

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-437

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 22-437

SUPPL #

HFD # 150

Trade Name Trelstar 22.5 mg; Every 24 weeks

Generic Name triptorelin pamoate for injectable suspension

Applicant Name Watson Laboratories, Inc.

Approval Date, If Known March 10, 2010

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)(1)

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

YES NO

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

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

d) Did the applicant request exclusivity?

YES NO

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

3 years

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# 020715 Trelstar Depot; 3.75 mg

NDA# 021288 Trelstar LA; 11.25 mg

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:

DEB-TRI6M-301

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:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

DEB-TRI6M-301

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

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

Investigation #1		!
		!
IND # 28,547	YES <input checked="" type="checkbox"/>	! NO <input type="checkbox"/>
		! Explain:

Investigation #2		!
		!
IND #	YES <input type="checkbox"/>	! NO <input type="checkbox"/>
		! Explain:

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

Investigation #1

YES

Explain:

!

!

! NO

! Explain:

Investigation #2

YES

Explain:

!

!

! NO

! Explain:

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

YES

NO

If yes, explain:

=====

Name of person completing form: Kim J. Robertson

Title: Consumer Safety Officer

Date: March 4, 2010

Name of Office/Division Director signing form: Robert L. Justice, M.D.

Title: Division Director

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

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22437

ORIG-1

WATSON
LABORATORIES
INC

TRELSTAR (b) (4)

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

/s/

KIM J ROBERTSON

03/11/2010

Exclusivity Form; NDA 022437; Trelstar 22.5 mg; Watson Labs

ROBERT L JUSTICE

03/11/2010

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 22-437 Supplement Number: _____ NDA Supplement Type (e.g. SE5): _____

Division Name: Division of Drug Oncology Products PDUFA Goal Date: October 19, 2009 Stamp Date: 9/12/2008

Proprietary Name: Trelstar (b) (4)

Established/Generic Name: triptorelin pamoate for Injection Suspension; 22.5 mg

Dosage Form: Suspension

Applicant/Sponsor: Watson Laboratories, Inc.

Indication(s) previously approved (please complete this question for supplements and Type 6 NDAs only):

- (1) _____
- (2) _____
- (3) _____
- (4) _____

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 1
(Attach a completed Pediatric Page for each indication in current application.)

Indication: The palliative treatment of advanced prostate cancer.

Q1: Is this application in response to a PREA PMR? Yes Continue
No Please proceed to Question 2.

If Yes, NDA/BLA#: _____ Supplement #: _____ PMR #: _____

Does the division agree that this is a complete response to the PMR?

- Yes. Please proceed to Section D.
- No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

Q2: Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW active ingredient(s) (includes new combination); indication(s); dosage form; dosing regimen; or route of administration?*

(b) No. PREA does not apply. **Skip to signature block.**

* **Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.**

Q3: Does this indication have orphan designation?

- Yes. PREA does not apply. **Skip to signature block.**
- No. Please proceed to the next question.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

Yes: (Complete Section A.)

No: Please check all that apply:

- Partial Waiver for selected pediatric subpopulations (Complete Sections B)
 - Deferred for some or all pediatric subpopulations (Complete Sections C)
 - Completed for some or all pediatric subpopulations (Complete Sections D)
 - Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
 - Extrapolation in One or More Pediatric Age Groups (Complete Section F)
- (Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

Necessary studies would be impossible or highly impracticable because:

- Disease/condition does not exist in children
- Too few children with disease/condition to study
- Other (e.g., patients geographically dispersed): _____

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

			Reason (see below for further detail):			
	minimum	maximum	Not feasible [#]	Not meaningful therapeutic benefit [*]	Ineffective or unsafe [†]	Formulation failed ^Δ
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief**

justification):**#** Not feasible:

- Necessary studies would be impossible or highly impracticable because:
- Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____

***** Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.*)

 Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for selected pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †
Population		minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Date studies are due (mm/dd/yy): _____							

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

* Other Reason: _____

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?.	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:			
Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as

pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:					
Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

Kim J. Robertson, CSO

(Revised: 6/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.

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

/s/

Kim Robertson
6/1/2009 03:07:16 PM
Pediatric Page NDA 22-437 TRELSTAR '09

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 22-437 BLA #	NDA Supplement # N/A BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Trelstar® 22.5 mg; Every 24 weeks Established/Proper Name: (triptorelin pamoate for injectable Dosage Form: Suspension		Applicant: Watson Laboratories, Inc. Agent for Applicant (if applicable):
RPM: Kim J. Robertson		Division: HFD-150
<p>NDA: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA # (s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.</p> <p style="text-align: center;"><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p> <p><u>On the day of approval</u>, check the Orange Book again for any new patents or pediatric exclusivity.</p>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>March 11, 2010</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; July 10, 2009

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, were promotional materials received? Note: For accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see 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): 3</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 <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request</p> <p>Comments:</p>	
<p>❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes, date
<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 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 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 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 type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	<input type="checkbox"/> N/A (no paragraph IV certification) <input 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>	<input type="checkbox"/> Yes <input type="checkbox"/> No
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ³	Yes
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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) 2nd Cycle-AP; March 10, 2010; 1 st Cycle-CR; July 10, 2009;
---	--

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. 	March 5, 2010
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	July 10, 2009
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A

³ Fill in blanks with dates of reviews, letters, etc.
Version: 12/4/09

<ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use (<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 checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in ttrack-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 	March 5, 2010
<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>) 	March 3, 2010
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input type="checkbox"/> RPM <input type="checkbox"/> DMEDP <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC March 08, 2010 <input type="checkbox"/> CSS <input checked="" type="checkbox"/> Other reviews DMEPA: March 3, 2010; SEALD: March 2, 2010
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>) 	N/A
<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 in on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC _____ If PeRC review not necessary, explain: <u>PeRC reviewed submission in 1st Cycle May 13, 2009. PeRC not needed 2nd cycle, because information did not change</u> • Pediatric Page (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>) 	<input type="checkbox"/> Verified, statement is acceptable
<ul style="list-style-type: none"> ❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>) 	Included
<ul style="list-style-type: none"> ❖ Internal memoranda, telecons, etc. 	N/A

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 12/4/09

❖ Minutes of Meetings		
• Pre-Approval Safety Conference (<i>indicate date of mtg; approvals only</i>)		X Not applicable
• 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 type="checkbox"/> No mtg
• EOP2 meeting (<i>indicate date of mtg</i>)		<input type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilot programs) (<i>indicates dates</i>)		N/A
❖ 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 March 10, 2010
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)		<input type="checkbox"/> None March 5, 2010
PMR/PMC Development Templates (<i>indicate total number</i>)		<input checked="" type="checkbox"/> None
Clinical Information⁵		
❖ Clinical Reviews		
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)		See CDTL Review
• Clinical review(s) (<i>indicate date for each review</i>)		February 22, 2010
• 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>)		Addressed in June 2009 Clinical Review of 1 st Cycle
❖ 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 checked="" type="checkbox"/> Not applicable
❖ Risk Management		
• REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>)		N/A
• REMS Memo (<i>indicate date</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
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)		<input checked="" type="checkbox"/> None requested

⁵ Filing reviews should be filed with the discipline reviews.
Version: 12/4/09

Clinical Microbiology		<input checked="" type="checkbox"/> None
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)		<input type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)		<input type="checkbox"/> None
Biostatistics		<input checked="" type="checkbox"/> None
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)		<input type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)		<input type="checkbox"/> None
Statistical Review(s) (<i>indicate date for each review</i>)		<input 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 March 05, 2010
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)		<input checked="" type="checkbox"/> None
Nonclinical		<input checked="" type="checkbox"/> None
❖ Pharmacology/Toxicology Discipline Reviews		
• ADP/T Review(s) (<i>indicate date for each review</i>)		<input type="checkbox"/> None
• Supervisory Review(s) (<i>indicate date for each review</i>)		<input type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)		<input type="checkbox"/> None
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)		<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)		<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting		<input type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)		<input 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 Memo; March 08, 2010
• Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>)		<input checked="" type="checkbox"/> None March 4, 2010
❖ 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</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	Addressed in CMC Review during 1 ST Review Cycle; June 16, 2009
<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>)	Date completed: March 8, 2010 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</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

Appendix A to Action Package Checklist

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

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

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

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

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

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

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

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

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

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22437

ORIG-1

WATSON
LABORATORIES
INC

TRELSTAR (b) (4)

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

/s/

KIM J ROBERTSON

03/11/2010

Action Package Checklist; NDA 022437; Trelstar 22.5 mg; Watson Labs; 2nd Review Cycle

Memorandum

To: NDA 22-437
From: Sarah Pope Miksinski, Ph.D.
Date: 3/8/2010
Re: NDA 22-437/11-SEP-2009 resubmission

NDA 22-437 was resubmitted on 11-SEP-2009 following a 10-JUL-2009 Complete Response letter. CMC review #1 (dated 16-JUN-2009) for the original 12-SEP-2008 submission identified a number of CMC deficiencies and captured an overall withhold recommendation from the Office of Compliance (OC). CMC review #2 (dated 04-MAR-2010) captured the resolution of the previous CMC deficiencies, and the NDA was recommended for approval from a CMC perspective pending minor labeling revisions and an acceptable (and updated) recommendation from the Office of Compliance.

This memo serves to update the status of the CMC review for the 11-SEP-2009 resubmission. Acceptable labeling (PI, container/carton labels) was submitted by the Applicant on 03-MAR-2010, and an acceptable recommendation was received from the Office of Compliance on 08-MAR-2010.

There are no outstanding CMC issues for this NDA, and this NDA is now recommended for approval from the CMC perspective.

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22437

ORIG-1

WATSON
LABORATORIES
INC

TRELSTAR (b) (4)

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

/s/

Sarah Pope Miksinski
03/08/2010

From: Robertson, Kim
Sent: Wednesday, March 03, 2010 7:28 PM
To: 'Melissa.Luras@watson.com'
Subject: RE: Cherri Petrie, Watson NDA 022437

Importance: High

Attachments: Trelstar Label NDA 22437 post.doc; 303294-carton-mixject-22-5.pdf

Hello Melissa:

Would you please convey the following information to Cherri, as it contains very important information?

Cherri:

We had a labeling meeting today with regard to the Trelstar label (please see attached). The division has made proposals that we will need Watson to address right away.

Also, with regard to your March 3, 2010 submission of the vial/carton labels, our CMC discipline reviewed the materials and stated that your Carton Mixject Label (attached) should read as follows, "Do Not Freeze TRELSTAR with MIXJECT"

The verbiage 'TRELSTAR with MIXJECT' succeeding 'Do Not Freeze' needs to be visible on the label. Watson may believe that the "Do Not Freeze" language alone clearly communicates the intent, but the CMC reviewers do not.

We therefore ask that you review the attached documents and provide us with an updated PI and Carton Mixject Label no later than Friday, 2:00PM, EST.

Thank you Melissa and Cherri,
Kim

From: Melissa.Luras@watson.com [mailto:Melissa.Luras@watson.com]
Sent: Tuesday, March 02, 2010 7:09 PM
To: Robertson, Kim
Subject: RE: Cherri Petrie, Watson NDA 022437

Hi Kim,

Thank you for your comments. We will submit our response with the proposed label storage statement first thing tomorrow.

Additionally, you informed Wendy Despain that there was a pending status for one of the sites in the GMP database. Do you have an update on whether the GMP pending status has been resolved and if not which site is involved?

