

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
202088Orig2s000

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

202088

NAME OF APPLICANT/NDA HOLDER

Citius Pharmaceuticals LLC

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)

Phentermine hydrochloride

ACTIVE INGREDIENT(S)

phentermine hydrochloride

STRENGTH(S)

15, 30 and 37,5 mg

DOSAGE FORM

oral disintegrating 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

b. Issue Date of Patent

c. Expiration Date of Patent

d. Name of Patent Owner

Address (of Patent Owner)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

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?	<input type="checkbox"/> Yes	<input type="checkbox"/> 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?	<input type="checkbox"/> Yes	<input type="checkbox"/> 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).	<input type="checkbox"/> Yes	<input type="checkbox"/> 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.)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.6 Does the patent claim only an intermediate?	<input type="checkbox"/> Yes	<input type="checkbox"/> 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.)	<input type="checkbox"/> Yes	<input type="checkbox"/> 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?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3.2 Does the patent claim only an intermediate?	<input type="checkbox"/> Yes	<input type="checkbox"/> 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.)	<input type="checkbox"/> Yes	<input type="checkbox"/> No

4. Method of Use

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4.2 Patent Claim Number(s) (as listed in the patent)	Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?	
	<input type="checkbox"/> Yes	<input type="checkbox"/> 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.)	

No Relevant Patents

or 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.	<input checked="" type="checkbox"/> Yes
--	---

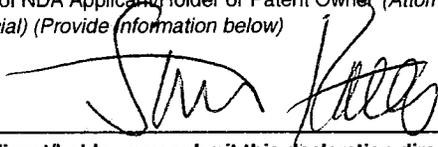
6. Declaration Certification

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



11 Aug 10

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).

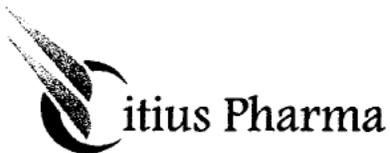
Check applicable box and provide information below.

<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 Citius Pharmaceuticals LLC, Steven Kates, PhD	
Address 63 Great Road	City/State Maynard, MA
ZIP Code 01754	Telephone Number 978 938 0338 (o); 978 760 3520 (c)
FAX Number (if available) 978 897 4952	E-Mail Address (if available) steve.kates@citiuspharma.com

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer (HFA-710)
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.



March 11, 2011

**RE: No Relevant Patents Certification
21 C.F.R. § 312.50(i)(1)(ii)**

In the opinion and to the best knowledge of Citius Pharmaceuticals LLC, there are no patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs.

If you have any questions or comments please contact me at 978 938 0338 (o) or 978 760 3520 (c).

Sincerely,

A handwritten signature in black ink, appearing to read "S. A. Kates", written over a horizontal line.

Steven A. Kates, Ph.D.
Vice President

11 March 11
Date

EXCLUSIVITY SUMMARY

NDA # 202088/Original-2

SUPPL #

HFD # 510

Trade Name Suprenza

Generic Name phentermine hydrochloride; 37.5 mg orally dissolving tablets

Applicant Name Citius Pharmaceuticals

Approval Date, If Known March 27,2012

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES NO

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

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

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.

Sponsor agrees - no clinical studies were conducted for this NDA

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:

N/A

d) Did the applicant request exclusivity?

YES NO

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

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

YES NO

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

N/A

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

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

YES NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES NO

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

NDA# 11613

Ionamin

NDA# 17352

Fastin

NDA#

2. Combination product.

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

YES NO

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

NDA#

NDA#

NDA#

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

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

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

YES NO

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

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

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

Investigation #2

!

YES

!

! NO

Explain:

! Explain:

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

YES

NO

If yes, explain:

=====

Name of person completing form: Patricia Madara
Title: Regulatory Project Manager
Date: March 27, 2012

Name of Office/Division Director signing form: Eric Colman
Title: Deputy Director, Division of Metabolism and Endocrinology Products

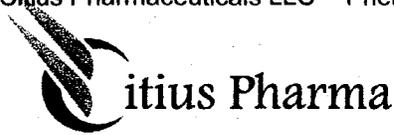
Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

PATRICIA J MADARA
03/27/2012

ERIC C COLMAN
03/27/2012



August 11, 2010

RE: DEBARMENT CERTIFICATION STATEMENT

Citius Pharmaceuticals LLC hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

If at any time after execution of this certification, Citius Pharmaceuticals LLC becomes aware that we or any person employed thereby, or, any affiliate person/firm is in the process of being debarred, Citius will notify its affected clients at once.

If you have any questions or comments please contact me at 978 938 0338 (o) or 978 760 3520 (c).

Sincerely,

A handwritten signature in black ink that reads "Steven A. Kates".

Steven A. Kates, Ph.D.
Vice President

11 Aug 10

Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 202088/Original#2 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: SUPRENZA Established/Proper Name: phentermine hydrochloride Dosage Form: orally dissolving tablet		Applicant: Citius Pharmaceuticals Agent for Applicant (if applicable):
RPM: Patricia Madara		Division: Metabolism and Endocrinology
<p><u>NDA and NDA Efficacy Supplements:</u></p> <p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s):</p> <p>Ionamin; NDA 011613</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>new formulation - orally dissolving tablet</p> <p><input type="checkbox"/> This application does not rely upon a listed drug. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> This application relies on (explain)</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: 3/27/12</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>3/29/12</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input type="checkbox"/> None CR: 6/13/11

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

² For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics³</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC </p> <p> NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies </p> <p> <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request </p> <p> BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies </p> <p> REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input type="checkbox"/> MedGuide w/o REMS <input type="checkbox"/> REMS not required </p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action (by OEP) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

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

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

Answer the following questions for **each** paragraph IV certification:

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ⁴	included
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) CR, 6/13/11; AP, 3/27/12
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	3/16/12; included
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	9/29/11; included
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A

⁴ Fill in blanks with dates of reviews, letters, etc.

❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	N/A
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	N/A
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
<ul style="list-style-type: none"> • Most-recent draft labeling 	3/2/12
❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. 	N/A
❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)	<input checked="" type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA 2/08/12 <input type="checkbox"/> DMPP/PLT (DRISK) N/A <input checked="" type="checkbox"/> ODPD (DDMAC) 2/27/12 <input type="checkbox"/> SEALD N/A <input checked="" type="checkbox"/> CSS 3/5/12 <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)	N/A
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte	<input type="checkbox"/> Not a (b)(2) 2/28/12
❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)	<input type="checkbox"/> Not a (b)(2) 3/27/12
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC _____ If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable

⁵ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Outgoing communications (<i>letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons</i>)	included
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 3/27/12
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None as above
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	see deputy director review
• Clinical review(s) (<i>indicate date for each review</i>)	3/07/12
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	6/01/11 (1 st cycle, clinical review)
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input type="checkbox"/> Not applicable 3/05/12
❖ Risk Management	
• REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>)	
• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)	
• Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested

⁶ Filing reviews should be filed with the discipline reviews.

Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Statistical Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None NAI
❖ DSI Clinical Pharmacology Inspection Review Summary <i>(include copies of DSI letters)</i>	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Supervisory Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None NAI
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary <i>(include copies of DSI letters)</i>	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>	<input type="checkbox"/> None 2/27/12
❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	5/9/11
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷</i>)	Date completed: 8-31-10+4-13-11 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁷ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

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

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

/s/

PATRICIA J MADARA
03/27/2012

Madara, Patricia

From: Madara, Patricia
Sent: Friday, March 16, 2012 12:44 PM
To: 'Steve Kates'
Subject: RE: NDA 202088 / Original #2 minor revision to the label. Agreement requested

NDA 202088 / Original #2

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Thanks for the very swift response. We acknowledge your agreement to the last minor revision to the label for NDA 202088 / Original #2.

