

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-350

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

**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
21-350

NAME OF APPLICANT / NDA HOLDER
SkyePharma 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)
██████████

ACTIVE INGREDIENT(S)
Fenofibrate

STRENGTH(S)
50mg & 160mg

DOSAGE FORM
Solid Oral Compressed 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 submit 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.

1. GENERAL

a. United States Patent Number Re. 35,338	b. Issue Date of Patent 09/24/1996	c. Expiration Date of Patent 09/24/2013
d. Name of Patent Owner RTP Pharma Corp.	Address (of Patent Owner) 4364 South Alston Avenue	
	City/State Durham, N.C.	
	ZIP Code 27713	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.) 10450 Science Center Drive	
	City/State San Diego, CA	
	ZIP Code 92121	FAX Number (if available) (858) 558-6617
 Steven W. Jensen	Telephone Number (858) 625-2424	E-Mail Address (if available) stevej@skypepharma.com
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 checked="" type="checkbox"/> No
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?	<input type="checkbox"/> Yes	<input checked="" 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 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, 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 Claim Number (as listed in the patent) Does the patent claim 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 proposed labeling.)

5. No Relevant Patents

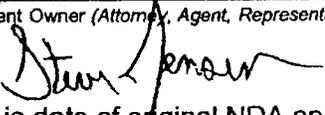
For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably 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

05/11/2004

NOTE: June 22, 2001 is date of original NDA application

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.

<input checked="" type="checkbox"/> NDA Applicant/Holder	<input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Steven W. Jensen	
Address 10450 Science Center Drive	City/State San Diego, CA
ZIP Code 92121	Telephone Number (858) 625-2424
FAX Number (if available) (858) 558-6617	E-Mail Address (if available) stevej@skyepharma.com

The public reporting burden for this collection of information has been estimated to average 9 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.

EXCLUSIVITY SUMMARY FOR NDA # 21-350

SUPPL # _____

Trade Name Triglide, Tablets, 50 & 160 mg

Generic Name fenofibrate

Applicant Name SkyePharma Inc.

HFD# 510

Approval Date If Known May 7, 2005

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 question about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?
YES / X / NO / ___ /

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

505(b)(2)

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 / X /

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

Studies were submitted as bioequivalence studies. In the original submission, Triglide was compared to Tricor (NDA 19-304). However in the resubmission, Triglide(re-formulation) was compared to Lipanthyl, a foreign-market version of Tricor (NDA 19-304). OCPB, ONDC, and OCC have accepted that study based on additional information submitted by the applicant to support the use of Lipanthyl as the comparator.

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 /X/

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 /X/

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 /X/

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 / X / NO / ___ /
If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#	<u>NDA 19-304</u>	<u>Tricor Capsules</u>
NDA#	<u>NDA 21-203</u>	<u>Tricor Tablets</u>
NDA#	<u>NDA 21-656</u>	<u>Tricor Tablets</u>
NDA#	<u>NDA 21-695</u>	<u>Antara Capsules</u>

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 / ___ / N/A / X /

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 NDA'S AND SUPPLEMENTS

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

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

YES /___/ NO /X/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS 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

its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1	:	
IND # _____	YES /___/	NO /___/ Explain: _____
	!	
	!	
Investigation #2	:	
IND # _____	YES /___/	NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	:	
YES /___/ Explain _____	!	NO /___/ Explain _____
_____	!	_____
_____	!	_____
Investigation #2	:	
YES /___/ Explain _____	!	NO /___/ Explain _____
_____	!	_____
_____	!	_____

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

YES /___/ NO /___/

If yes, explain: _____

Valerie Jimenez Date
Regulatory Project Manager
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

Form OGD-011347 Revised 05/10/2004

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

/s/

Mary Parks
6/6/05 06:11:07 PM

Exclusivity Checklist

NDA: 21-350				
Trade Name: 1 Tablets				
Generic Name: fenofibrate				
Applicant Name: RTP Pharma				
Division: HFD-510				
Project Manager: William C. Koch, R.Ph.				
Approval Date:				
PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?				
1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.				
a. Is it an original NDA?	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
b. Is it an effectiveness supplement?	Yes	<input type="checkbox"/>	No	<input checked="" type="checkbox"/>
c. If yes, what type? (SE1, SE2, etc.)				
Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")	Yes	<input type="checkbox"/>	No	<input checked="" type="checkbox"/>
If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.				
Explanation:				
If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:				
Explanation:				
d. Did the applicant request exclusivity?	Yes	<input type="checkbox"/>	No	<input checked="" type="checkbox"/>
If the answer to (d) is "yes," how many years of exclusivity did the applicant request?				
IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS.				
2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use?	Yes	<input checked="" type="checkbox"/>	No	<input type="checkbox"/>
If yes, NDA #	19-304			
Drug Name:	Tricor			
IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS.				
3. Is this drug product or indication a DESI upgrade?	Yes	<input type="checkbox"/>	No	<input type="checkbox"/>
IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS (even if a study was required for the upgrade).				

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES				
(Answer either #1 or #2, as appropriate)				
1. Single active ingredient product.		Yes		No
Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.		Yes		No
If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).				
Drug Product				
NDA #				
Drug Product				
NDA #				
Drug Product				
NDA #				
2. Combination product.		Yes		No
If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)		Yes		No
If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).				
Drug Product				
NDA #				
Drug Product				
NDA #				
Drug Product				
NDA #				
IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS. IF "YES," GO TO PART III.				
PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS				
To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."				
1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes." then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.		Yes		No
If "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS.				

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

a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?	Yes		No	
--	-----	--	----	--

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCKS.

Basis for conclusion:

b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?	Yes		No	
---	-----	--	----	--

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

If yes, explain:

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

If yes, explain:

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

Investigation #1, Study #:	
Investigation #2, Study #:	
Investigation #3, Study #:	

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

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

Investigation #1	Yes		No	
Investigation #2	Yes		No	
Investigation #3	Yes		No	

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

Investigation #1 -- NDA Number	
Investigation #2 -- NDA Number	
Investigation #3 -- NDA Number	

b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?			
Investigation #1	Yes	No	
Investigation #2	Yes	No	
Investigation #3	Yes	No	
If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:			
Investigation #1 -- NDA Number			
Investigation #2 -- NDA Number			
Investigation #3 -- NDA Number			
If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):			
Investigation #1			
Investigation #2			
Investigation #3			
4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.			
a. For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?			
Investigation #1	Yes	No	
IND#:			
Explain:			
Investigation #2	Yes	No	
IND#:			
Explain:			
Investigation #3	Yes	No	
IND#:			
Explain:			
b. For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?			
Investigation #1	Yes	No	
IND#:			
Explain:			
Investigation #2	Yes	No	
IND#:			
Explain:			
Investigation #3	Yes	No	
IND#:			
Explain:			

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

{See appended electronic signature page}

Signature of PM

Date:

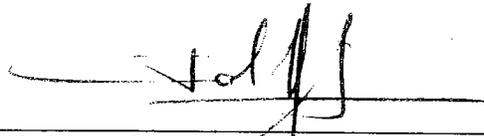
{See appended electronic signature page}

Signature of Division or Office Director

Date:

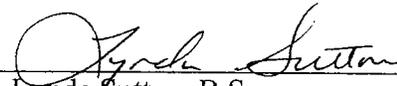
DEBARMENT CERTIFICATION

RTP Pharma Inc. 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 application¹.



MAY 02 2001

Pol-Henri Guivarch, M.D., M.B.A.
RTP Pharma Inc.
Vice President, Clinical Development
1000 chemin du Golf
Verdun, Quebec
Canada H3E 1H4



27 May 2001

Lynda Sutton, B.Sc.
Cato Research
Sr. Vice President, Regulatory Affairs and Project Planning
200 Westpark Corporate Center
4364 S. Alston Avenue
Durham, NC 27713
USA

¹ Wording is in accordance with that specified in 306(k)(1) of the Act and suggested in the draft Guidance for Industry *Submitting Debarment Certification Statements* (September 1998).

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-350 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: March 31, 2004 Action Date: October 1, 2004

HFD -510 Trade and generic names/dosage form. _____ (fenofibrate) Tablets

Applicant: SkyePharma, Inc. Therapeutic Class: 3

Indication(s) previously approved:

_____ is indicated as adjunctive therapy to diet for the reduction of LDL-C, Total-C, Triglycerides and Apo B in adult patients with primary hypercholesterolemia, mixed dyslipidemia, and hypertriglyceridemia (Fredrickson Types IIa, IIb, IV, and V).

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 3

Indication #1: Hypercholesterolemia

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: _____ Partial Waiver _____ Deferred _____ Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Adult studies ready for approval

Formulation needed

Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

Indication #2: Mixed Dyslipidemia

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns

Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____	kg _____	mo. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

Indication #3: Hypertriglyceridemia

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____	kg _____	mo. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for partial waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Adult studies ready for approval

Formulation needed

Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Valerie Jimenez
Regulatory Project Manager

cc: NDA 21-350
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

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

/s/

Valerie Jimenez
7/1/04 09:35:23 AM

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

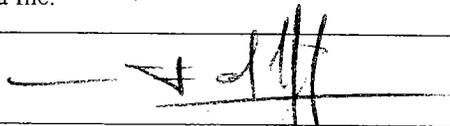
TO BE COMPLETED BY APPLICANT

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).

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Pol-Henri Guivarc'h, M.D., M.B.A.	Vice President, Clinical
FIRM/ORGANIZATION	
RTP Pharma Inc.	
SIGNATURE	DATE
	29 March 2001

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

Jimenez, Valerie

From: Galliers, Enid M
Date: Sunday, May 08, 2005 2:50 PM
To: 'Gordon Schooley'
Cc: Rita Pendergrass
Subject: RE: Please confirm receipt of N 21-350 AP letter. Thank you, EnidGalliers

Dear Gordon:

Your email confirmation is all I need. Thank you.

When I talked to Rita on Friday, I understood that you would distribute the letter by email to whoever needed it, so I did NOT fax it.

Thanks,

Enid Galliers

-----Original Message-----

From: Gordon Schooley [mailto:Gordon_Schooley@skyepharma.com]
Sent: Sunday, May 08, 2005 2:58 AM
To: GALLIERS@cder.fda.gov
Cc: Rita Pendergrass
Subject: Re: Please confirm receipt of N 21-350 AP letter. Thank you, EnidGalliers

Hi Enid,

Thanks for your long hours on Saturday. I did receive the e-mail copy of the letter on Saturday 7 May 2005. I am in London so I must rely on Rita Pendergrass to confirm receipt of a FAX copy. She lives quite a distance from the office. Would it be OK if she confirms receipt on Monday that the FAX was received on Saturday. Thanks. Gordon

Gordon L. Schooley, Ph.D.
Chief Scientific Officer
Tel: (858) 625-2414 ext. 3370
Mobile: (858) 353-0704
Fax: (858) 623-0376

The information in this e-mail and in any attachments is confidential and intended solely for the attention and use of the named addressee(s). This information may be subject to legal, professional or other privilege and further distribution of it is strictly prohibited without our authority. If you are not the intended recipient, you are not authorized to and must not disclose, copy, distribute or retain this message or any part of it, and should notify us immediately.