Best regards,

Melissa

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

To Melissa.Luras@watson.com

cc

03/02/2010 03:54 PM

Subject RE: Cherri Petrie, Watson NDA 022437

Hello Melissa:

If you would, please let Cherri know right away of the following response from our CMC reviewers with regard to her question as it pertains to NDA 22-437; Trelstar:

- Your proposed label storage statement is acceptable to ONDQA in that reference is made to USP CRT; the stability studies do not indicate significant thermal lability for the drug product; and the "do not freeze" statement is on the carton label in the mixject kit.

Thank you,
Kim

From: Melissa.Luras@watson.com [mailto:Melissa.Luras@watson.com]
Sent: Tuesday, March 02, 2010 12:48 PM
To: Robertson, Kim
Subject: RE: Cherri Petrie, Watson NDA 022437

Thank you Kim. We look forward to hearing from you.

Best regards,

Melissa Luras
Proprietary Regulatory Affairs, CMC
Watson Laboratories, Inc. - Salt Lake City, UT
Phone: 801-588-6729
Fax: 801-588-6232
email: Melissa.Luras@watson.com
"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

03/02/2010 10:22 AM

To: Melissa.Luras@watson.com
cc

Subject RE: Cherri Petrie, Watson NDA 022437

Thank you Melissa for this e-mail on behalf of Cherri. I will forward this to my chemist reviewers right away. I will provide feedback fro Cherri as soon as I hear from them.

Regards,
Kim

From: Melissa.Luras@watson.com [mailto:Melissa.Luras@watson.com]
Sent: Tuesday, March 02, 2010 12:18 PM
To: Robertson, Kim
Subject: Cherri Petrie, Watson NDA 022437

Dear Kim,

As discussed in our phone conversation earlier today, we are providing an email response to FDA's information request in advance of our formal submission. Please forward this information to the Chemistry Reviewer for their review and consideration.

In the information request, FDA provided the following comments on the carton and container labels:

The storage statement should be the same on the vial/carton labels and on the package insert. Since your stability studies support storage at USP controlled room temperature, we recommend that the package insert include the "excursions to 15-30°C" statement as on the vial/carton labels. In addition, the carton - mixject label should include the statement "Do not freeze TRELSTAR with MIXJECT". Please provide revised vial/carton labels in conjunction with a revised package insert.

Watson is currently preparing a written response to the agency, for submission on Tuesday March 2, 2010. In the interim, we would like to provide additional information for clarification on the points raised in the information request.

- It is Watson's intention to have the storage statement harmonized on all printed components, as noted in the request. For this reason, the vial/carton labels had already been revised - to harmonize with the storage statement listed on the package insert. These revisions have already been submitted to the printing vendor. Therefore, all components are aligned and prepared with the following storage statement: "Store at 20-25°C (68-77°F). [See USP Controlled Room Temperature.]" Watson is moving to this standardized storage statement across our product lines, in order to provide reference to the complete storage information presented in the USP text.
- Regarding the second point, the MIXJECT carton label and the MIXJECT label both include the following instructions in capitalized format, "DO NOT FREEZE." Watson believes this language clearly communicates the intended message.

As noted above and in our phone conversation, Watson is preparing a written response to the agency, for submission on Tuesday March 2, 2010. This response will include the information noted above, along with revised labeling for the affected components. Please advise if there are any concerns with this approach.

Should you have any additional questions or comments, please do not hesitate to contact me at the number provided below.

Sincerely,

Cherri Petrie
(801) 588-6633

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22437

ORIG-1

WATSON
LABORATORIES
INC

TRELSTAR (b) (4)

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

/s/

KIM J ROBERTSON

03/04/2010

Trelstar Outgoing Communication NDA 022437



NDA 022437

INFORMATION REQUEST

Watson Laboratories, Inc.
577 Chipeta Way
Salt Lake City, UT 84108

Attention: Wendy DeSpain, BS, MBA, RAC
Associate Director, Regulatory

Dear Ms. DeSpain:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Trelstar® (triptorelin pamoate for injectable suspension), 22.5 mg.

We also refer to your May 4, 2009 submission, containing revised carton and container labels that were updated at the request of the Agency in an April 22, 2009 teleconference.

We have reviewed the referenced material and have the following comment and request for information:

1. The storage statement should be the same on the vial/carton labels and on the package insert. Since your stability studies support storage at USP controlled room temperature, we recommend that the package insert include the "excursions to 15-30°C" statement as on the vial/carton labels. In addition, the carton - mixject label should include the statement "Do not freeze TRELSTAR with MIXJECT". Please provide revised vial/carton labels in conjunction with a revised package insert.

If you have any questions, call Kim J. Robertson, Consumer Safety Officer, at (301) 796-1441.

Sincerely,

{See appended electronic signature page}

Sarah C. Pope, Ph.D.
Branch Chief
Division of Pre-Marketing Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22437

ORIG-1

WATSON
LABORATORIES
INC

TRELSTAR (b) (4)

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

/s/

Sarah Pope Miksinski
03/01/2010

From: Robertson, Kim
Sent: Monday, March 01, 2010 3:23 PM
To: 'Wendy.DeSpain@watson.com'
Cc: 'Burke.Byrne@watson.com'
Subject: RE: NDA 22-437; Trelstar PI

Importance: High
Hi Wendy/Burke:

In case I didn't respond to this question regarding..... “We were wondering if you would be able to ask your clinical reviewer why the ^{(b) (4)} number was removed from Table 7 (pg. 18, "Summary of TRELSTAR Clinical Studies") and replaced with "not applicable". We would just like a better understanding of the reasoning.”

The response from the clinical reviewer was simply this.....the RR doesn't represent the primary endpoint; hence the reason the number was removed from the Table 7.

**Thanks,
Kim**

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Friday, February 26, 2010 1:47 PM
To: Robertson, Kim
Subject: RE: NDA 22-437; Trelstar PI

Thanks Kim! I wanted to let you know that I am traveling next week so I will be out of the office. However, I will be checking e-mail and voice mail. You can also reach me on my cell at 801-819-4401 at any time. If something is urgent and you can't reach me, please call Burke Byrne. His number is 801-588-6517 and his e-mail is burke.byrne@watson.com

Thanks again,
Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

To Wendy.DeSpain@watson.com
cc

02/26/2010 08:42 AM

Subject RE: NDA 22-437; Trelstar PI

I will ask and let you know as soon as I find out.

Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Thursday, February 25, 2010 6:14 PM
To: Robertson, Kim
Subject: RE: NDA 22-437; Trelstar PI

Hi Kim,

No problem.

We were wondering if you would be able to ask your clinical reviewer why the (b) (4) number was removed from Table 7 (pg. 18, "Summary of TRELSTAR Clinical Studies") and replaced with "not applicable". We would just like a better understanding of the reasoning.

Thanks so much,
Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

02/25/2010 03:44 PM

To Wendy.DeSpain@watson.com
cc

Subject RE: NDA 22-437; Trelstar PI

Yes please.
Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Thursday, February 25, 2010 5:24 PM
To: Robertson, Kim
Subject: Re: NDA 22-437; Trelstar PI

Hi Kim,

For the submission on Monday, will you need the label in SPL format?

Thanks,

Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

02/25/2010 02:27 PM

To Wendy.DeSpain@watson.com
cc

Subject NDA 22-437; Trelstar PI

Hello Wendy:

Please review your Trelstar PI inclusive of our FDA revisions. Please review the PI and return the label back to us no later than **Monday, March 1, 2010**.

Please note that there may be additional comments forthcoming with regard to your PI from our SEALD, DMEPA, and DDMAC colleagues.

Regards,

Kim

<<Trelstar PI 2-23-10 post.doc>>

Kim J. Robertson

Consumer Safety Officer

Division of Drug Oncology Products

Phone: (301) 796-1441

Fax: (301) 796-9845[attachment "Trelstar PI 2-23-10 post.doc" deleted by Wendy Despain/Salt Lake City/Watson]

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22437

ORIG-1

WATSON
LABORATORIES
INC

TRELSTAR (b) (4)

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

/s/

KIM J ROBERTSON

03/04/2010

Trelstar Outgoing Communications; NDA 022437

From: Robertson, Kim
Sent: Friday, February 19, 2010 6:58 PM
To: 'Wendy.DeSpain@watson.com'
Subject: RE: Trelstar NDA 22-437
[Thank you so much. Enjoy your weekend.](#)

[Kim](#)

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Friday, February 19, 2010 6:48 PM
To: Robertson, Kim
Subject: RE: Trelstar NDA 22-437

Hi Kim,

Great. Thanks so much.

Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

To Wendy.DeSpain@watson.com

cc

02/19/2010 03:36 PM

Subject RE: Trelstar NDA 22-437

[Wendy, please disregard this e-mail. I noticed that Watson did in fact submit revised C&C labeling on May 4, 2009 that reflects the frequency of TRELSTAR use indicated in WEEKS displayed prominently on the principal display panel.](#)

[Thank you,](#)
[Kim](#)

From: Robertson, Kim
Sent: Friday, February 19, 2010 3:41 PM
To: 'Wendy.DeSpain@watson.com'

Subject: RE: Trelstar NDA 22-437

Importance: High

Hello Wendy:

Can you please confirm for me that Watson Labs has not submitted any new/ updated carton and container labels, since the September 12, 2008 submission of the NDA?

Thank you,
Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Wednesday, February 10, 2010 5:55 PM
To: Robertson, Kim
Subject: RE: Trelstar NDA 22-437

Hi Kim,

Thanks so much for your help. I hope that you stay safe in the nasty weather.

Best regards,
Wendy
"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

02/10/2010 03:34 PM

To Wendy.DeSpain@watson.com
cc

Subject RE: Trelstar NDA 22-437

Hello Wendy:

Correspondence is going to be very hit-or-miss right about now, given the severe weather conditions in our area. The federal government has been on official shut down for the past 3 days, so none of my colleagues or I have seen one another since last week. I will forward this question to my CMC reviewers of your NDA for their feedback. I assure you, if the issues haven't been addressed, or we have additional issues, we will certainly let you know.

Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]

Sent: Tuesday, February 09, 2010 5:19 PM

To: Robertson, Kim

Subject: Trelstar NDA 22-437

Hi Kim,

I had a question that I was hoping you could answer:

The Complete Response for the Trelstar 22.5 mg NDA 22-437 noted that there were several withhold recommendations regarding facility inspections that needed to be addressed. We believe that these have been taken care of. Would you be able to confirm that there are indeed no outstanding withhold recommendations that would affect the approval of the Trelstar 22.5 mg NDA?

Thanks so much,
Wendy

From: Robertson, Kim

Sent: Tuesday, February 23, 2010 1:30 PM

To: 'Wendy.DeSpain@watson.com'

Subject: RE: Trelstar NDA 22-437

Currently, I have not heard of anything that will hinder our review time line for this NDA. I will however, pass this question on to my entire team during a team meeting. You are correct in that regard with PDUFA dates being extended, due to our blizzard. I have heard that it will affect quite a few applications.

Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]

Sent: Tuesday, February 23, 2010 10:55 AM

To: Robertson, Kim

Subject: RE: Trelstar NDA 22-437

Hi Kim,

We have heard several reports of delays and extensions to PDUFA dates due to the recent weather issues and a hole in the roof of the CDER building. Do you know if the FDA response to our Trelstar application will be delayed as a result of this?

Thanks,
Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

To Wendy.DeSpain@watson.com

cc

02/19/2010 04:58 PM

Subject RE: Trelstar NDA 22-437

Thank you so much. Enjoy your weekend.

Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Friday, February 19, 2010 6:48 PM
To: Robertson, Kim
Subject: RE: Trelstar NDA 22-437

Hi Kim,

Great. Thanks so much.

Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

02/19/2010 03:36 PM

To Wendy.DeSpain@watson.com
cc

Subject RE: Trelstar NDA 22-437

Wendy, please disregard this e-mail. I noticed that Watson did in fact submit revised C&C labeling on May 4, 2009 that reflects the frequency of TRELSTAR use indicated in WEEKS displayed prominently on the principal display panel.

Thank you,
Kim

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Subject: RE: Trelstar NDA 22-437
Importance: High

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Thank you,
Kim

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Best regards,
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02/10/2010 03:34 PM

To Wendy.DeSpain@watson.com
cc

Subject RE: Trelstar NDA 22-437

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Correspondence is going to be very hit-or-miss right about now, given the severe weather conditions in our area. The federal government has been on official shut down for the past 3 days, so none of my colleagues or I have seen one another since last week. I will forward this question to my CMC reviewers of your NDA for their feedback. I assure you, if the issues haven't been addressed, or we have additional issues, we will certainly let you know.

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To: Robertson, Kim
Subject: Trelstar NDA 22-437

Hi Kim,

I had a question that I was hoping you could answer:

The Complete Response for the Trelstar 22.5 mg NDA 22-437 noted that there were several withhold recommendations regarding facility inspections that needed to be addressed. We believe that these have been taken care of. Would you be able to confirm that there are indeed no outstanding withhold recommendations that would affect the approval of the Trelstar 22.5 mg NDA?

Thanks so much,
Wendy

From: Robertson, Kim
Sent: Thursday, February 25, 2010 4:28 PM
To: 'Wendy.DeSpain@watson.com'
Subject: NDA 22-437; Trelstar PI

Importance: High

Attachments: Trelstar PI 2-23-10 post.doc

Hello Wendy:

Please review your Trelstar PI inclusive of our FDA revisions. Please review the PI and return the label back to us no later than **Monday, March 1, 2010**. Please note that there may be additional comments forthcoming with regard to your PI from our SEALD, DMEPA, and DDMAC colleagues.

Regards,
Kim



Trelstar PI
3-10 post.doc

*Kim J. Robertson
Consumer Safety Officer
Division of Drug Oncology Products
Phone: (301) 796-1441
Fax: (301) 796-9845*

From: Robertson, Kim
Sent: Thursday, February 25, 2010 5:18 PM
To: 'Wendy.DeSpain@watson.com'
Subject: RE: NDA 22-437; Trelstar PI
[Thank you Wendy.](#)
[Kim](#)

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Thursday, February 25, 2010 4:51 PM
To: Robertson, Kim
Subject: Re: NDA 22-437; Trelstar PI

Hi Kim,

Thanks. We will review and submit by Monday.

Best regards,
Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

To Wendy.DeSpain@watson.com

cc

02/25/2010 02:27 PM

Subject NDA 22-437; Trelstar PI

Hello Wendy:

Please review your Trelstar PI inclusive of our FDA revisions. Please review the PI and return the label back to us no later than **Monday, March 1, 2010**.

Please note that there may be additional comments forthcoming with regard to your PI from our SEALD, DMEPA, and DDMAC colleagues.

Regards,

Kim

<<Trelstar PI 2-23-10 post.doc>>

Kim J. Robertson

Consumer Safety Officer

Division of Drug Oncology Products

Phone: (301) 796-1441

Fax: (301) 796-9845[attachment "Trelstar PI 2-23-10 post.doc" deleted by Wendy Despain/Salt Lake City/Watson]

From: Robertson, Kim
Sent: Tuesday, January 26, 2010 7:11 PM
To: 'Wendy.DeSpain@watson.com'
Subject: Corrected Trelstar Label...

Importance: High

Attachments: January 26 2010 Trelstar Class 2 Resub Label (post) .doc
Wendy, please disregard the first label that I sent to you.....please use **this** label to make any comments/revisions and provide us with a return label no later than **February 3, 2010**.

Thank you,
Kim



January 26
0 Trelstar Cla:

*Kim J. Robertson
Consumer Safety Officer
Division of Drug Oncology Products
Phone: (301) 796-1441
Fax: (301) 796-9845*

From: Robertson, Kim
Sent: Tuesday, January 26, 2010 7:03 PM
To: 'Wendy.DeSpain@watson.com'
Subject: RE: NDA 21-288 Trelstar with MixJect

Importance: High

Attachments: January 26 2010 Trelstar Class 2 Resub Label post.doc

[Wendy:](#)

Please see the attached Trelstar label. Please review and provide us with a return label no later than **February 3, 2010**.

Thank you,
Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Wednesday, January 20, 2010 1:28 PM
To: Robertson, Kim
Subject: RE: NDA 21-288 Trelstar with MixJect

No problem.

Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

To Wendy.DeSpain@watson.com
cc

01/20/2010 09:36 AM

Subject RE: NDA 21-288 Trelstar with MixJect

Thank you again Wendy. I will forward this along as well.

Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Wednesday, January 20, 2010 11:37 AM
To: Robertson, Kim
Subject: RE: NDA 21-288 Trelstar with MixJect

Hi Kim,

The "kit" is packaged in a molded plastic tray which contains the Mixject device, the sterile water for injection, and the Trelstar vial. The "108169 label-tray-mixject" label is located on the top outside (flat part) of the plastic tray. The syringe with the sterile water has a separate label that was included in the pdf entitled "vial-label-sterile-water". I have attached a picture that may help.

Best regards,
Wendy

"Robertson, Kim" <Kim.Robertson@fda hhs.gov>

01/19/2010 03:45 PM

To Wendy.DeSpain@watson.com

cc

Subject RE: NDA 21-288 Trelstar with MixJect

Wendy, one more question from my colleague:

Regarding the pdf file entitled "108169 label-tray-mixject"... where exactly are these labels on the product? On the syringe that contains the sterile water?

**Thank you,
Kim**

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Monday, January 18, 2010 9:59 AM
To: Robertson, Kim
Subject: Re: NDA 21-288 Trelstar with MixJect

Hi Kim,

For the trade name change for Trelstar LA (NDA 21-288) and Trelstar Depot (NDA 20-715), we submitted labels for the vial and two cartons (with Mixject and without) on May 5, 2009. The other kit labels, which include the Mixject tray label and sterile water for injection label, were not submitted since they did not change. I have attached the vial and carton labels.

For Trelstar 22.5 mg (NDA 22-437) we submitted labels for all kit components on September 12, 2010 (Sequence 0000; tray and sterile water labels) and May 4, 2009 (Sequence 0011; carton and vial labels). I have also attached these labels.

Please let me know if you need anything else.

Best regards,

Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

01/15/2010 02:03 PM

To Wendy.DeSpain@watson.com

cc

Subject NDA 21-288 Trelstar with MixJect

Hello Wendy:

I'm being asked by one of our reviewers in our OSE group if Watson ever submitted labels for the individual components within the kit? They readily see the Trelstar carton.

Please advise.

Thanks,

Kim

Kim J. Robertson

Consumer Safety Officer

Division of Drug Oncology Products

Phone: (301) 796-1441

Fax: (301) 796-9845

From: Robertson, Kim

Sent: Wednesday, January 20, 2010 11:36 AM

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01/19/2010 03:45 PM

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Best regards,

Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

01/15/2010 02:03 PM

To Wendy.DeSpain@watson.com

cc

Subject NDA 21-288 Trelstar with MixJect

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Please advise.

Thanks,

Kim

Kim J. Robertson

Consumer Safety Officer

Division of Drug Oncology Products

Phone: (301) 796-1441

Fax: (301) 796-9845

From: Robertson, Kim

Sent: Monday, January 18, 2010 9:55 PM

To: 'Wendy.DeSpain@watson.com'

Subject: RE: NDA 21-288 Trelstar with MixJect

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Regards,
Kim

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Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov>

To Wendy.DeSpain@watson.com

cc

01/15/2010 02:03 PM

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Please advise.

Thanks,

Kim

Kim J. Robertson

Consumer Safety Officer

Division of Drug Oncology Products

Phone: (301) 796-1441

Fax: (301) 796-9845

From: Robertson, Kim
Sent: Friday, January 15, 2010 4:04 PM
To: 'Wendy.DeSpain@watson.com'
Subject: NDA 21-288 Trelstar with MixJect

Importance: High
Hello Wendy:

I'm being asked by one of our reviewers in our OSE group if Watson ever submitted labels for the individual components within the kit? They readily see the Trelstar carton.

Please advise.

Thanks,
Kim

*Kim J. Robertson
Consumer Safety Officer
Division of Drug Oncology Products
Phone: (301) 796-1441
Fax: (301) 796-9845*

REQUEST FOR CONSULTATION

TO (Office/Division): Patrick Marroum CDER/OPS/ONDQA,
Angelica Dorantes CDER/OPS/ONDQA

FROM (Name, Office/Division, and Phone Number of Requestor): Debbie
Mesmer, ONDQA, 301-796-4023 on behalf of Terrance
Ocheltree, ONDQA

DATE November 30, 2009	IND NO.	NDA NO. 22-437	TYPE OF DOCUMENT NDA re-submission	DATE OF DOCUMENT Letter date Sept. 10, 2009; received Sept. 11, 2009
---------------------------	---------	-------------------	---------------------------------------	--

NAME OF DRUG Trelstar (triptorelin pamoate for injectable suspension)	PRIORITY CONSIDERATION Class 2 resubmission	CLASSIFICATION OF DRUG Oncology	DESIRED COMPLETION DATE PDUFA date is March 11, 2010
---	--	------------------------------------	--

NAME OF FIRM: Watson Labs

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input checked="" type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: We are requesting a Biopharmaceutics review for resubmitted NDA 22-437:

Items 11-13 of the CR letter dated 07/10/09 were comments regarding the IVIVC and dissolution specification based on the ClinPharm Review dated 06/25/09 (H.Mahayni). The applicant responded to these comments in the N015 amendment dated 09/10/09. There may also be supporting information in the N-013 amendment dated 07/09/09. The CMC reviewer requests a conclusion or comments on items 11-13 in order to complete his review. The submissions are electronic. \\CDSESUB1\EVSPROD\NDA022437. Please contact Debbie Mesmer regarding access to review materials, 301.796.4023. Please contact Mike Adams, CMC reviewer, for questions regarding the application.

SIGNATURE OF REQUESTOR
{See appended electronic signature page}

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22437

ORIG-1

WATSON
LABORATORIES
INC

TRELSTAR (b) (4)

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/s/

DEBORAH M MESMER
11/30/2009

TERRANCE W OCHELTRREE
11/30/2009



NDA 022437

ACKNOWLEDGE CLASS 2 RESPONSE

Watson Laboratories, Inc.
577 Chipeta Way
Salt Lake City, UT 84108

Attention: Wendy DeSpain, BS, MBA, RAC
Associate Director, Regulatory

Dear Ms. DeSpain:

We acknowledge receipt on September 11, 2009 of your September 10, 2009 resubmission to your new drug application for Trelstar® (triptorelin pamoate for injectable suspension), 22.5 mg.

We consider this a complete, Class 2 response to our July 10, 2009 action letter. Your response to the CMC information constitutes major amendments. Therefore, the user fee goal date is March 11, 2010.

If you have any questions, call Kim J. Robertson, Consumer Safety Officer, at (301) 796-1441.

