

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207768Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 207768

SUPPL #

HFD #

Trade Name Tuzistra XR

Generic Name Codeine Polistirex and Chlorpheniramine Polistirex

Applicant Name Tris Pharma, Inc.

Approval Date, If Known April 30, 2015

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.

The applicant performed four pharmacology studies, two pilot studies and two pivotal bioavailability studies to evaluate the relative bioavailability between the drug product and a reference product.

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

d) Did the applicant request exclusivity?

YES NO

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

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

YES NO

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

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

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

YES NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES NO

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

NDA#

NDA#

NDA#

2. Combination product.

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

YES X NO

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

NDA# 21369	Codeprex
NDA# 19111	Tussionex
NDA# 18928	Penntuss

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 X

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

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

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

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

YES NO

If yes, explain:

=====

Name of person completing form: Sadaf Nabavian
Title: Regulatory Project Manager
Date: April 16, 2015

Name of Office/Division Director signing form: DPARP/Lydia Gilbert-McClain
Title: Deputy Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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

/s/

SADAF NABAVIAN
04/30/2015

LYDIA I GILBERT MCCLAIN
04/30/2015

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 207768 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Tuzistra XR Established/Proper Name: Codeine Polistirex and Chlorpheniramine Polistirex Extended Release Dosage Form: Oral Suspension		Applicant: Tris Pharma, Inc. Agent for Applicant (if applicable):
RPM: Sadaf Nabavian		Division: Pulmonary, Allergy, and Rheumatology Products
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) BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)		<p><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></p> <ul style="list-style-type: none"> Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>notify CDER OND IO</i>) Date of check: _____</p> <p><i>Note: 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.</i></p>
❖ Actions		
<ul style="list-style-type: none"> Proposed action User Fee Goal Date is <u>April 30, 2015</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
❖ 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 _____		<input type="checkbox"/> Received
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, 505(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).

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.

Review priority: Standard Priority
 Chemical classification (new NDAs only): Type 3
(confirm chemical classification at time of approval)

- | | |
|---|---|
| <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 |
| <input type="checkbox"/> Breakthrough Therapy designation | |

NDAs: Subpart H

- Accelerated approval (21 CFR 314.510)
 Restricted distribution (21 CFR 314.520)

Subpart I

- Approval based on animal studies

- Submitted in response to a PMR
 Submitted in response to a PMC
 Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- Accelerated approval (21 CFR 601.41)
 Restricted distribution (21 CFR 601.42)

Subpart H

- Approval based on animal studies

- REMS: MedGuide
 Communication Plan
 ETASU
 MedGuide w/o REMS
 REMS not required

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 <i>(approvals only)</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications <i>(approvals only)</i>	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Indicate what types (if any) of information were issued	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
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): Approval; April 30, 2015
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 (<i>if it is division-proposed labeling, it should be in track-changes format</i>) 	<input checked="" type="checkbox"/> Included 4/30/2015
<ul style="list-style-type: none"> Original applicant-proposed labeling 	<input checked="" type="checkbox"/> Included 6/30/2014
❖ 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 checked="" type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> Most-recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>) 	<input checked="" type="checkbox"/> Included 4/29/2015
<ul style="list-style-type: none"> Original applicant-proposed labeling 	<input checked="" type="checkbox"/> Included 6/30/2014
❖ 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 	<input checked="" type="checkbox"/> Included 6/30/2014
❖ 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>) 	Acceptable; 9/19/2014 OSE/DMEPA Review: 9/15/2014
❖ Labeling reviews (<i>indicate dates of reviews</i>)	RPM: <input checked="" type="checkbox"/> None March 30, 2015 DMEPA: <input checked="" type="checkbox"/> February 23, 2015 DMPP/PLT (DRISK): <input checked="" type="checkbox"/> April 10, 2015 OPDP: <input checked="" type="checkbox"/> April 10, 2015 SEALD: <input type="checkbox"/> None X CSS: <input type="checkbox"/> None X Other: <input type="checkbox"/> None X
Administrative / Regulatory Documents	
❖ RPM Filing Review ⁴ /Memo of Filing Meeting (<i>indicate date of each review</i>) ❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	RPM Filing Review: March 30, 2015 <input type="checkbox"/> Not a (b)(2) Cleared on 3/23/2015 by Amy Bertha
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/>
❖ 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

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

<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>March 4, 2015</u> If PeRC review not necessary, explain: _____ 	
<ul style="list-style-type: none"> ❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, etc.) (<i>do not include previous action letters, as these are located elsewhere in package</i>) 	IRs: 4/30; 4/29/2015; 4/28/2015 (2); 4/21/2015 ; 4/3/2015; 3/13/2015; 2/19/2015; 1/30/2015 Letters: Proprietary Name Granted (9/19/2014); 74 Day Letter (9/11/2014); Acknowledgement Letter (7/9/2014)
<ul style="list-style-type: none"> ❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes) 	PeRC meeting minutes: 3/15/2015
<ul style="list-style-type: none"> ❖ Minutes of Meetings <ul style="list-style-type: none"> • If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) • Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) • EOP2 meeting (<i>indicate date of mtg</i>) • Mid-cycle Communication (<i>indicate date of mtg</i>) • Late-cycle Meeting (<i>indicate date of mtg</i>) • Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>) 	<input checked="" type="checkbox"/> N/A or no mtg <input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> N/A <input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> ❖ Advisory Committee Meeting(s) <ul style="list-style-type: none"> • Date(s) of Meeting(s) 	<input checked="" type="checkbox"/> No AC meeting
Decisional and Summary Memos	
<ul style="list-style-type: none"> ❖ Office Director Decisional Memo (<i>indicate date for each review</i>) 	
Division Director Summary Review (<i>indicate date for each review</i>)	April 30, 2015
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	April 9, 2015
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical	
<ul style="list-style-type: none"> ❖ Clinical Reviews <ul style="list-style-type: none"> • Clinical Team Leader Review(s) (<i>indicate date for each review</i>) • Clinical review(s) (<i>indicate date for each review</i>) • Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	<input type="checkbox"/> No separate review March 25, 2015 <input type="checkbox"/> None
<ul style="list-style-type: 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>) 	Clinical Review dated 3/25/15, Section 9.5, Financial Disclosure Review, Page 56

❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> N/A
❖ Risk Management <ul style="list-style-type: none"> REMS Documents and REMS Supporting Document (<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 type="checkbox"/> None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	<input checked="" type="checkbox"/> None
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
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 type="checkbox"/> No separate review
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 3/4/2015; 8/14/2014
❖ OSI Clinical Pharmacology Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> 11/5/2014
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 3/23/15; 3/17/2015; 8/5/2014
❖ 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
❖ OSI Nonclinical Inspection Review Summary (<i>include copies of OSI 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 type="checkbox"/> No separate review
• Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
• Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 3/25/2015; 8/14/2014
❖ Microbiology Reviews	<input checked="" type="checkbox"/> 2/13/2015
<input checked="" 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>)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>)	Biopharmaceutics dated 3/23/2015
❖ 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>)	CMC Review dated 3/25/15; Page 13
<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 type="checkbox"/> NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within 2 years of action date) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁵</i>)	Date completed: <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (date of most recent TB-EER must be within 30 days of action date) (<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)

⁵ 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.

Day of Approval Activities	
❖ For all 505(b)(2) applications: <ul style="list-style-type: none"> • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) 	<input checked="" type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>Notify CDER OND IO</i>)
<ul style="list-style-type: none"> • Finalize 505(b)(2) assessment 	<input checked="" type="checkbox"/> Done
❖ For Breakthrough Therapy(BT) Designated drugs: <ul style="list-style-type: none"> • Notify the CDER BT Program Manager 	<input type="checkbox"/> Done (<i>Send email to CDER OND IO and the CDER BT Program Manager</i>)
❖ For products that need to be added to the flush list (generally opioids): <ul style="list-style-type: none"> • Notify the Division of Online Communications, Office of Communications 	<input type="checkbox"/> Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<input checked="" type="checkbox"/> Done April 30, 2015
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	<input type="checkbox"/> Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	<input checked="" type="checkbox"/> Done April 30, 2015
❖ Ensure Pediatric Record is accurate	<input checked="" type="checkbox"/> Done
❖ Send approval email within one business day to CDER-APPROVALS	<input checked="" type="checkbox"/> Done April 30, 2015

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

/s/

SADAF NABAVIAN
04/30/2015



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: April 30, 2015

To: Ms. Norma J. Cappetti VP, Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tris Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-0374	Phone number: 301-796-2777
Subject: NDA 207768; FDA Labeling Comments	

Total no. of pages including cover: 3

Comments: Please confirm receipt.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 207768
Tuzistra XR
Tris Pharma, Inc.

Dear Ms. Cappetti:

Your submission dated, June 27, 2014, for Tuzistra XR suspension is currently under review. We are providing our labeling comments and recommendations.

Container

1. Delete the (b) (4) statement.
2. Change the “/” between the polistirex names to "and".

PI/PPI

3. Correct the line spacing discrepancies noted in different sections of the label (e.g. sections 7.2, 7.3, 8.1, 13.1) and make the line spacing consistent throughout the label.

Boxed Warning (BW)

4. The BW (in both the highlights and the actual boxed warning) should reference Section 5.1.
5. The heading should be centered and in upper case letters.
6. The BW should have the verbatim statement “*See full prescribing information for complete boxed warning.*” This statement should be centered immediately beneath the heading and appear in italics.

Submit revised labeling incorporating the changes via email to Sadaf.Nabavian@fda.hhs.gov by 1:00 p.m. EST, April 30, 2015, followed by official submission to the NDA. If there are any questions, contact Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, PharmD
Sr. Regulatory Project Manager

Drafted by: SNabavian/4.30.2015

Cleared by: JMaynard/4.30.2015
LJafari/4.30.2015

Finalized by: SNabavian/4.30.2015

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

/s/

SADAF NABAVIAN
04/30/2015



Food and Drug Administration
 Center for Drug Evaluation and Research
 Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: April 29, 2015

To: W. Scott Groner Director of Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tris Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-4690	Phone number: 301-796-2777
Subject: NDA 207768; FDA Labeling Comments	

Total no. of pages including cover: 3

Comments: Please confirm receipt.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this
 document to the addressee, you are hereby notified that any review,
 disclosure, dissemination, copying, or other action based on the content of
 this communication is not authorized. If you have received this document
 in error, please notify us immediately by telephone at (301) 796-2300.
 Thank you.

NDA 207768
Tuzistra XR
Tris Pharma, Inc.

Dear Mr. Groner:

Your submission dated, June 27, 2014, for Tuzistra XR suspension is currently under review. We are providing our comments and recommendations pertaining to the carton and container labels. Be advised that these labeling changes are not necessarily the Agency's final recommendations and that additional labeling changes may be forthcoming.

1. Revise the presentation of the proprietary name from lowercase (i.e. tuzistra XR) to title case (i.e. Tuzistra XR) to improve readability of the name. Words set in title case are easier to read.
2. Revise the presentation of the established name from lower case (i.e. codeine polistirex/chlorpheniramine polistirex) to title case (i.e. Codeine Polistirex/Chlorpheniramine Polistirex) to improve readability of the name. Words set in title case are easier to read.