Have a wonderful weekend.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

From: Steve Kates [mailto:steve.kates@citiuspharma.com]
Sent: Friday, March 16, 2012 12:41 PM
To: Madara, Patricia
Subject: RE: NDA 202088 / Original #2 minor revision to the label. Agreement requested
Importance: High

Dear Pat,
Please use this email as confirmation of receipt and that Citius agrees to the addition of "tachycardia" in Section 10.1 Acute Overdosage.

Please let me know if you need any additional information.

Regards,
Steve

Steve Kates, PhD
Citius Pharmaceuticals
978 938 0338 (o)
978 760 3520 (c)

From: Madara, Patricia [mailto:Patricia.Madara@fda.hhs.gov]
Sent: Friday, March 16, 2012 12:34 PM
To: 'Steve Kates'
Subject: NDA 202088 / Original #2 minor revision to the label. Agreement requested

NDA 202088 / Original #2

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Suprenza (phentermine HCl) ODT.

Also, reference is made to your September 28, 2011 amendment, which constituted a complete response to our June 13, 2011, action letter for NDA 202088 / Original #2. In addition, we refer to your submission dated March 2, 2012, received March 5, 2012, containing revised labeling for NDA 202088 / Original #2. This label contains all the revisions requested by the Division.

We are now requesting one additional, very minor change to the label. To section 10.1 (Acute Overdosage), we are adding "tachycardia" to to the third sentence (see below and attached label). Please confirm that this revision is acceptable.

10.1 Acute Overdosage

Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, and panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include **tachycardia**, arrhythmia, hypertension or hypotension, and circulatory collapse.

(we added tachycardia)

Please contact me if you have any questions.

Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

11 Page(s) of Draft Labeling have been Withheld in Full as b4
(CCI/TS) immediately following this page

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

/s/

PATRICIA J MADARA
03/16/2012

Madara, Patricia

From: Duvall, Beth A
Sent: Tuesday, February 28, 2012 2:58 PM
To: Maúara, Patricia
Cc: Bertha, Amy; Ripper, Leah W
Subject: NDA 202088/Original-2 - cleared for action

Hi Pat,

We discussed your application at yesterday's clearance meeting and you are cleared for action contingent on Citius Pharm submitting a 356h form that correctly identifies Ionamin Capsules (NDA 11613) as the listed drug relied-upon (rather than (b) (4) – same as they did for Original-1. The updated 356h form can come in with any submission, it does not need to be a stand-alone submission per se. And all future 356h forms they submit should be consistent with this. Furthermore, they must do this before approval.

Please also make the following changes to your draft 505(b)(2) assessment before archiving in DARRTS:

- Q4: Skip 4b since 4a is 'no'
- Q11: Modify your list of pharmaceutical alternatives under 'c' to note that there is a phentermine HCl NDA product, 200272 (Epic) listed in the Orange Book.

Let me know if you have any questions.

Beth

Beth Duvall

Associate Director for Regulatory Affairs
 CDER/Office of New Drugs
Direct Phone Number: (301) 796-0513
OND IO Phone Number: (301) 796-0700
Fax: (301) 796-9855

From: Madara, Patricia
Sent: Friday, February 24, 2012 2:19 PM
To: Duvall, Beth A
Cc: Bertha, Amy; Ripper, Leah W
Subject: RE: NDA 202088/Original-2 505b2 clearance question

They did submit a "no relevant patents statement." Thanks for your help. Pat

From: Duvall, Beth A
Sent: Friday, February 24, 2012 2:10 PM
To: Madara, Patricia
Cc: Bertha, Amy; Ripper, Leah W

Subject: RE: NDA 202088/Original-2 505b2 clearance question

Yes, this presents an inconsistency.

If the applicant was in fact relying on Ionamin in Original-1, and presumably the BA/BE studies bridged to it, then they are still relying on Ionamin in Original-2 and should submit a revised 356h form indicating as much. This is also true if their annotated labeling was referencing Ionamin. It follows that their patent cert/statement (which I assume they did in fact submit, according to your earlier assessment they submitted a 'no relevant patents' statement; please confirm) should be specific to reliance on Ionamin (and not (b)(4)) if they specified a listed drug in their patent cert/statement. Note that they don't necessarily have to specify the listed drug per se in a 'no relevant patents statement'.

Bottom line, they need to be consistent. At a minimum, it sounds like their 356h is inconsistent with their earlier submission/application and they'll need to send in a revised 356h form.

Beth

Beth Duvall

Associate Director for Regulatory Affairs
CDER/Office of New Drugs

Direct Phone Number: (301) 796-0513

OND IO Phone Number: (301) 796-0700

Fax: (301) 796-9855

From: Madara, Patricia
Sent: Friday, February 24, 2012 1:38 PM
To: Duvall, Beth A
Cc: Bertha, Amy; Ripper, Leah W
Subject: RE: NDA 202088/Original-2 505b2 clearance question

Oh Beth, why isn't anything quick and easy around this place. With the original submission, the annotated labeling referenced Ionamine. The original 356H incorrectly referenced (b)(4) and the sponsor submitted a corrected 356h, referencing Ionamine.

However, on the resubmission (Original-2) the 356H references (b)(4) and no annotated label was submitted. (My mistake for not catching this. Huge apologies.) It is hard to determine when (or why) the company started citing (b)(4) instead of Ionamin since the entire original submission (and the resubmission) are paper.

He does designate the application as a 505b2. Can I ask for a corrected 356h to cite Ionamin as the listed drug, as was used in the first cycle annotated label.

Thanks and apologies. Pat Madara

From: Duvall, Beth A
Sent: Friday, February 24, 2012 12:49 PM
To: Madara, Patricia
Cc: Bertha, Amy; Ripper, Leah W
Subject: NDA 202088/Original-2 505b2 clearance question

Hi Pat,

We'll be discussing your application at Monday's 505(b)(2) clearance meeting. I have one quick and easy question:

In the RS for Original-2, did Citius identify their application as a 505(b)(2) on their 356h form and did they identify Ionamin (NDA 11613) as the listed drug relied-upon in the application (also on 356h form, page one about mid-way)?

Beth

Beth Duvall

Associate Director for Regulatory Affairs
 CDER/Office of New Drugs
Direct Phone Number: (301) 796-0513
OND IO Phone Number: (301) 796-0700
Fax: (301) 796-9855

From: Madara, Patricia
Sent: Friday, February 03, 2012 3:57 PM
To: Duvall, Beth A
Cc: Madara, Patricia
Subject: NDA 202088/Original-2 505b2 assessment form
Importance: High

Hi Beth;

Here is the assessment form for NDA 202088/Original-2 (phentermine HCl) ODT, 37.5 mg dose only.

Background: In September 2010, a 505b2 NDA was submitted for phentermine HCL orally dissolving tablets (15, 30 and 37.5 mg). During the course of the review, it was determined that the 37.5 mg strength tablet (b) (4)

Therefore the NDA was split such that the 15 and 30 mg doses (Original-1) were approved on June 13, 2011, and the 37.5 mg dose (Original-2) received a complete response letter. On September 28, 2011, the applicant submitted a complete response for original-2 (b) (4)

The PDUFA goal date is 3/29/12. From all the conversations thus far, it appears the info submitted is sufficient and I would say it's headed toward approval.

Here is the 505b2 assessment form - almost a duplicate of the form approved by the committee for NDA 202088/Original-2. Please let me know if you need any additional information.

Many thanks. Pat Madara

Sharma, Khushboo

From: Sharma, Khushboo
Sent: Monday, February 27, 2012 10:56 AM
To: 'steve.kates@citiuspharma.com'
Cc: Madara, Patricia

Dear Mr. Kates,

Please refer to your NDA 202088 for Suprenza (phentermine hydrochloride) Tablets. We also refer to your February 10, 2012, correspondence requesting a Type B meeting to request a (b) (4) shelf life for Suprenza. We have considered your request and concluded that the meeting is unnecessary.

