mutual has selected the following two potential tradenames (listed in order of preference):

1. FIBRICOR[™] b(4)
2. _____

Draft labeling which included the preferred tradename, FIBRICOR[™], was submitted in an amendment to NDA 22-418 on 30 September 2008; copies of the Medication Error Prevention Analysis (MEPA) Report[™] and Proprietary Name Promotional Assessment Report for FIBRICOR[™] were also provided.

Copies of the Medication Error Prevention Analysis (MEPA) Report[™] and Proprietary Name Promotional Assessment Report for _____ are provided in Module 1.15 of this submission. b(4)

Dr. M. Parks
10 October 2008

Page 2 of 2

The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 10 October 2008. Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,

A handwritten signature in cursive script that reads "Robert Dettery" followed by a stylized flourish.

Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.



United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.
1100 Orthodox Street
Philadelphia, PA 19124
215-288-6500
www.urimutual.com

30 September 2008

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
Updated Stability Data and
Draft Labeling with Proposed Tradename, FIBRICOR™

b(4)

Dear Dr. Parks:

In accordance with provisions of 21 CFR 314, Mutual Pharmaceutical Company, Inc., (Mutual) of Philadelphia, Pennsylvania submitted a New Drug Application (NDA) for Fenofibric Acid Tablets, 35 mg and 105 mg (FIBRICOR™) for the treatment of hypercholesterolemia and hypertriglyceridemia on 15 August 2008. This NDA was submitted under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act as amended and as such, reliance is on the Agency's prior judgment of the safety and efficacy of TriCor®, the chosen reference listed drug (RLD).

On 27 August 2008, Mutual received notification from the Division that a proposed tradename was not included in the original NDA application. Mutual is submitting the draft labeling text, SPL, and container labels which include the proposed tradename, FIBRICOR™, in Module 1.14.1 of this amendment. A side-by-side comparison of the current labeling to the draft labeling text submitted in the original application is provided in Module 1.14.1.2. Copies of the Medication Error Prevention Analysis (MEPA) Report™ and Proprietary Name Promotional Assessment Report for FIBRICOR™ are included in Module 1.15.

Additionally, Mutual is submitting this amendment to NDA 22-418 to provide for the following Chemistry, Manufacturing, and Controls updates:

- 12-month long-term stability data for the three registration batches of 105-mg tablets (BB 788 0318, BB 788 0319, and BB 788 0320) are being submitted in Module 3.2.P.8.3.

• [] } b(4)

Mutual is submitting this application in electronic Common Technical Document (eCTD) format on the accompanying CD. _____ has produced the eCTD on behalf of Mutual, and has been approved through the FDA pilot program (reference pilot eCTD 900157) to provide electronic submissions in eCTD format. _____ may be contacted directly with requests that pertain to the electronic structure (via e-mail at _____ or _____). The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 30 September 2008. b(4)

Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,

Robert Dettery *aw*

Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.



United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street
Philadelphia, PA 19124

215-288-6500
www.urlmutual.com

18 September 2008

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

**Re: NDA 22-418
Fenofibric Acid Tablets, 35 mg and 105 mg
CMC Replacement Files for Original NDA**

Dear Dr. Parks:

In accordance with provisions of 21 CFR 314, Mutual Pharmaceutical Company, Inc., (Mutual) of Philadelphia, Pennsylvania submitted a New Drug Application (NDA) for Fenofibric Acid Tablets, 35 mg and 105 mg for the treatment of hypercholesterolemia and hypertriglyceridemia on 15 August 2008. This NDA was submitted under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act as amended and as such, reliance is on the Agency's prior judgment of the safety and efficacy of TriCor[®], the chosen reference listed drug (RLD).

On 17 September 2008, Mutual received notification from the Division that while a stability summary was provided in the original NDA application, the actual stability data were missing. This amendment provides Mutual's primary and supporting stability results for the proposed drug product that were inadvertently missed in the original submission; the amended section is Module 3.2.P.8.3.

