

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**201922Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

## EXCLUSIVITY SUMMARY

NDA 201922

SUPPL #

HFD # 540

Trade Name Ximino Extended-Release Capsules

Generic Name minocycline hydrochloride

Applicant Name Ranbaxy Laboratories Limited

Approval Date, If Known

### PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES  NO

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

505(b)(2)

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

YES  NO

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

This application is a 505(b)(2) which relies on the Agency's previous findings of safety and efficacy for the 135 mg strength of Solodyn (minocycline hydrochloride) Extended-Release Tablets (NDA 050808). BA/BE Studies were used to bridge Ximino Extended-Release Capsules to the highest strength (135 mg) of Solodyn Extended-Release Tablets. In-vitro dissolution studies were used for waiver of clinical studies with the lower strengths of Solodyn.

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

d) Did the applicant request exclusivity?

YES  NO

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

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

YES  NO

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

N/A

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

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

YES  NO

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

## **PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES**

(Answer either #1 or #2 as appropriate)

### 1. Single active ingredient product.

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

YES  NO

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

#(s).

NDA# 050808	Solodyn (minocycline hydrochloride) Extended-Release Tablets, 135 mg
NDA# 050444	Minocin (minocycline hydrochloride) Intravenous
NDA# 050781	Arestin (minocycline hydrochloride) Microspheres
NDA# 050649	Minocin (minocycline hydrochloride) Pellet-Filled Capsules

2. Combination product.

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

YES  NO

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

NDA#

NDA#

NDA#

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

**PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS**

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

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

YES  NO

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

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

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

YES  NO

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

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

YES  NO

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

YES  NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently

demonstrate the safety and effectiveness of this drug product?

YES  NO

If yes, explain:

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

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

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

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

Investigation #1 YES  NO

Investigation #2 YES  NO

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

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

Investigation #1 YES  NO

Investigation #2 YES  NO



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

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

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

YES  NO

If yes, explain:

=====

Name of person completing form: Matthew White  
Title: Regulatory Health Project Manager  
Date: 1/30/2012

Name of Office/Division Director signing form: Susan J. Walker, M.D.  
Title: Director, DDDP

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

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

MATTHEW E WHITE  
07/03/2012

GORDANA DIGLISIC  
07/03/2012

SUSAN J WALKER  
07/09/2012

# RANBAXY

A-41, PHASE VIII-A, INDUSTRIAL AREA, FOCAL POINT, S.A.S. NAGAR - 160 071, PUNJAB, INDIA  
PHONE: (91) 0172-5058136

December 8,2010

Division of Dermatology and Dental products  
Office of Drug evaluation III  
Center for Drug Evaluation and Research  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

## Debarment Certification

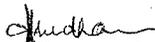
**Reference: Minocycline Hydrochloride Extended Release Capsules 45mg / 67.5mg / 90 mg/112.5 mg and 135 mg.**

Dear Sir/Madam:

In accordance with the requirement of section 306(k) of the Federal Food, Drug, and Cosmetic Act, Ranbaxy Laboratories Ltd. certifies that, Ranbaxy Laboratories did not use any person debarred under subsections (a) or (b) of section 306 in any capacity in connection with this NDA, nor will Ranbaxy Laboratories use any such person in connection with this NDA.

Furthermore, Ranbaxy Laboratories Ltd. certifies that, no employee of an affiliated company used by Ranbaxy who would have been among the employees overseeing work on data for the development or submission of this NDA, has been convicted within the last five years for acts described in subsection (a) and/or (b) of section 306.

Sincere regards,

  
Mogalipuvvu Sreedhar  
General Manager Production



**RANBAXY LABORATORIES LIMITED**  
REGISTERED OFFICE : SAHIBZADA AJIT SINGH NAGAR - 160 055 (PUNJAB) INDIA  
Website : <http://www.ranbaxy.com>

# RANBAXY

20, SECTOR-18, UDYOG VIHAR INDUSTRIAL AREA, GURGAON-122 015 (INDIA) PHONE : (91-124) 2342001-10, 4012501-10 FAX : (91-124) 2342017, 2342030  
RESEARCH & DEVELOPMENT CENTRE

January 17, 2011

Division of Dermatology and Dental Product  
Office of Drug Evaluation III  
Food and Drug Administration  
Center for Drug Evaluation and Research  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

## Debarment Certification

**Reference: Minocycline Hydrochloride Extended Release Capsules 45mg /  
67.5mg / 90 mg/112.5 mg and 135 mg./**

Dear Sir/Madam:

In accordance with the requirement of section 306(k) of the Federal Food, Drug, and Cosmetic Act, Ranbaxy Laboratories Ltd. certifies that, Ranbaxy Laboratories did not use any person debarred under subsections (a) or (b) of section 306 in any capacity in connection with this NDA, or will Ranbaxy Laboratories use any such person in connection with this NDA.

Furthermore, Ranbaxy Laboratories Ltd. certifies that, no employee of an affiliated company used by Ranbaxy who would have been among the employees overseeing work on data for the development or submission of this NDA, has been convicted within the last five years for acts described in subsection (a) and/or (b) of section 306.

Sincere regards

  
Rajender Singh  
Director  
Regulatory Affairs



OHM LABORATORIES, INC., 14 TERMINAL ROAD, NEW BRUNSWICK, NJ 08901, PHONE: (732) 514-4380, FAX: (732) 514-4405

January 06, 2011

Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Food and Drug Administration  
Center for Drug Evaluation and Research  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

### Debarment Certification

Reference: **NDA: 201922**

**Minocycline Hydrochloride Extended Release Capsules, 45 mg, 90 mg, 67.5 mg, 112.5 mg and 135 mg**

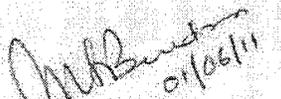
Dear Sir/Madam:

In accordance with the requirement of section 306(k) of the Federal Food, Drug, and Cosmetic Act, Ohm Laboratories, Inc. certifies that Ohm Laboratories, Inc. did not use any person debarred under subsections (a) or (b) of section 306 in any capacity in connection with this NDA, nor will Ohm Laboratories, Inc. use any such person in connection with this NDA.

Furthermore, Ohm Laboratories, Inc. certifies that no employee of an affiliated company used by Ohm Laboratories, Inc. who would have been among the employees overseeing work on data for the development or submission of this NDA, has been convicted within the last five years for acts described in subsection (a) and/or (b) of section 306.

This certificate is for both Terminal Road and Livingston Avenue facilities of Ohm Laboratories, Inc.