However, in order to assist you in your drug development program, we encourage you to submit a post approval submission as per the regulations regarding extending stability shelf life.

Please let me know if you have any questions. Please acknowledge the receipt of this email.

Thank you

*Khushboo Sharma
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment III
Phone (301)796-1270*

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

/s/

KHUSHBOO SHARMA
02/27/2012

Madara, Patricia

From: Madara, Patricia
Sent: Monday, January 09, 2012 8:20 PM
To: 'Steve Kates'
Subject: NDA202088/Original-2 - Request for Information

Importance: High

NDA 202088 / Original-2

INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for phentermine HCl ODT, 37.5 mg.

In addition, we reference your amendment dated September 28, 2011, submitted in response to our "complete response" letter issued on June 13, 2011. We are continuing our review and have the following requests for additional information:



Please contact me if you have any questions. Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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/s/

PATRICIA J MADARA
01/09/2012



NDA 202088/Original-2

**ACKNOWLEDGE –
CLASS 2 RESPONSE**

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Dr. Kates:

We acknowledge receipt on September 29, 2011, of your September 28, 2011, resubmission of your new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Suprenza (phentermine hydrochloride) ODT, 37.5 mg.

We consider this a complete, class 2 response to our June 13, 2011, action letter. Therefore, the user fee goal date is March 29, 2012.

If you have any questions, call me at (301) 796-1249.

Sincerely,

{See appended electronic signature page}

Patricia Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

PATRICIA J MADARA
10/12/2011

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 202088/original-1 and original-2 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Suprenza Established/Proper Name: phentermine hydrochloride Dosage Form: orally dissolving tablet		Applicant: Citius Pharmaceuticals Agent for Applicant (if applicable):
RPM: Patricia Madara		Division: Metabolism and Endocrinology
<p>NDA: NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s): Ionamin Provide a brief explanation of how this product is different from the listed drug. new formulation - orally dissolving tablet If no listed drug, explain. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: 6-13-11</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>June 13, 2011</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input checked="" type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input checked="" type="checkbox"/> None

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

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics²</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p><input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Communication Plan <input type="checkbox"/> Submitted in response to a Pediatric Written Request <input type="checkbox"/> ETASU <input type="checkbox"/> REMS not required</p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • Press Office notified of action (by OEP) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

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

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

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

Answer the following questions for **each** paragraph IV certification:

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ³	x
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) June 13, 2011
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	June 6,2011
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	

³ Fill in blanks with dates of reviews, letters, etc.

<ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>) 	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>) 	
<ul style="list-style-type: none"> • Most-recent draft labeling 	June 6, 2011
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) 	6-02-11 5-27-11
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input checked="" type="checkbox"/> RPM 6-13-11 <input checked="" type="checkbox"/> DMEPA 5-13-11 <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC 5-17-11 <input type="checkbox"/> SEALD <input checked="" type="checkbox"/> CSS 5-6-11 <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	clinical: 10-19-11 clin pharm: 10-22-11 ONDQA: 10-14-11 preclinical: 10-12-11 RPM: 11-30-11 cleared 5-23-11 <input type="checkbox"/> Not a (b)(2) <input type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm 	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>5-18-11</u> If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before</i>) 	<input checked="" type="checkbox"/> Included

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

<i>finalized)</i>	
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>)	all included
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	none
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 6-13-11 (deputy)
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 6-13-11
PMR/PMC Development Templates (<i>indicate total number</i>)	<input type="checkbox"/> None 6-8-11
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	6-13-11
• Clinical review(s) (<i>indicate date for each review</i>)	6-01-11
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	6-01-11 (clinical review)
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input type="checkbox"/> Not applicable 05-06-11

⁵ Filing reviews should be filed with the discipline reviews.

❖ Risk Management <ul style="list-style-type: none"> REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>) REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) 	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 05-18-11
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	<input type="checkbox"/> None 06-06-11
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	<input type="checkbox"/> None 4-12-11
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None requested

Product Quality		<input type="checkbox"/> None
❖ Product Quality Discipline Reviews		
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>		<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>		<input type="checkbox"/> None 5-12-11
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>		<input type="checkbox"/> None 5-09-11 biopharmaceutics 01-26-11
❖ Microbiology Reviews		<input checked="" type="checkbox"/> Not needed
<input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i>		
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>		
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>		<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)		
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>		5-09-11
<input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i>		
<input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i>		
❖ Facilities Review/Inspection		
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁶)</i>		Date completed: 8-31-10+4-13-11 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</i>		Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>		<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁶ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

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

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/s/

PATRICIA J MADARA
06/13/2011

Bishai, John

From: Karwoski, Claudia B
Sent: Wednesday, June 01, 2011 9:29 AM
To: Madara, Patricia; Egan, Amy
Cc: Bishai, John; Griffiths, LaShawn; Hampp, Christian; Frost, Kathleen R; Iyasu, Solomon; Golden, Julie; Colman, Eric C; Hulett, Melissa; Dempsey, Mary; Wysowski, Diane K; Karwoski, Claudia B
Subject: RE: Phentermine

Hi Amy and Patricia,

Three OSE divisions (DRISK, DEPI, and DPV 1) met to discuss

(b) (5)

(b) (5)

Claudia

From: Madara, Patricia
Sent: Thursday, May 26, 2011 12:18 PM
To: Dempsey, Mary; Wysowski, Diane K; Hulett, Melissa; Egan, Amy; Colman, Eric C; Golden, Julie
Cc: Bishai, John; Griffiths, LaShawn; Karwoski, Claudia B; Hampp, Christian; Frost, Kathleen R; Iyasu, Solomon
Subject: RE: Phentermine
Importance: High

5 Page(s) has been Withheld in Full as B5 immediately following this page

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/s/

JOHN M BISHAI

06/01/2011

From: Madara, Patricia
Sent: Tuesday, May 31, 2011 3:09 PM
To: 'Steve Kates'
Cc: Madara, Patricia
Subject: NDA 202088 (phentermine hydrochloride) orally dissolving tablets - Comments - Required
Importance: High
Attachments: Phentermine Drug Use PMR comments.pdf; Postmarketing Requirement_renal study.pdf

NDA 202088

ADVICE

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for phentermine HCl ODT. We are continuing to review your application and have comments related to required postmarketing studies. Please refer to the attached PDF documents.

Please contact me if you have any questions. Please confirm receipt of this email.

Sincerely,
Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

You will be required to conduct a nationally representative (or nationally projected) study of annual phentermine ODT use data that provides at a minimum:

- 1) Distribution of age (b) (4) sex, and BMI of phentermine ODT recipients
- 2) Distribution of specialties of physician prescribers as a proportion of doses and recipients
- 3) Average (median, mode, range) duration of the first use episode (continuous use until a gap of longer than 50% of days' supply of the previous prescription is reached)
- 4) Average (median, mode, range) size (dose, number of tablets, days of supply) of prescriptions, if possible, by prescription number up to 8
- 5) Number and distribution of patients by number of prescriptions in the first episode of use
- 6) Average (median, mode, range) gap in time between use episodes (continuous use until a gap of longer than 50% of days' supply of the previous prescription is reached)
- 7) Average (median, mode, range) total days of supply per patient
- 8) Average (median, mode, range) cumulative dose per patient
- 9) Dose distribution of initial prescriptions, dose distribution of prescriptions 2-5, dose distribution of prescriptions 6-10, and dose distribution of prescriptions 11 and over
- 10) Proportion of patients with 2 or more prescriptions who start on the lowest dose and remain on the same dose for subsequent prescriptions compared with the proportion who switch to higher doses for subsequent prescriptions
- 11) Concomitant drug use, including but not limited to other drugs used for weight loss, MAO inhibitors, and other drugs contraindicated or known to interact with phentermine
- 12) Concomitant alcohol use
- 13) Proportion of subjects prescribed an MAO inhibitor within 14 days of phentermine use
- 14) Concomitant diagnoses including cardiovascular disease, hypertension, hyperthyroidism, glaucoma, agitation, psychosis, history of drug abuse, history of alcohol abuse

Most analyses should be stratified by age, and then age and ~~gender, as appropriate~~

Results should be submitted annually, with each updated report including annual and cumulative data since launch of phentermine ODT, for a period of 3 years.