Mutual is submitting this application in electronic Common Technical Document (eCTD) format on the accompanying CD _____ as produced the eCTD on behalf of Mutual, and has been approved through the FDA pilot program (reference pilot eCTD 900157) to provide electronic submissions in eCTD format _____ may be contacted directly with requests that pertain to the electronic structure (via e-mail at _____) The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 18 September 2008.

b(4)

b(4)

Dr. M. Parks
18 September 2008

Page 2 of 2

Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,

Robert Dettery

Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.

DSI CONSULT

Request for Biopharmaceutical Inspections

DATE: September 5, 2008

TO: Associate Director for Bioequivalence
Division of Scientific Investigations, HFD-48

FROM: Kati Johnson, Project Manager, HFD-510

SUBJECT: **Request for Biopharmaceutical Inspections**
NDA 22-418
TBD (fenofibric acid) Tablets, 35 mg, 105 mg.

Study/Site Identification:

The study listed below is the pivotal BE study, and will form the basis for determining safety and efficacy of the product listed above.

Study #	Clinical Site (name, address, phone, fax, contact person, if available)	Analytical Site (name, address, phone, fax, contact person, if available)
MPC-028-07-1007	PRACS Institute, Ltd.,-Cetero Research 4801 Amber Valley Parkway Fargo, ND 58104 Anthony Godfrey, PharmD (investigator) P-701-239-4750 F-701-239-4955	

b(4)

Goal Date for Completion:

We request that the inspections be conducted and the Inspection Summary Results be provided by **5/15/09**. We intend to issue an action letter on this application by **6/15/09**.

Should you require any additional information, please contact Kati Johnson, 301-796-1234.

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/s/

Kati Johnson

9/5/2008 07:53:50 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

8/27/08
Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-418

NDA ACKNOWLEDGMENT

Mutual Pharmaceutical Company, Inc.
Attention: Robert Dettery
VP, Regulatory Affairs
1100 Orthodox Street
Philadelphia, PA 19124

Dear Mr. Dettery:

We have received your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Fenofibric Acid Tablets, 35 mg, 105 mg.

Date of Application: August 15, 2008

Date of Receipt: August 15, 2008

Our Reference Number: NDA 22-418

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on **October 14, 2008** in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(i)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

Please note that you are responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) (42 USC §§ 282(i) and (j)), which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85, 121 Stat. 904). Title VIII of FDAAA amended the PHS Act by adding new section 402(j) (42 USC § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) control numbers. 42 USC 282(j)(5)(B). You did not include such certification when you submitted this application. You may use Form FDA 3674, *Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank*, to

comply with the certification requirement. The form may be found at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trials referenced in this application. Additional information regarding the certification form is available at: http://internet-dev.fda.gov/cder/regulatory/FDAAA_certification.htm. Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information on registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrinology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

If you have any questions, call me at 301-796-1234.

Sincerely,

{See appended electronic signature page}

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
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/s/

Kati Johnson
8/27/2008 10:32:48 AM



15 August 2008

United Research Laboratories, Inc.
Mutual Pharmaceutical Company, Inc.
1100 Orthodox Street
Philadelphia, PA 19124
215-288-6500
www.urlmutual.com

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue, Building W022
Silver Spring, MD 20993

**Re: Original NDA Application (NDA 22-418)
Fenofibric Acid Tablets, 35 mg and 105 mg**

Dear Dr. Parks:

In accordance with provisions of 21 CFR 314, Mutual Pharmaceutical Company, Inc., (Mutual) of Philadelphia, Pennsylvania is submitting this New Drug Application (NDA) for Fenofibric Acid Tablets, 35 mg and 105 mg (trade name to be determined) for the treatment of hypercholesterolemia and hypertriglyceridemia. Fenofibric acid is the active moiety of fenofibrate, a lipid-lowering drug first approved by the Food and Drug Administration (FDA) in 1993. Fenofibrate is currently available in a number of tablet and capsule formulations. Since the parent drug (fenofibrate) is not present in plasma, the pharmacokinetic as well as pharmacodynamic properties of fenofibrate drug products are characterized by fenofibric acid levels and the pharmacological response to this active metabolite.

This NDA is being submitted under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act as amended and, as such, reliance is on the Agency's prior judgment of the safety and efficacy of TriCor[®], the chosen reference listed drug (RLD). For the purpose of this NDA, the TriCor[®] labeling currently in use, dated January 2008 (submitted to FDA in an Annual Report and available via National Library of Medicine's DailyMed website) is referenced.