Sincerely,

  
01/06/11  
Manjeet Bindra  
QA/QC, Vice President

# ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION <sup>1</sup>		
NDA # 201922 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Ximino Established/Proper Name: minocycline hydrochloride Dosage Form: Extended-Release Capsules		Applicant: Ranbaxy Laboratories Limited Agent for Applicant (if applicable): Scott Tomsky
RPM: Matthew White		Division: DDDP
<p><b>NDA:</b> NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p><b>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</b> Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Solodyn (minocycline hydrochloride) Extended Release Tablets, 135 mg (NDA 050808)</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>New dosage form</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><b><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></b></p> <p><b><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></b></p> <p><input checked="" type="checkbox"/> No changes    <input type="checkbox"/> Updated    Date of check: 7/11/12</p> <p><b>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.</b></p>
❖ Actions		
<ul style="list-style-type: none"> <li>• Proposed action</li> <li>• User Fee Goal Date is <u>July 14, 2012</u></li> </ul>		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> <li>• Previous actions (<i>specify type and date for each action taken</i>)</li> </ul>		<input type="checkbox"/> None    Refuse to File - 2/4/11

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

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a>). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics<sup>2</sup></p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): Acne Agents (4029041)</p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch  <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch  <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC         </p> <p>           NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510)  <input type="checkbox"/> Restricted distribution (21 CFR 314.520)            Subpart I <input type="checkbox"/> Approval based on animal studies  <input type="checkbox"/> Submitted in response to a PMR  <input type="checkbox"/> Submitted in response to a PMC  <input type="checkbox"/> Submitted in response to a Pediatric Written Request         </p> <p>           BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41)  <input type="checkbox"/> Restricted distribution (21 CFR 601.42)            Subpart H <input type="checkbox"/> Approval based on animal studies            REMS: <input type="checkbox"/> MedGuide  <input type="checkbox"/> Communication Plan  <input type="checkbox"/> ETASU  <input type="checkbox"/> REMS not required         </p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> <li>Office of Executive Programs (OEP) liaison has been notified of action</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>Press Office notified of action (by OEP)</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>Indicate what types (if any) of information dissemination are anticipated</li> </ul>	<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

<sup>2</sup> 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"> <li>Is approval of this application blocked by any type of exclusivity?</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> <li>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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA #                      and date exclusivity expires:
<ul style="list-style-type: none"> <li>(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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA #                      and date exclusivity expires:
<ul style="list-style-type: none"> <li>(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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA #                      and date exclusivity expires:
<ul style="list-style-type: none"> <li>(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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA #                      and date exclusivity expires:
<ul style="list-style-type: none"> <li>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></li> </ul>	<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"> <li>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.</li> </ul>	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> <li>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.</li> </ul>	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified  21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> <li>[505(b)(2) applications] If the application includes a <b>paragraph III</b> 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).</li> </ul>	<input checked="" type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> <li>[505(b)(2) applications] For <b>each paragraph IV</b> 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></li> </ul>	<input type="checkbox"/> N/A (no paragraph IV certification) <input checked="" type="checkbox"/> Verified

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

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

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

Yes     No

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

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

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

Yes     No

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

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

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

Yes     No

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

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

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

Yes     No

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

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

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

❖ Copy of this Action Package Checklist <sup>3</sup>	7/12/12
<b>Officer/Employee List</b>	
❖ 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
<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s) Approval: 7/11/12 RTF - 7/16/10
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	6/29/12
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	2/4/11
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	Solodyn PI - Approved 3/11

<sup>3</sup> Fill in blanks with dates of reviews, letters, etc.

<ul style="list-style-type: none"> <li>❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)</li> </ul>	<input type="checkbox"/> Medication Guide <input checked="" type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	6/29/12
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	2/4/11
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	Solodyn PI - Approved 3/11
<ul style="list-style-type: none"> <li>❖ Labels (<b>full color</b> carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most-recent draft labeling</li> </ul>	6/29/12
<ul style="list-style-type: none"> <li>❖ Proprietary Name             <ul style="list-style-type: none"> <li>• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>• Review(s) (<i>indicate date(s)</i>)</li> </ul> </li> </ul>	Acceptable - 10/26/11 Reviews: 10/26/11, 2/9/12
<ul style="list-style-type: none"> <li>❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)</li> </ul>	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA 8/15/11 <input checked="" type="checkbox"/> DRISK 10/3/11 <input checked="" type="checkbox"/> DDMAC 10/6/11 <input checked="" type="checkbox"/> SEALD 6/20/12 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
<b>Administrative / Regulatory Documents</b>	
<ul style="list-style-type: none"> <li>❖ Administrative Reviews (<i>e.g., RPM Filing Review<sup>4</sup>/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)</li> <li>❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte</li> <li>❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)</li> </ul>	RPM Filing Review: 10/6/11 RPM Filing Review Corrected: 7/10/12  <input type="checkbox"/> Not a (b)(2) 9/12/11 <input type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> <li>❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)</li> </ul>	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> <li>❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a></li> </ul>	
<ul style="list-style-type: none"> <li>• Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>• This application is on the AIP             <ul style="list-style-type: none"> <li>○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <div style="background-color: #cccccc; padding: 5px;">(b) (4)</div> <div style="background-color: #cccccc; padding: 5px;"></div>

<sup>4</sup> Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

	(b) (4)  <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> <li>❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> <li>• Date reviewed by PeRC <u>9/7/11</u> If PeRC review not necessary, explain: _____</li> <li>• Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)</li> </ul> </li> </ul>	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> <li>❖ 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>)</li> </ul>	<input checked="" type="checkbox"/> Verified, statement is acceptable
<ul style="list-style-type: none"> <li>❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>)</li> </ul>	5/18/10: No user fee 6/1/10: User fee received 8/9/10: Meeting granted 3/22/11: IR 4/8/11: Filing issues identified 4/26/11: Ack resubmission 5/27/11: IR 6/13/11: IR 6/21/11 IR 7/19/11: IR 8/4/11: IR 9/1/11: IR 9/15/11: IR 9/15/11: Ack tradename withdrawa 10/11/12: Review extension 12/14/11: AIP IR
<ul style="list-style-type: none"> <li>❖ Internal memoranda, telecons, etc.</li> </ul>	
<ul style="list-style-type: none"> <li>❖ Minutes of Meetings</li> </ul>	
<ul style="list-style-type: none"> <li>• Regulatory Briefing (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)</li> </ul>	<input type="checkbox"/> N/A or no mtg 8/31/10
<ul style="list-style-type: none"> <li>• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>• EOP2 meeting (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)</li> </ul>	
<ul style="list-style-type: none"> <li>❖ Advisory Committee Meeting(s)</li> </ul>	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> <li>• Date(s) of Meeting(s)</li> </ul>	
<ul style="list-style-type: none"> <li>• 48-hour alert or minutes, if available (<i>do not include transcript</i>)</li> </ul>	
<b>Decisional and Summary Memos</b>	
<ul style="list-style-type: none"> <li>❖ Office Director Decisional Memo (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Division Director Summary Review (<i>indicate date for each review</i>)</li> </ul>	<input type="checkbox"/> None 7/10/12
<ul style="list-style-type: none"> <li>• Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)</li> </ul>	<input type="checkbox"/> None 6/26/12
<ul style="list-style-type: none"> <li>• PMR/PMC Development Templates (<i>indicate total number</i>)</li> </ul>	<input checked="" type="checkbox"/> None