Postmarketing Requirement: Study to Assess Various Degrees of Renal Impairment on Phentermine Pharmacokinetics

Increases in exposure due to renal impairment are likely considering the urinary excretion of phentermine and dose adjustment is likely to be necessary for safe and effective use in patients with renal impairment.

You will be required to assess the effect of various degrees of renal impairment on phentermine pharmacokinetics. The required clinical trial should provide an estimate of exposure changes in patients with decreased renal function. The required clinical trial should provide information that form the basis for dosage adjustment in patients with renal impairment.

Provide the date for final protocol submission, clinical trial completion date and final study report submission date.

Madara, Patricia

From: Madara, Patricia
Sent: Thursday, May 05, 2011 2:51 PM
To: 'Steve Kates'
Subject: NDA 202088 (phentermine HCl orally dissolving tablet)

Importance: High

NDA 202088

INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for phentermine HCl ODT. We are continuing to review application and have the following urgent request for additional information:

(b) (4)

Please contact me if you have any questions. Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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/s/

PATRICIA J MADARA
05/05/2011

Madara, Patricia

From: Merchant, Lubna
nt: Friday, April 15, 2011 7:41 AM
Subject: Griffis, Melina; Tossa, Margarita; Holquist, Carol A; Madara, Patricia
Proprietary Name Review Suprenza (NDA 202088)

Good Morning,

This email is to notify you that the Division of Medication Error Prevention and Analysis (DMEPA) has determined that the proposed proprietary name, Suprenza (Phentermine), is acceptable from a look-alike and sound-alike perspective. In addition, our evaluation did not identify any other factors that render the name unacceptable at this time. Our decision is based upon the information submitted by the Applicant, DDMAC's promotional evaluation, DMEP's initial comments, and DMEPA's safety evaluation.

Please share this information with the Suprenza review team. If the review team believes the name is unacceptable based upon other factors (e.g. clinical, chemistry), please forward the concern and provide rationale.

We ask that you respond to the request within 7 days of the receipt of this communication so that we can finalize our review. We are willing to meet with the division to discuss, if needed.

Thank you
Lubna Merchant

Lubna Merchant, M.S., Pharm.D.
Drug Safety Evaluator
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
Food and Drug Administration
Office 301.796.5162
lubna.merchant@fda.hhs.gov



NDA 202088

MEETING MINUTES

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Dr. Kates:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for phentermine HCl orally dissolving tablet.

We also refer to the teleconference between representatives of your firm and the FDA on March 24, 2011. The purpose of the meeting was to discuss the adequacy of your proposed pediatric plan.

A copy of the official minutes of the telecom minutes is attached for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-1249.

Sincerely,

{See appended electronic signature page}

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
Meeting Minutes
Pediatric Guidance



**FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type C
Meeting Category: Guidance

Meeting Date and Time: March 24, 2011; 12:20 PM Eastern time
Meeting Location: teleconference

Application Number: 202088
Product Name: phentermine hydrochloride orally dissolving tablet (ODT)
Indication: adjunct to treatment of obesity
Applicant Name: Citius Pharmaceuticals, LLC

Meeting Chair: Eric Colman, M.D.
Meeting Recorder: Patricia Madara

CDER Attendees

Office of Drug Evaluation II; Division of Metabolism and Endocrinology Products

Eric Colman, M.D.	Deputy Director
Julie Golden, M.D.	Medical Officer
Todd Bourcier, Ph.D.	Pharmacology/Toxicology Team Leader
Mukesh Summan, Ph.D.; DAPT	Toxicologist
Patricia Madara, M.S.	Regulatory Project Manager

Office of Clinical Pharmacology; Division of Clinical Pharmacology II

Sally Choe, Ph.D.	Clinical Pharmacology Team Leader
Immo Zdrojewski, Ph.D.	Clinical Pharmacology Reviewer

Office of New Drugs; Pediatric and Maternal Health Staff

Lisa Mathis, CAPT, M.D.	Associate Director
Jeanine Best, MSN, RN, PNP	Senior Clinical Analyst
Mildred Wright, RN, MSN	Regulatory Health Project Manager
Courtney Suggs, Pharm.D., MPH	Regulatory Health Project Manager

Citius Pharmaceuticals, LLC Attendees

Reinier Beeuwkes, Ph.D.	President
Steven Kates, Ph.D.	Vice President
(b) (4)	Consultant - Medical
(b) (4)	Consultant – Regulatory
(b) (4)	Consultant – Toxicology

Background

On August 11, 2010, Citius Pharmaceuticals submitted an NDA under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for phentermine HCl orally dissolving tablets (ODT).

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the dosing, safety, and effectiveness of the product for the claimed indication in all relevant pediatric subpopulations unless this requirement is waived, deferred, or inapplicable.

(b) (4)

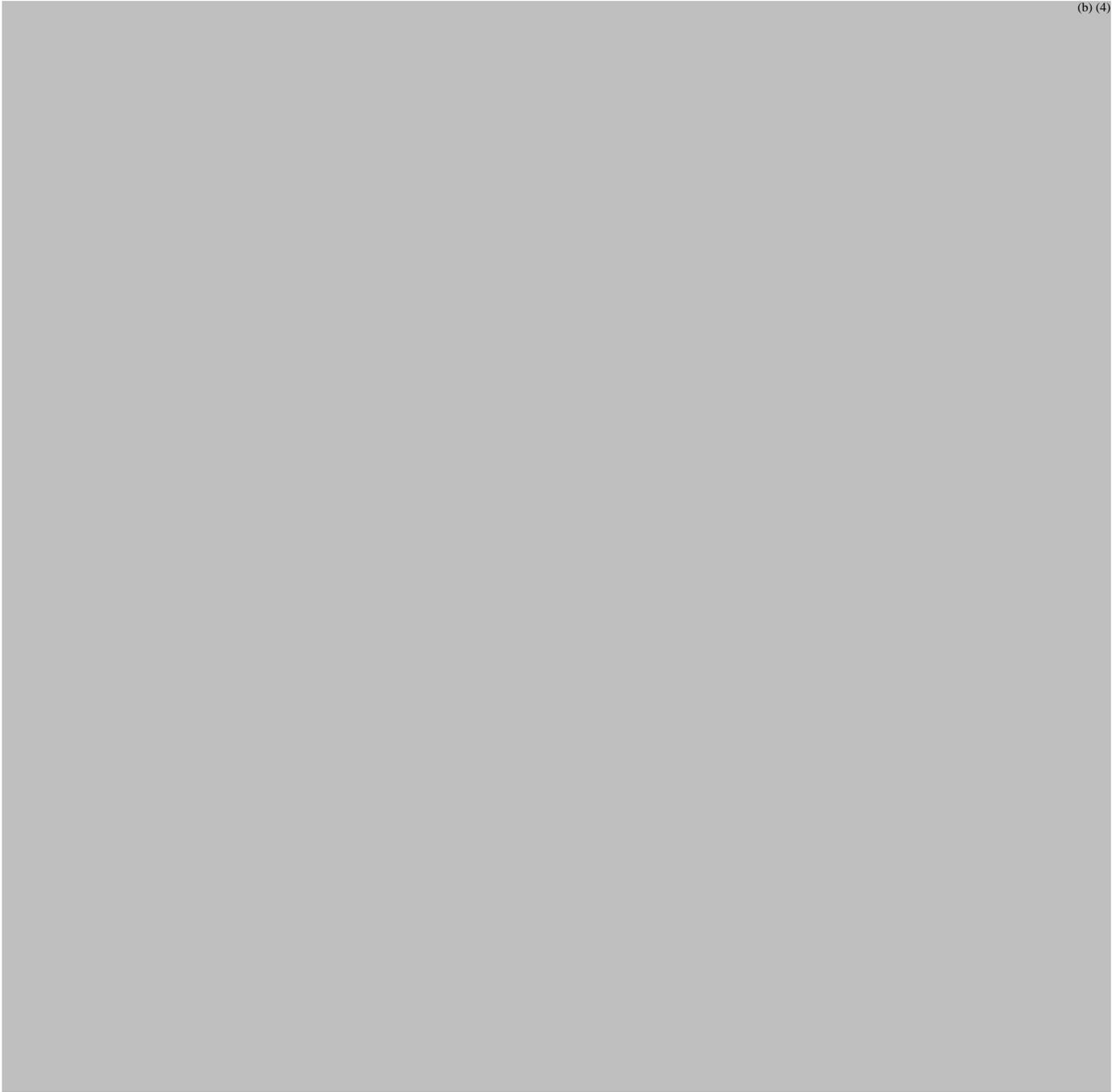
FDA requested this meeting with the applicant to provide guidance related to the submission of an acceptable pediatric plan. This was not considered a formal PDUFA meeting and no specific questions were submitted by the company. The Division sent preliminary clinical and nonclinical comments to Citius regarding their pediatric plan on March 21, 2011, in advance of this meeting.