Submit revised labeling incorporating the changes via email to Sadaf.Nabavian@fda.hhs.gov by COB, April 29, 2015, followed by official submission to the NDA. If there are any questions, contact Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, PharmD
Sr. Regulatory Project Manager

Drafted by: SNabavian/4.29.2015

Cleared by: LJafari/4.29.2015

Finalized by: SNabavian/4.29.2015

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

/s/

SADAF NABAVIAN
04/29/2015



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: April 28, 2015

To: W. Scott Groner Director of Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tris Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-4690	Phone number: 301-796-2777
Subject: NDA 207768; FDA Labeling Comments	

Total no. of pages including cover: 3

Comments: Please confirm receipt.

Document to be mailed: xYES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 207768
Tuzistra XR
Tris Pharma, Inc.

Dear Mr. Groner:

Your submission dated June 27, 2014, for Tuzistra XR suspension is currently under review. We are providing our labeling comments and recommendations in the attached marked up labeling. The proposed insertions are (underlined) and deletions are in (strike-out). Be advised that these labeling changes are not necessarily the Agency's final recommendations and that additional labeling changes may be forthcoming.

Submit revised labeling incorporating the changes shown in the attached marked up labels via email to Sadaf.Nabavian@fda.hhs.gov by noon, April 29, 2015, followed by official submission to the NDA. If there are any questions, contact Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, PharmD
Sr. Regulatory Project Manager

9 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/

SADAF NABAVIAN
04/28/2015



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II**

FACSIMILE TRANSMITTAL SHEET

DATE: April 28, 2015

To: W. Scott Groner Director of Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tris Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-4690	Phone number: 301-796-2777
Subject: NDA 207768; FDA Labeling Comments	

Total no. of pages including cover: 3

Comments: Please confirm receipt.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 207768
Tuzistra XR
Tris Pharma, Inc.

Dear Mr. Groner:

Your submission dated, June 27, 2014, for Tuzistra XR suspension is currently under review. We are providing our comment and recommendation pertaining to the carton label. Be advised that this labeling change is not necessarily the Agency's final recommendation and that additional labeling changes may be forthcoming.

1. Revise the carton label to state "14.7mg codeine and 2.8mg chlorpheniramine per 5 mL*". (b) (4)

Submit revised labeling incorporating the changes via email to Sadaf.Nabavian@fda.hhs.gov by noon, April 29, 2015, followed by official submission to the NDA. If there are any questions, contact Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, PharmD
Sr. Regulatory Project Manager

Drafted by: SNabavian/4.27.2015

Cleared by: LJafari/4.27.2015

Finalized by: SNabavian/4.28.2015

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

/s/

SADAF NABAVIAN
04/28/2015



Food and Drug Administration
 Center for Drug Evaluation and Research
 Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: April 21, 2015

To: W. Scott Groner Director of Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tris Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-4690	Phone number: 301-796-2777
Subject: NDA 207768; FDA Labeling Comments	

Total no. of pages including cover: 3

Comments: Please confirm receipt.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 207768; FDA Labeling Comments

NDA 207768
Tuzistra XR
Tris Pharma, Inc.

Dear Mr. Groner:

Your submission dated, June 27, 2014, for Tuzistra XR suspension is currently under review. We are providing our comments and recommendations pertaining to the carton and container labels. Be advised that these labeling changes are not necessarily the Agency's final recommendations and that additional labeling changes may be forthcoming.

1. Present the established name in a manner consistent with 21 CFR 201.10(g)(2), which requires that the established name be at least half the size of the letters comprising the proprietary name and have a prominence consistent with the proprietary name in terms of type, size, color, and font.
2. [REDACTED] (b) (4)
3. Change the carton labeling to be "Tuzistra® XR (codeine polistirex and chlorpheniramine polistirex) extended release oral suspension" with the strengths expressed as "14.7 mg codeine [REDACTED] (b) (4) and 2.8 mg chlorpheniramine [REDACTED] (b) (4)

Submit revised labeling incorporating the changes via email to Sadaf.Nabavian@fda.hhs.gov by Noon, April 24, 2015, followed by official submission to the NDA. If there are any questions, contact Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, PharmD
Sr. Regulatory Project Manager

Sr. Regulatory Project Manager, at 301-796-2777.

Drafted by: SNabavian/4.20.2015

Cleared by: LJafari/4.20.2015
Maynard/cc'd to the email string
CAbraham/CBertha/JPinto/4.20.2015

Finalized by: SNabavian/4.21.2015

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

/s/

SADAF NABAVIAN
04/21/2015



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: April 3, 2015

To: W. Scott Groner Director of Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tis Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-4690	Phone number: 301-796-2777
Subject: NDA 207768; FDA Comments	

Total no. of pages including cover: 3

Comments: Please confirm receipt.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 207768
Tuzistra ER Oral Suspension
Tris Pharma, Inc.

Dear Mr. Groner:

Your submission dated, June 27, 2014, for Tuzistra ER suspension is currently under review and we have the following comment.

- Upon further internal discussions, it appears that the proposed codeine polistirex and chlorpheniramine polistirex ER oral suspension may not trigger PREA. (b) (4)



If there are any questions, contact me at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, Pharm.D.
Sr. Regulatory Project Manager

Drafted by: SNabavian/4.3.2015

Cleared by: LJafari/4.3.2015

Finalized by: SNabavian/4.3.2015

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

/s/

SADAF NABAVIAN
04/03/2015



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: April 3, 2015

To: W. Scott Groner Director of Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tris Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-4690	Phone number: 301-796-2777
Subject: NDA 207768; FDA Labeling Comments	

Total no. of pages including cover: 19

Comments: Please confirm receipt.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 207768
Tuzistra ER Oral Suspension
Tris Pharma, Inc.

