

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205388Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 205388

SUPPL # N/A

Trade Name Omidria

Generic Name phenylephrine HCL and ketorolac tromethamine

Applicant Name Omeros Corporation

Approval Date, If Known May 30, 2014

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.

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

d) Did the applicant request exclusivity?

YES NO

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

3

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

YES NO

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

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

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

YES NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES NO

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

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# 203510 phenylephrine hydrochloride solution

NDA# 019700 Acular (ketorolac tromethamine ophthalmic solution) 0.5%

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:

Study C09-001: "A Study of Phenylephrine HCl's and Ketorolac Tromethamine's Ability, Alone and in Combination, to Maintain Mydriasis and Relieve Pain and Inflammation in Subjects Undergoing Unilateral Cataract Extraction with Lens Replacement"

Study OMS302-ILR-003: "A Phase 3 Randomized, Double-Masked, Placebo-Controlled Study of the Effect of OMS302 on Intraoperative Pupil Diameter and Early Postoperative Pain in Subjects Undergoing Intraocular Lens Replacement with Phacoemulsification"

Study OMS302-ILR-004: “A Phase 3 Randomized, Double-Masked, Placebo-Controlled Study of the Pharmacokinetics of OMS302 and the Effect of OMS302 on Intraoperative Pupil Diameter and Early Postoperative Pain in Subjects Undergoing Intraocular Lens Replacement with Phacoemulsification”

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 C09-001 YES NO

Investigation #2 OMS302-ILR-003 YES NO

Investigation #3 OMS302-ILR-004 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 C09-001 YES NO

Investigation #2 OMS302-ILR-003 YES NO

Investigation #3 OMS302-ILR-004 YES NO

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

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

Investigation #1 C09-001

Investigation #2 OMS302-ILR-003

Investigation #3 OMS302-ILR-004

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

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

Investigation #1
IND # 78227 YES ! NO
! Explain:

Investigation #2
IND # 78227 YES ! NO
! Explain:

Investigation #3
IND # 78227 YES ! NO
! Explain:

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

Investigation #1
!

YES
Explain:

! NO
! Explain:

Investigation #2

!
!
! NO
! Explain:

YES
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: **Jacquelyn Smith**
Title: **Senior Project Manager**
Date: May 29, 2014

Name of Office/Division Director signing form: **Renata Albrecht, M.D.**
Title: **Director, Division of Transplant and Ophthalmology Products**

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

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

/s/

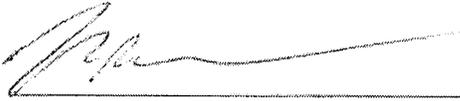
JACQUELYN E SMITH
05/29/2014

RENATA ALBRECHT
05/30/2014

3. DEBARMENT CERTIFICATION

Application Reference No.: NDA 205388

Omeros Corporation in accordance with the Generic Drug Enforcement Act of 1992 hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with the above-identified application.



Marcia S. Kelbon
Vice President, Patent and General Counsel
Omeros Corporation

July 10, 2013

Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 205388 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: Omidria Established/Proper Name: phenylephrine and ketorolac Dosage Form: 1% / 0.3% injection		Applicant: Omeros Corporation Agent for Applicant (if applicable):
RPM: Jacquelyn Smith		Division: Division of Transplant and Ophthalmology Products
<p><u>NDA and NDA Efficacy Supplements:</u></p> <p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>	<p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>NDA# 203510-- phenylephrine hydrochloride Solution; 019700-- Acular (ketorolac tromethamine ophthalmic solution) 0.5%</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>This product provides for a change in dosage form, from topical ophthalmic to ocular irrigating solution and it is a new combination.</p> <p><input type="checkbox"/> This application does not rely upon a listed drug. <input checked="" type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> This application relies on (explain)</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: 5/30/14</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>	
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>May 30, 2014</u> 	<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR	
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 	<input checked="" type="checkbox"/> None	

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

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

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics ³</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): Type 4- New Combination</p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC </p> <p> NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies </p> <p> <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request </p> <p> BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies </p> <p> REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input type="checkbox"/> MedGuide w/o REMS <input type="checkbox"/> REMS not required </p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action (by OEP) 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

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

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

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

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

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

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

CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ⁴	<input checked="" type="checkbox"/>
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s)
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	4/29/14
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	7/30/13
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A