The proposed indications for Mutual's fenofibric acid tablets are identical to those currently approved for fenofibrate and include:

- Treatment of hypercholesterolemia, specifically as adjunctive therapy to diet to reduce elevated low density lipoprotein cholesterol (LDL-C), total cholesterol (Total-C), triglycerides, and apolipoprotein B (apo B), and to increase high density lipoprotein cholesterol (HDL-C) in adult patients with primary hypercholesterolemia or mixed dyslipidemia; and
- Treatment of hypertriglyceridemia, specifically as adjunctive therapy to diet for treatment of adult patients with hypertriglyceridemia.

The proposed doses are identical to those currently approved for fenofibrate on the basis of demonstrated bioequivalence to TriCor[®] 48 mg and 145 mg tablets. Specifically, for the treatment of primary hypercholesterolemia or mixed hyperlipidemia, the initial dose of fenofibric acid is 105 mg per day. For the treatment of hypertriglyceridemia, the initial dose is 35 to 105 mg per day. Dosage should be individualized according to patient response, and should be adjusted if necessary following repeat lipid determinations at 4 to 8 week intervals. The maximum dose is 105 mg per day. Fenofibric acid tablets may be taken without regard to meals.

On behalf of Mutual, _____, has manufactured batches of the drug substance under current good manufacturing practice (cGMP). The DMF _____ provides full chemistry, manufacturing and controls (CMC) information for fenofibric acid drug substance; additional details are provided in Module 3.2.S. In this NDA, Mutual is presenting _____

b(4)

_____ is _____, holder of DMF _____

b(4)

Three registration batches of each strength of drug product were manufactured by Mutual in June-July 2007 under current Good Manufacturing Practices at a pilot scale of _____ tablets (35 mg/105 mg); this is a representative pilot scale of the intended commercial production (approximately _____ tablets). One batch of each strength, Batch BB 787 0307 (35 mg) and batch BB 788 0318 (105 mg), was used in the pharmacokinetic and/or clinical pharmacology studies in support of the NDA. Information regarding the drug product manufacturing and packaging is provided in Module 3.2.P.

b(4)

The proposed 35 mg tablet is described as white, round, debossed 'AR 787' on one side and blank on the other side. The 105 mg tablet is described as white, modified oval, debossed 'AR 788' on one side and blank on the other side. The tablets are packaged in _____ bottles, _____ containing 30 to

b(4)

1000 tablets per bottle, with _____. The lower tablet count bottle configurations for the 35 mg tablets are the _____ bottles containing 30 or 60 tablets and the _____ bottles containing 90 tablets. The lower tablet count bottle configurations for the 105 mg tablets are the _____ bottles containing 30 tablets, the _____ bottles containing 60 tablets and the _____ bottles containing 90 tablets. These bottles are equipped with _____. Mutual is presenting at this time both primary and supportive stability results following the schedule agreed upon by the FDA, i.e., 6-month ICH stability results for three batches of each proposed strength, 35 mg and 105 mg, stored in the proposed packaging configurations. These results will be updated for the 12-month long term stability results as data become available and before the fifth month in the review clock; and up to 12/18-month stability data for the supportive bracketing tablet strengths.

b(4)

Mutual conducted two nonclinical single-dose pharmacokinetic studies, one in rats and one in dogs, to confirm that the repeated-dose toxicology studies performed with

fenofibrate in these two species are also applicable for the direct administration of fenofibric acid; for comparative purposes, fenofibrate was included in each study. Repeated-dose toxicokinetic studies in mice, rats, and rabbits were conducted to bridge to the carcinogenicity and reproductive toxicity information that is included in the approved label for TriCor[®]. All nonclinical studies performed for Mutual were compliant with current good laboratory practice (GLP). These studies are discussed in Module 2.6 of this NDA; full study reports are provided in Module 4.