> "Galliers, Enid M" <GALLIERS@cder.fda.gov> 5/7/2005 5:16:55 PM >>>
"MMS <skyepharma.com>" made the following annotations.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

Skye Pharma Inc.
Attention: Gordon L. Schooley, Ph.D.
Chief Scientific Officer
10450 Science Center Drive
San Diego, CA 92121

Dear Dr. Schooley:

We acknowledge receipt on March 7, 2005, of your March 4, 2005, resubmission to your new drug application for Triglide (fenofibrate) Tablets, 50mg and 160 mg.

We consider this a complete, class 1 response to our December 14, 2004, action letter. Therefore, the user fee goal date is May 7, 2005.

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

Sincerely,

{See appended electronic signature page}

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

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

/s/

Valerie Jimenez
3/15/05 11:11:36 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

Skye Pharma Inc.
Attention: Gordon L. Schooley, Ph.D.
Chief Scientific Officer
10450 Science Center Drive
San Diego, CA 92121

Dear Dr. Schooley:

We acknowledge receipt on February 3, 2005, of your January 28, 2005, submission to your new drug application (NDA) for Triglide (fenofibrate) Tablets, 50mg and 160 mg.

We do not consider this a complete response to our action letter. Therefore, the review clock will not start until we receive a complete response. The deficiencies listed below still need to be addressed.

We also refer to the February 17, 2005, telephone conversation between Skye Pharma (Drs. Michael Vachon and Gordon Schooley) and the Agency (Dr. Mamta Gautam-Basak and Valerie Jimenez) in which we discussed your January 28, 2005, submission.

We are reiterating certain deficiencies from our December 14, 2004, action letter below with additional clarifications. To complete your response (and restart the review clock), please address these items.

1. Item #1 (December 14, 2004, FDA letter)

With limited dissolution data provided, it appeared that the 160 mg tablets dissolved similarly in 0.025 M SLS [redacted] media. Therefore, the dissolution method using the lower SLS concentration of 0.025 M is recommended. Since the dissolution data of 50 mg tablets using 0.025 M is lacking, provide data for three batches [redacted] /batch) of the 50 mg strength under the condition of USP apparatus 2 at 50 rpm in 0.025 M SLS medium. The biowaiver for the 50 mg tablets will be determined based on similarity between the dissolution profiles of the 50 mg and 160 mg tablets using USP Apparatus 2 at 50 rpm in 0.025 M SLS medium.

In your response to item #1 above, you provided dissolution profiles of 1 x 160mg from Lot #H904 (batch H569 in [redacted] bottle) and 3 x 50 mg from Lots # H556, H565, and H976.

However, to evaluate the similarity of dissolution profiles between strengths and set appropriate dissolution specification for the 50 mg tablets, dissolution data for 1x 50 mg tablet (i.e., a single 50 mg tablet) are required. In addition, critical information for these tested batches including formulation, manufacturing process, and batch sizes were not provided in the biopharmaceutics section of your January 28, 2005, submission.

Clarification of FDA request:

- Provide dissolution profiles for three batches ([REDACTED] /batch) of 1 x 50 mg tablet (i.e., a single tablet) using USP Apparatus 2 at 50 rpm in 0.025 M SLS medium. Additionally, relevant information including formulation, manufacturing process, and batch sizes for 160 mg tablet Lot #H904 (batch H569) and 50 mg tablet Lots #H556, #H565, and #H976 should be provided. If you choose to use different batches to evaluate the dissolution profile of 1 x 50 mg tablet, the same information should be provided for these additional batches.
- Based on these test results, provide revised dissolution specifications.

2. Item #2 (December 14, 2004, FDA letter)

The application lacks sufficient evidence that the drug product (Lipanthyl 200M) used in the bioequivalence (BE) study (FEN101-C1-001) is the same drug product from the CMC perspective as the reference drug, Tricor (fenofibrate, micronized) Capsules, 200 mg (Abbott's NDA 19-304). Please provide information on the equivalence between the two products. We reference the letter dated April 12, 2002, addressed "To whom it may concern" under [REDACTED] letterhead. Please provide the basis on which these representations are made. Additionally, provide evidence that the Lipanthyl 200M and Tricor 200 mg capsule products are identical in qualitative and quantitative composition with regard to both active and inactive ingredients. Also provide evidence that the manufacturing processes and controls are the same for both products. Useful evidence to help support your assertions might be, for example: Evidence that the drug substance used for both products meets the same specifications, comparative batch records, comparative detailed manufacturing descriptions, and comparisons of process controls. In addition, provide certificates of analysis for Lipanthyl 200M and Tricor 200 mg capsules using the U.S. NDA approved procedures for Tricor 200 mg capsules, as well as evidence of authorization to access the Tricor 200 mg NDA specifications (NDA 19-304).

In your response to item #2 (above), you stated: "Additionally, SkyePharma has confirmed the suitability of Lipanthyl 200M (lot # 76149) and Tricor 200mg (lot#705843E2) by subjecting the products to the same test conditions as used for Triglide in order to establish identity, potency, purity and dissolution per the performance criteria listed in the attached certificate of analysis."

Your response included:

- The certificate of analysis of Lipanthyl (batch#66467) containing test results obtained by [REDACTED]
- Dissolution comparison profile for Tricor and Lipanthyl.

However, your response did not provide analytical test results on Lipanthyl lot#76149 and Tricor lot#705843E2.

Clarification of FDA request:

Provide full specification test results for Lipanthyl 200M (lot # 76149) and Tricor 200mg (lot#705843E2). You agreed to submit this information in our teleconference on February 17, 2005.

2. Item #4 (December 14, 2004, FDA letter)

Lower the drug product moisture content acceptance criterion below [REDACTED] w/w. Tablet moisture levels at or above [REDACTED] w/w may cause the tablets to become sticky and result in damage to the tablets when [REDACTED]

In your response to item #4 (above), you stated:

- For the bottle packaging: "SkyePharma proposes the limit to be not more than [redacted] w/w for tablets in the to-be-marketed [redacted] container. The highest moisture level achieved to date for IDD-P fenofibrate tablets was [redacted] w/w at 6-months accelerated storage conditions at 40°C/75%RH where all tablet parameters continued to meet specifications."
- For the blister packaging: "The 12-month real-time stability results for the 25°C/60%RH shelf condition indicate tablets with moisture levels as high as [redacted] w/w continue to meet the hardness specification. Therefore it appears that a [redacted] moisture specification is more appropriate than the original specification proposed for this product before the 12-month stability data was available."

As discussed in the teleconference referenced above, your proposed acceptance criteria for the drug product specifications should be based on data obtained thus far, as packaged in the to-be-marketed container/closure presentations. The Agency explained that the drug product specifications should be the same for all presentations.

Clarification of FDA request:

Provide complete, current drug product specifications. The specifications should also include revised criteria for appearance specification with [redacted]. These criteria were omitted in your January 28, 2005, submission. (See also under item #5).

3. Item #5 (December 14, 2004, FDA letter)

Provide updated drug substance specifications and drug product specifications for release and stability.

Regarding drug substance specifications:

You did not provide complete, current drug substance specifications in your response.

Clarification of FDA request:

Provide complete drug substance specifications (list of tests, methods, and the acceptance criteria).

Regarding drug product specifications:

- In your response regarding the drug product specifications, you introduced a new color evaluation system, with color codes [redacted]. You provided an amendment to monograph 672 to describe the new [redacted] color evaluation system; however, you did not provide the relevant color chips and updated monograph 672.

Clarification of FDA request.

- Provide [redacted] standard color chips corresponding to code 0 (N9.25), 1(5Y9/1.5), 2(5Y9/2.5), 3(5Y9/3), 4(5Y9/3.5), and 5(5Y9/4), as part of the appearance method in the updated monograph 672. (In addition to, or instead of, providing the color chips electronically, these chips may be submitted in paper.)

- While you revised your appearance coding system for color to the new color system, you omitted the previous used code [REDACTED] and code [REDACTED] (coding system you proposed in your amendment dated July 30, 2004).

Clarification of FDA request:

[REDACTED]

Additionally,

- We noted in your stability data (at 25°C/60% relative humidity) for batch H904 a value for the mode of the API particle size of [REDACTED] at 12 months. That value is out of acceptance criteria (NMT [REDACTED]). Please clarify/explain.
- Please help us locate the "in-use stability data" (i.e., submission date, volume, page) that you said had been submitted previously during the February 17, 2005, teleconference.
- Provide drug product samples (in bottles [REDACTED]) of primary stability batches as requested by e-mail on February 22, 2005, and include batch numbers and date of manufacture.

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

Sincerely,

{See appended electronic signature page}

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

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

/s/

Enid Galliers
2/25/05 05:32:48 PM
Signing for V. Jimenez



DEPARTMENT OF HEALTH & HUMAN SERVICES

2/9/05
Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

SkyePharma Inc.
Attention: Gordon L. Schooley, Ph.D.
Chief Scientific Officer
10450 Science Center Drive
San Diego, CA 92121

Dear Dr. Schooley:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triglide (fenofibrate) Tablets, 50 mg and 160 mg.

We also refer to the teleconference between representatives of your firm and the FDA on January 18, 2005. The purpose of the meeting was to discuss the December 14, 2004, action letter for your Triglide (fenofibrate) Tablets application.

The official minutes of that meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

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

Sincerely,

(See appended electronic signature page)

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

Enclosure

MEMORANDUM OF TELECONFERENCE MINUTES

DATE: January 18, 2005

APPLICATION NUMBER: NDA 21-350, Triglide (fenofibrate) Tablets

BETWEEN:

Name: Gordon Schooley, Ph. D., Chief Scientific Officer
~~Michael Vachon, M.Sc.Pharm. Ph.D. Project CMC Specialist~~
Antoine Poncy, SkyePharma Manufacturing Facility
Alan Roberts, Marketing partner representative
Diana Fordyce, Ph.D., RAC, Coordinator of Regulatory Correspondence

Phone: (877) 331-6867
Representing: SkyePharma

AND

Name: Mary Parks, M.D., Deputy Director and Medical Team Leader
Mamta Gautam-Basak, Ph. D., Chemistry Team Leader
Wei Qiu, Ph. D., Biopharmaceutics Reviewer
Elsbeth Chikhale, Ph. D., Chemistry Reviewer
Kim Dettelbach, Attorney, Office of Chief Counsel
Elaine Tseng, Regulatory Counsel, Office of Regulatory Policy
Enid Galliers, Chief, Regulatory Project Management Staff
Valerie Jimenez, Regulatory Project Manager

Division of Metabolic and Endocrine Drug Products, HFD-510

SUBJECT: December 14, 2004, Action letter: End-of-Review Meeting

BACKGROUND: On June 22, 2001, the sponsor, SkyePharma, submitted a New Drug Application (NDA) for Triglide (fenofibrate) Tablets which was reviewed and received an Approvable action on April 24, 2002. A response was submitted on March 31, 2004, and resulted in an Approvable action on December 14, 2004. The action letter outlined deficiencies that needed to be addressed in the resubmission. The firm submitted a December 15, 2004, request for an End-of-Review meeting.