Dear Mr. Groner:

Your submission dated June 27, 2014, for Tuzistra ER suspension is currently under review. We are providing our labeling comments and recommendations in the attached marked up labeling. The proposed insertions are (underlined) and deletions are in (strike-out). Be advised that these labeling changes are not necessarily the Agency's final recommendations and that additional labeling changes may be forthcoming.

Submit revised labeling incorporating the changes shown in the attached marked up labels via email to Sadaf.Nabavian@fda.hhs.gov by COB, April 10, 2015, followed by official submission to the NDA. If there are any questions, contact Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, PharmD
Sr. Regulatory Project Manager

Drafted by: SNabavian/4.3.2015

Cleared by: LJafari/4.3.2015

Finalized by: SNabavian/4.3.2015

17 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/

SADAF NABAVIAN
04/03/2015

**PeRC Meeting Minutes
March 4, 2015**

PeRC Members Attending:

Lynne Yao

Rosemary Addy

Jane Inglese

Hari Cheryl Sachs

Wiley Chambers

Tom Smith

Karen Davis-Bruno

Peter Starke [REDACTED] NON RESPONSIVE

Andrew Mulberg

Gregory Reaman

[REDACTED] NON RESPONSIVE

Shrikant Pagay

Andrew Mosholder

Freda Cooner

Gilbert Burckart for Lily Mulugeta

[REDACTED] NON RESPONSIVE

Robert Nelson

Maura O'Leary [REDACTED] NON RESPONSIVE

Tuzistra XR, [REDACTED] NON)