From a clinical perspective, bioequivalence of the 105-mg fenofibric acid tablet with the RLD, TriCor[®] 145 mg, has been demonstrated in two single-dose studies performed in healthy adult subjects under fasted and fed conditions. These studies, along with eight additional pharmacokinetic and/or clinical pharmacology studies and five *in vitro* studies, are discussed individually in Section 2.7 and final study reports are provided in Module 5. The 35-mg fenofibric acid tablet is composition proportional to the 105-mg fenofibric acid tablet, *in vitro* dissolution profiles are similar using suitable methodology, and pharmacokinetics are linear over the proposed dose range. Therefore, Mutual is requesting "biowaiver" of any further *in vivo* studies for the 35-mg fenofibric acid tablet, as provided in Module 1 of this submission.

Fenofibric acid tablets do not represent a meaningful therapeutic benefit over existing treatments for pediatric patients and are not likely to be used in a substantial number of patients since primary intervention focuses on changing the diet. Therefore, Mutual is requesting a waiver of a pediatric assessment of fenofibric acid tablets, 35 mg and 105 mg. The request for pediatric waiver is provided in Module 1.

Mutual is submitting this application in electronic Common Technical Document (eCTD) format on the accompanying CD. _____ as produced the eCTD on behalf of Mutual, and has been approved through the FDA pilot program (reference pilot eCTD 900157) to provide electronic submissions in eCTD format. _____ may be contacted directly with requests that pertain to the electronic structure (*via* e-mail at _____ or _____). Enclosed please find the original NDA application. The electronic files submitted for this application have been scanned for viruses with AVG Antivirus, using virus definitions of 15 August 2008.

b(4)

b(4)

b(4)

Please do not hesitate to contact me with any questions. I can be reached by telephone at (215) 288-6500 / (800) 523-3684.

Sincerely,



Robert Dettery
Vice President, Regulatory Affairs
Mutual Pharmaceutical Company, Inc.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

1/15/08

IND 76,749

Mutual Pharmaceutical Company, Inc.
Attention: Robert Dettery
VP, Regulatory Affairs
1100 Orthodox Street
Philadelphia, PA 19124

Dear Mr. Dettery:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Fenofibric Acid Tablets, _____ and _____

b(4)

We also refer to the draft pre-NDA meeting responses that were sent to you on January 11, 2008, and to your e-mail the same day requesting that the meeting be cancelled.

The official minutes of the pre-meeting are enclosed. They are identical with the exception of a clarification you requested regarding Question #10.

If you have any questions, call me at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

Kati Johnson
Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure - Meeting Minutes

BACKGROUND: The sponsor is developing a 505(b)(2) application, and has conducted pharmacokinetic studies comparing their drug to TriCor (NDA 21-656). According to the background package, they will be developing the 35-mg and 105-mg strength fenofibric acid tablets, and the latter strength tablet is bioequivalent to Tricor 145-mg under fasted and standard meal conditions. The proposed NDA is planned for June 2008.

NOTE: the strengths now proposed for development (35 and 105 mg) are different than those listed in the initial December 8, 2006 IND application _____ and in subsequent submissions. b(4)

Below are the preliminary responses sent to you on January 11, 2008. Your request for clarification of our response to Question #10 is underlined and our response is double underlined.

This material consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for January 14, 2008 between representative from Mutual Pharmaceutical Company, Inc. and the Agency. This material is shared to promote a collaborative and successful discussion at the meeting. The minutes of the meeting will reflect agreements, important issues, and any action items discussed during the meeting and may not be identical to these preliminary comments. If these answers and comments are clear to you and you determine that further discussion is not required, you have the option of cancelling the meeting (contact Kati Johnson). If you determine that discussion is needed for some of the original questions, we will have the meeting. It is important to remember that some meetings, particularly milestone meetings, are valuable even if the pre-meeting communications are considered sufficient to answer the questions. Note that if there are any major changes to your development plan, the purpose of the meeting, or the questions based on our preliminary responses, we may not be prepared to discuss or reach agreement on such changes at the meeting. If any modifications to the development plan or additional questions for which you would like FDA feedback arise prior to the meeting, contact the Regulatory Project Manager to discuss the possibility of including these for discussion at the meeting.

Your questions are followed by our **bolded** responses.