DISCUSSION: The sponsor stated that a response to the December 14, 2004, action letter would be submitted approximately January 27 or 28, 2005, addressing the deficiencies contained in the Triglide action letter. After participant introductions, the sponsor requested discussion of 3 main categories; (1) biopharmaceutics/chemistry questions, (2) labeling, and (3) response review timeline. The Agency began with discussion of the deficiency items (1-9) in the action letter.

- Item #1: Dr. Qiu recommended that the sponsor submit dissolution data for three batches (batch) of 50 mg tablets using a lower concentration SLS (0.025 M). The sponsor agreed to submit dissolution data for 3 batches of 50 mg and 160 mg tablets as well as the dissolution similarity documentation. Dr. Qiu found the sponsor's proposal acceptable. Additionally, dissolution specifications for the 50 mg and 160 mg and the biowaiver request for the 50 mg tablet strength would be determined based on the dissolution data at the lower concentration SLS.
- Item #2: Dr. Chikhale informed the sponsor that information from the Freedom Of Information (FOI) for NDA 19-304 that is referenced cannot be used to support the Triglide application

because the sponsor does not have the right of reference. The sponsor affirms that Lipanthyl 200M is the same product, manufactured at the same site, and meets the same specifications as Tricor 200 mg capsules (NDA 19-304). Furthermore, attestation was submitted to the Agency on March 31, 2004, in the form of a letter from Fournier Laboratoires. The sponsor mentioned that the fax cover sheet for this letter will indicate the authenticity of this letter, and will confirm the relationship between the sponsor and Fournier. Dr. Gautam-Basak mentioned that review of all supporting evidence will be required to make a final decision.

- Item #3: Dr. Chikhale requested the submission of data to establish the identity and degree of discoloration. Moreover, if the sponsor suspected egg lecithin degradation products are causing the discoloration of the tablets, to identify and quantify the degradation products in the colored tablets. The sponsor agreed to submit those data, a gradation scale with matching color key as well as literature references.
- Item #4: Drs. Gautam-Basak and Chikhale stated that their previous request for an additional decimal place, was intended to clarify what the sponsor meant by "NMT [redacted]". Dr. Chikhale stated that submitted data indicated that NMT [redacted] was actually NMT [redacted]. Therefore, the moisture acceptance criteria are recommended to be NMT [redacted] and in the future (post approval), with the submission of additional data, the acceptance criteria may be revised. The sponsor stated that they had data indicating that tablets with more than [redacted] moisture, still met the other drug product specifications. Dr. Gautam-Basak suggested that along with the data a justification should be provided with the proposed acceptance criterion.
- Item #5: Dr. Chikhale asked the sponsor to submit updated specifications for the drug product and drug substance (list of test, acceptance criteria, and analytical procedures) and recommended [redacted] for moisture acceptance criteria.
- Dr. Gautam-Basak gave the response to two additional requests from the sponsor regarding CMC:
 - (1) [redacted]

(2) The sponsor requested confirmation that their proposal regarding the intended product expiry dating is supported by the stability data to date. Additionally, expiry dating will be extended as confirmatory stability data comes available. Dr. Gautam-Basak stated that the proposed expiry dating is not supported by currently submitted stability data. Since the drug product fails during accelerated stability studies, the expiry dating can not be projected and should be based on real time data. Furthermore, extrapolation is usually more helpful using assay values or degradation product values, than for physical properties. The sponsor declared that the blister sample was used strictly for physician sample only. Dr. Gautam-Basak asked for the submission of all available stability data to support the proposed expiry date with any justification.

(2) The sponsor requested confirmation that their proposal regarding the intended product expiry dating is supported by the stability data to date. Additionally, expiry dating will be extended as confirmatory stability data comes available. Dr. Gautam-Basak stated that the proposed expiry dating is not supported by currently submitted stability data. Since the drug product fails during accelerated stability studies the expiry dating can not be projected and should be based on; real time data. Furthermore, extrapolation is usually more helpful using assay values or degradation product values, than for physical properties. [redacted]

Dr. Gautam-Basak asked for the submission of all available stability data to support the proposed expiry date with and justification.

NDA 21-350

- Item #6: [REDACTED]
- Item #7: Ms. Galliers requested financial disclosure information for study FEN101-C1-001; Lipanthyl Capsules, 200 mg.
- Item #8: Regarding labeling, all queries were deferred until item 6, above, is resolved.
- Item #9: The sponsor agreed to submit color mock-ups of the container and carton labels with the proprietary name "Triglide".
- [REDACTED]

Valerie Jimenez
Regulatory Project Manager

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/s/

Valerie Jimenez
2/9/05 11:22:42 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

1/3/05

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

SkyePharma Inc.
Attention: Steve W. Jensen
Director, Global Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

Dear Mr. Jensen:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triglide (fenofibrate) Tablets, 50 mg and 160 mg.

We also refer to your December 15, 2004, correspondence, received December 17, 2004, requesting a meeting to discuss the December 14, 2004, action letter for your Triglide (fenofibrate) Tablets application. In addition, you requested a discussion of your counter proposal and clarification to the Clinical Pharmacology labeling section from the Biopharmaceutics reviewer.

Based on the statement of purpose, objectives, and proposed agenda, we consider the meeting a type C meeting as described in our guidance for industry titled *Formal Meetings with Sponsors and Applicants for PDL* (FDA, 2001) (February, 2000). The meeting is scheduled for:

Date: January 18, 2005
Time: 11:00 am to 12:00 noon
Phone Arrangement: Home phone and all-in phone number

Tentative CDER Participants

- Eric Curtis, Director, Division of New Drug Chemistry
- Maura Gorman-Bischoff, Chief, Chemistry Team Leader
- Robert Chikara, Chief, Chemistry Reviewer
- Harold G. ... Team Leader
- ...
- ...
- ...

Best Available Copy

NDA 21-350

Page 2

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

Sincerely,

(See attached electronic signature page)

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

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/s/

Valerie Jimenez
1/3/05 03:03:35 PM

Jimenez, Valerie

From: dfordyce@cato.com
Sent: Wednesday, December 15, 2004 11:22 AM
To: Jimenez, Valerie
Subject: Triglide/NDA 21-350 Action Letter

Return Receipt

Your Triglide/NDA 21-350 Action Letter
document:
was Diana Fordyce/CRL/Cato
received by:
at: 12.15.2004 11:21:30 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

INFORMATION REQUEST LETTER

Skye Pharma Inc.
Attention: Gordon L. Schooley, Ph.D.
Chief Scientific Officer
10450 Science Center Drive
San Diego, CA 92121

Dear Dr. Schooley:

Please refer to your June 22, 2001 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triglide (fenofibrate) Tablets, 50mg and 160 mg.

We also refer to your March 31, 2004, submission.

We are reviewing the Biopharmaceutical section of your March 31, 2004, submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

During our review, we have noted that you conducted dissolution studies using only one dissolution method (USP Apparatus 2 at 50 rpm in [REDACTED] sodium lauryl sulfate medium). To optimize the dissolution method for the current product, we recommend that you investigate two other dissolution conditions (e.g., lower SLS concentrations). Please submit individual dissolution profiles for tablets from 3 batches ([REDACTED] batch).

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

Sincerely,

{See appended electronic signature page}

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

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/s/

Mary Parks
11/4/04 02:40:30 PM
for Dr. Orloff



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

INFORMATION REQUEST LETTER

SkyePharma Inc.
Attention: Steve W. Jensen
Director, Global Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

Dear Mr. Jensen:

Please refer to your June 22, 2001 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Triglide (fenofibrate) Tablets, 50 mg and 160 mg.

We also refer to your March 31 and July 30, 2004, amendments.

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

1. Provide USP<671> test results for the proposed [REDACTED] packaging.
2. The release and stability specifications for appearance should include as part of the acceptance criteria: [REDACTED]
3. The certificates of analysis (COA) provide in appendix P report particle size as [REDACTED] percentile, whereas the release specifications (pg. 29 of the resubmission) use 'mean of mode' as the parameter for particle size. The parameter(s) reported in the COA, the regulatory drug product release specifications, and the stability specifications should be consistent.
4. Clarify whether the tablets are package in bulk after manufacturing? If so, provide information on the bulk packaging material, storage conditions, and time limit for storage in bulk.
5. Resubmit the available moisture content stability data with at least one decimal precision, rather than data rounded to whole number.
6. If available, provide 9-month (room temperature) stability data for the to-be marketed drug product.
7. Regarding the drug product manufacturing process, clarify the following:
 - a. Does the addition of mannitol, maltodextrin, and croscarmellose sodium [REDACTED]

- b. What is the in-process control for drug substance particle size? Is it: Volume weighted mean NMT [REDACTED] and [REDACTED] percentile NMT [REDACTED] (as indicated in table 4A-22) or is it [REDACTED] (how measured?) as indicated in the manufacturing process description (pg. 18 of the March 31, 2004 submission)?

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

Sincerely,

Mamta Gautam-Basak, Ph.D.
Chemistry Team Leader II for the
Division of Metabolic and Endocrine Drug Products,
HFD-510
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Mamta Gautam-Basak
10/20/04 02:57:26 PM

10/15/04



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

SkyePharma Inc.
Attention: Steve W. Jensen
Director, Global Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

Dear Mr. Jensen:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [redacted] (fenofibrate) Tablets, 50 mg and 160 mg, [redacted]

We also refer to your July 30, 2004, submission containing a request for trade name change.

We have reviewed the referenced material and find the proposed proprietary name Triglide™ acceptable. Additionally, we have the following comments and recommendations. Labeling comments will be conveyed under separate cover.

General Comment

Please ensure the 90-tablet bottle unit-of-use has a child-resistant cap (CRC) to be compliant with the Poison Prevention Act.

Blister Label (50 mg and 160 mg)

1. Since this product is to be dispensed to a patient, please ensure that the packaging is child-resistant.
2. [redacted]

n

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

Sincerely,

(See appended electronic signature page)

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

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/s/

Mary Parks
10/15/04 01:12:40 PM
for Dr. Orloff



DEPARTMENT OF HEALTH & HUMAN SERVICES

8/18/04

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

SkyePharma Inc.
Attention: Steve W. Jensen
Director, Global Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

Dear Mr. Jensen:

Please refer to your June 22, 2001, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [REDACTED] (fenofibrate) Tablets, 50 mg and 160 mg.

We also refer to your submission dated March 31, 2004, received April 1, 2004, which was a complete response to our April 1, 2004, action letter.

On August 2, 2004, we received your July 30, 2004 major amendment to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is January 1, 2005.

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

Sincerely,

{See appended electronic signature page}

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

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/s/

Valerie Jimenez
8/18/04 12:43:38 PM

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: Aug. 6, 2004	DESIRED COMPLETION DATE: September 15, 2004	ODS CONSULT #: 01-0117-2
PDUFA DATE: October 1, 2004		

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

THROUGH: Valerie Jiminez
Project Manager
HFD-510

PRODUCT NAME:

Triglide™
(Fenofibrate Tablets)
50 mg and 160 mg

NDA #: 21-350

SPONSOR: SkyePharma

SAFETY EVALUATOR: Tia M. Harper-Velazquez, Pharm.D.