Sincerely,

{See appended electronic signature page}

Kim J. Robertson
Consumer Safety Officer
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22437

ORIG-1

WATSON
LABORATORIES
INC

TRELSTAR (b) (4)

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/s/

KIM J ROBERTSON

10/29/2009

Acknowledgement of Class 2 Resubmission for NDA 22-437; Trelstar



NDA 22-437

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Watson Laboratories, Inc.
577 Chipeta Way
Salt Lake City, Utah 84108

ATTENTION: Wendy DeSpain, BS., M.B.A., R.A.C.
Associate Director, Proprietary Regulatory Affairs

Dear Ms. DeSpain:

Please refer to your New Drug Application (NDA) dated September 12, 2008, received September 12, 2008, submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for Triptorelin Pamoate for Injectable Suspension 22.5 mg.

We also refer to your May 4, 2009, correspondence, received May 5, 2009, requesting a reconsideration of the proposed proprietary name, Trelstar.

We have completed our review of this proposed proprietary name and have concluded that the proposed proprietary name, Trelstar, is acceptable contingent upon approval of this NDA and your supplements for NDA 21-288/S-015 and NDA 20-715/S-018.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Sandra Griffith, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-2445. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager Kim Robertson at (301) 796-1441.

Sincerely,
See appended electronic signature page

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

Carol Holquist
7/23/2009 12:13:22 PM

ACTION PACKAGE CHECKLIST

Application Information		
NDA # 22-437	NDA Supplement # N/A	If NDA, Efficacy Supplement Type
Proprietary Name: Trelstar® 22.5 mg; Every 24 weeks Established Name: (triptorelin pamoate for injectable suspension) Dosage Form: Suspension		Applicant: Watson Laboratories, Inc.
RPM: Kim J. Robertson		Division: HFD-150 Phone # (301) 796-1441
NDAs: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) (A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)		505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): Provide a brief explanation of how this product is different from the listed drug. <input type="checkbox"/> If no listed drug, check here and explain: Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct. <input type="checkbox"/> Confirmed <input type="checkbox"/> Corrected Date:
❖ User Fee Goal Date: ❖ Action Goal Date (if different)		July 12, 2009 July 10, 2009
❖ Actions		
<ul style="list-style-type: none"> • Proposed action 		<input type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <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
❖ Advertising (<i>approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (<i>indicate dates of reviews</i>)		<input type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 3 NDAs, BLAs and Supplements: <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2 <input type="checkbox"/> Orphan drug designation 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 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 NDAs and NDA Supplements: <input type="checkbox"/> OTC drug Other: Other comments:	
❖ Application Integrity Policy (AIP)	
<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"> Exception for review (<i>file Center Director's memo in Administrative Documents section</i>) OC clearance for approval (<i>file communication in Administrative Documents section</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
<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 	<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"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

❖ Exclusivity	
<ul style="list-style-type: none"> • NDAs: Exclusivity Summary (approvals only) (<i>file Summary in Administrative Documents section</i>) 	N/A
<ul style="list-style-type: none"> • Is approval of this application blocked by any type of exclusivity? <ul style="list-style-type: none"> • NDAs/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> • NDAs: 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>) • NDAs: 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>) • NDAs: 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>) 	<p>No <input type="checkbox"/> Yes</p> <p>No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____</p> <p>No <input type="checkbox"/> Yes If, yes, NDA # _____ and date exclusivity expires: _____</p> <p>No <input type="checkbox"/> Yes If, yes, NDA # _____ and date exclusivity expires: _____</p> <p>No <input type="checkbox"/> Yes If, yes, NDA # _____ and date exclusivity expires: _____</p>
❖ Patent Information (NDAs and NDA supplements 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. • [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). 	<p>21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified</p> <p>21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)</p> <p><input type="checkbox"/> No paragraph III certification Date patent will expire _____</p>
<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>) • [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. <p>Answer the following questions for each paragraph IV certification:</p> <p>(1) Have 45 days passed since the patent owner’s receipt of the applicant’s</p>	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

<p>notice of certification?</p> <p>(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)).</p> <p><i>If “Yes,” skip to question (4) below. If “No,” continue with question (2).</i></p> <p>(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)?</p> <p><i>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).</i></p> <p><i>If “No,” continue with question (3).</i></p> <p>(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?</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)).</p> <p><i>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.</i></p> <p>(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)?</p> <p><i>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).</i></p> <p><i>If “No,” continue with question (5).</i></p> <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</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
--	---

<p>within the 45-day period).</p> <p>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).</p> <p>If “Yes,” a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.</p>	
Summary Reviews	
❖ Summary Reviews (e.g., Office Director, Division Director) (<i>indicate date for each review</i>)	Division Director: July 10, 2009
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (<i>indicate date</i>)	
Labeling	
❖ Package Insert	
<ul style="list-style-type: none"> Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	July 6, 2009
<ul style="list-style-type: none"> Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	June 29, 2009
<ul style="list-style-type: none"> Original applicant-proposed labeling Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	September 12, 2008
❖ Patient Package Insert	N/A
<ul style="list-style-type: none"> Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> Original applicant-proposed labeling Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
❖ Medication Guide	N/A
<ul style="list-style-type: none"> Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> Original applicant-proposed labeling Other relevant labeling (e.g., most recent 3 in class, class labeling) 	
❖ Labels (full color carton and immediate-container labels)	
<ul style="list-style-type: none"> Most-recent division-proposed labels (only if generated after latest applicant submission) 	
<ul style="list-style-type: none"> Most recent applicant-proposed labeling 	May 4, 2009
❖ Labeling reviews and minutes of any labeling meetings (<i>indicate dates of reviews and meetings</i>)	<input type="checkbox"/> DMETS <input type="checkbox"/> DSRCs <input type="checkbox"/> DDMAC <input type="checkbox"/> SEALD <input checked="" type="checkbox"/> Other reviews DMEPA: March 20, 2009 <input type="checkbox"/> Memos of Mtgs

Administrative Documents	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) (<i>indicate date of each review</i>)	May 27, 2009
❖ NDA and NDA supplement approvals only: Exclusivity Summary (<i>signed by Division Director</i>)	X Included
❖ AIP-related documents <ul style="list-style-type: none"> Center Director's Exception for Review memo If AP: OC clearance for approval 	
❖ Pediatric Page (all actions)	X 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>)	X Verified, statement is acceptable
❖ Postmarketing Commitment Studies	<input type="checkbox"/> None
<ul style="list-style-type: none"> Outgoing Agency request for post-marketing commitments (<i>if located elsewhere in package, state where located</i>) Incoming submission documenting commitment 	
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	November 12, 2008; March 23, 2009; June 16, 2009
❖ Internal memoranda, telecons, email, etc.	
❖ Minutes of Meetings	
<ul style="list-style-type: none"> Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) 	N/A
<ul style="list-style-type: none"> Pre-NDA/BLA meeting (<i>indicate date</i>) 	<input type="checkbox"/> No mtg February 19, 2008 & May 14, 2008 (CMC)
<ul style="list-style-type: none"> EOP2 meeting (<i>indicate date</i>) 	X No mtg
<ul style="list-style-type: none"> Other (e.g., EOP2a, CMC pilot programs)—Ofc. Of Surveillance and Epidemiology 	Type C Meeting Minutes- May 19, 2009
❖ Advisory Committee Meeting	X No AC meeting
<ul style="list-style-type: none"> Date of Meeting 48-hour alert or minutes, if available 	
❖ <u>Federal Register</u> Notices, DESI documents, NAS/NRC reports (if applicable)	
CMC/Product Quality Information	
❖ CMC/Product review(s) (<i>indicate date for each review</i>)	June 16, 2009 ; Branch Chief Review: July 9, 2009
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer (<i>indicate date for each review</i>)	X Biopharmaceutics Review June 25, 2009
❖ BLAs: Product subject to lot release (APs only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Environmental Assessment (check one) (original and supplemental applications)	
<ul style="list-style-type: none"> X Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>) 	June 16, 2009
<ul style="list-style-type: none"> <input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>) 	N/A
<ul style="list-style-type: none"> <input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>) 	N/A
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) (<i>indicate date of each review</i>)	June 22, 2009 <input type="checkbox"/> Not a parenteral product
❖ Facilities Review/Inspection	
<ul style="list-style-type: none"> NDAs: Facilities inspections (include EER printout) 	Date completed: July 7, 2009 <input type="checkbox"/> Acceptable X Withhold recommendation

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> • Facility review (<i>indicate date(s)</i>) • Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>) 	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation N/A	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed
Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	Memo to File: May 7, 2009
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	X None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	X No carc
❖ ECAC/CAC report/memo of meeting	N/A
❖ Nonclinical inspection review Summary (DSI)	X None requested
Clinical Information	
❖ Clinical review(s) (<i>indicate date for each review</i>)	Med. Offc. Review: June 29, 2009 ; CDTL Review: July 7, 2009 ; DRUP Review: June 19, 2009
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	Page 15 of Clinical Review
❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)	X None
❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)	X Not needed
❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)	N/A
❖ Risk Management Plan review(s) (including those by OSE) (<i>indicate location/date if incorporated into another review</i>)	N/A
❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date of each review</i>)	X Not needed
❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested
• Clinical Studies	June 29, 2009
• Bioequivalence Studies	N/A
• Clin Pharm Studies	N/A
❖ Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> Combined with Clinical Review dated- June 29, 2009
❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None June 30, 2009

Appendix A to Action Package Checklist

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

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

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

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

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

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

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

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

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

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

/s/

Kim Robertson

7/13/2009 04:21:51 PM

Action Package Checklist for Trelstar (triptorelin pamoate for injectable
suspension) 22.5 mg NDA 22-437 '09

NDA 22-437 (Tracked Correspondence #73)

Medical Officer's Memorandum: Response to Consult Request

Date Consult Requested: May 21, 2009

Date Completed: June 19, 2009

From: Harry Handelsman, Clinical Reviewer
Division of Reproductive and Urologic Products (DRUP)

Mark S. Hirsch, Clinical Team Leader, DRUP

Scott Monroe, Director, DRUP

To: Y. Max Ning, Clinical Reviewer
Division of Drug Oncology Products (DDOP)

Virginia E. Maher, Clinical Team Leader, DDOP

Robert Justice, Director, DDOP

Re: NDA 22-437, Watson Laboratories, Inc
Trelstar 22.5 mg (triptorelin pamoate for injection)
Request for consultation regarding castration rates in an NDA

1. Background

On September 12, 2008, NDA 22-437 (Trelstar [triptorelin pamoate] 22.5 mg for the palliative treatment of advanced prostate cancer) was submitted to DDOP. Triptorelin is a GnRH receptor agonist, approved as Trelstar 3.75 mg (1 month) and 11.25 mg (3-month) depot formulations.

Watson Laboratories now seeks the approval of Trelstar 22.5 mg, a 6-month depot formation. The NDA is supported by a single, pivotal, Phase 3 study, DEB-TRI6M-301, entitled "*A Multicentre, Open, Non-Comparative, Phase III Study on the Efficacy, Pharmacokinetics and Safety of Two Injections of Triptorelin Embonate 22.5mg 6-Month Formulation in Patients with Advanced Prostate Cancer.*" DEB-TRI6M-301 was conducted in 120 subjects at 13 centers in South Africa. Patients received two intramuscular injections of Trelstar 22.5mg at 24-week intervals. The primary objective of the study was to demonstrate that Trelstar 22.5mg is effective in achieving medical castration (serum total testosterone <1.735 nmol/l) on Day 29, and in maintaining medical castration from Month 2 to Month 12.