Regulatory Comments

A 505(b)(2) application would be an acceptable approach at this time based on the information provided. The Division recommends that sponsors considering the submission of an application through the 505(b)(2) pathway consult the Agency's regulations at 21 CFR 314.54, and the October 1999 Draft Guidance for Industry "Applications Covered by Section 505(b)(2)" available at <http://www.fda.gov/cder/guidance/index.htm>. In addition, FDA has explained the background and applicability of section 505(b)(2) in its October 14, 2003, response to a number of citizen petitions challenging the Agency's interpretation of this statutory provision (see Dockets 2001P-0323, 2002P-0447, and 2003P-0408 (available at <http://www.fda.gov/ohrms/dockets/dailys/03/oct03/102303/02p-0447-pdm0001-vol1.pdf>)).

If you intend to submit a 505(b)(2) application that relies for approval on FDA's finding of safety and/or effectiveness for one or more listed drugs, you must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s). You should establish a "bridge" (e.g., via comparative bioavailability data) between your proposed drug product and each listed drug upon which you propose to rely to demonstrate that such reliance is scientifically justified. If you intend to rely on literature or other studies for which you have no right of reference but that

are necessary for approval, you also must establish that reliance on the studies described in the literature is scientifically appropriate.

Your pre-NDA briefing package suggests that you are proposing to reference information from the Summary Basis of Approval (SBA) or FDA reviewers' public summaries for NDA 19-304 and NDA 21-656 for support of safety and/or effectiveness. We note that a 505(b)(2) applicant that seeks to rely upon the Agency's finding of safety and/or effectiveness for a listed drug, may rely only on that finding as is reflected in the approved labeling for the listed drug.

If you intend to rely on the Agency's finding of safety and/or effectiveness for an additional listed drug(s) such as NDA 19-304 or published literature describing a listed drug(s), you should identify the listed drug(s) in accordance with the Agency's regulations at 21 CFR 314.54. It should be noted that the regulatory requirements for a 505(b)(2) application (including, but not limited to, an appropriate patent certification or statement) apply to each listed drug upon which a sponsor relies.

Chemistry, Manufacturing and Controls

1. Mutual would like the Division's feedback regarding the acceptability of the proposed regulatory specifications for the drug substance and drug product.

Response: The acceptability of the proposed drug substance (DS) specifications will be determined as part of FDA's review of the NDA.

Include these additional tests: heavy metals, halides (Cl), particle size, sulphates, sulfated ash. Impurities above 0.10% in the DS should be identified and any impurity above 0.15% should be qualified (ICH Q3A)

The acceptability of the proposed drug product (DP) specifications will be determined as part of FDA's review of the NDA.

Include these additional tests: tablet hardness and water content. Provide more data (time points, paddle speed) in order to evaluate the acceptability of the dissolution specifications (method and acceptance criteria). Using 100 rpm seems to result in a less discriminating method; 50 rpm might be more appropriate/discriminating. Provide complete dissolution profiles in your application. We noted that there is no sign-off on the data on pg. 002080.

2. Is the amount of stability data to be included in the NDA at submission sufficient to allow filing?
Is Mutual's proposed stability program for the drug product acceptable?

Response: Yes, the proposed stability data in the initial NDA submission are sufficient for filing and will be used for expiry date determination. Additional data may be submitted within 5 months. However, while every effort will be made to review additional stability data, their review will depend on the timeliness of the submission, extend of the submitted data, and available resources of the reviewer.

The time points and storage conditions in the proposed stability program for the drug product is acceptable, however, the drug product specifications should be modified as discussed in Response 1.

Nonclinical Pharmacology and Toxicology

3. Does the Division agree that the single dose pharmacokinetic studies are required for the NDA?
If yes, are the designs of the studies, including dose selection and plans for plasma analysis acceptable?

Response: The single dose pharmacokinetic bridging studies in animals where fenofibrate and fenofibric acid will be administered at equimolar doses and metabolic profiles characterized are not required, but will help establish the comparisons between fenofibrate and fenofibric acid.

4. Are the designs of the toxicokinetic bridging studies acceptable, including plans to limit the carcinogenicity bridging studies to only one strain of mice and rats? Does the Division have any recommendations with respect to dose selection for any of the studies?

Response: Your planned bridging toxicokinetic studies including the carcinogenicity bridging studies in animals are acceptable.