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

<ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>) 	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	N/A
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	N/A
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>) 	
<ul style="list-style-type: none"> • Most-recent draft labeling 	4/25/14
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. 	11/8/13
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input checked="" type="checkbox"/> RPM 10/2/13 <input checked="" type="checkbox"/> DMEPA 4/7/14 <input type="checkbox"/> DMPP/PLT (DRISK) <input checked="" type="checkbox"/> ODPD (DDMAC) 4/14/14 <input type="checkbox"/> SEALD <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	10/7/13
<ul style="list-style-type: none"> ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte 	<input type="checkbox"/> Not a (b)(2) 5/7/14
<ul style="list-style-type: none"> ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	<input type="checkbox"/> Not a (b)(2) 6/4/14
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm 	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>10/30/13</u> If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>) 	<input checked="" type="checkbox"/> Verified, statement is acceptable

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

❖ Outgoing communications (<i>letters, including response to FD RR (do not include previous action letters in this tab), emails, faxes, telecons</i>)	<input checked="" type="checkbox"/>
❖ Internal memoranda, telecons, etc.	<input type="checkbox"/>
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg 2/28/13
• EOP2 meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg 12/7/11
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	N/A
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 5/30/14
Deputy Division Director Review	<input type="checkbox"/> None 5/27/14
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 5/27/14
PMR/PMC Development Templates (<i>indicate total number</i>)	<input type="checkbox"/> None
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	
• Clinical review(s) (<i>indicate date for each review</i>)	5/9/14
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	Clinical Review: 5/9/14 N/A
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	
• REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>)	N/A
• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)	N/A
• Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	<input checked="" type="checkbox"/> None N/A
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	<input type="checkbox"/> None requested 4/14/14

⁶ Filing reviews should be filed with the discipline reviews.

Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None 4/25/14
Clinical Pharmacology <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 4/22/14
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 4/21/14
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (include copies of OSI letters)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews (indicate date for each review)	<input type="checkbox"/> None 5/30/14; 4/22/14
❖ Microbiology Reviews	<input type="checkbox"/> Not needed 12/16/13
<input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (indicate date of each review)	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) (indicate date of each review)	N/A
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<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>)	4/22/14
<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 or EER Summary Report only; do NOT include EER Detailed Report) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷</i>)	Date completed: 5/30/14 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

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

Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

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

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

/s/

JACQUELYN E SMITH
06/04/2014



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

COMMUNICATION TRANSMITTAL SHEET

DATE: April 22, 2014

To: Catherine A. Melfi, PhD VP, Regulatory Affairs & Quality Systems	From: Jacquelyn Smith, M.A., Senior Project Manager
Company: Omeros Corp.	Division of Transplant and Ophthalmology Products
Phone Number: 206-676-5045	Phone Number: 301-796-1600
Email: cmelfi@omeros.com	Email: jacquelyn.smith@fda.hhs.gov

NDA 205388, Omidria

Total no. of pages including cover: 3

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

Dear Dr. Melfi:

Please refer to NDA 205388, Omidria (phenylephrine-ketorolac ophthalmic injection) 1% / 0.3 %, received July 30, 2013.

We have the following information request. We are requesting a response as soon as possible.

Information Request

1. For Study OMS302-ILR-003, please provide a table similar to Table 7 (Supportive Analyses of Pupil Diameter (mm) During Surgery, Full Analysis Set Population found on page 51 of body of study report) **but without subjects with Distorted Video Images and without Dr. Marisco's subjects.**
2. For Study OMS302-ILR-004, please provide a table similar to Table 8 (Supportive Analyses of Pupil Diameter (mm) During Surgery, Full Analysis Set Population found on page 56 of body of study report) **but without subjects with Distorted Video Images and without Dr. Marisco's subjects.**
3. Please provide a re-analysis for OMS302-ILR-004 for the Primary endpoint {Mean Area Under the Curve (AUC) Analysis of Change From Baseline in Pupil Diameter (mm) During Surgery} and Co-Primary Endpoint {Mean Area Under the Curve (AUC) Analysis of Ocular Pain VAS Score Within 12 Hours Postoperatively} excluding Dr. Marciso's patients.