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Triglide™. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
2. Revised labels and labeling were not submitted with this consult request. Please refer to Consult # 01-0117-1, dated July 27, 2004, for comments.
3. DDMAC finds the proprietary name Triglide™ acceptable from a promotional perspective.

Denise P. Toyer, Pharm.D.
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

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

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: August 30, 2004

NDA: 21-350

NAME OF DRUG: **Triglide™**
(Fenofibrate Tablets)
50 mg and 160 mg

NDA SPONSOR: SkyePharma

I. INTRODUCTION

This consult was written in response to a request from the Division of Metabolic and Endocrine Drug Products, for an assessment of the proprietary name "Triglide™" regarding potential name confusion with other proprietary or established drug names. Originally, the sponsor submitted the trade names **██████████** (primary choice) and **██████████** (alternate choice) for review. Both proposed names were found unacceptable by DMETS on February 14, 2002 (ODS Consult # 01-0117) and July 27, 2004 (ODS Consult # 01-0117-1). Triglide™ is the third name reviewed for SkyePharma's fenofibrate tablets. Revised container labels, blister strip labels, carton and insert labeling were not submitted for review. The sponsor has submitted additional information, including an independent analysis conducted by the Drug Safety Institute, for review and comment.

PRODUCT INFORMATION

Triglide™ is the proposed name for fenofibrate tablets. It is indicated as adjunctive therapy to diet for the reduction of LDL-C, Total-C, triglycerides, and Apo B in adult patients with primary hypercholesterolemia or mixed dyslipidemia. For adult patients, the initial dose is 50 mg to 160 mg once daily. Dosage should be individualized according to patient response, and should be adjusted if necessary following repeat lipid determinations and four to eight week intervals. Triglide™ will be available as a tablet in strengths of 50 mg and 160 mg.

II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{i,ii} as well as several FDA databasesⁱⁱⁱ for existing drug names which sound-alike or look-alike to "Triglide™" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent

ⁱ MICROMEDEX Integrated Index, 2004. MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

ⁱⁱ Facts and Comparisons, online version. Facts and Comparisons, St. Louis, MO.

ⁱⁱⁱ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support proprietary name consultation requests, New Drug Approvals 1998-2004, and the electronic online version of the FDA Orange Book.

and Trademark Office's Text and Image Database^{iv} and the data provided by Thomson & Thomson's SAEGISTM Online Service^v were also conducted. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Triglide. Potential concerns regarding drug marketing and promotion related to the proposed name was also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name acceptable from a promotional perspective.
2. The Expert Panel identified five proprietary names that have potential for confusion with Triglide. These products are listed in Table 1 (see below), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult Dose*	Other **
Triglide (Rx)	Fenofibrate Tablets 50 mg and 160 mg	Take one tablet daily.	
Prinzide (Rx)	Lisinopril and Hydrochlorothiazide Tablets 10 mg/12.5 mg, 20 mg/12.5 mg, and 20 mg/25 mg	Take one tablet once daily	**L/A, S/A
Trilyte (Rx)	Polyethylene Glycol 3350 420 grams	After fasting for 3 to 4 hours, take 240 mL every 10 minutes or 20 mL to 30 mL per minute by NG tube until rectal discharge is clear.	**L/A, S/A
Tridil (Rx)	Nitroglycerin Injection	<u>Initial</u> 25 mg/250 mL in D5W at 5-10 mL/hour or 5 micrograms/minute and advance 3-5 mL/hr every five minutes until chest pain resolved. <u>Maintenance</u> 5-100 micrograms/minute	**L/A, S/A
Timolide (Rx)	Timolol and Hydrochlorothiazide Tablets 10 mg/25 mg	Take 2 tablets daily in 1 or 2 divided doses	**L/A, S/A
Ticlid (Rx)	Ticlopidine Tablets 250 mg	Take one tablet twice daily with food.	**L/A
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

B. PHONETIC ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

^{iv} WWW location <http://www.uspto.gov>.

^v Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search modules return a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. No additional names of concern were identified in POCA that were not discussed in EPD.

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Triglide with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 129 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Triglide (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u></p> 	<p>Triglide 160 mg, take one by mouth daily, dispense #30.</p>
<p><u>Inpatient RX:</u></p> 	

2. Results:

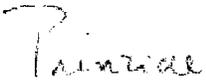
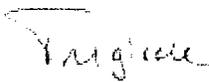
None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S product. See Appendix A for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name “Triglide”, the products considered to have potential for name confusion with Triglide were: Prinzide, Trilyte, Tridil, Timolide, and Ticlid. Upon further review of the names gathered from EPD and POCA, the names, Tridil and Ticlid were not reviewed further due to a lack of convincing look-alike and sound-alike similarities, in addition to numerous product differences such as product strength, route of administration, dosage form, and indication of use.

We conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of incorrect interpretations from the written and verbal studies were misspelled/phonetic variations of the proposed name, Triglide.

1. Prinzide was identified to look similar and sound similar to the proposed name Triglide. Prinzide is a combination drug product, containing lisinopril and hydrochlorothiazide, and is indicated for the treatment of hypertension. It is available as an oral tablet, in strengths of 10 mg/12.5 mg, 20 mg/12.5 mg, and 20 mg/25, which is administered once daily. Both names contain eight letters and two syllables. The second and third letters (“ri”) as well as the last three letters of the names are identical (“ide”), adding to both the orthographic and phonetic similarity. The first letter of each name (“P” vs. “T”) can look similar when written, although the first syllable is distinguishable when pronounced (“Prin” vs. “Tri”). In addition, the presence of the down stroke letter “g” and upstroke letter “l” in Triglide helps to distinguish the names from each other in appearance. The products share an overlapping route of administration (oral) and dosage form (tablet), however they differ in strength (10 mg/12.5 mg, 20 mg/12.5 mg, and 20 mg/25 vs. 50 mg and 160 mg). The minimal sound-alike similarities between the names, in addition to the difference in product strength, decrease the potential for confusion between Prinzide and Triglide.

<u>Prinzide</u>	<u>Triglide</u>
	

P R I N Z I D E
T R I G L I D E

2. Trilyte was identified to sound and look similar to the proposed name, Triglide. Trilyte is the proprietary name for the Schwarz Pharma brand of polyethylene glycol 3350. It is indicated as a bowel cleanser, used before colonoscopy. The recommended adult dose is 240 mL taken every ten minutes, after fasting for three to four hours until rectal discharge is clear. Both names consist of three syllables and begin with the combination “Tri”. The ending of the names (“lyte” vs. “glide”) are orthographically similar due to the letters “l”, “e”, which are present in both names, as well as the upstroke letters “t” (in Trilyte) and “d” (in Triglide). Although both products are taken orally, Trilyte and Triglide differ in dosage form (liquid vs. tablet), dosing regimen (every 10 minutes vs. once daily), packaging (420 gram carton vs. blister strips in cartons of 30 count and tablets in bottles of 90 count), and indication of use (bowel cleanser vs. lipid lowering agent).

Although there are some look-alike and sound-alike similarities between the names, the aforementioned product differences will minimize the potential for confusion between Trilyte and Triglide.

Trilyte Triglide
Trilyte Triglide

TRILYTE
TRIGLIDE

3. Timolide was identified to have look-alike and sound-alike similarities to the proposed name, Triglide. Timolide is a combination drug product containing timolol, a non-cardioselective beta-blocker and hydrochlorothiazide, a diuretic. It is indicated for the treatment of hypertension. Timolide is available as a tablet in a strength of 10 mg/25 mg. The recommended adult dose is two tablets daily given as one dose or in two divided doses. The look-alike and sound-alike similarities between the names can be attributed to the fact that both names begin with the letter “T”, and end in the letter combination “lide”. Although the first syllable of each name contains the letter “i”, it is located in different positions in each name. Despite these similarities, overall, the beginnings of the names are different from each other when spoken (“Timo” vs. “Tri”). In addition, the down stroke of the letter “g” (in Triglide) helps to further distinguish the names from each other when written. Timolide and Triglide share an overlapping route of administration (oral), dosage form (tablet), and dosing regimen (once daily). However, they differ in strength (10 mg/25 mg vs. 50 mg and 160 mg). Since Triglide is available in two strengths, a strength would likely be indicated on a prescription order, unlike Timolide, which is available in only one strength. A strength would not necessarily have to be noted on a prescription order for Timolide. The potential for confusion and error between Timolide and Triglide is reduced due to the minimal look-alike and sound-alike similarities between the names, in addition to the difference in product strength.

Timolide Triglide
Timolide Triglide

E. INDEPENDENT NAME ANALYSIS

The sponsor submitted an independent analysis conducted by the Drug Safety Institute, a subsidiary of the Brand Institute, Inc. The analysis discusses the following names that were not identified as potential sound-alike or look-alike products by DMETS: Artilide, Astroglide, Avalide, Gliadel, Glibornuride, Glipizide, Glyburide, Glynase, Indapamide, Microzide, Minizide, Nipride, Pergolide, Repaglinide, Tegamide, Thiacyde, Thiazide, Tiaramide, Tilidine, Ti-Lite, Tizide, Tralonide, Triad, Trialodine, Triamonide, Trianide, Tricor, Triderm, Tridione, Trifed, Trigesic, Trileptal, Trilisate, Trilog, Trilone, Trimazide, Trimetamide, Trimethamide, Trimidar, Trimline, Trinalin, Triolipid, Triple, Tripodrine, Tritec, Tri-Vite, Troglitazone, Tropicamide, and Twilite. It should be noted that three participants in the written prescription study identified the proposed name as Tricor; and one participant in the verbal study identified the proposed name as Glyburide.

Tricor and the proposed name, Triglide look similar to each other due to the identical letter combination at the beginning of each name ("Tri"). The names differ in number of letters (six vs. eight), and the ending of the names are phonetically and orthographically distinguishable from each other ("cor" vs. "glide"). The products share an overlapping route of administration (oral), dosage form (tablets), dosing regimen (once daily), product strength (160 mg), active ingredient (fenofibrate) and indication of use (cholesterol lowering agent). Despite the similarities, the orthographic differences in the endings of each name will help to distinguish the two products.

Glyburide was identified in the verbal study to have sound-alike similarity to the proposed name, Triglide. The beginning of the names share a rhyming quality ("Gly" vs. "Tri") and both names end with the letter combination "ide". The names differ in number of syllables (three vs. two), and the middle of the names are phonetically distinguishable from one another ("bur" vs. "gl"). Both products are available as oral tablets which are administered daily. Although there are overlapping numerals (5 mg vs. 50 mg), overall the products differ in strength (1.25 mg, 2.5 mg, and 5 mg vs. 50 mg and 160 mg), and indication of use (diabetes vs. lipid lowering). Despite the rhyming quality between the names and overlapping product characteristics, the sound-alike similarities between the names is minimal, and thus decreases the potential for confusion.

Therefore, DMETS concurs with the overall findings of the Drug Safety Institute study that the potential for confusion between Triglide and the aforementioned names is minimal.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

Revised labels and labeling were not submitted with this consult request. Please refer to Consult # 01-0117-1, dated July 27, 2004, for comments.