Discussion

(b) (4)

The pediatric plan must describe protocols designed to assess dosing, safety and efficacy of phentermine HCl ODT in relevant pediatric populations.

(b) (4)



The company thanked FDA for their guidance and the meeting ended.

JCEM

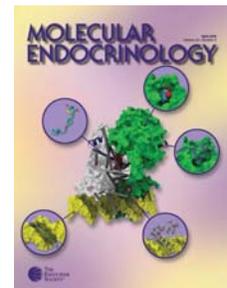
THE JOURNAL
OF CLINICAL
ENDOCRINOLOGY
& METABOLISM

Prevention and Treatment of Pediatric Obesity: An Endocrine Society Clinical Practice Guideline Based on Expert Opinion

Gilbert P. August, Sonia Caprio, Ilene Fennoy, Michael Freemark, Francine R. Kaufman, Robert H. Lustig, Janet H. Silverstein, Phyllis W. Speiser, Dennis M. Styne and Victor M. Montori

J. Clin. Endocrinol. Metab. 2008 93:4576-4599 originally published online Sep 9, 2008; , doi: 10.1210/jc.2007-2458

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Reference ID: 2925754

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/s/

PATRICIA J MADARA
03/30/2011

Madara, Patricia

From: Madara, Patricia
Sent: Monday, March 21, 2011 4:19 PM
To: 'Steve Kates'
Cc: Madara, Patricia
Subject: NDA 202088 (phentermine HCl ODT)
Importance: High
Attachments: ped plan_FDA.pdf; Preclinical comments.pdf

NDA 202088

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for (b) (4) (phentermine HCl) ODT.

In addition, reference the teleconference scheduled for Thursday, March 24, 2011, at 12:20 PM eastern time, between Citius Pharmaceuticals and FDA.

To assist your preparation for a meaningful discussion, I have attached documents containing clinical and preclinical recommendations related to your proposed pediatric assessment plan.

At the tcon, FDA hopes to provide helpful information to Citius regarding (b) (4) (b) (4). However, if you have any specific questions you would like addressed at the meeting, please submit them as soon as possible, via email.

Please contact me if you have any questions. **Please confirm receipt of this email.**

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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3/21/2011

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/s/

PATRICIA J MADARA
03/21/2011

Madara, Patricia

m: Tossa, Margarita
: Thursday, March 10, 2011 11:31 AM
ject: Madara, Patricia
FW: NDA 202-088

*forwarded
to
Lubna merchant*

Importance: High

I will forward it to DMEPA reviewer (Rick Abate).

Thank you,

Rita.

From: Madara, Patricia
Sent: Thursday, March 10, 2011 11:26 AM
To: Tossa, Margarita
Subject: FW: NDA 202-088
Importance: High

Hi Rita;

I believe there is already a consult to DMEPA for NDA 202088 (phentermine HCl). (b) (4)
[REDACTED] Can you tell me if you need another consult.

anks, Pat

From: Egan, Amy
Sent: Wednesday, March 09, 2011 4:54 PM
To: Golden, Julie; Colman, Eric C
Cc: Madara, Patricia; Bishai, John
Subject: RE: NDA 202-088

Shall we forward this on to DMEPA?

From: Chikhale, Elsbeth G
Sent: Wednesday, March 09, 2011 1:18 PM
To: Golden, Julie; Egan, Amy; Colman, Eric C
Cc: Tran, Suong T; Madara, Patricia
Subject: NDA 202-088

Hi Julie, Amy and Eric,

I just wanted to make you aware of the following possible issue for Clinical/Safety in NDA 202088 phentermine ODT 15 mg/tablet, 30 mg/tablet and 37.5 mg/tablet:

- The applicant states in a recent amendment (received on 2/22/11) that the 37.5 mg strength ODT (b) (4)

[REDACTED] (b) (4)

Thanks,
Elsbeth

Appears this way on original

Madara, Patricia

From: Colman, Eric C
Sent: Wednesday, March 09, 2011 5:02 PM
To: Egan, Amy; Golden, Julie
Cc: Madara, Patricia; Bishai, John
Subject: Re: NDA 202-088

Sent to DMEPA

Good ideer

From: Egan, Amy
Sent: Wednesday, March 09, 2011 04:53 PM
To: Golden, Julie; Colman, Eric C
Cc: Madara, Patricia; Bishai, John
Subject: RE: NDA 202-088

Shall we forward this on to DMEPA?

From: Chikhale, Elsbeth G
Sent: Wednesday, March 09, 2011 1:18 PM
To: Golden, Julie; Egan, Amy; Colman, Eric C
Cc: Tran, Suong T; Madara, Patricia
Subject: NDA 202-088

Hi Julie, Amy and Eric,

I just wanted to make you aware of the following possible issue for Clinical/Safety in NDA 202088 phentermine ODT 15 mg/tablet, 30 mg/tablet and 37.5 mg/tablet:

- o The applicant states in a recent amendment (received on 2/22/11) that the 37.5 mg strength ODT

(b) (4)

[Redacted]

(b) (4)

[Redacted]

Thanks,
Elsbeth

Madara, Patricia

From: Madara, Patricia
Sent: Tuesday, March 08, 2011 1:22 PM
To: 'Steve Kates'
Cc: Madara, Patricia
Subject: NDA 202088 - Request for Information

Importance: High

NDA 202088

INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for (b)(4) (phentermine HCl) ODT.

We are reviewing your application and have the following requests for additional information:

- Your amendment dated December 29, 2010 states, "Citius will submit updated 12-month long term stability data for the two remaining batches by April 2011." **We must receive this information by April 1, 2011 in order to insure review before the PDUFA goal date.**
- Your amendment dated February 18, 2011 contains "Revised Specification" Tables on pages 5 - 7. These tables incorrectly state the disintegration time to be (b)(4). **In previous communication, Citius had assured FDA that the disintegration time was (b)(4). Please correct these tables and resubmit as soon as possible.**
- As noted previously, your 356H, lists phentermine HCL as the reference listed drug product that is the basis for the submission. This is incorrect. **You must also supply the tradename of an NDA that was found to be safe and effective by the FDA on your 356H. Submit the revised 356H within one week.**
- As requested previously, **You must certify that you are not infringing on any patents for phentermine held by other companies. Your application must contain a certification or statement addressing any of the following patent scenarios that apply to your drug. See the Code of Federal Regulations 21, part 314.50. Submit the appropriate certification(s) within one week.**

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)(ii): No relevant patents statement

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)

21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the NDA holder/patent owner

Please contact me if you have any questions.

Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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/s/

PATRICIA J MADARA
03/08/2011



NDA 202088

INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Dr. Kates:

Please refer to your new drug application (NDA) dated August 11, 2010, received August 13, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (b) (4) (phentermine hydrochloride) ODT, 15 mg, 30 mg, 37.5 mg.

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

- Revise the appearance acceptance criteria for the 37.5 mg tablets to include the shape of the tablet.
- Clarify whether the 37.5 mg tablets are (b) (4)
- Revise the acceptance criterion for phentermine dissolution testing from (b) (4) to "NLT (b) (4) dissolved in 15 min."
- Submit a revised table with drug product specifications to include all above changes.

If you have any questions, call Patricia Madara, Regulatory Project Manager, at (301) 796-1249.

Sincerely,

{See appended electronic signature page}

Ali Al Hakim, Ph.D.
Chief, Branch VII
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

ALI H AL HAKIM
02/08/2011

Madara, Patricia

From: Madara, Patricia
Sent: Friday, January 28, 2011 1:35 PM
To: 'Steve Kates'
Subject: NDA 202088 (phentermine HCl) ODT

Importance: High

NDA 202088

INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for (b)(4) (phentermine HCl) ODT.

We continue to review your application and have the following clinical questions:

- **What were the adverse events that occurred pre-dose in studies 01806KH and 018089D?**
- **Were these included in the adverse event tables?**

Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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PATRICIA J MADARA
01/28/2011

Madara, Patricia

From: Madara, Patricia
Thursday, January 20, 2011 10:51 AM
'Steve Kates'
Subject: NDA 202088 - Information request
Importance: High

NDA 202088

INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Steve:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for (b)(4) (phentermine HCl) ODT.

We are reviewing your application and have the following request for information:

- **Please provide the qualifications of the staff that performed the oral mucosal examinations for all the treatment arms.**

Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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/s/

PATRICIA J MADARA
01/20/2011

Refer ~~to~~ 289393

Madara, Patricia

From: Madara, Patricia
Sent: Monday, December 13, 2010 10:15 AM
To: 'Steve Kates'
Subject: RE: NDA 202088 status update
Importance: High

Hi Steve;

Please see my responses below in bold red font. Also, I have another request for clarification from the clinical pharmacology review team:

- **We are trying to analyze data submitted previously, however, the treatments are described as T1,T2, and R in the report but A, B, and C in the dataset. We cannot determine which treatment is which. Can you please clarify which treatment in the dataset corresponds to the same treatment in the report?**

Please contact me if you have any questions. **Please confirm receipt of this email.**

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

From: Steve Kates [mailto:steve.kates@citiuspharma.com]
Sent: Friday, December 10, 2010 2:24 PM
To: Madara, Patricia
Subject: RE: NDA 202088 status update

Dear Pat,

Please find below a reply to your questions from the December 9, 2010 email correspondence.

Can you tell me when the request for tradename review will be submitted?

Citius has contracted to an outside organization to review the phentermine HCl ODT tradename. Due to the expected holiday schedule, we anticipate that a report will be submitted to the FDA by January 30, 2011. Please let me know if this will satisfy the requirements of the reviewers. We apologize for the delay regarding this issue but recent responses to information requests limit our ability to provide this documentation. If this is unacceptable, we can ask the outside contractor to determine if they can expedite the process. **I will forward this timeframe to OSE - I don't think it will be a problem. I will let you know if there are any issues.**

Reference ID: 2876508

12/13/2010

Review containers and cartons

Can you please clarify the needs of the division? In a response to information request dated October 11, 2010 regarding information on the impurities/degradants – container closure system, a detailed description of the bottles and caps used for packaging is described in Appendix 1 (Volume 1, Response to Information Request Amendment 3, October 11, 2010):

Item	Page
(b) (4)	018
	044
	073
	112

I have also attached a color mockup of the label with the proposed name for one strength (15 mg) for the two bottle sizes (30 and 100 tablets/bottle). Do you need to receive actual bottles and caps with labels attached for your review? If so, we will need time to obtain them from our manufacturer in Switzerland.

Please let me know if this is the information the Office of Surveillance and Epidemiology is requesting. **OSE requires color mock ups of the containers and cartons (if there are cartons) for review. They will require mock ups like those above for all sizes and strengths. You may submit them in paper but please include an electronic copy via email.**

Regards,
Steve

Steve Kates, PhD
Citius Pharmaceuticals
978 938 0338 (o)
978 760 3520 (c)

From: Madara, Patricia [mailto:Patricia.Madara@fda.hhs.gov]
Sent: Thursday, December 09, 2010 10:18 AM
To: 'Steve Kates'
Subject: NDA 202088 status update
Importance: High

Hi Steve;

Can you tell me when the request for tradename review will be submitted? Also, I have been informed by the Office of Surveillance and Epidemiology that they would like to review your containers and cartons prior to completion of the tradename review. Please submit color mock ups using your proposed name. These can be submitted in paper but we would appreciate an unofficial version sent via email.

Please contact me if you have any questions or concerns.

Please confirm receipt of this email.

Sincerely;

Pat Madara
Reference ID: 2876508
Regulatory Project Manager
Division of Metabolism and Endocrinology Products

12/13/2010

Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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/s/

PATRICIA J MADARA
12/13/2010



NDA 202088

INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Dr. Kates:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (b) (4) (phentermine hydrochloride) ODT, 15 mg, 30 mg, 37.5 mg.

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

In order for us to comment on the appropriateness of the choice of the dissolution method and proposed dissolution specification, the following information needs to be provided in the NDA:

- Full development (justifying choice of method parameters) and validation reports for the *in-vitro* dissolution method and specifications.
- Full *in-vitro* dissolution data set (preferably in electronic format) and the *in-vitro* dissolution profiles.

If you have any questions, call Patricia Madara, Regulatory Project Manager, at 301-796-1249.

Sincerely,

{See appended electronic signature page}

Ali Al-Hakim, PhD.
Chief, Branch 7, Division 3
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

ALI H AL HAKIM
11/03/2010



NDA 202088

FILING COMMUNICATION

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Dr. Kates:

Please refer to your new drug application (NDA) dated August 11, 2010, received August 13, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (b) (4) (phentermine hydrochloride) ODT, 15 mg, 30 mg, 37.5 mg.

We also refer to your submissions dated September 29, and October 11, 12, and 13(2), 2010.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is June 13, 2011.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by May 16, 2011.

During our filing review of your application, we identified the following potential review issues and have the following requests for additional information:

Clinical Pharmacology

1. Please submit the datasets for all three bioavailability studies in electronic format.

Chemistry, Manufacturing and Controls

1. Your claim of categorical exclusion from the requirement to prepare an environmental assessment cites “21 CFR, Part 25, Subpart B, 25.24(c)(4)”, which does not exist. Submit a revised claim with the correct regulation citation, information to support the requested exclusion (e.g., a calculation of estimated environmental concentrations of the drug), and a statement that, to the best of your knowledge, no extraordinary circumstance exists that would warrant the preparation of an environmental assessment.
2. Provide the location in the NDA of the photostability study report for the drug product.
3. The term “retest period” does not apply to the drug product. Revise your NDA where appropriate to replace “retest period” with the correct term “expiration dating period” when discussing the drug product.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

Required Pediatric Assessments

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that you have not addressed how you plan to fulfill this requirement. Your section 1.9 does not contain a pediatric plan. Within 30 days of the date of this letter, please submit (1) a full waiver request, (2) a partial waiver request and a deferral request along with a pediatric development plan for the pediatric age groups not covered by the partial waiver request, or (3) a deferral request along with a pediatric drug development plan covering the full pediatric age range. A pediatric drug development plan must address the indication(s) proposed in this application.