We are providing the above information by email for your convenience. Contact me at 301-796-1002 if you have any questions regarding the contents of this transmission. Thank you.

Regards,

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products
FDA/CDER/OND/OAP

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

/s/

JACQUELYN E SMITH
04/22/2014



NDA 205388

INFORMATION REQUEST

Omeros Corporation
Attention: Catherine A. Melfi
Vice President, Regulatory Affairs & Quality Systems
201 Elliott Avenue West
Seattle, WA 98119

Dear Dr. Melfi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Omidria® (phenylephrine /ketorolac) Injection.

We are reviewing the Chemistry, manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response by April 17, 2014, in order to continue our evaluation of your NDA.

1. We note that the available batch analyses and long term (25°C/60% RH) stability data, albeit limited, support tighter control of the (b)(4) individual unspecified degradation products and total degradation products. We also note that levels of degradants present in clinical trial materials were considerably below the currently proposed levels. In addition your assessment of acceptable levels based on systemic exposure of approximately 1% does not address local (i.e., ocular) exposure and potential toxicity. Based on our assessment, limits of not more than (b)(4) of ketorolac and not more than (b)(4) of individual unspecified degradation products are appropriate. A limit of not more than (b)(4) total degradation products is also appropriate. Please revise the drug product specification accordingly.
2. Based on the available long term, intermediate and accelerated stability data, an expiration dating period of 18 months when drug product is stored at 25°C/60% RH is granted. While the long term and intermediate data appear satisfactory through 12 months, the (b)(4) preclude a longer expiration dating period until additional satisfactory long term stability data are obtained.

3. Please revise the drug product stability commitment to include testing for leachables on at least one batch of product, stored upright and inverted, throughout the proposed shelf-life.
4. Based on the results obtained by the Division of Pharmaceutical Analysis (DPA), we have the following requests:
 - a. Please identify the peak in the chromatograms that elutes at (b) (4) minutes. This peak is observed to form over time in samples analyzed by DPA (and appears in chromatograms on pages 8 and 10 (m3.2.P.5.2)).
 - b. In addition, unknown impurity / degradation product peaks greater than (b) (4) were also observed at retention times of approximately (b) (4) minutes and (b) (4) minutes. Please indicate whether these are drug substance process impurities or if they are degradation products.
 - c. As noted in ICH Q6A, Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, “it is normally not considered necessary to test the drug product for synthesis impurities that are controlled in the drug substance and are not degradation products.” Per Q3B(R2), “a rationale should be provided for exclusion of those impurities that are not degradation products (e.g., process impurities from the drug substance and impurities arising from excipients). Accordingly, please provide a tabulation of all peaks (retention time, relative retention time) in the drug product chromatogram that are considered drug substance process impurities and those that are degradation products, and provide justification for the peak assignments (for example, submit chromatograms of each drug substance (including aged and/or stressed samples) using the proposed regulatory procedure for the drug product, along with chromatograms of the drug product (including aged and/or stressed samples) obtained under the same chromatographic conditions).

If you have any questions, call Navdeep Bhandari, Regulatory Health Project Manager, at (240) 402 -3815.

Sincerely,

{See appended electronic signature page}

Rapti D. Madurawe, Ph.D.
Branch Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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

/s/

RAPTI D MADURawe
04/04/2014



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

COMMUNICATION TRANSMITTAL SHEET

DATE: March 24, 2014

To: Catherine A. Melfi, PhD VP, Regulatory Affairs & Quality Systems	From: Jacquelyn Smith, M.A., Senior Project Manager
Company: Omeros Corp.	Division of Transplant and Ophthalmology Products
Phone Number: 206-676-5045	Phone Number: 301-796-1600
Email: cmelfi@omeros.com	Email: jacquelyn.smith@fda.hhs.gov

NDA 205388, Omidria

Total no. of pages including cover: 3

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

Dear Dr. Melfi:

Please refer to NDA 205388, Omidria (phenylephrine-ketorolac ophthalmic injection) 1% / (b)(4) received July 30, 2013.

We have the following information request. We are requesting a response by Thursday, March 27th.