V. RECOMMENDATIONS

- A. DMETS has no objections to the use of the proprietary name, Triglide. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
- B. Revised labels and labeling were not submitted with this consult request. Please refer to Consult # 01-0117-1, dated July 27, 2004, for comments.
- C. DDMAC finds the proprietary name Triglide acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

Tia M. Harper-Velazquez, Pharm.D.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

8/5/04

Office of Drug Safety

MEMO

To: David Orloff, MD
Director, Division of Metabolic and Endocrine Drug Products, HFD-510

From: Nora Roselle, PharmD
Safety Evaluator, Division of Medication Errors and Technical Support, Office of Drug Safety, HFD-420

Through: Denise Toyer, PharmD
Deputy Director, Division of Medication Errors and Technical Support, Office of Drug Safety, HFD-420
Carol A. Holquist, RPh
Director, Division of Medication Errors and Technical Support, Office of Drug Safety, HFD-420

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

Date: July 27, 2004

Re: ODS Consult 01-0117-1, [REDACTED] (Fenofibrate Tablets) 50 mg and 160 mg; NDA 21-350.

This memorandum is in response to a June 30, 2004, request from your Division for a re-review of the proprietary name, [REDACTED]. The proposed proprietary name, [REDACTED] and the alternate name, [REDACTED] were previously found unacceptable by DMETS on February 25, 2002 (ODS Consult # 01-0117).

A memo from the medical officer dated April 8, 2002, states that due to differences between [REDACTED] as well as a low probability of serious safety concerns, the Division of Metabolic and Endocrine Drug Products has no objections to the proposed proprietary, [REDACTED].

Since the original review, DMETS has not identified any additional proprietary or established names that have the potential for confusion with [REDACTED] that would render the name objectionable. However, we restate our concerns with regards to the sound-alike similarities between [REDACTED]. DMETS acknowledges that the product characteristics of these two products are different. Product characteristics (e.g., frequency and strength) often help to differentiate products. However, DMETS is learning from postmarketing experience that the potential for error between names goes beyond the context for use (strengths, frequency, etc.) when the names are very similar. Examples of these types of name pairs include the following:

- A nurse called the pharmacy to ask for a morning dose of Diprivan (intravenous general anesthetic) that was "missing". Upon checking the patient's electronic drug profile, the pharmacist could not find an order for Diprivan. He learned that the "missing" drug was being used for bladder spasms and realized the patient was on Ditropan (oral agent used for urinary incontinence). (ISMP Medication Safety Alert, Volume 7, Issue 6, March 20, 2002)
- A patient was ordered Keppra 500 mg (tablets) every 12 hours but Kaletra was dispensed. The brand name sound-alike probably contributed to the error. Kaletra is available as a combination capsule (133.3 mg/33.3 mg) and oral solution (20 mg/mL and 80 mg/mL).

Additionally, two participants from the verbal study interpreted [REDACTED] and two other participants interpreted the sample as [REDACTED] which sounds very similar to [REDACTED]. These misinterpretations occurred despite the different strength and frequency. DMETS notes that the medical team leader memo states that the “safety concerns associated with inadvertent administration of [REDACTED] do not appear life-threatening and are more likely a tolerability issue that would result in the patient discontinuing the medication.” Despite the lack of a serious outcome, the medication error would have occurred.

It is also important to note that in our original review, we did not have access to our Phonetic/Orthographic Computer Analysis (POCA) which is one tool that we currently use to evaluate our proposed names. Asacol was considered to have significant phonetic and orthographic similarities to [REDACTED] when evaluated with the algorithm.

Additionally, in reviewing the container label, carton and insert labeling for [REDACTED] DMETS has identified some areas of possible improvement in the interest of minimizing potential user error. Labels and labeling for the bottles of 90 tablets were not submitted for review and comment.

A. GENERAL COMMENT

1. We recommend clearly differentiating the two different strengths by using a contrasting color, boxing, or some other means. Currently the presentation of both the 50 mg and 160 mg are identical, which increases the potential of selection errors.
2. It appears that the 90-tablet bottle is a unit-of-use. Please ensure this bottle has a child-resistant cap (CRC) to be compliant with the Poison Prevention Act.

B.

[REDACTED]

C.

[REDACTED]

In summary, DMETS does not recommend the use of the proprietary name, [REDACTED]. DDMAC finds the proprietary name, [REDACTED] acceptable from a promotional perspective. Additionally, we recommend implementation of the label and labeling revisions noted above. We would be willing to meet with the Division for further discussion if needed. If you have any questions or need clarification, please contact Sammie Beam at 301-827-3242.

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/s/

Nora L. Roselle
8/5/04 09:14:56 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
8/5/04 12:52:53 PM
DRUG SAFETY OFFICE REVIEWER
for Carol Holquist



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

INFORMATION REQUEST LETTER

SkyePharma Inc.
Attention: Steve W. Jensen
Director, Global Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

Dear Mr. Jensen:

Please refer to your March 31, 2004 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [REDACTED] (fenofibrate) Tablets, 50 mg and 160 mg.

We also refer to your submission dated May 19, 2004.

During the review biopharmaceutics portion of your submission, we found study FEN101-C25 is not acceptable because the batch size [REDACTED] used in this study is extremely small. We recommend that you conduct another study to evaluate relative bioavailability comparing [REDACTED] Tablets to the reference listed drug. Also provide data for food effect and dosage form equivalence for [REDACTED] Tablets. The batch size of the [REDACTED] Tablets tested must equal or exceed [REDACTED] of the commercial batch size.

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

1. The following cannot be located in the NDA, please provide the following information or the exact location in your submission:
 - Monograph 336-1 (test method for [REDACTED] referenced on pg. 58).
 - Monograph 033-9 (test method for purified water EP, referenced on pg. 88).
 - SOP [REDACTED] and SOP [REDACTED] referenced in table 4A-22, and also indicate/provide methods used.
 - Stability protocols No. 529 and No. 531 (referenced on pg. 1605).
2. Provide a better (readable) copy of the flow chart of manufacturing process (Figure 4A-2, pg. 15).
3. In appendix J, there are several typographical errors in the specifications of a number of raw materials; provide clarification and revised information should be resubmitted (e.g., see below)
 - Mannitol, USP [REDACTED]
 - Maltodextrin, NF [REDACTED]
 - Carboxymethylcellulose sodium, USP [REDACTED]
 - Lactose monohydrate, NF [REDACTED]
4. Your proposed expiration date is not supported by the submitted stability data. Provide available long term stability data on batches of the to-be-marketed formulation.
5. In appendix O (pg. 1611 and 1659), you mention the appearance of a yellowish molting after storage of the tablets at accelerated conditions. Provide clarification and a report of investigation on probable cause of discoloration of the drug product.

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/s/

Mary Parks
7/2/04 07:56:47 AM
for Dr. Orloff

5/9/05

Division of Metabolic & Endocrine Drug Products

PROJECT MANAGER LABELING REVIEW

Application Number: NDA 21-350

Name of Drug: Triglide® (fenofibrate tablets), 50 mg and 160 mg

Sponsor: SkyePharma, Inc.

Materials Reviewed:

Submission Date(s): Final Printed Labeling (FPL): Package Insert (PI), FPL 90-count container labels, 50 mg and 160 mg, Submitted March 4, 2005; received March 5, 2005.

Background and Summary

Triglide is indicated as adjunctive therapy to diet for the reduction of LDL-C, Total-C, Triglycerides, and ApoB in adult patients with primary hypercholesterolemia or mixed dyslipidemia (Fredrickson Types IIa and IIb). Additionally, it is indicated as adjunctive therapy to diet for treatment of adult patients with hypertriglyceridemia (Fredrickson Types IV and V hyperlipidemia). This application was originally submitted on June 22, 2001, and received an Approvable action on April 24, 2002. The firm submitted a response on March 31, 2004, reflecting the Agency's proposed changes resulting in a second Approvable action on December 14, 2004. The sponsor requested a teleconference to discuss the deficiencies in the December 14, 2004, action letter. The teleconference was held on January 18, 2005. On January 28 and March 4, 2005, the sponsor submitted a response to the December 14, 2004, action letter which includes proposed labeling reflecting the requested changes discussed in the teleconference.

Review

Package Insert

The Agency's proposed labeling issued in the December 14, 2004, action letter was compared to the applicant's labeling dated March 4, 2005.

1. The firm has changed the established name to "fenofibrate" and added "tablets" to the proprietary name, "Triglide." It is now "TRIGLIDE (fenofibrate) Tablets".

This is a change made in response to an FDA comment on the December 14, 2004, FDA labeling, and it is acceptable.

2. Under DESCRIPTION, Inactive Ingredients section, the underlined text was added:

"Inactive Ingredients: Each tablet also contains crospovidone, lactose, monohydrate, mannitol, maltodextrin, carboxymethylcellulose sodium, egg lecithin, croscarmellose sodium, sodium lauryl sulfate, ..."

This addition is acceptable per the Chemists review page 12, dated December 6, 2004, by Elsbeth Chikhale, Ph.D.

3. Under **CLINICAL PHARMACOLOGY** section, **Pharmacokinetics, Effect of Food on Absorption** subsection, the second paragraph was changed:

~~_____~~

to:

"The extent of absorption of TRIGLIDE (AUC) is comparable between fed and fasted conditions. Food increases the rate of absorption of TRIGLIDE approximately 55%."

4. Under **CLINICAL TRIALS** section, the first paragraph was changed:

from:

~~_____~~

to:

"In a single-dose pharmacokinetics study in healthy volunteers, TRIGLIDE 160 mg tablet was shown to have comparable bioavailability to a single dose of 200 mg fenofibrate capsule, micronized."

5. Under **WARNINGS** section, **Concomitant HMG-CoA Reductase Inhibitors (Statins)** subsection, the following paragraph (previously the second paragraph) was deleted:

~~_____~~

The above changes, items 3 through 5, were agreed upon in the January 18, 2005, teleconference. Additionally, the changes were confirmed per the biopharmaceutics memorandum dated April 21, 2005, by Wei Qiu, Ph.D.

6. Under **DOSAGE AND ADMINISTRATION**, the third paragraph has been removed.

~~_____~~

This change is acceptable per the teleconference dated January 18, 2005.

7. In the **HOW SUPPLIED** section, the following changes were made:

a. The tablets are debossed with "FH 50" or "FH 60" instead o ~~_____~~

This change is acceptable.

- b. The NDC numbers are given.

This change is acceptable.

to:

“Store at 20-25°C (68-77°F); excursions permitted to 15-30°C (59-86°F). [See USP Controlled Room Temperature]. Protect from light and moisture.”

These changes are acceptable, except “...excursions permitted to...” should be changed to state “. ~~_____~~

8. In the **HOW SUPPLIED** section, the following underlined text has been changed:

“Manufactured for First Horizon Pharmaceuticals® Corporation by SkyePharma Production SAS, France. Made in France.

This change is acceptable per 21 CFR 201.1(h)(5).

9. An identifier, “FF-PI-1”, and revision date, “Rev 01/05”, were added.

This is an acceptable change.