<b>Clinical Information<sup>5</sup></b>	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (indicate date for each review)	
• Clinical review(s) (indicate date for each review)	6/26/12 Filing Reviews: 4/1/11, 7/14/10
• Social scientist review(s) (if OTC drug) (indicate date for each review)	<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 (indicate date of review/memo)	6/26/12
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (indicate date of each review)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (indicate date of each review)	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management <ul style="list-style-type: none"> <li>• REMS Documents and Supporting Statement (indicate date(s) of submission(s))</li> <li>• REMS Memo(s) and letter(s) (indicate date(s))</li> <li>• Risk management review(s) and recommendations (including those by OSE and CSS) (indicate date of each review and indicate location/date if incorporated into another review)</li> </ul>	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (include copies of DSI letters to investigators)	<input checked="" type="checkbox"/> None requested
<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input type="checkbox"/> None
<b>Biostatistics</b> <input checked="" type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 10/4/11 1/23/12: AIP review 6/19/12: Review Addendum Filing Review: 7/6/10, 4/4/11
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input type="checkbox"/> None 9/2/11

<sup>5</sup> Filing reviews should be filed with the discipline reviews.

<b>Nonclinical</b> <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
• Supervisory Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 10/4/11 Filing Reviews: 7/6/10, 3/31/11
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary ( <i>include copies of DSI letters</i> )	<input checked="" type="checkbox"/> None requested
<b>Product Quality</b> <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 9/30/11
• Branch Chief/Team Leader Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 9/28/11
• Product quality review(s) including ONDQA biopharmaceutics reviews ( <i>indicate date for each review</i> )	<input type="checkbox"/> None CMC: 9/28/11 1/20/12: AIP review 1/31/12: EES inspection and packaging review 6/19/12: Review Addendum 7/3/12: Review Addendum Filing Review: 7/8/10, 3/29/11 Biopharmaceutics: 8/31/11 Filing Review: 4/5/11
❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) ( <i>indicate date of each review</i> ) <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion ( <i>indicate review date</i> )( <i>all original applications and all efficacy supplements that could increase the patient population</i> )	9/28/11
<input type="checkbox"/> Review & FONSI ( <i>indicate date of review</i> )	
<input type="checkbox"/> Review & Environmental Impact Statement ( <i>indicate date of each review</i> )	

❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (date completed must be within <b>2 years</b> of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites <sup>6</sup> )	Date completed: 12/9/11 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (date of most recent TB-EER must be within <b>30 days</b> of action date) (original and supplemental BLAs)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (check box only, do not include documents)	<input type="checkbox"/> Completed <input checked="" type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

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

## Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

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

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/s/  
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MATTHEW E WHITE  
07/12/2012

86 Pages Have Been Withheld In Full As b4 and b5 Immediately Following This Page



NDA 201922

**INFORMATION REQUEST**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ximino (minocycline hydrochloride) Extended Release Capsules, 45mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

We are reviewing your NDA resubmission and have the following information requests. We request a written response by December 23, 2011 in order to continue our evaluation of your NDA.

1. Provide a tabulated list of the manufacture and test sites of the drug substance, drug product, and reference standards used in or as the development, pivotal, and registration batches of the drug product with inclusion of pertinent batch numbers and manufacture or test dates.
2. If any material was manufactured or provided from or tested by Ranbaxy Laboratories Limited's **Paonta Sahib** or **Dewas** facilities located in India describe how that material was used in sufficient detail to understand the connection to NDA 201922. For example, "This standard was used to analyze drug substance Batch ABC which was used to produce drug product Batch XYZ. Drug product Batch XYZ was used for dissolution method development."

If you have any questions, call Matthew White, Regulatory Project Manager, at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Gordana Diglisic, M.D.  
Clinical Team Leader  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/  
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GORDANA DIGLISIC  
12/14/2011



NDA 201922

**PROPRIETARY NAME REQUEST  
CONDITIONALLY ACCEPTABLE**

Ranbaxy Laboratories Limited  
c/o Ranbaxy Inc  
600 College Road East  
Princeton, NJ 08540

ATTENTION: Scott D. Tomsky  
US Agent for Ranbaxy Laboratories Limited

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) dated May 10, 2010, received May 10, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Minocycline Hydrochloride Extended-release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

We also refer to your August 9, 2011, correspondence, received August 9, 2011, requesting review of your proposed proprietary name, Ximino. We have completed our review of the proposed proprietary name, Ximino and have concluded that it is acceptable.

The proposed proprietary name, Ximino, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your August 9, 2011 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Janet Anderson, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0675. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Matthew White at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

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

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/s/  
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CAROL A HOLQUIST  
10/26/2011



NDA 201922

**REVIEW EXTENSION –  
MAJOR AMENDMENT**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your February 4, 2011 New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (minocycline hydrochloride) Extended Release Capsules, 45mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

On September 26, 2011, we received your September 23, 2011 unsolicited major amendment to this application. The receipt date is within three months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is March 4, 2012.

In addition, in accordance with the “PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES – FISCAL YEARS 2008 THROUGH 2012,” the timeline for communicating labeling changes and/or postmarketing requirements/commitments, provided in our April 8, 2011 filing communication letter, no longer applies and no new timeline will be provided.

If you have any questions, call Matthew White, Regulatory Project Manager, at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Barbara Gould, M.B.A.H.C.M  
Chief, Project Management Staff  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/  
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MARGO L OWENS

10/11/2011

Signing for Barbara Gould, CPMS



NDA 201922

## INFORMATION REQUEST

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky  
US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (minocycline hydrochloride) Extended Release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

FDA investigators have identified significant violations to the bioavailability and bioequivalence requirements of Title 21, Code of Federal Regulation, Part 320 in bioanalytical studies conducted by Cetero Research in Houston, Texas (Cetero).<sup>1</sup> The pervasiveness and egregious nature of the violative practices by Cetero has led FDA to have significant concerns that the bioanalytical data generated at Cetero from April 1, 2005 to June 15, 2010, as part of studies submitted to FDA in New Drug Applications (NDA) and Supplemental New Drug Applications (sNDA) are unreliable. FDA has reached this conclusion for three reasons: (1) the widespread falsification of dates and times in laboratory records for subject sample extractions, (2) the apparent manipulation of equilibration or “prep” run samples to meet pre-determined acceptance criteria, and (3) lack of documentation regarding equilibration or “prep” runs that prevented Cetero and the Agency from determining the extent and impact of these violations.