5. The particle size of the fenofibrate used in the original studies is not known. The fenofibrate drug substance to be used in these studies will be _____ and obtained from a supplier with an approved DMF; _____
Please confirm the acceptability of this approach.

b(4)

Response: The approach is acceptable.

6. Does the Division agree that no additional toxicology studies, other than the mouse micronucleus assay, are required for NDA filing?

Response: The mouse micronucleus assay is not required for filing of this NDA, since you are referring to the approved reference listed drug Tricor. However, if the test is performed, the labeling text will be modified to reflect the results.

We agree that no additional toxicity studies are required for this 505(b)(2) NDA. However, please note that any novel excipients/impurities/degradants present in the final marketed formulation above the qualification thresholds will require qualification. These studies would include in vitro genotoxicity, and a 2-4 week toxicity study in one species (as per ICH Q3A and ICH Q3B) unless literature can be provided to adequately support safety of these excipients/impurities/degradants.

Biopharmaceutics and Pharmacokinetics

7. Please confirm that the approach to establishing bioequivalence is appropriate.

Response: We agree with the BE approach.

8. Please confirm that the approach to determining the effect of food and plans for inclusion of the information in the label will be acceptable.

Response: We agree with the approach to determine the effect of food. The information that will be included in the label will be a review issue.

9. Is the approach to providing information to support a request for waiver of the need for in vivo bioequivalence studies acceptable?

Response: Biowaiver of the 35 mg fenofibric acid tablets based on composition proportionality and similar dissolution profile is acceptable if linearity of fenofibric acid pharmacokinetics is demonstrated. If linearity is not demonstrated, a clinical study with the 35 mg tablet formulation will be required. This study can be a PK study comparing the pharmacokinetics of fenofibric acid 35 mg tablet to the 105 mg tablet formulation.

10. Does FDA agree that an *in vivo* drug-drug interaction study is necessary to assess the clinical significance of the inhibition of CYP2B6? If yes, does the Division have any recommendations with respect to study design, including the choice of bupropion as a substrate?

Response: As the [I]/K_i w² —, we recommended that you conduct the drug interaction study to address the CYP2B6 inhibition potential of fenofibric acid. Based on drug interaction guidance the model probe substrate for CYP2B6 inhibition is efavirenz. Please justify the use of bupropion in the proposed drug interaction study. b(4)

Clarification request: You requested whether a one-way drug interaction study using single doses of efavirenz (rather than multiple doses) is acceptable.

FDA Response: A drug interaction study using steady-state concentrations of inhibitor (Fenofibric acid) and single dose of substrate (Efavirenz) is acceptable. You may submit the protocol for review if you like, however, allow at least 8 weeks for our comments.

11. Mutual seeks confirmation that no other *in vivo* clinical pharmacology studies are required for NDA filing other than those already ongoing or planned.

Response: No. Please refer to response to Q 9. Apart from the study mentioned in Q9, we recommend that a dosage form equivalence study be conducted i.e., comparing the PK of three 35 mg fenofibric acid tablets to one 105 mg fenofibric acid tablet.

Clinical Studies

12. As bioequivalence will be demonstrated and the same indication and dosing instructions sought, is an Integrated Summary of Efficacy required?

Response: No

13. Mutual will prepare an Integrated Summary of Safety describing the publicly available information for fenofibrate. Safety results from the clinical pharmacology studies will also be included, however, Mutual does not plan to pool the data from these studies. Is this acceptable?

Response: Yes

Administrative

14. Mutual seeks confirmation that the organization of the future NDA as well as the proposed SDTM format SAS XPORT files are acceptable.

Response: It appears acceptable

##

Linked Applications

Sponsor Name

Drug Name

IND 76749

MUTUAL
PHARMACEUTICAL CO
INC

FENOFIBRIC ACID TABLETS

b(4)

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U i jt !jt !b!sf qsf t f oubjpolpgbo!f rfduspojd!sf dpse!u bux bt !t jhof e
f rfduspojdbm!boe!u jt !qbfh !jt !u f !n bojg t ubjpolpgu f !f rfduspojd
t jhobw sf /

.....
/s/

KATI JOHNSON
01/15/2008