If you request a full waiver, we will notify you if the full waiver is denied and a pediatric drug development plan is required.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. If you wish to qualify for pediatric exclusivity please consult INSERT DIVISION NAME. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

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

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

If you have any questions, call Patricia Madara, Regulatory Project Manager, at 301-796-5332.

Sincerely,

{See appended electronic signature page}

Eric Colman, M.D.
Deputy Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

ERIC C COLMAN
10/26/2010

Madara, Patricia

From: Madara, Patricia
Sent: Friday, October 08, 2010 3:44 PM
To: 'Steve Kates'
Subject: Information required for NDA 202088 prior to the filing date

Importance: High

Steve;

As I mentioned in my voice message left last evening at your office phone #, we will need to receive the information described below by October 13th in order to perform a cursory review and determine acceptability for filing.

Provide information on the impurities/degradants that are specific to this drug product formulation, including qualification information on impurities/degradants in the drug substance and drug product or a justification for the lack of such safety studies.

Please let me know if you have any problems accessing voice messages.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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/s/

PATRICIA J MADARA
10/08/2010

Madara, Patricia

From: Madara, Patricia
Sent: Tuesday, October 05, 2010 1:30 PM
To: Madara, Patricia
Subject: RE: Teleconference call follow-up

sent to firm via fax.

See responses below

From: Steve Kates [mailto:steve.kates@citiuspharma.com]
Sent: Monday, October 04, 2010 1:44 PM
To: Madara, Patricia
Subject: Teleconference call follow-up

Dear Pat,

I would like to thank you and your team again for Friday's teleconference. Two brief questions as a follow-up.

1. Will you be providing any meeting notes? If not, I can provide a memo for the file.

We had not planned on issuing minutes for such an informal tcon but a memo will be placed in the file.

^ Could you send me (email is fine) for clarity purposes the pharm/tox question that was asked at the end of the call?

Provide information on the impurities/degradants that are specific to this drug product formulation, including qualification information on impurities/degradants in the drug substance and drug product or a justification for the lack of such safety studies.

Regards,
Steve

Steve Kates, PhD
Citius Pharmaceuticals
978 938 0338 (o)
978 760 3520 (c)

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/s/

PATRICIA J MADARA

10/08/2010

These responses to the company's questions were sent via email and fax.

Reference ID: 2848062

Reference ID: 3113872

Madara, Patricia

From: Madara, Patricia
Sent: Monday, October 04, 2010 10:48 AM
To: 'steve.kates@citiuspharma.com'
Cc: Madara, Patricia; Galliers, Enid M
Subject: RE: NDA 202088 (phentermine HCl) ODT

Importance: High

Hi Steve;

We have received your labeling for (b) (4) (submitted electronically). However, as mentioned in the email below, previous phone calls, and published guidances, ALL versions (SPL, WORD, PDF) must be in PLR format. Please resubmit in PLR format prior to the filing date.

Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

From: Madara, Patricia
Sent: Thursday, September 23, 2010 3:53 PM
To: 'steve.kates@citiuspharma.com'
Cc: Madara, Patricia
Subject: FW: NDA 202088 (phentermine HCl) ODT
Importance: High

Hi Steve - this was sent on 9/07. Please provide a timeline for response.

From: Madara, Patricia
Sent: Tuesday, September 07, 2010 11:27 AM
To: Madara, Patricia; 'Steve Kates'
Subject: RE: NDA 202088 (phentermine HCl) ODT

Hi Steve;

Can you please confirm receipt of the original email below. Also, please provide a timeline for response.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Phone: 301-796-1249

From: Madara, Patricia
Sent: Thursday, August 26, 2010 10:16 AM
To: 'Steve Kates'
Cc: Madara, Patricia
Subject: RE: NDA 202088 (phentermine HCl) ODT
Importance: High

Hi Steve;

Please confirm receipt of this email. Also, just a reminder regarding the labeling submission, per the regulations, it must be in PLR format.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

From: Madara, Patricia
Sent: Wednesday, August 25, 2010 5:20 PM
To: 'Steve Kates'
Cc: Madara, Patricia
Subject: NDA 202088 (phentermine HCl) ODT
Importance: High

NDA 202088

NDA INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Dr. Kates:

Please refer to your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for (phentermine HCl) orally dissolving tablets (ODT).

We are currently beginning our review of your application and have the following requests for additional information. Please respond promptly since these are filing issues.

- **In support of your 505(b)(2) application for an Orally Disintegrating Tablet (ODT) of phentermine hydrochloride, provide a justification for designating your product an ODT. According the FDA final (December 2008) "Guidance for Industry Orally Disintegrating Tablets", the defining characteristics of this dosage form is the rapid disintegration in saliva without the need for chewing or liquids, and the definition includes an in-vitro disintegration time**

of approximately 30 seconds or less, when based on the USP disintegration test method or alternative.

(b) (4)

- As required by 21 CFR 314.54 (i.e., for a 505(b)(2) application), submit the proposed or actual master production record of the commercial drug product. As required by 21 CFR 314.50, submit the executed batch records for each batch of the drug product used to conduct the pivotal bioavailability or bioequivalence study.
- The ICH final (November 2003) Guidance Q1A(R2) Stability Testing of New Drug Substances and Products states "The long-term testing should cover a minimum of 12 months' duration on at least three primary batches at the time of submission". The primary drug product stability data in the 11-AUG-2010 NDA submission include 3-month long-term data for two (out of the three) primary batches of each dosage strength. Provide a justification for your request to file the NDA with such limited stability data.

Please respond to our information requests informally, via email, but also submit the correspondence officially to your NDA and cite this email in the cover letter. The amendment can be coded "**Quality Information / Response to Information Request.**"

Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

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/s/

PATRICIA J MADARA
10/08/2010

Madara, Patricia

From: Tran, Suong T
At: Friday, October 01, 2010 11:07 AM
Colman, Eric C; Bourcier, Todd; Summan, Mukesh
Madara, Patricia;-Al Hakim, Ali H; Chikhale, Elsbeth G; Ghosh, Tapash; Zdrojewski, Immo;
Choe, Sally
Subject: filing NDA 202088 phentermine HCl ODT

Hi everyone-

Based on the additional info received from the applicant during the CMC t-con today, ONDOQA will recommend filing this NDA (as soon as we receive the applicant's amendment that has the info in writing):

- The designation "ODT" will apply to this product based on a revised analytical method that would have FDA's 30-second disintegration threshold.
- Additional 6-month accelerated and long-term stability data will be submitted by November (for the stability batches that currently have 3-month data in the NDA).
- One copy of the master batch records will be submitted.

I forwarded the PharmTox filing deficiency to the applicant, that the following is required for filing: Information on the impurities/degradants that are specific to this drug product formulation, including qualification information on impurities/degradants in the drug substance and drug product or a justification for the lack of such safety studies. The applicant indicated that some information was submitted in the NDA but may be difficult for FDA to find. They will send Pat the exact location of the information in the NDA and they will also submit additional information if currently missing in the NDA. The package will be submitted for the PharmTox evaluation prior to the filing date.