Serious questions remain about the validity of any data generated in studies by Cetero Research in Houston, Texas during this time period. In view of these findings, FDA is informing holders of approved and pending NDAs of these issues.

The impact of the data from these studies (which may include bioequivalence, bioavailability,

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<sup>1</sup> These violations include studies conducted by Bioassay Laboratories and BA Research International specific to the Houston, Texas facility.

drug-drug interaction, specific population, and others) cannot be assessed without knowing the details regarding the study and how the data in question were considered in the overall development and approval of your drug product. At this time, the Office of New Drugs is searching available documentation to determine which NDAs are impacted by the above findings.

To further expedite this process, we ask that you inform us if you have submitted any studies conducted by Cetero Research in Houston, Texas during the time period of concern (April 1, 2005 to June 15, 2010). Please submit information on each of the studies, including supplement number (if appropriate), study name/protocol number, and date of submission. With respect to those studies, you will need to do one of the following: (a) re-assay samples if available and supported by stability data, (b) repeat the studies, or (c) provide a rationale if you feel that no further action is warranted.

**Please respond to this query within 30 days from the date of this letter.**

This information should be submitted as correspondence to your NDA. In addition, please provide a desk copy to:

Office of New Drugs  
Center for Drug Evaluation and Research  
10903 New Hampshire Avenue  
Bldg. 22, Room 6300  
Silver Spring, MD 20993-0002

If you have any questions, call Barbara Gould, Chief, Project Staff Management, at (301) 796-4224.

Sincerely,

*{See appended electronic signature page}*

Susan J. Walker, M.D., F.A.A.D.  
Director  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/  
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BARBARA J GOULD

09/15/2011

p.p. DIVISION DIRECTOR Susan J. Walker



NDA 201922

**PROPRIETARY NAME REQUEST  
WITHDRAWN**

Ranbaxy Laboratories Limited  
c/o Ranbaxy Inc, US Agent  
600 College Road East  
Princeton, NJ 08540

ATTENTION: Scott D. Tomsky  
US Agent for Ranbaxy Laboratories Limited

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) dated May 10, 2010, received May 10, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Minocycline Hydrochloride Extended-release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

We acknowledge receipt of your August 9, 2011 correspondence, on August 9, 2011, notifying us that you are withdrawing your request for a review of the proposed proprietary name [REDACTED] (b) (4). This proposed proprietary name request is considered withdrawn as of August 9, 2011.

We also acknowledge receipt of your August 9, 2011 correspondence, on August 9, 2011, requesting review of Ximino, the secondary name submitted in your June 9, 2011 submission.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Janet Anderson, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0675. For any other information regarding this application, contact Matthew White in the Office of New Drugs (OND) Regulatory Project Manager at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

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

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/s/  
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CAROL A HOLQUIST  
09/15/2011



NDA 201922

**REQUEST FOR NDA SAFETY UPDATE**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your new drug application (NDA) for (minocycline hydrochloride) Extended Release Capsules, 45mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your pending NDA by submitting all safety information you now have regarding your new drug. The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.
2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
  - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
  - Present tabulations of the new safety data combined with the original NDA data.
  - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
  - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature study discontinuation by incorporating the dropouts from the newly completed studies. Describe any new trends or patterns identified.
4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.
5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.

6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
7. Provide English translations of current approved foreign labeling not previously submitted.

Please submit this information as soon as possible. If you have any questions, call Matthew White, Regulatory Project Manager, at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Barbara Gould, M.B.A.H.C.M.  
Chief, Project Management Staff  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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BARBARA J GOULD  
09/01/2011



NDA 201-922

## INFORMATION REQUEST

Ranbaxy Laboratories Limited  
c/o Ranbaxy Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to Ranbaxy Laboratories Limited's New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Minocycline Hydrochloride Extended Release Capsules.

Please also refer to Ranbaxy Laboratories Limited's July 5, 2011, submission and to the teleconference held between Ranbaxy Laboratories Limited, Ranbaxy Inc. and the FDA on August 3, 2011. We are reviewing the Chemistry, Manufacturing and Controls sections of NDA 201-922 and have the following comments and information requests.

Please submit your official responses by the August 10, 2011, timeline that you proposed during the August 3, 2011, teleconference (with the exception of August 25, 2011, as agreed for 1d). We would like to re-iterate that responses officially submitted later than August 31, 2011, may not be considered in this review cycle.

1. During the teleconference held on August 3, 2011, you stated that you had developed a new HPLC method for quantitation of impurities in the drug product, and that the concerned unknown impurity found in the drug product was a known related substance that originated from the drug substance. Based on the information provided, we would like to further request the following information:
  - a. The HPLC chromatograms with peak assignments and retention times, from both the original and the revised HPLC methods used for quantitation of the impurities in the drug product, for the batches (#2024828, #2119411 and #2131397) of the drug substance used in the manufacture the registration batches of the drug product.
  - b. The HPLC chromatograms with peak assignments and retention times, from both the original and the revised HPLC methods used for quantitation of the impurities in the drug product, for the long-term and accelerated stability samples from batches

- #2065673, #2132003 and #2142165 of the drug product packaged in bottle (30 capsules/bottle) and blister at current time point (month 6 for the accelerated stability samples). All the chromatograms submitted should be scaled properly to show the impurity peaks.
- c. Any additional information that can confirm that the concerned unknown impurity in the drug product is the known related substance that originated from the drug substance.
  - d. A comparison of levels of impurities in the registration stability samples (from all the packaging configurations, batches and strengths of the extended release capsules tested under long-term testing condition at current time point and accelerated testing condition at month 6), determined using both the original and the revised HPLC methods for quantitation of impurities present in the drug product.
2. The requested holding time of (b) (4) for the intermediates and the extended release capsules is not justified. Tabulate the holding time for the intermediates and the finished capsules during manufacturing the registration batches of the drug product. The holding time for the intermediates and the finished capsules (b) (4) than the one used during manufacturing the registration batches of the drug product.
  3. Provide the derivation of the formulas used to calculate the levels of (b) (4) present in the drug substance.
  4. Update the in-process controls provided in 3.2.p.3.4 to include the in-process control(s) for the (b) (4) during manufacture of the extended release capsules.
  5. Update the drug product specification tables for all the strengths of the extended release capsules to include the revised test method (the revised HPLC method); acceptance criteria for any unknown impurity and (b) (4); and test methods and acceptance criteria for microbial limit tests.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Matthew White, Regulatory Project Manager the Office of New Drugs (Matthew.White@fda.hhs.gov).

If you have any questions or would prefer a teleconference to discuss these issues, please contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

*{See appended electronic signature page}*

Moo-Jhong Rhee, Ph.D.  
Chief, Branch IV  
Division of New Drug Quality Assessment II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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/s/  
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MOO JHONG RHEE  
08/04/2011  
Chief, Branch IV



NDA 201-922

**INFORMATION REQUEST**

Ranbaxy Laboratories Limited  
c/o Ranbaxy Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Minocycline Hydrochloride Extended Release Capsules.