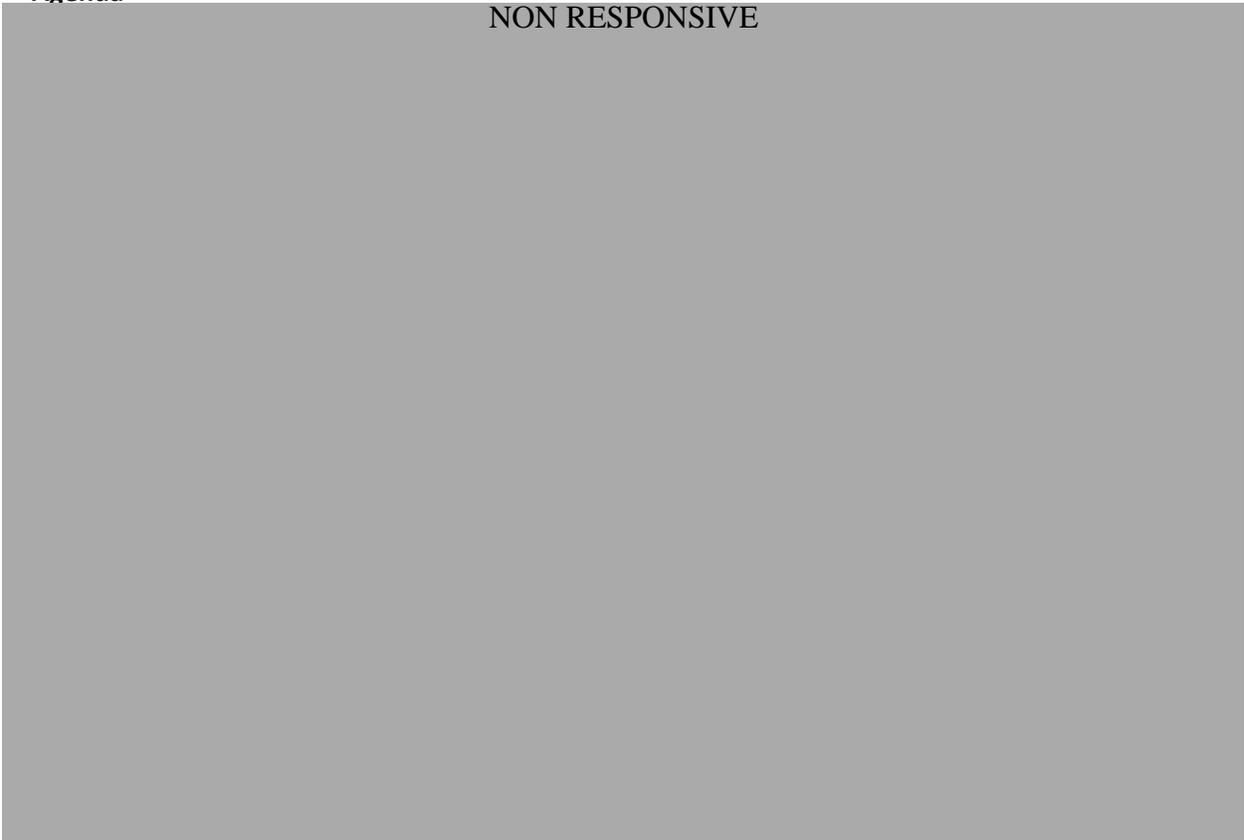
Dianne Murphy

RESPONS

[REDACTED] NON RESPONSIVE

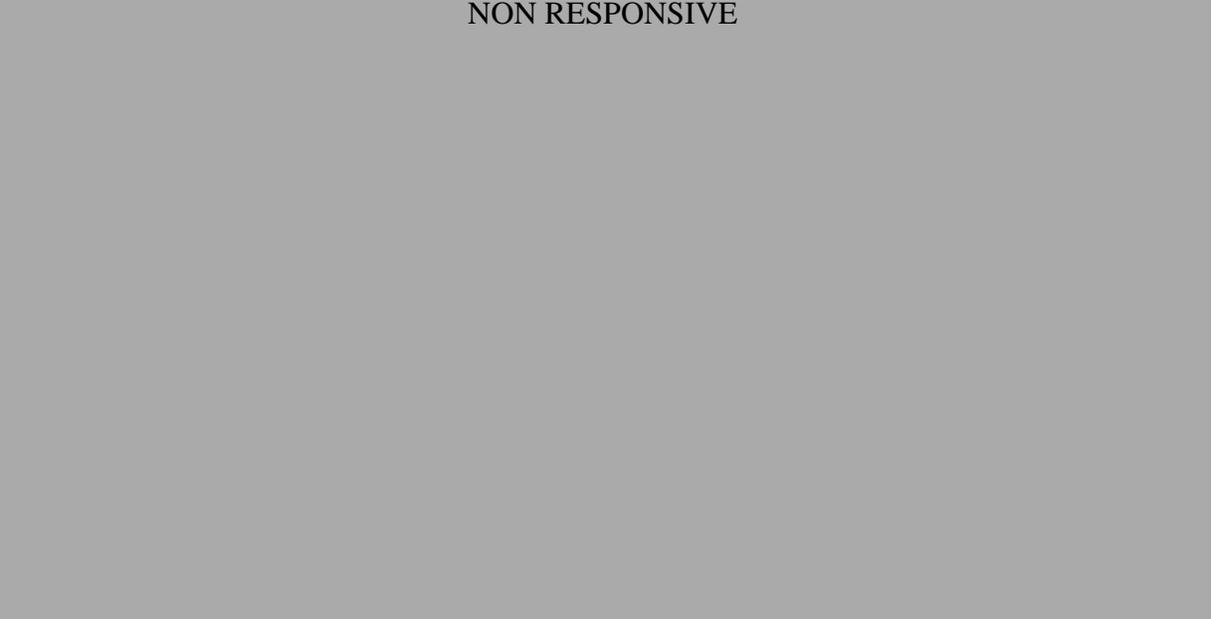
Agenda

NON RESPONSIVE



NDA	207768	Tuzistra XR (codeine polistirex and chlorpheniramine polistirex ER) (b) (4) [Redacted] *Agreed iPSP	Relief of cough and [Redacted] [Redacted] upper respiratory allergies	(b) (4)
-----	--------	---	---	---------

NON RESPONSIVE



3 Page(s) has been Withheld in Full as NON-RESPONSIVE immediately following this page

NON RESPONSIVE

Tuzistra XR (codeine polistirex and chlorpheniramine polistirex ER) (b) (4)

- NDA 207768 seeks marketing approval for Tuzistra XR (codeine polistirex and chlorpheniramine polistirex ER) for relief of cough and (b) (4) upper respiratory allergies.
- (b) (4)
- The application has a PDUFA goal date of April 30, 2015.
- *PerRC Recommendations:*
 - Upon further review, the PerRC noted that the change in codeine strength for which this application seeks marketing approval does not trigger PREA because the dosing regimen is also not changed. In view of this, the PerRC recommended that the Division issue a WR for pediatric studies for codeine polistirex and chlorpheniramine polistirex ER because these studies would be clear public health benefit (see discussion above).

NON RESPONSIVE

2 Page(s) has been Withheld in Full as NON-RESPONSIVE 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/

JANE E INGLESE
03/15/2015



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: March 13, 2015

To: W. Scott Groner Director of Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tis Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-4690	Phone number: 301-796-2777
Subject: NDA 207768; FDA Labeling Comments	

Total no. of pages including cover: 3

Comments: Please confirm receipt.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 207768
Tuzistra ER Oral Suspension
Tris Pharma, Inc.

Dear Mr. Groner:

Your submission dated, June 27, 2014, for Tuzistra ER suspension is currently under review. We are providing our labeling comments and recommendations in the attached marked up labeling. The proposed insertions are (underlined) and deletions are in (strike-out). Be advised that these labeling changes are not necessarily the Agency's final recommendations and that additional labeling changes may be forthcoming.

Submit revised labeling incorporating the changes shown in the attached marked up labels via email to Sadaf.Nabavian@fda.hhs.gov by COB, March 20, 2015, followed by official submission to the NDA. If there are any questions, contact Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, PharmD
Sr. Regulatory Project Manager

Drafted by: SNabavian/3.13.2015

Cleared by: LJafari/3.13.2015

Finalized by: SNabavian/3.13.2015

27 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/

SADAF NABAVIAN
03/13/2015



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: February 19, 2015

To: W. Scott Groner Director of Regulatory Affairs	From: Sadaf Nabavian, Pharm.D. Regulatory Project Manager
Company: Tis Pharma, Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Email: TrisRA@trispharma.com	Fax number: 301-796-9728
Phone number: 732-940-4690	Phone number: 301-796-2777
Subject: NDA 207768; Information Request	

Total no. of pages including cover: 3

Comments: Please confirm receipt.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 207768
Tuzistra ER Oral Suspension
Tris Pharma, Inc.

Dear Mr. Groner:

Your submission dated, June 27, 2014, for Tuzistra ER suspension is currently under review and we have the following comment.

1. The specification for the excipient (b)(4), found in DMF 27314, Section 3.2.P.4.1, includes a limit for (b)(4) of NMT (b)(4) ppm. Table 1 of DMF 27314, Section 3.2.P.1, lists a total of (b)(4) of (b)(4) (b)(4) per 20 ml of drug product (maximum daily dose). Therefore, the maximum total daily intake of (b)(4) would be:

(b)(4)

Provide justification for the safety of this level of (b)(4) µg/day) in the COD-CPM ER Suspension.