Su

INTERNAL MEMORANDUM OF MEETING MINUTES

MEETING DATE: October 01, 2010
TIME: 10:00 AM, eastern time
LOCATION: Teleconference
APPLICATION: NDA 202088
DRUG NAME: (b) (4) (phentermine HCl) ODT
TYPE OF MEETING: Guidance

MEETING CHAIR: Ali Al Hakim, Ph.D.

MEETING RECORDER: Patricia Madara

CDER Attendees

Office of New Drug Quality Assessment; Division 3, Branch 7

Ali Al Hakim, Ph.D. Chief, Branch 7, Division 3
Suong Tran, Ph.D. CMC Lead, Branch 7

Office of Drug Evaluation II; Division of Metabolism and Endocrinology Products

Patricia Madara, M.S. Regulatory Project Manager

External Attendees:

Steven Kates, Ph.D. Citius Pharmaceuticals
Federico Stroppolo Apex Pharmaceuticals – Technical Director
Andrea Righetti Apex Pharmaceuticals, Quality Assurance Manager

Background:

On August 11, 2010, Citius Pharmaceuticals submitted a new 505(b)(2) application for a phentermine HCl orally dissolving tablet (ODT), (15 mg, 30 mg, and 37.5 mg). Upon initial review of the chemistry section, specifically the disintegration characteristics, it was noted that (b) (4) as published in the FDA guidance.

The teleconference sought to clear up this discrepancy since the NDA would not qualify as a 505b2 if it did not meet this criterion and would not be filed.

Discussion:

Drs. Al Hakim and Tran explained that the orally dissolving tablet (ODT) must dissolve within 30 seconds in order to meet the criteria for an ODT. If it did not dissolve in 30 seconds or less, it would just be considered a regular tablet and the application should be submitted to the Office of Generic Drugs.

First, the Apex Pharmaceuticals scientists noted that work on this product had begun over three years ago – before the current guidance was finalized. However, they have since re-examined

the procedure used

(b) (4)

Citius Pharmaceuticals (NDA applicant), in conjunction with Alpex, will write an amendment explaining the changes and include a justification for the differences. This new specification will be submitted prior to the October 13, 2010, filing deadline.

Next, Dr. Tran asked about the study submitted in which the ODT was taken with water. Dr. Kates explained that they had conducted a study with and without water but water was not required for the tablet to dissolve.

In addition, Dr. Tran asked the company to submit the master batch records (one copy) and confirm in writing that the process in that batch was identical to the commercial batches.

Finally, Dr. Tran asked the company to submit more stability data (only 3-month data was submitted with the NDA). The company responded that they would be sending more in November. They would have 6-month accelerated and room temperature data for all batches.

Dr. Tran also relayed a preclinical pharmacology / toxicology deficiency that must be addressed in order to file the NDA. As specified by the preclinical review team, the company must provide information on the impurities/degradants that are specific to this drug product formulation, including qualification information on impurities/degradants in the drug substance and drug product or a justification for the lack of such safety studies.

Dr. Kates confirmed that the company would submit this information prior to the filing deadline.

The teleconference ended.

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/s/

PATRICIA J MADARA
11/04/2010



NDA 202088

NDA ACKNOWLEDGMENT

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Dr. Kates:

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

Name of Drug Product: (b)(4) (phentermine hydrochloride) ODT, 15 mg, 30 mg, 37.5 mg

Date of Application: August 11, 2010

Date of Receipt: August 17, 2010

Our Reference Number: NDA 202088

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on October 16, 2010, in accordance with 21 CFR 314.101(a).

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

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

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

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>

If you have any questions, call me at (301) 796-1249.

Sincerely,

{See appended electronic signature page}

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-202088	ORIG-1	CITIUS PHARMACEUTICA LS LLC	PHENTERMINE HCL 15,30,37.5 mg ODT

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/s/

PATRICIA J MADARA
08/25/2010

Madara, Patricia

From: Madara, Patricia
Sent: Wednesday, August 25, 2010 5:20 PM
To: 'Steve Kates'
Cc: Madara, Patricia
Subject: NDA 202088 (phentermine HCl) ODT

Importance: High

NDA 202088

NDA INFORMATION REQUEST

Citius Pharmaceuticals, LLC
Attention: Steven A. Kates, Ph.D.
Vice President
63 Great Road
Maynard, MA 01754

Dear Dr. Kates:

Please refer to your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for (phentermine HCl) orally dissolving tablets (ODT).

We are currently beginning our review of your application and have the following requests for additional information. Please respond promptly since these are filing issues.

- **In support of your 505(b)(2) application for an Orally Disintegrating Tablet (ODT) of phentermine hydrochloride, provide a justification for designating your product an ODT. According the FDA final (December 2008) "Guidance for Industry Orally Disintegrating Tablets", the defining characteristics of this dosage form is the rapid disintegration in saliva without the need for chewing or liquids, and the definition includes an in-vitro disintegration time of approximately 30 seconds or less, when based on the USP disintegration test method or alternative.** (b) (4)

- **As required by 21 CFR 314.54 (i.e., for a 505(b)(2) application), submit the proposed or actual master production record of the commercial drug product. As required by 21 CFR 314.50, submit the executed batch records for each batch of the drug product used to conduct the pivotal bioavailability or bioequivalence study.**
- **The ICH final (November 2003) Guidance Q1A(R2) Stability Testing of New Drug Substances and Products states "The long-term testing should cover a minimum of 12 months' duration on at least three primary batches at the time of submission". The primary drug product stability data in the 11-AUG-2010 NDA submission include 3-month long-term data for two (out of the three) primary batches of each dosage strength. Provide a justification for your request to file the NDA with such limited stability data.**

Please respond to our information requests informally, via email, but also submit the correspondence officially to your NDA and cite this email in the cover letter. The amendment can be coded "**Quality Information / Response to Information Request.**"

Please confirm receipt of this email.

Sincerely;

Pat Madara
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-1249

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-202088	ORIG-1	CITIUS PHARMACEUTICA LS LLC	PHENTERMINE HCL 15,30,37.5 mg ODT

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/s/

PATRICIA J MADARA
08/25/2010

MEMORANDUM

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

DATE: 8/24/2010

TO: Steven Kates, Vice President, Citius Pharmaceuticals LLC, Ph# 978-938-0338

THROUGH : Khushboo Sharma, Regulatory Project Manager, ONDQA

FROM: Khushboo Sharma, Regulatory Project Manager, ONDQA

SUBJECT: Memo of Telecon: Request for clarification on establishments information

APPLICATION/DRUG: NDA 202-088

**Memo of Telecon:

The following clarifications were requested in a telephone conversation from Khushboo Sharma, RPM, ONDQA, to Steven Kates, Vice President, Citius Pharmaceutical regarding establishment information submitted to the original NDA on FDA Form 356h Attachment:

1. Confirm that the [REDACTED] (b) (4) were the only two sites for commercial drug substance and drug product manufacturing and testing. Additionally no other sites are hidden in the referenced DMF or other sections of the application.
2. Provide contact name, phone number, fax number and FEI or DUNNS (if available) for both the sites mentioned above an an amendment to the application.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-202088	ORIG-1	CITIUS PHARMACEUTICA LS LLC	PHENTERMINE HCL 15,30,37.5 mg ODT

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/s/

KHUSHBOO SHARMA
08/24/2010

1.3.4 Financial Disclosure Certification (of Investigators) (FDA Form 3454 and Form 3455)

Form 3454 – Attached

Form 3455 – Not applicable

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

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

Please mark the applicable checkbox.

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

Clinical Investigators	Mark T. Leibowitz, M.D. - CEDRA Corporation	

- (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 Steven Kates, PhD	TITLE Vice President
FIRM/ORGANIZATION Citius Pharmaceuticals LLC, 63 Great Road, Maynard, MA 01754	
SIGNATURE 	DATE (mm/dd/yyyy) 08/11/2010

Paperwork Reduction Act Statement

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