We are reviewing the Biopharmaceutics section of your submission and have the following comments and information requests. We request your written response by August 12, 2011, in order to continue our evaluation of your NDA.

The IVIVC study is not acceptable due to the following facts:

[REDACTED] (b) (4)

[REDACTED]

Without an IVIVC justification, the widened dissolution acceptance criteria you proposed are not adequate.

We recommend the following dissolution acceptance criteria:

0.5 h: [REDACTED] (b) (4)  
1.5 h: [REDACTED] (b) (4)  
3.0 h: NLT [REDACTED] (b) (4)

using the conditions you proposed as shown below:

Apparatus: USP 1 (basket)  
Rotation: 100 rpm  
Medium: 0.1 N HCl  
Volume: 900 mL  
Temperature:  $37 \pm 0.5^{\circ}\text{C}$

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Matthew White, Regulatory Project Manager the Office of New Drugs (Matthew.White@fda.hhs.gov).

If you have any questions or would prefer a teleconference to discuss these issues, please contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

*{See appended electronic signature page}*

Moo-Jhong Rhee, Ph.D.  
Chief, Branch IV  
Division of New Drug Quality Assessment II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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MOO JHONG RHEE  
07/19/2011  
Chief, Branch IV



NDA 201922

**INFORMATION REQUEST**

Ranbaxy Laboratories Limited  
c/o Ranbaxy Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Minocycline Hydrochloride Extended Release Capsules.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a written response by July 5, 2011, in order to continue our evaluation of your NDA.

1. Update the drug substance specification to be in line with the latest drug substance specification provided by the DMF holder.
2. Tighten the acceptance criterion of any unknown impurity from NMT (b) (4) to NMT (b) (4) in the drug substance specification.
3. Include the particle size test to the proposed reduced testing for the drug substance.
4. Provide the exact test method and procedure for the test on description of the drug substance.
5. Provide information regarding the reference standards of the known impurities used in the validation study of the HPLC method employed to determine drug substance impurities.
6. Provide detailed information regarding preparation of the standard solutions of the known impurities used in the validation study of the HPLC method employed to determine drug substance impurities.
7. Provide relative response factors for all the known impurities in the drug substance.
8. Provide in-process controls that are implemented for the manufacture of the extended release capsules.

9. Provide in-process controls implemented to ensure (b) (4) (b) (4) are filled into each capsule.
10. Tighten the acceptance criterion of any unknown impurity from NMT (b) (4) to NMT (b) (4) in the drug product specification. Alternatively, identify and qualify the unknown impurity or impurities if the proposed acceptance criterion of any unknown impurity is set higher than (b) (4).
11. Change the acceptance criterion for the known impurity, (b) (4) from (b) (4) to (b) (4) in the drug product specification.
12. Add microbial limits tests and acceptance criteria to the drug product specification.
13. Provide the exact test method and procedure for the test on description of the drug product.
14. Provide information regarding the reference standard of the known impurity, (b) (4) used to control the drug product.
15. Provide peak purity results for the known impurities in the forced degradation study, which was part of the validation studies of the HPLC method used for quantitation of the degradatants in the drug product.
16. Update validation results on specificity of the UV method, used to quantitate the amount of drug released from the extended release capsules, to include the strengths of 67.5 mg and 112.5 mg of the capsules.
17. The packaging materials provided by (b) (4) have not been used in the stability studies. Therefore, the packaging materials provided by (b) (4) should not be used in commercial production until they are qualified through stability studies.
18. Clarify if the proposed blister pack is child-resistant.
19. Provide pertinent CFR food additive regulations for the components used in the container closure systems (including the components used in the desiccant) of the drug product.
20. Clarify if the registration stability batches of the drug product were prepared with aged intermediates or the capsules that had been held in shipment packs for (b) (4) before final packaging for registration stability studies. The requested holding time of (b) (4) for the intermediates and the extended release capsules is not acceptable without supportive stability data obtained from pilot or production scale batches of the drug product prepared with aged intermediates or capsules that have been held for the proposed holding time in shipment pack before final packaging.

21. Clarify the ratio between [REDACTED] (b) (4) used in the [REDACTED] (b) (4). The ratio between [REDACTED] (b) (4) used in the executed batches of the minitablets was different from the one listed in the batch formula provided in 3.2. P. 3.2. Confirm the ratio that will be used for commercial production.
22. Provide the forecast of yearly US sale of all Ranbaxy's drug products containing minocycline hydrochloride for five years, and calculate Expected Introduction Concentration using the forecast.

If you have any questions, call Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

*{See appended electronic signature page}*

Moo-Jhong Rhee, Ph.D.  
Chief, Branch IV  
Division of New Drug Quality Assessment II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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MOO JHONG RHEE  
06/21/2011  
Chief, Branch IV



NDA 201922

**INFORMATION REQUEST**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, U.S. Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (minocycline hydrochloride) Extended Release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

We are reviewing your request for waiver of bioavailability studies and have the following comments and information requests. We request a written response by June 27, 2011 in order to continue our evaluation of your NDA.

1. The dissolution data in the submission are not legible. Provide clear copies with legible font and the raw data in SAS transport file format.
2. Provide the dissolution profile comparisons between the proposed formulation and the reference formulation and between the strengths requesting waiver of bioavailability studies and those with bioequivalence data using an appropriate method, such as f2 factor. When the f2 factor is used, only one measurement should be considered after (b) (4) dissolution for both the products.

If you have any questions, call Matthew White, Regulatory Project Manager, at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Gordana Diglisic, M.D.  
Clinical Team Leader  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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GORDANA DIGLISIC  
06/13/2011



NDA 201922

**INFORMATION REQUEST**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (minocycline hydrochloride) Extended Release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

We also refer to your May 11, 2011 submission, containing your responses to information requested in the filing communication dated April 08, 2011.

We are reviewing the Nonclinical section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA. Submit a written response Nonclinical information requests by June 1, 2011.

- In your response to the nonclinical information requested in the filing communication dated April 8, 2011, you provided information for the degradant impurity (b) (4) in your drug product and the listed drug product. However, you should provide a full impurity profile comparison between the listed drug product and your drug product. It should include levels for each of the degradant and non-degradant impurities, and total impurities. The degradant and non-degradant impurities should be identified by their name and not by their code number.

If you have any questions, call Matthew White, Regulatory Project Manager, at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Gordana Diglisic, M.D.  
Clinical Team Leader  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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GORDANA DIGLISIC  
05/27/2011



NDA 201922

**ACKNOWLEDGE RESUBMISSION  
AFTER REFUSE-TO-FILE**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, U.S. Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

We have received your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act in response to our July 16, 2010, refusal to file letter for the following:

Name of Drug Product: (minocycline hydrochloride) Extended Release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg

Review Priority Classification: Standard

Date of Application: February 4, 2011

Date of Receipt: February 4, 2011

Our Reference Number: NDA 201922

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 April 5, 2011 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be December 4, 2011.