Conclusion

An Approval letter should be drafted. FPL was submitted in the March 4, 2005, submission. The current Identifiers are:

Presentation	Identifier
PI	FF-PI-1, Rev. 01/05
Container: 50 mg	FF-L05-2, Rev. 01/05
Container: 160 mg	FF-L16-3, Rev. 01/05

Valerie Jimenez
Regulatory Project Manager, HFD-510

Drafted: V.J./April 18, 2005

Revised/Initialed: E.G/ May 4, 6, 8, and 9, 2005

Finalized: May X, 2005

Filename: C:/Askpol-N21350/Triglide-N21350/NDA.LR.doc

CSO LABELING REVIEW

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/s/

Valerie Jimenez
5/9/05 02:50:35 PM
CSO

4/22/04



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

SkyePharma Inc.
Attention: Steve W. Jensen
Director, Global Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

Dear Mr. Jensen:

We acknowledge receipt on April 1, 2004, of your March 31, 2004, resubmission to your new drug application for [REDACTED] (fenofibrate) Tablets.

We consider this a complete, class 2 response to our April 24, 2002, action letter. Therefore, the user fee goal date is October 1, 2004.

We are reviewing your submission and have the following requests for additional information. Please provide:

1. A paper desk copy of the Chemistry, Manufacturing, and Controls (CMC) portion of your (March 31, 2004, submission) with pagination.
2. A summary table of all CMC changes (e.g., formulation changes, manufacturing process changes, storage conditions, and manufacturing and testing sites) with a side-by-side comparison to the original submission and reference to location of information in the March 31, 2004. All information must be provided in English.
3. Final particle size distribution for your fenofibrate product after disintegration.
4. The formulation used in the Pharmacokinetics (PK) study FEN101-C25.
5. Batch size for Batch LFTF2 (Lot #94.172) used for study FEN101-C25.
6. Patent Information Form FDA 3542a and any necessary new patent certifications.
7. Mock-ups of the carton and bottle labels for 90-count trade bottles of 50 mg and 160 mg tablets.

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

NDA 21-350

Page 2

effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirement. We are waiving the requirement for pediatric studies for this application.

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

Sincerely,

{See appended electronic signature page}

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

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/s/

Valerie Jimenez
4/22/04 02:58:54 PM .

4/20/04



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-350

SkyePharma, Inc.
Attention: Steve W. Jensen
Director, Global Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

Dear Mr. Jensen:

We acknowledge receipt on April 1, 2004, of your March 31, 2004, correspondence notifying the Food and Drug Administration that the corporate name and address has been changed from

SkyePharma Canada Inc.
1000 chemin du Golf
Verdun (Quebec)
Canada H3E 1H4

Cato Research, U.S. Agent
200 Westpark Corporate Center
4364 S. Alston Avenue
Durham, NC 27713-2280

to

SkyePharma, Inc.
10450 Science Center Drive
San Diego, CA 92121

for the following new drug application:

NDA 21-350 for (fenofibrate) Tablets, 50 mg and 160 mg.

We have revised our records to reflect this change.

We request that you notify your suppliers and contractors who have DMFs referenced by your application of the change so that they can submit a new letter of authorization (LOA) to their Drug Master File(s).

NDA 21-350

Page 2

Address all communications concerning this NDA as follows:

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

Center for Drug Evaluation and Research

Division of Metabolic and Endocrine Drug Products, HFD-510

Attention: Division Document Room, 8B-45

5600 Fishers Lane

Rockville, Maryland 20857

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

Sincerely,

{See appended electronic signature page}

Valerie Jimenez

Regulatory Project Manager

Division of Metabolic and Endocrine Drug
Products

Office of Drug Evaluation II

Center for Drug Evaluation and Research

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/s/

Valerie Jimenez
4/20/04 07:51:03 AM

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/s/

William Koch
4/1/02 03:40:07 PM
CSO

Koch, William

From: Orloff, David G
Sent: Monday, April 01, 2002 12:33 PM
To: Parks, Mary H; Ahn, Hae Young; Qiu, Wei
Cc: Koch, William
Subject: RE: IDD-P fenofibrate

One more point of clarification. Our current thinking is that the data they have submitted supports bioequivalence to the reference listed drug in the fed state for both. In other words, the only head-to-head study they did for the purposes of inferring efficacy of their product was fed to fed. So the label should say take with food (to get an effect equivalent to Tricor (which is taken with food). If they did theirs fasted to Tricor fed and showed equivalence, then we could say take with or without food, though in the absence of proof that the food effect was not clinically significant, the label might still have to say that if the response is inadequate when taken without regard to meals, consideration may be given to taking always with food.

DGO

-----Original Message-----

From: Parks, Mary H
Sent: Monday, April 01, 2002 12:21 PM
To: Ahn, Hae Young; Qiu, Wei
Cc: Koch, William; Orloff, David G
Subject: IDD-P fenofibrate

Hae Young and Wei,

I just spoke with David regarding the food effect of IDD-P fenofibrate. He feels that this food effect, no matter how small, is still a food effect for which we have no clinical data to state (as the sponsor has proposed) that it's clinically insignificant. Such, the sponsor would need to prove to us that there is no clinical effect in IDD-P fenofibrate given with or without meals. This can be achieved by their doing a clinical trial under fed and fasted conditions and comparing the lipid-altering efficacy in both groups to show no difference.

Another potential way for establishing no clinical effect is for the sponsor to conduct a relative bioavailability study between IDD-P fenofibrate under fasted conditions to Tricor under fed conditions. The thinking here is that if IDD-P fenofibrate under fasted conditions (lower C_{max}) gives comparable bioavailability to Tricor under fed conditions (the setting for which we have clinical data - at least the nonmicronized one) then we could allow them to state "taken with or without meals" because we'll know that the fasted levels of IDD-P fenofibrate are bioequivalent to the fed levels of Tricor. We would be interested in knowing whether BPH sees any problems with this approach.

I think a clinical trial would give us more definitive information but admittedly, this would take longer than a pK study. Can you discuss this among the OCPB group to get some input on this issue? Although these guys will get an AE (at least) we should try to come up with some solution for their proposed labeling on food effect.

Thanks,
Mary

Koch, William

From: Koch, William
Sent: Wednesday, February 13, 2002 2:52 PM
To: Beam, Sammie
Subject: IND 60,743 (NDA 21-350); Final Trade Name Check

Sammie,

UF(10) date: April 25, 2002

Original ODS Consult Number 01-0117

Proposed trade name: 

Thank You

Bill

William C. Koch, R.Ph.
Regulatory Project Manager
Lipid Altering Agents II Group
Anabolic Steroids Group
Cachexia/AIDS Wasting Group
Division of Metabolic
and Endocrine Drug Products, HFD-510
Office of Drug Evaluations II
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 827-6412
Fax: (301) 443-9282
Email: KOCHW@CDER.FDA.gov

11/5/01

Meeting Date: September 28, 2001 Time: 02:30PM Location: PKLN Room #14B-45

NDA 21-350
IDD-P Fenofibrate (Insoluble Drug Delivery-Microparticle fenofibrate tablets)

Type of Meeting: Guidance Telephone Conference, CMC

External Participant: RTP Pharma Inc.

Meeting Chair: Duu-Gong Wu, Ph.D., Chemistry Team II Leader

External Participant Lead: Michael G. Vachon, M.Sc.Phm., Ph.D., Vice President, Process Development

Meeting Recorder: William C. Koch, R.Ph., Regulatory Project Manager

FDA Attendees and titles:

- Enid Galliers, Chief, Project Management Staff
- Wei Qiu, Ph.D., Biopharmaceutics Reviewer
- Duu-Gong Wu, Ph.D., Chemistry Team Leader
- Pardha Komanduri, Ph.D., Chemistry Reviewer
- Hae Young Ahn, Ph.D., Biopharmaceutics Team Leader
- William C. Koch, R.Ph., Regulatory Project Manager

External participant Attendees (by phone) and titles:

- Pol-Henri Guivarc'h, M.D., M.B.A., Vice President, Clinical Development
- Michael G. Vachon, M.Sc.Phm., Ph.D., Vice President, Process Development
- Gary Robinson, Ph.D., Senior Scientist
- Diana Fordyce, Ph.D., R.A.C., Senior Regulatory Scientist

Meeting Objectives:

To discuss the commercial scale manufacturing process for the drug product.

Discussion Points:



1 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process

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/s/

Duu-gong Wu
11/5/01 11:08:26 AM

Koch, William

From: Komanduri, Pardhasara
Sent: Wednesday, October 31, 2001 5:24 PM
To: Wu, Duu Gong
Cc: Duffy, Eric P; Koch, William
Subject: NDA # 21-350

Duu Gong,

I just checked with Ms. Lynda Sutton from CATO research and she indicated that the issue is still unresolved as to what they will be doing about the manufacturing facility confusion, they are having. She mentioned that she will check with the concerned staff and get back to me. As we discussed during the Telecon. the sponsor wants to engage both the facilities for the production of Drug Product [REDACTED]. But none of the two facilities are ready for inspection at the present time. When the NDA was submitted, the [REDACTED] facility was ready and the application was filed. During the course, the sponsor has started moving some of the equipment to the new facility [REDACTED] and we have been informed when the equipments were in transit. Apparently, as per the conversation I had today and the conversations Bill had in the past, the sponsor does not want to bring back the equipment to [REDACTED] facility to get the inspection completed.

I just checked with Bill, and according to the information he has, the facilities will be ready for inspection only by 31st December 2001 (either they bring back the equipment to the old facility or they install it in the new facility). This is pretty much the feed back we got from them during the Telecon and apparently that did not change. The facility at [REDACTED] is only half ready in the sense that the [REDACTED] are still being carried out there and that portion of it can be inspected but then, the [REDACTED] in which the [REDACTED] are planned, will not be ready till December 31st.

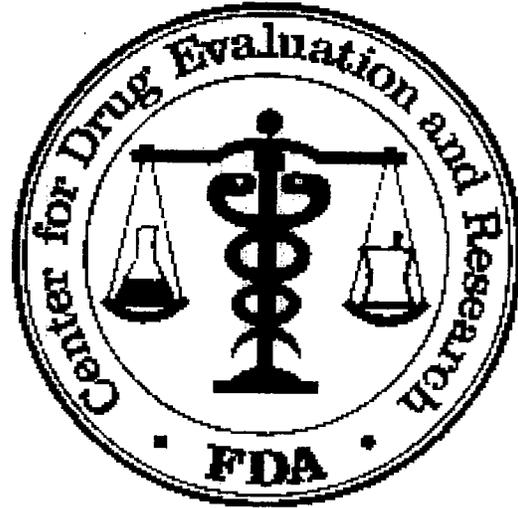
As per our discussion a minute ago, I will get some documentation from the sponsor to this effect.

Thanks

Pardha

FOOD AND DRUG ADMINISTRATION
DIVISION OF METABOLIC AND
ENDOCRINE DRUG PRODUCTS
5600 FISHERS LANE, HFD-510
ROCKVILLE, MARYLAND 20857-1706

DATE: November 13, 2001



Comments:

Attached are the minutes of the telephone conference regarding NDA 21-350 which was held on September 28, 2001, at 02:30 PM.

Please don't hesitate to call with any questions.