On May 21, 2009, DDOP conveyed a consult request to DRUP with two questions regarding efficacy results observed in DEB-TRI6M-301.

2. Responses to Specific Questions from DDOP

- 1. Relevant to the medical castration rates demonstrated by the two approved Trelstar products, are the medical castration rates demonstrated in the Trelstar 22.5mg application sufficient for approval?**

In their consult requests DDOP provided summarized efficacy data from the previous and current Trelstar new drug applications, as follows:

Table 1: Medical Castration Rates Related to the Approved Trelstar Products

	Trelstar Depot (3.75 mg)	Trelstar LA (11.25 mg)
Castration rate on Day 29	91.2%	97.7%
Castration maintenance rate (Day 57-253)	96.4%	94.4%
Note: no 95% intervals were found		

Table 2: Medical Castration Rates Demonstrated With the Current Trelstar 22.5 mg NDA

	Trelstar 22.5 mg ITT (N=120)	A sensitivity analysis: Trelstar 22.5 mg ITT (N=120)
Castration rate on Day 29 (95% CI)	97.5% (92.8%; 99.5%)	Not Applicable
Castration maintenance rate (Day 57-253) (95% CI)	93.3% (88.1%; 97.3%)	96.7% (91.7%; 99.3%)

DDOP noted that they had conducted a “sensitivity analysis” wherein 4 individual patients who had escaped castrate suppression by having a single isolated serum T value between 1-2 fold greater than 1.735 nmol/L were treated as successes.

Response: For the Trelstar 22.5mg analyses shown, the testosterone values used were those obtained with the LCMS method of the central laboratory in the (b) (4) (b) (4), not those obtained with the automated (b) (4) immunoassay used in the local central laboratory in the (b) (4) (b) (4). If one considers just the (b) (4) testosterone values, then the percentages of successful “achievers” and “maintainers” in the current Trelstar NDA are comparable to those

reported in the previous Trelstar applications as well as those reported for other approved products. See our Additional Comment below.

2. **The medical reviewer does not think that one isolated testosterone escape with a magnitude of > 1.735 but < 3.5 nM during the 48 week study period is clinically meaningful, since the magnitude is still considerably low as compared to the level for a confirmation of hypogonadism (< 6.9 nM or 200ng/dL). Technically, the castration cut-off of <1.735 nM or 50 ng/dL is relatively arbitrary, not well evidenced with large studies. Based on the Pub-med literature, not all patients who had successful orchiectomy had testosterone levels below 1.735 nM or 50 ng/dL. In addition, there might be other reasons for the blip observed in the patients. In the current case, the timing of the escape did not appear to relate to any incidence of adverse reactions or disease worsening in the patients. Therefore, the reviewer considers the sensitivity analysis may represent an acceptable castration rate of the new formulation, appropriate for consideration in regulatory decision-making for the product. Please comment on the phenomenon of minimum isolated testosterone escape and its clinical and regulatory relevancies.**

DDOP provided testosterone values for each of 6 individual patients who had escaped castrate suppression by having a single isolated serum T value > 1.735 nmol/l. Four of these patients (patient identifier shown in lavender font) had a single isolated T value between 1-2 fold > 1.735 nmol/l. The following table shows the T values for these patients.

Day	(ID 06402)	06604	(ID 06608)	08604	11606	13613
0	35.581	14.113	9.381	28.201	23.36	40.591
1	22.423	14.112	14.195	18.867	18.522	27.553
29	1.19	0.774	0.668	0.828	1.303	1.108
57	0.625	0.398	0.333	0.611	2.333	0.706
85	0.841	0.339	0.451	0.59	0.447	0.46
113	0.663	0.385	6.119	0.365	0.756	3.354
141	0.546	0.393	0.252	0.307	0.316	0.469
169	0.374	1.938	0.373	0.753	0.551	0.648
171	0.787	0.328	1.625	1.966	1.231	.
197	0.902	0.176	0.456	0.377	0.629	0.522
225	0.797	0.219	0.272	0.613	0.699	0.653
253	0.656	0.338	0.442	0.49	0.658	0.463
281	0.769	0.471	0.724	0.664	0.894	1.553
309	0.836	0.338	0.275	0.683	0.652	0.486
337	42.047	0.382	0.388	0.801	1.077	0.792

Response: Using the testosterone values obtained from (b) (4) there are 6 individual “non-maintainers” who had single isolated T levels > 1.735 nmol/L and two additional “non-maintainers” who had more than one T level >1.735 nmol/L. Four of these patients show an isolated “low grade” escape (T level between 1.735 nmol/L and 3.5 nmol/L). We agree that it is reasonable for clinical judgment to play a role in the assessment of these cases.

3. Additional Comment

We note that the submission contains two complete sets of testosterone data, one from (b) (4) (immunoassay method) and one from (b) (4) (LCMS method). On page 29 of 378 of the Clinical Study Report (CSR) for DEB the Sponsor states:

“Serum testosterone levels were measured in two central laboratories (b) (4)

The local central laboratory on the (b) (4) [automated immunoassay, (b) (4) from Aug 2006, LOQ 0.35 nmol/L] provided the Investigators with values for the daily follow-up of the patients, and these local laboratory values were also used to assess the eligibility of the patients for the study.

However, it is known that the routine assays particularly in the hypogonadal testosterone range have poor precision. The (b) (4) method used by (b) (4), although validated, has shown a positive bias (overestimation of the testosterone values) when compared with the reference method, the liquid chromatography/tandem mass spectrometry [LC/MS], which has been validated especially for the low hypogonadal range [Reference 6]. Therefore, Debiopharm decided to have back-up samples for each testosterone sample analyzed with the more cumbersome but also more accurate LC/MS method to double-check the (b) (4) values. In all the analyses other than those regarding the inclusion of the patients, testosterone values obtained with the LC/MS of the central laboratory in the (b) (4) were used (b) (4) and LC-MS/MS analyses, LOQ 0.1 nmol/L (30 pg/ml), section 16.1.10].”

While this reasonable explanation was provided in the CSR, we find nothing in the protocol or protocol amendments to this end. The Sponsor states that the (b) (4) assay was prone to higher T levels (due to “overestimation”), and it appears true that the T levels were higher for the (b) (4) data compared to the (b) (4) data. It is clear that an analysis of the (b) (4) data would show lower percentages of success for both “achieve” (perhaps 93%) and “maintain” (perhaps 82%) compared to the same analysis of the (b) (4) data. This issue raises several questions, but in our view, the key question is: Which assay methodology more accurately reflects a castrate T level (≤ 1.735 nmol/L)?

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

/s/

Harry Handelsman
6/19/2009 03:13:17 PM
MEDICAL OFFICER

Mark S. Hirsch
6/19/2009 03:14:10 PM
MEDICAL OFFICER
I concur.

Scott Monroe
6/19/2009 03:18:15 PM
MEDICAL OFFICER

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # **22-437** Supplement # **N/A** Efficacy Supplement Type **N/A**

Proprietary Name: **TRELSTAR®** (b)(4)
Established Name: **(triptorelin pamoate for injectable suspension)**
Strengths: **22.5 mg**

Applicant: **Watson Laboratories, Inc.**
Agent for Applicant (if applicable): **N/A**

Date of Application: **September 12, 2008**
Date of Receipt: **September 12, 2008**
Date clock started after UN: **N/A**
Date of Filing Meeting: **November 12, 2008**
Filing Date: **November 12, 2008**

Action Goal Date (optional): User Fee Goal Date: **July 12, 2009**

Indication(s) requested: **TRELSTAR®** (b)(4) **(triptorelin pamoate for injectable suspension)**
22.5 mg, is for the palliative treatment of patients with advanced prostate cancer, (b)(4)

Type of Original NDA: (b)(1) (b)(2)
AND (if applicable)
Type of Supplement: (b)(1) (b)(2)

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. 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). If the application or efficacy supplement is a (b)(2), complete Appendix B.

Review Classification: S P
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: **3**
Other (orphan), OTC, etc.)

Form 3397 (User Fee Cover Sheet) submitted: YES NO

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

NOTE: If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required by contacting the User Fee staff in the Office of Regulatory Policy. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application.

Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the User Fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2) application? YES NO
If yes, explain: **NDA 20-715, Trelstar Depot; 3.75 mg, Approved 6/15/2000 & NDA 21-288, Trelstar LA; 11.25 mg, Approved 7/29/01**

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- Does another drug have orphan drug exclusivity for the same indication? YES NO
- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:
- If yes, has OC/DMPQ been notified of the submission? YES NO
- Does the submission contain an accurate comprehensive index? YES NO
If no, explain:
- Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.
- Submission complete as required under 21 CFR 314.50? YES NO
If no, explain:
- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES NO

2. This application is an eNDA or combined paper + eNDA YES
This application is: All electronic Combined paper + eNDA
This application is in: NDA format CTD format
Combined NDA and CTD formats

Does the eNDA, follow the guidance?
(<http://www.fda.gov/cder/guidance/2353fnl.pdf>) YES NO

If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format?

Additional comments: N/A

3. This application is an eCTD NDA. YES NO

If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments: N/A

- Patent information submitted on form FDA 3542a? YES **X** NO
- Exclusivity requested? YES, **X** Years **3**
NO

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

- Correctly worded Debarment Certification included with authorized signature? YES **X** NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.” Applicant may not use wording such as “To the best of my knowledge . . .”

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES **X** NO
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES **X** NO
- Is this submission a partial or complete response to a pediatric Written Request? YES NO **X**

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES **X** NO
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)

NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.

- Field Copy Certification (that it is a true copy of the CMC technical section) YES NO **X**
- PDUFA and Action Goal dates correct in tracking system? YES **X** NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.

- List referenced IND numbers: 28,547

- Are the trade, established/proper, and applicant names correct in COMIS? YES **X** NO
If no, have the Document Room make the corrections.

- End-of-Phase 2 Meeting(s)? Date(s) _____ NO **X**
If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) **February 19, 2008, & May 14, 2008** NO
(CMC)
If yes, distribute minutes before filing meeting.
- Any SPA agreements? Date(s) _____ NO
If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES NO
If no, request in 74-day letter.
- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
Was the PI submitted in PLR format? YES NO
If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:
- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES NO
- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES NO
- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS? N/A YES NO
- Risk Management Plan consulted to OSE/IO? N/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA YES NO

If Rx-to-OTC Switch or OTC application:

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES NO
- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
If no, did applicant submit a complete environmental assessment? YES NO

- If EA submitted, consulted to EA officer, OPS? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
 - If a parenteral product, consulted to Microbiology Team? YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: November 12, 2008

NDA #: 22-437

DRUG NAMES: TRELSTAR® (triptorelin pamoate for injectable suspension) 22.5 mg

APPLICANT: Watson Laboratories, Inc.

BACKGROUND: Watson Laboratories, Inc. has submitted an NDA for TRELSTAR® (triptorelin pamoate for injectable suspension) 22.5 mg. This new sustained release formulation is purportedly designed to release 22.5 mg of triptorelin over a period of 168 days (6 months). Watson is seeking approval for the palliative treatment of advanced prostate cancer. (b) (4)

Primary objective: To assess the efficacy of 3 different triptorelin pamoate 6-month formulations in achieving castrate levels of testosterone (≤ 1.735 nmol/l) 28 days (Day 29) after study drug injection and in maintaining the castrate levels of serum testosterone from Day 57 to Day 169 in patients with advanced prostate cancer. **Secondary objectives:** To assess the testosterone pharmacodynamics and pharmacokinetics, the change in PSA levels and the safety profile of 3 different triptorelin pamoate 6-month formulations in patients with advanced prostate cancer.