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. Once the application has been filed we will notify you whether we have waived the pediatric study requirement for this application.

Please cite the NDA number listed above 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 Dermatology and Dental Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

If you have any questions, call Matthew White, Regulatory Project Manager, at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Matthew White  
Regulatory Project Manager  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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MATTHEW E WHITE  
04/26/2011



NDA 201922

**FILING COMMUNICATION**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) dated February 1, 2011 received February 4, 2011 submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (minocycline hydrochloride) Extended Release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

We also refer to your submissions dated February 18, March 1, 4, and 28, 2011.

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, December 4, 2011 is the user fee goal date.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by October 11, 2011.

During our filing review of your application, we identified the following potential review issues and have the following requests for information: Please respond to the following requests for information by May 12, 2011.

### **Chemistry, Manufacturing and Controls (CMC)**

1. Clarify whether the 500 count bottle is for pharmacy dispensing.
2. Clarify whether the blister pack configuration is child resistant.
3. Your claim for categorical exclusion for your NDA from the preparation of an Environmental Assessment cannot be granted on the basis of 21 CFR 25.31(e). This regulation supports categorical exclusion from Environmental Assessment for INDs. Resubmit the claim with an appropriate basis and supporting information for a NDA. Be reminded that any claim of categorical exclusion based on 21 CFR 25.31(b) will need to be supported by an expected introduction concentration (EIC) calculation and five years of production forecast.

### **Nonclinical**

4. Provide an impurity profile comparison between the listed drug product and your drug product. Additional nonclinical bridging toxicology studies may be needed if there are any significant differences in the impurity profile for the listed drug product compared to the impurity profile for your drug product.

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

During our preliminary review of your submitted labeling, we have identified the following labeling format issues:

### **Highlights Section:**

5. The Highlights must be limited in length to one-half page, in 8 point type, two-column format. [21 CFR 201.57(a)(1)]
6. Highlights Limitation Statement: The name of the drug product must be bolded and in upper case.

### **Full Prescribing Information (FPI) Section:**

7. For the “Clinical Trials Experience” subsection, the following verbatim statement should precede the presentation of adverse reactions:  
“Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.”

8. For the “Postmarketing Experience” subsection, include the following verbatim statement:

“The following adverse reactions have been identified during post approval use of minocycline hydrochloride. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.”

9. The following statement should appear at the beginning of Section 17 for prominence:

“See FDA-Approved Patient Labeling (Patient Information)”

We request that you resubmit labeling that addresses these issues by May 27, 2011. The resubmitted labeling will be used for further labeling discussions.

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

If you have any questions, call Matthew White, Regulatory Project Manager, at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Susan J. Walker, M.D., F.A.A.D.  
Director  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/  
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SUSAN J WALKER  
04/08/2011



NDA 201922

**INFORMATION REQUEST**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (minocycline hydrochloride) Extended Release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg.

We are reviewing the Biopharmaceutics and Clinical sections of your submission and have the following information requests. We request a written response by March 28, 2011 in order to continue our evaluation of your pending NDA.

**Biopharmaceutics**

1. Provide all the data for the in-vitro in-vivo correlation (IVIVC) report, including in vivo data for each subject and in vitro data for each unit both for the model building and the validation. The data can be provided in SAS transport file format.
2. It is noted that in the pharmaceutical development report provided in 3.2.P.2, you investigated the effects of different manufacturing process. However, the investigation was focused on (b) (4) Conduct (b) (4) and provide all the parameters for each batch, even though they are not the one to be investigated. The data can be provided in SAS transport file format.

**Clinical**

3. Clarify whether ages (b) (4) requested for pediatric waiver are the intended ages in view of labeling indication for treatment of (only inflammatory lesions of non-nodular moderate to severe) acne vulgaris in patients 12 years of age and older.

If you have any questions, call Matthew White, Regulatory Project Manager, at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Gordana Diglisic, M.D.  
Clinical Team Leader  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/  
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GORDANA DIGLISIC  
03/22/2011



NDA 201922

**MEETING MINUTES**

Ranbaxy Laboratories Limited  
Attention: Scott D. Tomsky  
Sr. Director, Regulatory Affairs  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (minocycline hydrochloride) Extended Release Capsules, 135 mg.

We also refer to the teleconference between representatives of your firm and the FDA on August 31, 2010. The purpose of the meeting was to discuss the deficiencies provided in the Refuse to File Letter.

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

If you have any questions, call Matthew White, Regulatory Project Manager at (301) 796-4997.

Sincerely,

*{See appended electronic signature page}*

Susan J. Walker, M.D., F.A.A.D.  
Director  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research



FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

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**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** TYPE A  
**Meeting Category:** Other (Refuse to File)

**Meeting Date and Time:** August 31, 2010, 1:00 PM  
**Meeting Location:** Teleconference

**Application Number:** NDA 201922  
**Product Name:** (minocycline HCl) Extended Release Capsules, 135 mg  
**Indication:** Treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris

**Sponsor/Applicant Name:** Ranbaxy Laboratories Limited

**Meeting Chair:** Susan J. Walker, M.D.  
**Meeting Recorder:** Matthew White

**FDA ATTENDEES**

Susan J. Walker, M.D., F.A.A.D., Director, DDDP  
Patricia Brown, M.D., Clinical Reviewer, DDDP  
Gordana Diglisic, M.D., Clinical Reviewer, DDDP  
Shulin Ding, Ph.D., CMC Lead, DNDQA II  
Raymond Frankewich, Ph.D., Quality Reviewer, DNDQA II  
Carin Kim, Ph.D., Biostatistics Reviewer, DB III  
Dennis Bashaw, Pharm. D., Director, DCP 3  
Doanh Tran, Ph.D., Clinical Pharmacology Team Leader, DCP3  
Chinmay Shukla, Ph.D., Clinical Pharmacology Reviewer, DCP3  
Barbara Gould, M.B.A.H.C.M., Chief, Project Management Staff, DDDP  
Margo Owens, Project Management Team Leader, DDDP  
Matthew E. White, Regulatory Health Project Manager, DDDP

**SPONSOR ATTENDEES**

Sudershan Arora, President R&D, Ranbaxy Laboratories Limited, India  
Tausif Monif, Vice President, Clinical Pharmacology & Pharmacokinetics,  
Ranbaxy Laboratories Limited, India  
Rajender Singh, Director, Regulatory Affairs, Ranbaxy Laboratories  
Limited, India  
Scott D. Tomsy, Sr. Director, Regulatory Affairs, Ranbaxy Inc., USA  
Usha Sankaran, Associate Director, Regulatory Affairs, Ranbaxy Inc.,  
USA

**Purpose of the Meeting:**

The purpose of this meeting is to discuss comments provided in the Refuse to File letter dated July 14, 2010.