TO:

Name: Lynda Sutton, B.S.
Senior Vice President
Fax No.: (919) 361-2290
Phone No.: (919) 361-2286
Location: Cato Research

FROM:

Name: William C. Koch, R.Ph.
Regulatory Project Manager
Fax No.: (301)-443-9282
Phone No.: (301)-827-6412

Pages (including this cover sheet): five (5)

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DMEDP, HFD-510

Industry Meeting Tracking System Data Entry Documentation
(IMTS)

Project Manager: Koch

Meeting Request Receipt Date: 09/18/01

Requester: Industry CDER (circle one)

Notification Date: 09/24/01 (date industry was notified)

Meeting Status: (circle one)

Cancel- Late Package

~~Cancel~~ Other (give reason): _____

Granted

Denied

Withdrawn

Formal Meeting Date: 09/28/01 (actual meeting date)

Application Type: NDA IND (circle one) Application No: 21-350

Sponsor's Name: (Fill in if there is no application type)

Meeting Types: (circle one)

- | | |
|---------------|------------------------------|
| 90 DAY | 90 DAY |
| ADPRO | ADVERTISING/PROMOTION |
| BIOEQ | BIOPHARM/BIOEQUIVALENCE |
| CMC | CHEMISTRY |
| COMPL | COMPLIANCE |
| CP | CRITICAL PATH |
| ELECT | ELECTRONIC SUBMISSION |
| EOP1 | END OF PHASE 1 |
| EOP2 | END OF PHASE 2/PRE-PHASE 3 |
| EOR | END OF REVIEW |
| FC | FILING CONFERENCE |
| <u>GUID</u> | <u>GUIDANCE</u> |
| LABEL | LABELING |
| 560FB | OTC MONOGRAPH FEEDBACK |
| OTHER | OTHER |
| PHTOX | PHARM/TOX |
| PH_4 | PHASE 4 |
| P-IND | PRE-IND |
| P-NDA | PRE-NDA/SUPPLEMENT |
| SAFTY | SAFETY ISSUES |
| SPC | SPECIAL PROTOCOL, CHEMISTRY |
| SPM | SPECIAL PROTOCOL, MEDICAL |
| SPX | SPECIAL PROTOCOL, PHARM/TOX |

Meeting Minutes Issued Date: 11/13/01
(date mtg minutes were sent to participants)

Meeting ID _____

9/19/01

Meeting Date: August 17, 2001 Time: 09:30AM Location: PKLN Room #14B-45
NDA 21-350 IDD-P Fenofibrate (Insoluble Drug Delivery-Microparticle fenofibrate tablets)
Type of Meeting: Guidance Telephone Conference
External Participant: RTP Pharma Inc.
Meeting Chair: Hae Young Ahn, Ph.D., Biopharmaceutics Team Leader
External Participant Lead: Pol-Henri Guivarc'h, M.D., M.B.A., Vice President, Clinical Development
Meeting Recorder: William C. Koch, R.Ph., Regulatory Project Manager

FDA Attendees and titles:

Hae Young Ahn, Ph.D., Biopharmaceutics Team Leader
William C. Koch, R.Ph., Regulatory Project Manager

External participant Attendees (by phone) and titles:

Pol-Henri Guivarc'h, M.D., M.B.A., Vice President, Clinical Development
Michael G. Vachon, M.Sc.Pharm., Ph.D., Vice President, Process Development
Gary Robinson, Ph.D., Senior Scientist
Lynda Sutton, B.Sc., Senior Vice President, Regulatory Affairs and Project Planning
Diana Fordyce, Ph.D., R.A.C., Senior Regulatory Scientist

Meeting Objectives:

To discuss biopharmaceutics review issues.

Discussion Points:

The Division stated that because the dissolution profiles for the 160mg and 50mg formulations are different and the 50mg formulation has not been tested clinically, a biowaiver for the 50mg formulation cannot be granted. Therefore, the 50mg formulation cannot be approved without pharmacokinetic data.

The Division recommended that the applicant complete a pharmacokinetic study, under fed conditions. The pharmacokinetic data could be obtained by completing one of the following two possible bioequivalence studies:

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/s/

William Koch
9/18/01 02:39:22 PM
CSO

Hae-Young Ahn
9/19/01 12:27:30 PM
BIOPHARMACEUTICS

William Koch
9/19/01 04:09:44 PM
CSO

Electronic Mail Message

Date: 8/24/01 5:01:03 PM
From: William C. Koch (KOCHW)
To: dfordyce (dfordyce@mail.cato.com)
Subject: NDA 21-350; Safety Updates

Diana,

Please submit the 4-month (first) safety update as per 21 CFR 314.50(5)(vi)(b) with added new safety information.

The final study report for the requested biopharm study will be submitted separately, as a minor amendment, in December 2001 as agreed upon.

The second safety up date, required by Division policy and provided for in the above referenced CFR paragraph, must be submitted no earlier than 90-days before the 10-month goal date. This second safety update would include safety data reported since the first safety update including any safety data from the requested biopharm study.

Bill

Electronic Mail Message

Date: 8/24/01 4:00:42 PM
From: William C. Koch (KOCHW)
To: dfordyce (dfordyce@mail.cato.com)
Cc: David Orloff (ORLOFFD)
Cc: Enid Galliers (GALLIERS)
Cc: Kati Johnson (JOHNSONKA)
Subject: NDA 21-350; Notice of Certification of Noninfringement

Diana,

In answer to your question of earlier today regarding documentation of receipt of notice, the Division will accept as adequate documentation of the date of receipt a letter acknowledging receipt by the person provided the notice [21 CFR 314.52(e)].

Such an acknowledgment letter and a pre-paid FedEx mailer could be provided along with the Notice of Certification to the party(ies) provided the notice.

Bill

Electronic Mail Message

Date: 8/22/01 4:53:31 PM
From: William C. Koch (KOCHW)
To: dfordyce (dfordyce@mail.cato.com)
Subject: NDA 21-350

Diana,

As a follow-up to our telephone conversation of August 9, 2001, the review of this application will be completed on a standard 10-month cycle. Therefore, the first action on this application will occur on or about April 25, 2002.

Bill

Electronic Mail Message

Date: 8/20/01 1:59:46 PM
From: William C. Koch (KOCHW)
To: See Below
Subject: NDA 21-350: Modification of goal dates

TEAM,

It has become necessary to change the "FINAL Reviews DUE from TL" goal date for the IDD-P Fenofibrate application to:

March 04, 2002.

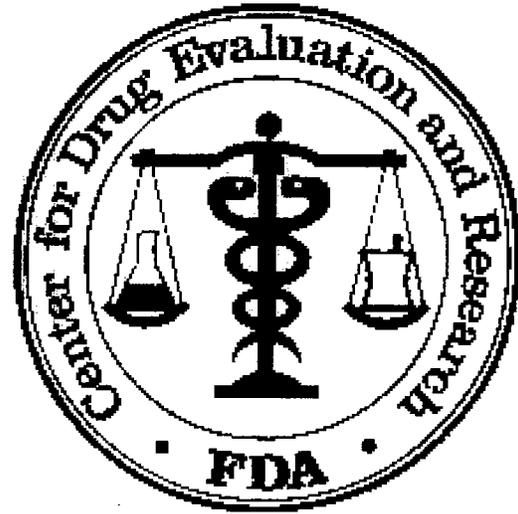
I apologize for any inconvenience this will cause!!

Bill

To: Mary Parks (PARKSM)
To: Karen Davis-Bruno (DAVISBRUNOK)
To: Indra Antonipillai (ANTONIPILLAI)
: Hae Young Ahn (AHNH)
: Wei Qiu (QIUW)
To: Shiao Shen (SHEN)
To: Pardhasarad Komanduri (KOMANDURIP)
To: Stephen Moore (MOOREST)
To: Todd Sahlroot (SAHLROOTT)
To: Enid Galliers (GALLIERS)

FOOD AND DRUG ADMINISTRATION
DIVISION OF METABOLIC AND
ENDOCRINE DRUG PRODUCTS
5600 FISHERS LANE, HFD-510
ROCKVILLE, MARYLAND 20857-1706

DATE: September 19, 2001



Comments:

Attached are the minutes of the telephone conference regarding NDA 21-350 which was held on August 17, 2001, at 09:30 AM.

Please don't hesitate to call with any questions. ~Bill

TO:

Name: Lynda Sutton, B.S.
Senior Vice President

Fax No.: (919) 361-2290

Phone No.: (919) 361-2286

Location: Cato Research

FROM:

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

Fax No.: (301)-443-9282

Phone No.: (301)-827-6412

Pages (including this cover sheet): four (4)

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□ Chemistry

Submitted information is adequate for filing

Establishment Evaluation Requests (EER) – sites will be requested

Environmental Assessment (EA/FONSI) – Categorical exclusion requested.

□ Biopharmaceutics

Submitted information is adequate for filing, however, it is recommended that the sponsor conduct either a bioequivalence (BE) study to compare the 50mg IDD-P Fenofibrate with the 67mg Tricor Capsule or a dosage form equivalence study to compare one 160mg tablet with three of the 50mg tablets.

□ Biostatistics

No filing issues.

□ DSI

No clinical inspections are required

REGULATORY SECTION

2. Priority or Standard Review schedule: Standard

3. Clinical Audit sites (list):

None required

4. Advisory Committee Meeting: No

5. Review Timelines/Review Goal Date (with labeling):

Consults Due:	N/A
Reviews Completed:	March 7, 2002
To Division Director:	March 15, 2002
To Office Director:	N/A
10 month calendar due:	April 26, 2002

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

/s/

William Koch
8/16/01 04:14:11 PM

6/29/01



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-350

Cato Research, agent for
RTP Pharma Inc.
Attention: Lynda Sutton
Senior Vice President, Regulatory Affairs and Project Planning
200 Westpark Corporate Center
4364 South Alston Avenue
Durham, NC 27713-2280

Dear Ms. Sutton:

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

Name of Drug Products: IDD-P fenofibrate (insoluble drug delivery-microparticle fenofibrate) tablets, 50mg, 160mg.

Name of Applicant: RTP Pharma Inc.

Review Priority Classification: Standard (S)

Date of Application: June 22, 2001

Date of Receipt: June 25, 2001

Our Reference Number: NDA 21-350

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on August 24, 2001, in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be April 25, 2001, and the secondary user fee goal date will be June 25, 2001.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). If you have not already fulfilled the requirements of 21 CFR 314.55, please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination

whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the application. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

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

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

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room 14B-19
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call me at (301) 827-6412.