ATTENDEES:

ASSIGNED REVIEWERS (including those not present at filing meeting): See Below↓

Discipline/Organization

Reviewer

Medical:	Yang (Max) Ning, M.D.
Secondary Medical:	V. Ellen Maher, M.D.
Statistical:	Yu-Ling Chang, Ph.D.
Pharmacology:	Timothy Kropp, Ph.D
Statistical Pharmacology:	N/A
Chemistry:	William (Mike) Adams, Ph.D.
Environmental Assessment (if needed):	
Biopharmaceutical:	
Microbiology, sterility:	Vinayak Pawar, Ph.D.
Microbiology, clinical (for antimicrobial products only):	N/A
DSI:	Robert S.K. Young, M.D.
OPS:	N/A
Regulatory Project Management:	Kim J. Robertson, CSO
Other Consults:	DDMAC, DMETS/OSE, DMEPA

Per reviewers, are all parts in English or English translation? YES NO

If no, explain: N/A

CLINICAL		FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>	
• Clinical site audit(s) needed? If no, explain:		YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>	
• Advisory Committee Meeting needed?	YES, date if known _____			NO	<input checked="" type="checkbox"/>	
• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?		N/A	<input checked="" type="checkbox"/>	YES	<input type="checkbox"/>	
				NO	<input type="checkbox"/>	
CLINICAL MICROBIOLOGY	N/A	<input checked="" type="checkbox"/>	FILE	<input type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
STATISTICS	N/A	<input type="checkbox"/>	FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
BIOPHARMACEUTICS		FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>	
• Biopharm. study site audits(s) needed?		YES	<input type="checkbox"/>	NO	<input checked="" type="checkbox"/>	
PHARMACOLOGY/TOX	N/A	<input type="checkbox"/>	FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
• GLP audit needed?		YES	<input type="checkbox"/>	NO	<input type="checkbox"/>	
CHEMISTRY		FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>	
• Establishment(s) ready for inspection?		YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>	
• Sterile product?		YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>	
• If yes, was microbiology consulted for validation of sterilization?		YES	<input checked="" type="checkbox"/>	NO	<input type="checkbox"/>	

ELECTRONIC SUBMISSION:

Any comments: **N/A**

REGULATORY CONCLUSIONS/DEFICIENCIES:

(Refer to 21 CFR 314.101(d) for filing requirements.)

- The application is unsuitable for filing. Explain why:
The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.
- No filing issues have been identified.
- Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.

2. If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
3. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
4. If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)
5. Convey document filing issues/no filing issues to applicant by Day 74.

Kim J. Robertson
Consumer Safety Officer

Appendix A to NDA Regulatory Filing Review

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

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

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

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

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

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

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

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

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the

original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),

- (2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or
- (3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

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

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

1. Does the application reference a listed drug (approved drug)? YES NO

If “No,” skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):
3. Is this application for a drug that is an “old” antibiotic (as described in the draft guidance implementing the 1997 FDAMA provisions? (Certain antibiotics are not entitled to Hatch-Waxman patent listing and exclusivity benefits.) YES NO

If “Yes,” skip to question 7.

4. Is this application for a recombinant or biologically-derived product? YES NO

If “Yes “contact your ODE’s Office of Regulatory Policy representative.

5. The purpose of the questions below (questions 5 to 6) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.
- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved? YES NO

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

If “No,” to (a) skip to question 6. Otherwise, answer part (b and (c)).

- (b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval? YES NO

- (c) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES NO

If “Yes,” (c), list the pharmaceutical equivalent(s) and proceed to question 6.

If “No,” to (c) list the pharmaceutical equivalent and contact your ODE’s Office of Regulatory Policy representative.

Pharmaceutical equivalent(s):

6. (a) Is there a pharmaceutical alternative(s) already approved? YES NO

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

If “No,” to (a) skip to question 7. Otherwise, answer part (b and (c)).

- (b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval? YES NO

- (c) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES NO

If “Yes,” to (c), proceed to question 7.

NOTE: *If there is more than one pharmaceutical alternative approved, consult your ODE’s Office of Regulatory Policy representative to determine if the appropriate pharmaceutical alternatives are referenced.*

If “No,” to (c), list the pharmaceutical alternative(s) and contact your ODE’s Office of Regulatory Policy representative. Proceed to question 7.

Pharmaceutical alternative(s):

7. (a) Does the application rely on published literature necessary to support the proposed approval of the drug product (i.e. is the published literature necessary for the approval)? YES NO

If “No,” skip to question 8. Otherwise, answer part (b).

(b) Does any of the published literature cited reference a specific (e.g. brand name) product? Note that if yes, the applicant will be required to submit patent certification for the product, see question 12.

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

9. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA may refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)).) YES NO

10. Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application may be refused for filing under 21 CFR 314.101(d)(9)). YES NO

11. Is the application for a duplicate of a listed drug whose only difference is YES NO

that the rate at which the product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application may be refused for filing under 21 CFR 314.101(d)(9).

12. Are there certifications for each of the patents listed in the Orange Book for the listed drug(s) referenced by the applicant (see question #2)? (This is different from the patent declaration submitted on form FDA 3542 and 3542a.) YES NO

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

- Not applicable (e.g., solely based on published literature. See question # 7)
- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)
Patent number(s):

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

- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).
Patent number(s):
- Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):
- 21 CFR 314.50(i)(1)(ii): No relevant patents.
- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

14. Did the applicant:

- Identify which parts of the application rely on the finding of safety and effectiveness for a listed drug or published literature describing a listed drug or both? For example, pharm/tox section of application relies on finding of preclinical safety for a listed drug.

YES NO

If "Yes," what is the listed drug product(s) and which sections of the 505(b)(2) application rely on the finding of safety and effectiveness or on published literature about that listed drug

Was this listed drug product(s) referenced by the applicant? (see question # 2)

YES NO

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

N/A YES NO

15. (a) Is there unexpired exclusivity on this listed drug (for example, 5 year, 3 year, orphan or pediatric exclusivity)? Note: this information is available in the Orange Book.

YES NO

If "Yes," please list:

Application No.	Product No.	Exclusivity Code	Exclusivity Expiration

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/s/

Kim Robertson

5/27/2009 03:08:21 PM

CSO

Trelstar-NDA Regulatory Filing Review; NDA 22-437 '09



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA#(s) 21-288, 20-715, 22-437

Watson Laboratories, Inc.
ATTENTION: Wendy DeSpain, B.S., M.B.A., R.A.C.
Associate Director, Proprietary Regulatory Affairs
577 Chipeta Way
Salt Lake City, Utah 84108

Dear Ms. DeSpain:

Please refer to the following:

Your New Drug Application (NDA) 21-288 dated June 29, 2000, received June 29, 2000, submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for triptorelin pamoate 11.25MG.

Your New Drug Application (NDA) 20-715 dated June 24, 1996, received June 26, 1996, submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for triptorelin pamoate 3.75MG.

Your New Drug Application (NDA) 22-437 dated September 12, 2008, received September 12, 2008, submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for triptorelin pamoate 22.5 mg injection.

We also refer to the teleconference meeting between representatives of your firm and the FDA on April 22, 2009. The purpose of the meeting was to discuss your firm's Nomenclature plan as it related to FDA's objections of the proprietary names and the labeling.

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

If you have any questions, call Sandra Griffith, Safety Regulatory Project Manager, at (301) 796-2445.

Sincerely,

{See appended electronic signature page}

Carol Holquist

Director

Division of Medication Error Prevention and
Analysis

Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

NDA/IND NUMBER (DELETE THIS LINE IF THERE IS NO APPLICATION)

Page 2

Enclosure

MEMORANDUM OF MEETING MINUTES

Appointment Date/Time: Wednesday 22 April 2009, 11:30AM EST

Type of Meeting: Type C Teleconference

Application(s): NDAs 21-288, 20-715, and 22-437

Product/ Name: Trelstar LA; 11.25 mg, Trelstar Depot; 3.75 mg, Trelstar (triptorelin pamoate) 22.5 mg

Sponsor: Watson Laboratories, Inc.

Purpose: To discuss with the Sponsor their 2 April 2009 Trelstar Nomenclature Plan.

FDA Attendees:

OSE - Office of Surveillance and Epidemiology

Sandra Griffith, BSN., RN, Safety Regulatory Project Manager

Carol Holquist RPh., Division Director DMEPA

Kellie Taylor, Pharm D., Team Leader DMEPA

Cathy A. Miller, RN, MPH, Safety Evaluator DMEPA

OND - Office of New Drugs:

Kim Robertson, Consumer Safety Officer, DDOP

Yang-Min (Max) Ning, M.D., Clinical Reviewer, DDOP

Virginia Maher, M.D., Clinical Team Leader, DDOP

Terrance Ocheltree, Ph.D., Pharmaceutical Assessment Lead, DPAMS

William M. Adams, Ph.D., Chemistry Reviewer, DPAMS

Anthony Murgo, M.D., Associate Director, DDOP

Michelle Bell, Correspondence Control Specialist Fellow

Watson Laboratories Attendees:

Wendy DeSpain, B.S., M.B.A., R.A.C., Associate Director, Regulatory Affairs

Charles Ebert, Ph.D., Senior Vice President, Research and Development

Kevin Barber, Ph.D., R.A.C., P.M.P., Executive Director, Regulatory Affairs

Cherri Petrie, R.A.C., Director, Regulatory Affairs CMC

Burke Byrne, M.B.A., R.A.C., Manager, Regulatory Affairs CMC

(b) (4)

Summary of Discussion: DMEPA and DDOP met in a teleconference with Watson Pharmaceuticals to discuss FDA's objections to the proposed proprietary name 'Trelstar' for pending new drug application NDA 22-437, as outlined in our correspondence dated March 23, 2009, as well as our objection to Watson's proposal to change the proprietary names for currently marketed products, Trelstar Depot (NDA 20-715) and Trelstar LA (NDA 21-288) to 'Trelstar' as outlined in our correspondence dated March 31, 2009.

Summary of Discussion continued: FDA explained that the original proposed name ‘Trelstar’ (b) (4) dated November 12, 2008, was objected to because of potential promotional concerns surrounding the (b) (4) claim. FDA further acknowledged review of the Sponsor’s rebuttal to our objection to having all three Triptorelin Pamoate products managed under the single name “Trelstar” as presented in their letter dated April 2, 2009. In this April submission, the Sponsor outlined precedence for similar nomenclature and labeling for products such as Lupon, Zoladex and Eligard. FDA clarified our objection to this proposal, which was based on the consideration of varying delayed-release formulation features of the 22.5 mg strength product and possible risk of interchangeability among the three different strengths in the clinical setting. FDA explained to the Sponsor that we have reconsidered our decision after review of these products and internal discussions, and are willing to accept the Sponsor’s proposed name ‘Trelstar’ for all three Triptorelin Pamoate products contingent upon the following:

- 1) The Sponsor should submit to the NDA 22-437 a revised integrated product insert label that reflects information on all three Triptorelin Pamoate strengths (3.75 mg, 11.25 mg and 22.5 mg). After internal discussions between DMEPA and DDOP and discussions with the Sponsor, the agreement was made that the Sponsor would submit their draft combined insert labeling by approximately May 4, 2009 in order to give the FDA an opportunity to review it before the first labeling meeting, scheduled on May 7, 2009. The Sponsor agreed.
- 2) The Sponsor should submit to the NDA 22-437 revised container labels and carton labeling, with the frequency of use indicated in WEEKS displayed prominently on the principal display panel in addition to the strength, similar to the features illustrated on the Eligard product line.
- 3) The Sponsor should submit labeling supplements to NDA 21-288 and NDA 20-715 (i.e., 3.75 mg and 11.25 mg strengths), with the strength and frequency (in WEEKS) of use prominently displayed on the principal display panel, similar to features illustrated on the Eligard product line. Along with the proposed carton/container labeling, the Sponsor will also submit combined package insert labeling for all three Triptorelin Pamoate strengths.
- 3) The Sponsor will revise their previously submitted Nomenclature Implementation plan, providing detailed clarifications of their marketing and communication plans to targeted parties of interest (healthcare providers, pharmacists, patients, etc) for the name changes to the current Trelstar Depot and Trelstar LA products, in conjunction with the introduction into the market of the pending third strength product. The FDA discussed concerns with product confusion should the new strength ‘Trelstar’ be introduced to the market while Trelstar Depot and Trelstar LA are still under the old proprietary name.