Submit your response via email to Sadaf.Nabavian@fda.hhs.gov by COB, Thursday, February 26, 2015, followed by an official submission to the NDA. If there are any questions, contact Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

(See appended electronic signature)

Sadaf Nabavian, PharmD
Sr. Regulatory Project Manager

Drafted by: SNabavian/2.19.2015

Cleared by: LJafari/2.19.2015

Finalized by: SNabavian/2.19.2015

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

/s/

SADAF NABAVIAN
02/19/2015

MEMORANDUM OF TELECON

DATE: November 13, 2014

APPLICATION NUMBER: NDA 207768

DRUG: Codeine polistirex and chlorpheniramine polistirex, ER Oral Suspension

BETWEEN:

Tris Pharma

Scott Groner, Director, Regulatory Affairs
Norma J Cappetti, VP of Regulatory Affairs
Yulia Pincus, PhD, Sr. Manager, Regulatory Affairs
Andrea Nelso, Manager, Product Development
Sally Berry, MD, PhD, Chief Medical Officer

Vernalis Therapeutics, Inc.

Donna Radzik, Senior Vice President, Pharmaceutical Quality Operations
Pascal Borderies, Senior Vice President Medical Affairs

AND

Division of Pulmonary, Allergy, and Rheumatology Products

Satjit Brar, PhD, Clinical Pharmacology Team Leader
Ritesh Jain, PhD, Clinical Pharmacology Reviewer
Janet Maynard, MD, MHS, Clinical Team Leader
Sadaf Nabavian, PharmD, Regulatory Health Project Manager

SUBJECT: Post Mid-Cycle Meeting Teleconference

Discussion regarding clinical pharmacology studies

The Division requested a post mid-cycle teleconference with the Sponsor to provide an update on the review of the pending NDA, and communicate potential review issues that were identified during the mid-cycle meeting from the clinical pharmacology perspective. The following comments were conveyed to the Sponsor:

- The results of the food effect study (3007117) indicates that presence of a high-fat, high-calorie meal leads to a 26% increase in exposure of the codeine component in your extended release product. Considering the safety risks associated with codeine, this observed food effect is a potential review issue.

- In addition, the results of the multiple-dose study (3007116) indicates that the systemic concentrations of codeine from your extended release product, are lower than those observed with the respective immediate release formulations in the last few hours of the 12 hour dosing interval. The implications of the lower systemic concentrations is a potential review issue.

The Division noted that no additional data or justifications are needed at this time and our reviews are ongoing.

Discussion regarding pediatric studies

The Division also informed Tris Pharma of an ongoing internal discussion regarding  (b) (4)



Sadaf Nabavian, Pharm.D.
Regulatory Project Management Officer

Drafted: Nabavian/1.16.2015
Initialed: LJafari/1.16.2015
SBrar/1.29.2015
JManynard/1.29.2015
Finalized: Nabavian/1.30.2015

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

/s/

SADAF NABAVIAN
01/30/2015



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 207768

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Tris Pharma, Inc.
2033 Route 130
Suite D
Monmouth Junction, NJ 08852

ATTENTION: W. Scott Groner
Director of Regulatory Affairs

Dear Mr. Groner:

Please refer to your New Drug Application (NDA) dated June 27, 2014, received June 30, 2014, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Codeine Polistirex and Chlorpheniramine Polistirex Extended-Release Suspension, 20 mg/4 mg per 5 mL.

We also refer to your July 9, 2014, correspondence, received July 10, 2014, requesting review of your proposed proprietary name, Tuzistra XR.

We have completed our review of the proposed proprietary name, Tuzistra XR and have concluded that it is acceptable.

If any of the proposed product characteristics as stated in your July 9, 2014, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Nichelle Rashid, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3904. For any other information regarding this application, contact Sadaf Nabavian, Regulatory Project Manager in the Office of New Drugs, at (301) 796-2777.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

TODD D BRIDGES on behalf of KELLIE A TAYLOR
09/19/2014



NDA 207768

**FILING COMMUNICATION –
NO FILING REVIEW ISSUES IDENTIFIED**

Tris Pharma, Inc.
2033 Route 130, Suite D
Monmouth Junction, New Jersey, 08852

Attention: W. Scott Groner
Director, Regulatory Affairs

Dear Mr. Groner:

Please refer to your New Drug Application (NDA) dated June 27, 2014, received June 30, 2014, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Codeine Polistirex and Chlorpheniramine Polistirex ER Oral Suspension (20 mg codeine phosphate and 4 mg chlorpheniramine maleate per 5 mL).

We also refer to your amendments dated July 10 and August 14, 2014.

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 April 30, 2015.

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, mid-cycle, 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 April 2, 2015.

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

We request that you submit the following information:

1. Provide detailed report of dissolution method validation.
2. Provide detailed report of the IVIVC model development and Validation.
3. Provide justification for the Extended Release (ER) claim of your product.

PRESCRIBING INFORMATION

Your proposed prescribing information (PI) must conform to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). We encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.

During our preliminary review of your submitted labeling, we have identified the following labeling issues and have the following labeling comments or questions:

1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.
2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission.
3. All headings in HL must be **bolded** and presented in the center of a horizontal line (each horizontal line should extend over the entire width of the column). The headings should be in UPPER CASE letters.
4. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., “**Revised: 9/2013**”).
5. Initial U.S. Approval in HL must be bolded, and include the verbatim statement “Initial U.S. Approval:” followed by the 4-digit year.
6. For the Patient Counseling Information statement you must include one of the following verbatim statement: “**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**”
7. The Table of Content (TOC) should be in a two-column format.
8. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (through), articles (a, an, and the), or conjunctions (for, and)].
9. The following heading must be **bolded** and appear at the beginning of the Full Prescribing Information Section Heading: “**FULL PRESCRIBING INFORMATION**”. This heading should be in UPPER CASE.

We request that you resubmit labeling (in Microsoft Word format) that addresses these issues by October 3, 2014. The resubmitted labeling will be used for further labeling discussions. Use the SRPI checklist to correct any formatting errors to ensure conformance with the format items in regulations and guidances.