**General**

**Question 3:**

The Refusal to File letter states that it consists of only a partial listing of deficiencies and that there may be additional deficiencies that are not listed in the letter. Has the Agency identified any other deficiencies in the submission that they can share at this time?

**Response:**

The pertinent filing issues have been addressed in the refuse to file letter.

**Regulatory**

**Question 4:**

The Refusal to File letter also states “*Your application does not contain a signed Debarment Certification and Financial Disclosure forms from the applicant*”. Ranbaxy understands that the Agency would like a signed Debarment Certification from the applicant, rather than the applicant’s US Agent. In addition, Ranbaxy wishes to point out that the Financial Disclosures signed by the applicant were provided on June 30, 2010. Can the Agency confirm if they have received this information?

**Response:**

Yes. The Agency acknowledges receipt of your signed financial disclosure forms.

**Chemistry, Manufacturing and Controls (CMC)**

**Question 5:**

The original NDA application includes 6 months accelerated stability data for the 135 mg strength. Ranbaxy has also now generated 6 months accelerated stability data on the 45 mg and 90 mg strengths which will be included in the amendment that Ranbaxy plans to submit following this meeting. As mentioned earlier Ranbaxy is also working on other intermediate strengths – 67.5 mg and 112.5 mg for which at present time, 3 months stability data is available. It should be noted that all strengths of the drug product are dose proportional. Based on this information, will the Agency accept submission of the 67.5 mg and 112.5 mg strengths with 3 months stability data and the updated data will be provided when it becomes available?

**Response:**

The NDA should be complete at time of submission.

Regarding stability data for the 45, 90, and 135 mg strength capsules: a reasonable expiration date cannot be established unless at least 12 months data for samples stored at controlled room temperature conditions (25 C / 65% RH) and 6 months data for samples stored at accelerated conditions (40 C / 75% RH) is provided. This data must be provided early enough in the NDA review period to allow a reasonable evaluation from all appropriate disciplines.

Confirm that the 45 mg and 90 mg strength capsules (b) (4) (b) (4) that have been described previously in this NDA.

**Meeting Discussion:**

Sponsor proposed to submit 6 months of stability data with room temperature storage and 6 months of accelerated storage. Sponsor will amend the application with 12 months of room temperature storage.

The agency agrees.

**Pharmacology/Toxicology**

There are no Pharmacology/Toxicology questions presented in this briefing package.

**Clinical Pharmacology/Biopharmaceutics**

**Question 1:**

Ranbaxy believes that it has conducted BE studies sufficient to support the 135 mg strength, filed pursuant to Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act and is relying on the agency's findings for a previously approved drug (Solodyn) to make this application sufficiently complete to permit a substantive review. Based on the information provided above, does the Agency agree?

**Response:**

No. We do not agree.

We had raised this issue in our advice/information request letter dated January 14, 2010 following review of your IND 107472 received by FDA on 12/14/2009. We note that study no. 1974/09 (fasting) was initiated on December 1, 2009 and study no. 1975/09 (fed) was initiated on December 10, 2009, before the IND was received by the Agency. Furthermore, you completed both studies before you received the advice/information request letter from the Agency on 1/14/2010. You did not address our comments to the IND prior to the NDA submission.

Since drug bioavailability is formulation dependent and different populations may respond differently to your formulation and the listed drug formulation, demonstrating bioequivalence (BE) of your formulation to the listed drug in an ethnically homogenous population of South Asian males can not be extrapolated as demonstrating BE in an ethnically diverse population of both males and females.

We advise you to conduct new BE studies under fasting and fed conditions with your to-be-marketed 135 mg formulation. The new pivotal BE studies should be conducted in a population representative of the United States population and should include similar proportions of males and females.

**Meeting Discussion:**

The sponsor clarified their rationale for the program submitted in this application. There was discussion concerning informational needs and study design. The Agency commented that the sponsor can conduct two separate studies as recommended or they may conduct a single four arm study (fasting and fed) in a diverse population (race and gender).

**Question 2:**

As explained earlier, Ranbaxy plans to amend the application following the outcome of this meeting to include the 45 mg and 90 mg strengths. This amendment will include a study to evaluate doses 45 mg, 90 mg and 135mg test and 135 mg reference under fasting condition, so as to assess the pharmacokinetic behavior of the product. When submitted, will the Agency consider the application complete in order to permit its substantive review?

**Response:**

Since your 45 mg, 90 mg and 135 mg capsule formulations contain (b) (4) minitabs, respectively, within each capsule (b) (4) and assuming that the 3 strengths have similar dissolution profile, your proposed study appears appropriate to support the 45 mg and 90 mg capsule strengths.

**Clinical**

There are no Clinical questions presented in this briefing package.

**Biostatistics**

There are no Biostatistics questions presented in this briefing package.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201922	GI-1	RANBAXY LABORATORIES LTD	MINOCYCLINE ER CAPSULES 135 mg

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/s/

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SUSAN J WALKER  
09/03/2010



NDA 201922

**MEETING REQUEST GRANTED**

Ranbaxy Inc.  
Attention: Scott D. Tomsky  
Sr. Director, Regulatory Affairs  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Minocycline Hydrochloride Extended Release Capsules, 135mg.

We also refer to your July 23, 2010, correspondence requesting a meeting to discuss the Refusal to File Letter. Based on the statement of purpose, objectives, and proposed agenda, we consider the meeting a type A meeting.

The meeting is scheduled as follows:

**Date:** August 31, 2010  
**Time:** 1:00 pm  
**Location:** 10903 New Hampshire Avenue  
White Oak Building 22  
Silver Spring, Maryland 20903

Please e-mail any updates to your attendees at [Barbara.Gould@fda.hhs.gov](mailto:Barbara.Gould@fda.hhs.gov), at least one week prior to the meeting. For each foreign visitor, complete and email me the enclosed Foreign Visitor Data Request Form, at least two weeks prior to the meeting. A foreign visitor is defined as any non-U.S. citizen or dual citizen who does not have a valid U.S. Federal Government Agency issued Security Identification Access Badge. If we do not receive the above requested information in a timely manner, attendees may be denied access.

Please have all attendees bring valid photo identification and allow 15-30 minutes to complete security clearance. Upon arrival at FDA, provide the guards with either of the following numbers to request an escort to the conference room: Barbara Gould or Martha Carter at 301-796-2110.

Submit background information for the meeting (three paper copies or one electronic copy to the application and 15 desk copies to me) at least 2 weeks prior to the meeting. If the materials

presented in the information package are inadequate to prepare for the meeting or if we do not receive the package by August 17, 2010, we may cancel or reschedule the meeting.