FDA discussed that administratively, the sponsor would need to resubmit their April 2, 2009 General Correspondence as a “Request for Re-consideration of a Proprietary Name” to the NDA with new labels, and also send a “Request for Re-Consideration of a Proprietary Name” for Trelstar LA and Trelstar Depot.

OSE Safety Regulatory Project Manager: Sandra J Griffith

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/s/

Carol Holquist
5/19/2009 05:21:07 PM

REQUEST FOR CONSULTATION

TO (Office/Division): **HFD-580, Jennifer Mercier, CPMS**

FROM (Name, Office/Division, and Phone Number of Requestor): **HFD-150/Kim J. Robertson; 6-1441**

DATE
May 19, 2009

IND NO.

NDA NO.
22-437

TYPE OF DOCUMENT
New NDA Submission

DATE OF DOCUMENT
September 12, 2008

NAME OF DRUG
**Trelstar (triptorelin pamoate
for injectable suspension)
22.5 mg**

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
June 3, 2009

NAME OF FIRM: **Watson Laboratories, Inc.**

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: DDOP requests that DRUP join us during our OODP Rounds to comment on the applicant's response rate (in light of other approvals), and to comment on the clinical impact of the isolated testosterone failures seen in the patients on this trial.

The M.O. is Yang-Min (Max) Ning, M.D.; 6-2321
The EDR link is: \\Cdsesub1\evsprod\NDA022437\0000

SIGNATURE OF REQUESTOR
Kim J. Robertson

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Kim Robertson

5/19/2009 11:56:44 AM

19May09 DRUP Consult-Trelstar NDA 22-437 '09

MEMO TO FILE
NDA 22-437

Drug: triptorelin pamoate for injectable suspension (trade name under discussion)

Sponsor: Watson Laboratories, Inc.

Date: 8 April 2009

Reviewer: Timothy Kropp, Ph.D., Toxicologist

Subject: Pharmacology/Toxicology Review of NDA 22-437

NDA 22-437 does not contain any new information on the toxicology of the product. Three pharmacokinetic studies have been submitted, indicating decreased levels of testosterone in response to the new formulation of triptorelin. The NDA relies on pharmacology and toxicology information submitted for triptorelin pamoate under NDA 20-715. There are no formulation differences that would be expected to change the pharmacological or toxicological activity between previous formulations and the formulation that is being proposed under NDA 22-437. Only the duration of activity should be expected to change. One of the excipients, (b) (4) Poly(D,Llactide-coglycolide), is a novel polymer in this formulation but the DMF relied upon (DMF (b) (4)) has been reviewed and relied upon for approved products in the past (significantly, it has been referred to for NDA 021731, an approved 6-month depot formulation of 45 mg leuprolide acetate). Furthermore, there is no change in proposed indication (palliative treatment of advanced prostate cancer). Given these facts, the pharmacology/toxicology review conducted for NDA 20-715 is sufficient and an additional pharmacology and toxicology review for this NDA is not needed.

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/s/

Timothy Kropp
4/16/2009 12:54:27 PM
PHARMACOLOGIST

Haleh Saber
5/7/2009 03:37:39 PM
PHARMACOLOGIST

From: Griffith, Sandra J
Sent: Wednesday, April 08, 2009 3:03 PM
To: 'Wendy.DeSpain@watson.com'
Cc: Robertson, Kim
Subject: RE: NDA 22-437 Trelstar
[Hi Wendy,](#)

FDA meeting attendees will be as follows:

OSE- Office of Surveillance and Epidemiology
Sandra Griffith, SRPM
Cathy Miller, MPH BSN., Senior Regulatory Reviewer
Kellie Taylor, Pharm D., DMEPA Team Lead.

OND - Office of NEW Drugs
Kim Robertson, CSO/PM
Virginia Maher, Lead Medical Officer
Anthony Murgo, Medical Officer
Yang-Ming (Max) Ning, Medical Officer
William M. Adams, Chemist
Terrance Ocheltree, Chemist
Sarah Pope, Chemist

Thanks,
Sandra

Sandra J Griffith, BSN, RN.
LCDR, USPHS
Safety Regulatory Project Manager
FDA CDER OSE, Bld 22 Rm 4476.
10903 New Hampshire Ave,
Silver Spring Maryland 20993-0002
301 796-2445

From: Robertson, Kim
Sent: Tuesday, April 07, 2009 5:02 PM
To: Wendy.DeSpain@watson.com; Griffith, Sandra J
Subject: RE: NDA 22-437 Trelstar

Thank you Wendy. We are all in receipt of the official meeting request via the Gateway. We look forward to speaking with you soon.

Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Tuesday, April 07, 2009 3:58 PM
To: Robertson, Kim; Griffith, Sandra J
Subject: RE: NDA 22-437 Trelstar

Hi Kim and Sandra,

I will be submitting the attached Type C meeting request through the electronic gateway today to Trelstar NDA 22-437. As noted in this letter, our meeting attendees will be the following:

Charles Ebert, Ph.D., Senior Vice President, Research and Development
Kevin Barber, Ph.D., R.A.C., P.M.P., Executive Director, Regulatory Affairs
Wendy DeSpain, B.S., M.B.A., R.A.C., Associate Director, Regulatory Affairs
Cherri Petrie, R.A.C., Director, Regulatory Affairs CMC
Burke Byrne, M.B.A., R.A.C., Manager, Regulatory Affairs CMC

Best regards,
Wendy

"Robertson, Kim"
<Kim.Robertson@fda.hhs.gov>

To Wendy.DeSpain@watson.com
cc "Griffith, Sandra J" <Sandra.Griffith@fda.hhs.gov>
Subject RE: NDA 22-437 Trelstar

04/03/2009 02:38 PM

Yes Wendy; please still submit the request. Sandra will need a submission to attach any side-notes/mins. to for our database.

Thanks,
Kim

From: Wendy.DeSpain@watson.com [mailto:Wendy.DeSpain@watson.com]
Sent: Friday, April 03, 2009 1:23 PM
To: Robertson, Kim
Subject: Re: NDA 22-437 Trelstar

Hi Kim,

Thank you so much for passing this information along to us. We will hold off on contacting Med-EERS, and we look forward to the teleconference that is being scheduled for the week of April 20, 2009. As a side note, I have not yet submitted a formal Type C meeting request. Will this be necessary?

Best regards,
Wendy

"Robertson, Kim" <Kim.Robertson@fda.hhs.gov> 04/03/2009 11:03 AM

To Wendy.DeSpain@watson.com
cc

Subject NDA 22-437 Trelstar

Hello Wendy:

Today, the OND and OSE reviewers of your NDA met internally to discuss Watson's Trelstar Nomenclature Plan, received April 2, 2009. There is some confusion regarding our concerns about the proprietary name of your product. Consequently, we recommend that you discuss these concerns with us during your Type C teleconference.

We also recommend that Watson Laboratories postpone contacting Med-EERS until after the teleconference. If after the teleconference, Watson Laboratories decides to contract with Med-ERRS, Watson will do so with a full understanding of our concerns.

Ms. Sandra Griffith of the OSE is in the process of scheduling the teleconference meeting for the week of April 20, 2009. She will provide the specifics with regard to the actual date and time as soon as possible.

Regards,

Kim

Kim J. Robertson

Consumer Safety Officer

Division of Drug Oncology Products

Phone: (301) 796-1441

Fax: (301) 796-9845

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/s/

Kim Robertson

4/8/2009 03:28:20 PM

CSO

Proprietary/Tradename Discussions re: Trelstar NDA 22-437 -Sponsor Type C
Meeting Granted-OND&OSE Reviewers



NDA 22-437

**PROPRIETARY NAME REQUEST
- UNACCEPTABLE**

Watson Laboratories, Inc.
577 Chipeta Way
Salt Lake City, Utah 84108

ATTENTION: Wendy DeSpain, BS, M.B.A., R.A.C.
Associate Director, Proprietary Regulatory Affairs

Dear Ms. DeSpain:

Please refer to your New Drug Application dated September 12, 2008, received September 12, 2008, submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for triptorelin pamoate 22.5 mg injection.

We also refer to your December 23, 2008, correspondence, received December 23, 2008, requesting review of your proposed proprietary name, Trelstar. We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

You have proposed to use the proprietary name Trelstar for this new 22.5 mg strength product as well as revise the proprietary name of your currently marketed products, Trelstar Depot 3.75 mg and Trelstar LA 11.25 mg, to Trelstar. The 22.5 mg strength has a new extended-release formulation with a mechanism of action that is different from the 3.75 mg and 11.25 mg strengths and is not interchangeable with the currently marketed products. Managing all three products under one 'Trelstar' proprietary name or naming this product 'Trelstar' alone while retaining the currently marketed proprietary names, creates the potential for product confusion that could lead to medication errors such as improper dose administration, wrong product selection or wrong formulation selection. Product confusion and inappropriate substitution could occur between the 22.5 mg strength and the currently marketed 3.75 mg and 11.25 mg strength products. By using the same name clinicians may mistakenly conclude that the three products vary only in their strength and can be used interchangeably and combine smaller strengths to an achievable 22.5 mg dose (i.e., 2 x 11.25 mg). Since the 22.5 mg strength has a different extended-release formulation, such strength combinations would not effectively provide the same extended-release 22.5 mg dose intended for release over a 24 week period.

Given these concerns, we recommend the following:

- a. Submit a proprietary name that contains a modifier that aligns accurately with the product's clinically proven claims (i.e., Trelstar 'NEW MODIFIER'). Given that the Trelstar product line is already marketed with two modifiers (LA and Depot) to convey the extended-release nature of the formulation, please provide data that demonstrates that the proposed modifier provides adequate differentiation among the Trelstar product line and has a meaning that is consistently and readily understood by healthcare practitioners.
- b. That you submit another proposed proprietary name for the 22.5 mg strength product.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Sandra Griffith, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 301 796-2445. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager.