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

Please respond only to the above requests for 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.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI), and patient package insert (PPI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), and patient package insert, and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

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 Division of

Pulmonary, Allergy, and Rheumatology Products. 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.

We acknowledge receipt of your request for a [REDACTED] ^{(b) (4)} for this application. Once we have reviewed your request, we will notify you if the [REDACTED] ^{(b) (4)} is denied.

If you have any questions, call Sadaf Nabavian, Regulatory Project Manager, at (301) 796-2777.

Sincerely,

{See appended electronic signature page}

Lydia Gilbert-McClain, M.D.
Deputy Director
Division of Pulmonary, Allergy, and
Rheumatology Products
Office of Drug Evaluation II
Center of Drug Evaluation and Research

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

/s/

LYDIA I GILBERT MCCLAIN
09/11/2014



NDA 207768

NDA ACKNOWLEDGMENT

Tris Pharma, Inc.
2033 Route 130
Monmouth Junction, New Jersey, 08852

Attention: W. Scott Groner
Director of Regulatory Affairs

Dear Mr. Groner:

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: Codeine Polistirex and Chlorpheniramine Polistirex ER Oral Suspension (20 mg codeine phosphate/4 mg chlorpheniramine maleate per 5 ml)

Date of Application: June 27, 2014

Date of Receipt: June 30, 2014

Our Reference Number: NDA 207768

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 August 29, 2014, 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.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

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 Pulmonary, Allergy, and Rheumatology 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>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, call Sadaf Nabavian, Sr. Regulatory Project Manager, at (301) 796-2777.

Sincerely,

{See appended electronic signature page}

Sadaf Nabavian, Pharm.D.
Sr. Regulatory Project Manager
Division of Pulmonary, Allergy, and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

SADAF NABAVIAN
07/09/2014

6/9/14

**PeRC BPCA/Pediatric Study Plan Subcommittee Meeting Minutes
May 28, 2014**

PeRC Members Attending:

Robert Nelson

Jane Inglese

Rosemary Addy

Hari Cheryl Sachs

Wiley Chambers

Tom Smith

Peter Starke

Gregory Reaman

Daiva Shetty

Kristiana Brugger

Ruthanna Davi

Freda Cooner

Lily Mulugeta

Maura O'Leary

Dianne Murphy

Michelle Roth-Cline **Non Responsive**

Agenda
NON RESPONSIVE



IND	(b) (4)	Codeine Polisterix_Chlorphiramine Polisterix Agreed iPSP (Full Waiver)	(b) (4) of cough and upper respiratory (b) (4) (b) (4) common cold (b) (4)
-----	---------	---	---

Non Responsive

2 Page(s) has been Withheld in Full as NON-RESPONSIVE immediately following this page

Non Responsive

Codeine Polisterix Chlorphiramine Polisterix Agreed iPSP (b) (4)

- Proposed Indication: (b) (4) of cough and upper respiratory (b) (4)
(b) (4) common cold (b) (4)
- *PeRC Recommendations:*
 - The PeRC concurred with the agreed iPSP.

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

/s/

JANE E INGLESE
06/09/2014

5/29/2014



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

IND (b) (4)

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Tris Pharma, Inc.
2033 Route 130
Suite D
Monmouth Junction, New Jersey 08852

ATTENTION: W. Scott Groner
Director Regulatory Affairs

Dear Mr. Groner:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Codeine Polistirex and Chlorpheniramine Polistirex Extended Release Suspension, 20 mg/4 mg per 5 mL.

We also refer to your December 12, 2013, correspondence, received December 13, 2013, requesting review of your proposed proprietary name, Tuzistra XR.

We have completed our review of the proposed proprietary name, Tuzistra XR and have concluded that it is acceptable.

A request for proprietary name review for Tuzistra XR should be submitted once the NDA is submitted.

If any of the proposed product characteristics as stated in your December 12, 2013, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Nichelle Rashid, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3904. For any other information regarding this application, contact Laura Musse, Regulatory Project Manager in the Office of New Drugs, at (240) 402-3720.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

KELLIE A TAYLOR
05/29/2014



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND (b) (4)

ADVICE

Tris Pharma, Inc
2033 Route 130
Monmouth Junction, NJ 08852

Attention: William Scott Groner
Director of Regulatory Affairs

Dear Mr. Gronor:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for codeine polisterex and chlorpheniramine polisterex.

We also refer to your amendment dated December 3, 2014, containing initial Pediatric Study Plan (iPSP) for codeine polisterex and chlorpheniramine polisterex.

(b) (4)

(b) (4)

As sponsor of this IND, you are responsible for compliance with the FDCA (21 U.S.C. §§ 301 et. seq.) as well as the implementing regulations [Title 21 of the Code of Federal Regulations (CFR)]. A searchable version of these regulations is available at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm>. Your responsibilities include:

- Reporting any unexpected fatal or life-threatening suspected adverse reactions to this Division no later than 7 calendar days after initial receipt of the information [21 CFR 312.32(c)(2)].

If your IND is in eCTD format, submit 7-day reports electronically in eCTD format via the FDA Electronic Submissions Gateway (ESG). To obtain an ESG account, see information at the end of this letter.