Submit the 15 desk copies to the following address:

Tisha Washington  
Food and Drug Administration  
Center for Drug Evaluation and Research  
White Oak Building 22, Room: 5177  
10903 New Hampshire Avenue  
Silver Spring, Maryland 20903

If you have any questions, call me at (301) 796-1019.

Sincerely,

*{See appended electronic signature page}*

Tisha Washington  
Technical Information Specialist  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

ENCLOSURE: Foreign Visitor Data Request Form

## FOREIGN VISITOR DATA REQUEST FORM

VISITORS FULL NAME (First, Middle, Last)	
GENDER	
COUNTRY OF ORIGIN/CITZENSHIP	
DATE OF BIRTH (MM/DD/YYYY)	
PLACE OF BIRTH (city and country)	
PASSPORT NUMBER COUNTRY THAT ISSUED PASSPORT ISSUANCE DATE: EXPIRATION DATE:	
VISITOR ORGANIZATION/EMPLOYER	
MEETING START DATE AND TIME	
MEETING ENDING DATE AND TIME	
PURPOSE OF MEETING	
BUILDING(S) & ROOM NUMBER(S) TO BE VISITED	
WILL CRITICAL INFRASTRUCTURE AND/OR FDA LABORATORIES BE VISITED?	
HOSTING OFFICIAL (name, title, office/bldg, room number, and phone number)	
ESCORT INFORMATION (If different from Hosting Official)	

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201922	GI-1	RANBAXY LABORATORIES LTD	MINOCYCLINE ER CAPSULES 135 mg

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/s/

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TISHA L WASHINGTON  
08/09/2010



NDA 201922

**REFUSAL TO FILE**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your May 10, 2010, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (minocycline hydrochloride) Extended Release Capsules, 135 mg.

After a preliminary review, we find your application is not sufficiently complete to permit a substantive review. Therefore, we are refusing to file this application under 21 CFR 314.101(d) for the reasons below. Please note that the following is only a partial listing of deficiencies, and that there may be additional deficiencies with your submission that are not listed below:

21 CFR 314.101(d)(3): The application is incomplete because it does not on its face contain information required under section 505(b) and 21 CFR 314.50.

1. Your bioequivalence studies do not contain adequate evaluation for safety and/or effectiveness of the population intended to use the drug, including pertinent subsets, such as gender, age and racial subsets, or the subset of patients weighing less than 200 pounds (91 kg).

You conducted your bioequivalence studies 1974/09 and 1975/09 in an ethnically homogeneous population of South Asians. This population is not representative of the United States population. Furthermore, your bioequivalence studies included only male subjects. However, you are seeking approval for an indication that affects both male and female patients.

You provided information to support only the 135mg dose, which would not provide the appropriate dose for patients weighing less than 200 pounds (91 kg).

2. Your application does not contain a signed Debarment Certification and Financial Disclosure forms from the applicant.

We will refund 75% of the total user fee submitted with the application.

Within 30 days of the date of this letter, you may request in writing a meeting about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If, after the meeting, you still do not agree with our conclusions, you may request that the application be filed over protest. In that case, the filing date will be 60 days after the date you requested meeting. The application will be considered a new original application for user fee purposes, and you must remit the appropriate fee.

If you have any questions, please call Barbara Gould, Chief, Project Management Staff at (301) 796-4224.

Sincerely yours,

*{See appended electronic signature page}*

Susan Walker, M.D., F.A.A.D.  
Director  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201922	ORIG-1	RANBAXY LABORATORIES LTD	MINOCYCLINE ER CAPSULES 135 mg

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/s/

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BARBARA J GOULD  
07/14/2010

SUSAN J WALKER  
07/16/2010



NDA 201922

**RECEIPT OF USER FEES**

Ranbaxy Laboratories Limited  
c/o Ranbaxy, Inc.  
Attention: Scott D. Tomsky, US Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

Please refer to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug and Cosmetic Act for TRADE NAME (minocycline hydrochloride) Extended Release Capsule, 135 mg.

You were notified in our letter dated May 18, 2010 that your application was not accepted for filing due to non-payment of fees. This is to notify you that the Agency has received all fees owed and your application has been accepted as of May 20, 2010.

Unless we notify you within 60 days of the above date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on July 19, 2010 in accordance with 21 CFR 314.101(a).

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

Please cite the NDA number listed above 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 Dermatology and Dental Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

If you have any questions, contact Barbara Gould, Regulatory Project Manager, at (301) 796-4224.

Sincerely,

*{See appended electronic signature page}*

Barbara Gould, MBAHCM  
Chief, Project Management Staff  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-201922	----- ORIG-1	----- RANBAXY INC	----- MINOCYCLINE ER CAPSULES 135 mg

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/s/  
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BARBARA J GOULD  
06/01/2010



NDA 201922

**UNACCEPTABLE FOR FILING**

Ranbaxy Laboratories Limited  
c/o Ranbaxy Inc.  
Attention: Scott D. Tomsky  
U.S. Agent  
600 College Road East  
Princeton, NJ 08540

Dear Mr. Tomsky:

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

Name of Drug Product: minocycline hydrochloride extended release capsules, 135 mg

Date of Application: May 7, 2010

Date of Receipt: May 10, 2010

Our Reference Number: NDA 201922

We have not received the appropriate user fee for this application. An application is considered incomplete and cannot be accepted for filing until all fees owed have been paid. Therefore, this application is not accepted for filing. We will not begin a review of this application's adequacy for filing until FDA has been notified that the appropriate fee has been paid. Payment should be submitted to the following address:

Food and Drug Administration  
P.O. Box 70963  
Charlotte, NC 28272-0963

Checks sent by a courier should be addressed to:

Wachovia QLP Lockbox – D1113-022  
Food and Drug Administration, Lockbox 70963  
1525 West WT Harris Blvd  
Charlotte, NC 28262

**NOTE: Please include the User Fee I.D. Number, the Application number, and the FDA P.O. Box number (P.O. Box 70963) on the enclosed check. It would be helpful if you included the user fee cover sheet (Form FDA 3397) with your payment.**

The receipt date for this submission (which begins the review for filability) will be the date the review division is notified that payment has been received by the bank.

Please cite the NDA number listed above 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 Dermatology and Dental Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

If you wish to send payment by wire transfer, or if you have any other questions, please call Bev Friedman or Mike Jones at 301-796-3602.

If you have any questions, contact Cristina Attinello, Regulatory Project Manager, at (301) 796-3986.

Sincerely,

*{See appended electronic signature page}*

Susan J. Walker, M.D., F.A.A.D.  
Director  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201922	ORIG-1	RANBAXY INC	MINOCYCLINE ER CAPSULES 135 mg

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/s/

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SUSAN J WALKER  
05/18/2010