Sincerely,

(See appended electronic signature page)

William C. Koch, R.Ph.
Regulatory Project Manager
Division of Metabolic
and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

William Koch
6/29/01 05:14:25 PM

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

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

<p>1. APPLICANT'S NAME AND ADDRESS RTP Pharma Inc. 1000 chemin du Golf Verdun (Quebec) Canada H3E 1H4</p>	<p>3. PRODUCT NAME IDD-P fenofibrate</p>
<p>2. TELEPHONE NUMBER (Include Area Code) (514) 362-9818</p>	<p>4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).</p>
<p>5. USER FEE I.D. NUMBER 4132</p>	<p>6. LICENSE NUMBER / NDA NUMBER N021350</p>

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)	

FOR BIOLOGICAL PRODUCTS ONLY

<input type="checkbox"/> WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION	<input type="checkbox"/> A CRUDE ALLERGENIC EXTRACT PRODUCT
<input type="checkbox"/> AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY	<input type="checkbox"/> AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT
<input type="checkbox"/> BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92	

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
(See reverse side if answered YES)

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

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

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

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

<p>SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE Pol-Henri Guivarc'h, M.D., M.B.A.</p>	<p>TITLE Vice-President, Clinical</p>	<p>DATE 2 May 2001</p>
--	---	----------------------------

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

/s/

Mary Parks

4/24/01 11:01:56 AM

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST #3

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST #3		
NDA 21-350	Efficacy Supplement Type SE-	Supplement Number
Drug: Triglide (fenofibrate) Tablets		Applicant: SkyePharma, Inc.
RPM: Valerie Jimenez	HFD- 510	Phone # (301) 827-9090
Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2)	Reference Listed Drug (NDA #, Drug name): Tricor Tablets, NDA 21-203	
❖ Application Classifications:		
• Review priority	<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority	
• Chem class (NDAs only)	3s	
• Other (e.g., orphan, OTC)		
❖ User Fee Goal Dates		
		May 7, 2005
❖ Special programs (indicate all that apply)		
		<input checked="" type="checkbox"/> None
		Subpart H
		<input type="checkbox"/> 21 CFR 314.510 (accelerated approval)
		<input type="checkbox"/> 21 CFR 314.520 (restricted distribution)
		<input type="checkbox"/> Fast Track
		<input type="checkbox"/> Rolling Review
		<input type="checkbox"/> CMA Pilot 1
		<input type="checkbox"/> CMA Pilot 2
User Fee Information		
• User Fee	<input type="checkbox"/> Paid	
• User Fee waiver	<input type="checkbox"/> Small business	
	<input type="checkbox"/> Public health	
	<input type="checkbox"/> Barrier-to-Innovation	
	<input type="checkbox"/> Other	
• User Fee exception	<input type="checkbox"/> Orphan designation	
	<input checked="" type="checkbox"/> No-fee 505(b)(2)	
	<input type="checkbox"/> Other	
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
• This application is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
• Exception for review (Center Director's memo)		
• OC clearance for approval		
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.		
		<input checked="" type="checkbox"/> Verified
❖ Patent		
• Information: Verify that form FDA-3542a was submitted.	<input checked="" type="checkbox"/> Verified	
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted.	21 CFR 314.50(i)(1)(i)(A)	
	<input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input checked="" type="checkbox"/> IV	
	21 CFR 314.50(i)(1)	
	<input type="checkbox"/> (ii) <input type="checkbox"/> (iii)	
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	<input checked="" type="checkbox"/> Verified	

Exclusivity (approvals only)	
• Exclusivity summary	5/2/05
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!	() Yes, Application # _____ (X) No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	
❖ Actions	
• Proposed action	(X) AP () TA () AE () NA
• Previous actions (specify type and date for each action taken)	AE, 4/24/02; AE, 12/14/04
• Status of advertising (approvals only)	() Materials requested in AP letter () Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	() Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	() None () Press Release () Talk Paper () Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling <i>PI + bottle labels</i>	3/31/04, 3/4/05
• Original applicant-proposed labeling	01/22/01
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (indicate dates of reviews and meetings)	2/25/02, 8/5/04, 9/28/04, 4/28/05
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	3/31/04, 5/19/04
• Reviews	2/25/02, 8/5/04, 9/28/04, 4/28/05
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes) 5/21/01, 6/29/01, 1/25/02, 4/20/04, 4/22/04, 7/2/04, 8/18/04, 10/15/04,	11/4/04, 2/25/05, 3/15/05
❖ Memoranda and Telecons	9/20/04, 10/13/04, 10/18/04, 12/6/04
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	1/30/01
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other (Cons/Guidance)	9/19/01, 11/5/01, 4/1/02

Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	
Summary Reviews	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	4/4/02, 4/8/02
Clinical Reviews	
❖ Clinical review(s) (indicate date for each review)	4/3/02
❖ Microbiology (efficacy) review(s) (indicate date for each review)	N/A
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	N/A
❖ Risk Management Plan review(s) (indicate date/location if incorporated in another rev)	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	6/29/04, 7/1/04
❖ Demographic Worksheet (NME approvals only)	N/A
❖ Statistical review(s) (indicate date for each review)	N/A
❖ Biopharmaceutical review(s) (indicate date for each review)	6/30/04, 3/11/02, 11/30/04, 4/12/05
❖ Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	N/A
Clinical Inspection Review Summary (DSI)	
• Clinical studies	4/1/02
• Bioequivalence studies	4/1/02
CMC Review	
❖ CMC review(s) (indicate date for each review)	4/10/02, 5/2/05
Environmental Assessment	
• Categorical Exclusion (indicate review date)	CMC review; 4/10/04
• Review & FONSI (indicate date of review)	
• Review & Environmental Impact Statement (indicate date of each review)	
❖ Microbiology (validation of sterilization & product sterility) review(s) (indicate date for each review)	N/A
❖ Facilities inspection (provide EER report)	Date completed: 12/7/04 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ Methods validation	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input checked="" type="checkbox"/> Not yet requested
Nonclinical Pharm/tox Information	
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	6/28/04, 10/19/01, 10/4/01, 2/6/01
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	N/A
❖ CAC/ECAC report	N/A

4/8/05

NDA REGULATORY REVIEW

Appendix A to NDA Regulatory Filing Review

NDA 21-350 Triglide (fenofibrate) Tablets, 50 mg and 160 mg
Sponsor: SkyePharma Inc.

HISTORY:

On June 22, 2001, Cato Research Ltd., agent to RTP Pharma Inc., submitted a New Drug Application (NDA) to the Food and Drug Administration (FDA) for their drug product, Insoluble Drug Delivery-Microparticle (IDD-P™) fenofibrate Tablets. The indication was for the treatment of hyperlipidemia (Fredrickson Type IV and V). The sponsor proposed that IDD-P™ fenofibrate provides for increased bioavailability (BA) and, therefore a lower dose of IDD-PTM fenofibrate tablet (160 mg) is required for equivalent extent of absorption to that of Tricor® Capsule (200 mg), additionally, the sponsor claims IDD-P™ fenofibrate demonstrates no significant food effect on extent of absorption. On April 24, 2002, the application was granted an Approvable action. On May 28, 2002, Cato Research Ltd., submitted correspondence advising the Agency that RTP Pharma, henceforth named SkyePharma Canada, Inc. transferred all rights and obligations for NDA 21-350 to SkyePharma Inc.

The sponsor submitted a complete response on March 31, 2004, to the April 24, 2002, action letter which prompted a 6 month-review of the application yielding a userfee goal date of October 1, 2004. The complete response focused on the deficiencies contained in the action letter but included a re-formulation of the product. Review of the resubmission noted that the sponsor had conducted BE studies with Lipanthyl (200 mg), a foreign-marketed product not approved in the United States. Furthermore, the sponsor stated that Lipanthyl (200 mg) is the same drug product as the reference listed drug (RLD) Tricor (200 mg) Capsule (Abbott Laboratories Inc., NDA 19-304).

The Agency requested information in order to complete the Chemistry, Manufacturing, and Controls (CMC) and Biopharmaceutics discipline reviews on July 2, August 18, October 15 (2), and October 20, 2004. The information request letters sent to the sponsor dated October 15, 2004, requested an explanation of the difference in the appearance of the reference capsules used in studies FEN101-C1-001 and FEN101-C25. Moreover, it requested an explanation why none of the reference products had any imprint on the capsules. An October 20, 2004, letter requested CMC data, i.e., USP test results, release and stability specifications, the certificates of analysis (COA), and moisture content stability; and November 4, 2004, letter requested that the sponsor investigate two other dissolution conditions. The sponsor submitted their responses on July 30, October 15, and 26, and November 16, 2004. Because the July 30 submission was a major amendment, the clock was extended 3-months yielding a user fee goal date of January 1, 2005. Another Approvable (AE) action letter issued on December 15, 2004.

**Appendix B to NDA Regulatory Review
Questions for 505(b)(2) Applications**

1. Does the application reference a listed drug (approved drug)? YES

If "No," skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):
NDA 19-304: Tricor (fenofibrate micronized) Capsules, 67 mg, 134 mg, and 200 mg/
Approved December 31, 1993. NDA 19-304 was cited in the 356h form.
ANDA 075753: Fenofibrate Capsules, 67 mg, 134 mg, and 200 mg/Approved April 9, 2002.
ANDA 75-753 was mentioned in the March 31, 2004, cover letter but not in the 356h.
3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.
- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved?
NDA 21-203 Tricor Tablets, 54 mg and 160 mg/Approved September 4, 2001

YES

The first AE letter issued by the Agency on April 24, 2002, did not raise the issue of referencing the pharmaceutical equivalent or attendant patent certification requirements. However, that issue was raised in the second AE letter (issued December 15, 2004) after consultation with OCC.

(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))

If "No," skip to question 4. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? NO
(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

The pharmaceutical equivalent was approved after this NDA was filed. ORP and OCC have been consulted on this issue.

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)?

YES

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

4. (a) Is there a pharmaceutical alternative(s) already approved? YES

NDA 19-304 Tricor (fenofibrate micronized) Capsules, 67 mg, 134 mg, and 200 mg/
Approved December 31, 1993.

NDA 21-656 Tricor Tablets, 48 mg, and 145 mg/Approved November 5, 2004.

ANDNA 075753 Fenofibrate, 67 mg, 134 mg, and 200 mg/Approved April 9, 2002.

NDA 21-695 Antara (fenofibrate) Capsules, 43 mg, 87 mg, and 130 mg/Approved November 30, 2004.

(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.)

If "No," skip to question 5. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES
(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

The first approved pharmaceutical alternative is cited.

NOTE: If there is more than one pharmaceutical alternative approved, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product?

NO

If "No," skip to question 6.

If "Yes," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.

- (b) Is the approved drug product cited as the listed drug? NO

6. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").

This application provides for a change in dosage form and strength. This application also proposes that the different formulation allows for similar bioavailability relevant to the reference drug but without a "food effect".

7. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)). NOT at the time of filing.
8. Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 21 CFR 314.101(d)(9)). NO
9. Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). NO
10. Are there certifications for each of the patents listed for the listed drug(s)? YES

The certifications for each patent listed for the listed drug is for NDA 19-304 only (a pharmaceutical alternative).

11. 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.)

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)

21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)

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: 4,895,726-NDA 19-304 Tricor (fenofibrate micronized) Capsules

Expires January 19, 2009

Owner: Abbott Laboratories

Paragraph IV submitted May 2, 2001

Notification submitted: September 6, 2001

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

_____ 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)

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

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

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference?

YES

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

NO

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

In the original application-YES

In the resubmission, the BE study compared its re-formulated product to a foreign-marketed version of the listed drug.

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

NO

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

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

N/A

- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.

N/A

- EITHER

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

IND # _____ N/A

OR

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

N/A

14. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES

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

/s/

Valerie Jimenez
4/8/05 07:34:33 AM
CSO