If your IND is not in eCTD format:

- you should submit 7-day reports by a rapid means of communication, preferably by facsimile or email. You should address each submission to the Regulatory Project Manager and/or to the Chief, Project Management Staff;
- if you intend to submit 7-day reports by email, you should obtain a secure email account with FDA (see information at the end of this letter);
- if you also send copies of these reports to your IND, the submission should have the same date as your facsimile or email submission and be clearly marked as "Duplicate."
- Reporting any (1) serious, unexpected suspected adverse reactions, (2) findings from other clinical, animal, or in-vitro studies that suggest significant human risk, and (3) a clinically important increase in the rate of a serious suspected adverse reaction to this Division and to all investigators no later than 15 calendar days after determining that the information qualifies for reporting [21 CFR 312.32(c)(1)]. If your IND is in eCTD format, submit 15-day reports to FDA electronically in eCTD format. If your IND is not in eCTD format, you may submit 15-day reports in paper format; and

- Submitting annual progress reports within 60 days of the anniversary of the date that the IND went into effect (the date clinical studies were permitted to begin) [21 CFR 312.33].

Secure email between CDER and sponsors is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications (except for 7-day safety reports for INDs not in eCTD format).

The FDA Electronic Submissions Gateway (ESG) is the central transmission point for sending information electronically to the FDA and enables the secure submission of regulatory information for review. If your IND is in eCTD format, you should obtain an ESG account. For additional information, see <http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/>.

If you have any questions, contact Laura Musse, Regulatory Health Project Manager, at (240) 402-3720

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

BADRUL A CHOWDHURY
02/26/2014

2/11/14

PeRC BPCA/Pediatric Study Plan Subcommittee
Meeting Minutes
January 29, 2014

PeRC Members Attending:

- Lynne Yao
- Rosemary Addy
- Hari Cheryl Sachs [REDACTED] NON RESPONSIVE
- George Greeley
- Robert "Skip" Nelson [REDACTED] NON RESPONSIVE
- Jane Inglese
- Wiley Chambers
- Tom Smith
- Karen Davis-Bruno
- Shrikant Pagay
- Lily Mulugeta
- Dianne Murphy [REDACTED] NON RESPONSIVE
- William J. Rodriguez
- Maura O'Leary
- Gregory Reaman [REDACTED] NON RESPONSIVE
- Coleen LoCicero [REDACTED] NON RESPONSIVE
- Peter Starke

BPCA/Initial Pediatric Study Plan

9:00			Biosimilars Presentation	Leah Christl
9:35			Suggested indications to the list of Full Waivers (Review & Accept)	
9:45	IND	(b) (4)	Codeine Polisterix/Chlorpheramine Polisterix iPSP (Full Waiver)	(b) (4) of cough and upper respiratory (b) (4) common cold (b) (4)

[REDACTED] NON RESPONSIVE

Codeine Polisterix/Chlorpheramine iPSP (Full Waiver)

- Proposed Indication: (b) (4) of cough and upper respiratory (b) (4) common cold and inhaled allergens
- PeRC Recommendations:

- See comments on the iPSP sent to the Division on January 29, 2014.

○ [REDACTED] (b) (4)

- [REDACTED] (b) (4)

○ [REDACTED] However, these plans may be amended in the future based several factors including changes to the cough and cold monograph.

- [REDACTED] (b) (4)

[REDACTED]

[REDACTED]

NON RESPONSIVE

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

/s/

GEORGE E GREELEY
02/11/2014

5/30/14



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND (b) (4)

ADVICE/INFORMATION REQUEST

Tris Pharma, Inc
2033 Route 130
Monmouth Junction, NJ 08852

Attention: William Scott Groner
Director of Regulatory Affairs

Dear Mr. Groner:

Please refer to your New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for codeine polisterex and chlorpheniramine polisterex.

We also refer to your submission dated December 3, 2014, containing the Initial Pediatric Study Plan (iPSP) for codeine polisterex and chlorpheniramine polisterex for the (b) (4) relief of cough and to your amendments dated March 28, and May 9, 2014, containing revised iPSPs. We acknowledge receipt of your May 15, 2014 amendment containing your Agreed iPSP.

We have completed our review of the submission, and we confirm our agreement to your Agreed iPSP. We have no further comments on your PSP. A clean copy of the Agreed iPSP is attached for your reference.

As sponsor of this IND, you are responsible for compliance with the FDCA (21 U.S.C. §§ 301 et. seq.) as well as the implementing regulations [Title 21 of the Code of Federal Regulations (CFR)]. A searchable version of these regulations is available at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm>. Your responsibilities include:

- Reporting any unexpected fatal or life-threatening suspected adverse reactions to this Division no later than 7 calendar days after initial receipt of the information [21 CFR 312.32(c)(2)].

If your IND is in eCTD format, submit 7-day reports electronically in eCTD format via the FDA Electronic Submissions Gateway (ESG). To obtain an ESG account, see information at the end of this letter.

If your IND is not in eCTD format:

- you should submit 7-day reports by a rapid means of communication, preferably by facsimile or email. You should address each submission to the Regulatory Project Manager and/or to the Chief, Project Management Staff;
- if you intend to submit 7-day reports by email, you should obtain a secure email account with FDA (see information at the end of this letter);
- if you also send copies of these reports to your IND, the submission should have the same date as your facsimile or email submission and be clearly marked as “Duplicate.”
- Reporting any (1) serious, unexpected suspected adverse reactions, (2) findings from other clinical, animal, or in-vitro studies that suggest significant human risk, and (3) a clinically important increase in the rate of a serious suspected adverse reaction to this Division and to all investigators no later than 15 calendar days after determining that the information qualifies for reporting [21 CFR 312.32(c)(1)]. If your IND is in eCTD format, submit 15-day reports to FDA electronically in eCTD format. If your IND is not in eCTD format, you may submit 15-day reports in paper format; and
- Submitting annual progress reports within 60 days of the anniversary of the date that the IND went into effect (the date clinical studies were permitted to begin) [21 CFR 312.33].

If you have any questions, contact Laura Musse, Regulatory Health Project Manager, at (240) 402-3720

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

45 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page