Sincerely,

See appended electronic signature p

Robert Justice, MD
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Office of New Drugs
Center for Drug Evaluation and Research

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/s/

Robert Justice
3/23/2009 06:04:34 PM

DSI CONSULT: Request for Clinical Inspections

Date: January 16, 2009

To: Tejashri Purohit-Sheth, M.D., Branch Chief, GCPB2, DSI

cc: Robert S. K. Young, M.D., GCPB2, DSI

Through: Y. Max Ning, M.D., Clinical Reviewer, DDOP
Robert L. Justice, M.D., Division Director, DDOP

From: Kim Robertson, Consumer Safety Officer, DDOP

Subject: **Request for Clinical Site Inspections**
NDA 22-437
Sponsor: Watson Laboratories, Inc.
Drug: Triptorelin Pamoate for Injectable suspension 22.5
NME: No
Review: Standard
Study Population: adults with prostate cancer

PDUFA: July 12, 2009
Action Goal Date: June 23, 2009
Inspection Summary Goal Date: May 22, 2009

I. Background Information

Triptorelin is a GnRH receptor agonist. Its 1-month (3.75 mg) and 3-month (11.25 mg) formulations have been approved and marketed in the United States and Europe for treatment of patients with advanced prostate cancer. In order to further reduce the number of injections for convenience to both the patients, the sponsor has developed a new triptorelin embonate formulation, designed to release triptorelin over a period of 6 months.

In this application, the sponsor provided evidence of the efficacy and safety of a 6-month triptorelin formulation based on an open-label, uncontrolled Phase 3 study that enrolled 120 patients with advanced prostate cancer who received two intramuscular injections of the preparation at an interval of 6 months after study initiation.

Protocol/Site Identification:

Site # (Name, Address, Phone number, email, fax#)	Protocol #	Number of Subjects	Indication
Center # 11: Dr Johann.H. van Wyk, Suite 207, Wilmedpark Hospital, C/o Ametis and Marmer Street, Wilkoppies, Klerksdorp, 2570 Republic of South Africa.	DEB- TRI6M-301	23 patients received Trelstar (b) (4) 22.5 mg	Palliative treatment of patients with advanced prostate cancer
Center # 05: Dr Johann. Bahlmann, 20 Varing Avenue, George, 6529 Republic of South Africa.	DEB- TRI6M-301	16 patients received Trelstar (b) (4) 22.5 mg	Palliative treatment of patients with advanced prostate cancer

II. Site Selection/Rationale

The listed two sites essential for approval have been identified for inspection as per the clinical review team.

Domestic Inspections:

Reasons for inspections (please check all that apply):

- Enrollment of large numbers of study subjects
- High treatment responders (specify):
- Significant primary efficacy results pertinent to decision-making
- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, significant human subject protection violations or adverse event profiles.
- Other (specify):

International Inspections:

Reasons for inspections (please check all that apply):

- There are no domestic data

Request for Clinical Inspections

- Only foreign data are submitted to support an application. The key study was conducted solely in one country.
- Domestic and foreign data show conflicting results pertinent to decision-making
- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, or significant human subject protection violations.

Other (specify): The two centers had a total 39 of the 120 patients enrolled in the key study in support of the efficacy claim of the 6-month formulation, with few patients having 2 or more testosterone escape around month 6 or after.

Note: International inspection requests or requests for five or more inspections require sign-off by the OND Division Director and forwarding through the Director, DSI.

Should you require any additional information, please contact Kim Robertson (regulatory project manager) at 301-796-1441 or Y. Max Ning (medical reviewer) at 301-796-2321.

Concurrence: (as needed)

Y. Max Ning, M.D. _____ Medical Reviewer

Robert L. Justice, M.D. _____ Division Director (for foreign inspection requests only)

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/s/

Robert Justice
1/21/2009 06:04:24 PM

REQUEST FOR CONSULTATION

TO (Office/Division): HFD-805/OPS/NDMS/Attn: James McVey, Ph.D.

FROM (Name, Office/Division, and Phone Number of Requestor): HFD-150/DDOP/Kim Robertson, 6-1441

DATE
November 12, 2008

IND NO.

NDA NO.
22-437

TYPE OF DOCUMENT
New NDA

DATE OF DOCUMENT
September 12, 2008

NAME OF DRUG
Trelstar (b)(4) 22.5 mg

PRIORITY CONSIDERATION
Standard Review

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
April 12, 2009

NAME OF FIRM: Watson Laboratories, Inc.

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

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|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

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| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: At this time, DDOP is requesting to have a Microbiology review of the newly submitted NDA application for Trelstar (b)(4) 22.5 mg. Specifically, this consult's request is providing for the following: the sterilization of the vials and stoppers of the drug product, (b)(4) and lyophilization of the drug product, the sterile water for the injection syringe (DMF 8084), and the (b)(4) of the drug product.

Williams (Mike) Adams, Ph.D. is the primary CMC reviewer for this NDA. Please see Dr. Adams, if any DMFs need to be referenced.

Clinical reviewer: Yang-Min (Max) Ning, M.D; CSO: Kim Robertson

SIGNATURE OF REQUESTOR
Kim Robertson, CSO

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER



Appears This Way On Original

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/s/

Kim Robertson

11/12/2008 06:43:28 PM

12November08 Micro Consult for Trelstar (b)(4) NDA 22-437



FILING COMMUNICATION

NDA 22-437

Watson Laboratories, Inc.
577 Chipeta Way
Salt Lake City, UT 84108

Attention: Kevin Barber, Ph.D., R.A.C., P.M.P
Executive Director, Proprietary Regulatory Affairs

Dear Dr. Barber:

Please refer to your new drug application (NDA) dated September 12, 2008, received September 12, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Trelstar® (b) (4) (triptorelin pamoate for injectable suspension) 22.5 mg.

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 July 12, 2009.

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

1. DDMAC objects to the proposed trade name "Trelstar (b) (4)" because (b) (4). DDMAC acknowledges that "Trelstar Depot" and "Trelstar LA" are currently on the market. However, adding (b) (4) to "Trelstar" misleadingly implies that the drug (b) (4) for its approved indication, the palliative treatment of advanced prostate cancer. (b) (4) the proposed trade name is misleading.

Please note that the Federal Food Drug and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made, whether through a proposed trade name or otherwise; this includes suggestions that a drug is better, more effective, useful in a broader range of conditions or patients, safer, has fewer, or lower incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n); 21 CFR 202.1(e)(5)(i);(e)(6)(i)].

The Division of Drug Oncology Products has taken into consideration the recommendation of DDMAC; however, the tradename remains a review issue with the primary division. Watson Laboratories will be notified with a division decision as the review of your NDA progresses.

2. Please provide a statement confirming that all facilities are ready for GMP inspection.
3. Please provide the recommended storage conditions and retest period for the drug substance.
4. Please provide the profile of all impurities at or above the analytical method's limit of quantitation for each drug product lot listed in table 3.2.P.5.4-1.
5. For validation report 02-002549/01 (triptorelin assay in drug product), please provide copies of chromatograms from the specificity and robustness evaluations.
6. For validation report 02-002550/01 (related substances in drug product), please provide copies of chromatograms from the specificity, limit of detection, limit of quantitation, and robustness evaluations.
7. For validation report 02-002552/02 (dissolution), please provide copies of chromatograms from the specificity and robustness evaluations.
8. For validation report 02-002970/01 (pamoic acid assay in drug substance), please provide copies of chromatograms from the robustness evaluation.
9. For validation report 02-002985/01 (related substances in drug substance), please provide copies of chromatograms from the specificity, limit of detection and limit of quantitation evaluations, and provide data to establish method robustness.
10. Please identify the columns used in HPLC methods 02-002264, 02-002651, 02-002878, 02-002828, 02-002232, 02-002236 and 02-002889.
11. Please provide a method validation study for method 02-002889 and include copies of chromatograms from the specificity and ruggedness evaluations.

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.

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

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

If you have any questions, call Kim J. Robertson, Consumer Safety Officer, at (301) 796-1441.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D.
Division Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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/s/

Robert Justice

11/12/2008 06:19:14 PM

REQUEST FOR CONSULTATION

TO (Office/Division): HFD-42/DDMAC/Attn: JuWon Lee

FROM (Name, Office/Division, and Phone Number of Requestor): HFD-150/DDOP/Kim Robertson, 6-1441

DATE
October 20, 2008

IND NO.

NDA NO.
22-437

TYPE OF DOCUMENT
New NDA

DATE OF DOCUMENT
September 12, 2008

NAME OF DRUG
Trelstar (b) (4) 22.5 mg

PRIORITY CONSIDERATION
Standard Review

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
March 15, 2009

NAME OF FIRM: Watson Laboratories, Inc.

REASON FOR REQUEST

I. GENERAL

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| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
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| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

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| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
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| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
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III. BIOPHARMACEUTICS

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| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

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| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
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| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

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| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
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COMMENTS / SPECIAL INSTRUCTIONS: At this time, the DDOP is requesting that DDMAC review the proposed product labeling and any relevant advertising for this NDA. Please find the submission in the EDR for any other pertinent information you may need to complete your review.

Clinical reviewer: Yang-Min (Max) Ning, M.D; CSO: Kim Robertson
Please see attached labeling for your convenience.

14 page(s) of Draft Labeling have been Withheld in Full immediately following this page as B4 (CCI/TS)

SIGNATURE OF REQUESTOR
Kim Robertson, CSO

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

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/s/

Kim Robertson
10/20/2008 05:15:31 PM
20Oct08 DDMAC Consult

REQUEST FOR CONSULTATION

TO (Office/Division): OSE Consult; Tradename,
Carton/Container, PPI Attn: Carol Holquist, Pharm.D.

FROM (Name, Office/Division, and Phone Number of Requestor): HFD-
150/DDOP/Kim Robertson, 6-1441

DATE
October 20, 2008

IND NO.

NDA NO.
22-437

TYPE OF DOCUMENT
New NDA

DATE OF DOCUMENT
September 12, 2008

NAME OF DRUG
Trelstar (b) (4) 22.5 mg

PRIORITY CONSIDERATION
Standard Review

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
March 15, 2009

NAME OF FIRM: Watson Laboratories, Inc.

REASON FOR REQUEST

I. GENERAL

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| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

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| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

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| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

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|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
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| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
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COMMENTS / SPECIAL INSTRUCTIONS: At this time, the DDOP is requesting OSE to please perform the following actions as they pertain to this newly submitted NDA: 1) Review and comment on the proposed proprietary name "Trelstar (b) (4)"; 2) Review and comment on the enclosed carton, container, and vial information; 3) Review the PPI. The PDUFA date of July 12, 2009 and the medical reviewer is Yang-Min (Max) Ning.

Please see the attached link for your convenience. Any additional information can be found in the EDR.

SIGNATURE OF REQUESTOR
Kim Robertson, CSO

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Kim Robertson
10/20/2008 05:03:15 PM
200ct08 OSE Consult



NDA 22-437

NDA ACKNOWLEDGMENT

Watson Laboratories, Inc.
577 Chipeta Way
Salt Lake City, UT 84108

Attention: Kevin Barber, Ph.D., R.A.C., P.M.P.
Executive Director, Proprietary Regulatory Affairs

Dear Dr. Barber:

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

Name of Drug Product: Trelstar® (b) (4) (triptorelin pamoate for injectable suspension) 22.5 mg

Date of Application: September 12, 2008

Date of Receipt: September 12, 2008

Our Reference Number: NDA 22-437

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 November 11, 2008 in accordance with 21 CFR 314.101(a).

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

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 Drug Oncology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

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

If you have any questions, call Kim J. Robertson, Consumer Safety Officer, at (301) 796-1441.

Sincerely,

{See appended electronic signature page}

Capt. Frank Cross, Jr., M.A. MT (ASCP)
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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/s/

Kim Robertson

9/29/2008 03:46:47 PM

Ack. Letter for NDA 22-437--Trelstar

(b) (4)