Information Request

Your latest 356(h) dated 3/24/14 lists NDAs 203510 (Phenylephrine Hydrochloride) and 019700 (Acular) as the listed drug products that are the basis for the submission

You also state in Module 2.2 that, “the components of OMS302 have been on the market for several years and have well established profiles through extensive nonclinical and clinical experience. Phenylephrine and KE both have a long history of use as topical agents in ophthalmology and there is a significant body of literature on their individual clinical pharmacology.”

Please provide the link between each of the listed drug products (i.e. phenylephrine, ketorolac), the literature that you are citing, and your product. Specifically, how are you bridging between the difference in dosage forms to be able to rely on the listed products and the literature for your labeling?

We are providing the above information by email for your convenience. Contact me at 301-796-1002 if you have any questions regarding the contents of this transmission. Thank you.

Regards,

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products
FDA/CDER/OND/OAP

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

/s/

JACQUELYN E SMITH
03/24/2014

Smith, Jacquelyn

From: Smith, Jacquelyn
Sent: Wednesday, March 19, 2014 7:16 AM
To: Cathy Melfi-TLS (cmelfi@tls.omeross.com)
Cc: ssullivan@tls.omeross.com
Subject: N 205388 Product Strength - Revised request for Omeros

Hi Cathy,

Please re-calculate the strengths of the active ingredients, as the free acid and the free base, in the drug product as % w/v. Please submit the calculations and propose revised labeling.

Regards,

Jacquelyn

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Food and Drug Administration
Division of Transplant and Ophthalmology Products
10903 New Hampshire Avenue
White Oak, Bldg. 22, Room 6114
Silver Spring, Maryland 20993
Telephone: 301-796-1002
Fax: 301-796-9881
Email: jacquelyn.smith@fda.hhs.gov

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

/s/

JACQUELYN E SMITH
03/19/2014



NDA 205388

INFORMATION REQUEST

Omeros Corporation
Attention: Catherine A. Melfi
Vice President, Regulatory Affairs & Quality Systems
201 Elliott Avenue West
Seattle, WA 98119

Dear Dr. Melfi:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Omidria[®] (phenylephrine HCl/ketorolac tromethamine) Injection.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a prompt written response by March 14, 2014, in order to continue our evaluation of your NDA.

The reported compatibility of Omidria with balanced salt solution (BSS) is based on admixture homogeneity (assay uniformity) and stability (assay) over 24 hours (3.2.P.2.6). Please test admixtures of Omidria in BSS and BSS Plus for sub-visible particulate contamination using the methodology in USP<789> Particulate Matter in Ophthalmic Solutions.

If you have any questions, call Navdeep Bhandari, Regulatory Health Project Manager, at (240) 402 -3815.

Sincerely,

{See appended electronic signature page}

Rapti D. Madurawe, Ph.D.
Branch Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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

/s/

BALAJEE SHANMUGAM
02/27/2014



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

COMMUNICATION TRANSMITTAL SHEET

DATE: January 15, 2014

To: Catherine A. Melfi, PhD VP, Regulatory Affairs & Quality Systems	From: Jacquelyn Smith, MA, Senior Project Manager
Company: Omeros Corp.	Division of Transplant and Ophthalmology Products
Phone Number: 206-676-5045	Phone Number: 301-796-1600
Email: cmelfi@omeros.com	Email: jacquelyn.smith@fda.hhs.gov

NDA 205388, Omidria

Total no. of pages including cover: 3

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

Dear Dr. Melfi:

Please refer to NDA 205388, Omidria (phenylephrine-ketorolac ophthalmic injection) 1% / (b) (4) received July 30, 2013.

We have the following information request:

Information Request

1. Please provide a re-analysis for Study OMS302-ILR-003 for the Primary endpoint {Mean Area Under the Curve (AUC) Analysis of Change From Baseline in Pupil Diameter (mm) During Surgery} and Secondary Endpoint {Mean Area Under the Curve (AUC) Analysis of Ocular Pain VAS Score Within 12 Hours Post-operatively} excluding Dr. Marciso's patients (Site 198, 39 patients).
2. In CSR for OMS302-ILR-003 Table 39, data appears to be missing in the table for systolic BP, diastolic BP, and HR for the timepoint of 15 minutes after the end of procedure for active and placebo. Please provide this data or provide an explanation for the n of 1 and n of 0.

We are providing the above information by email for your convenience. Contact me at 301-796-1002 if you have any questions regarding the contents of this transmission. Thank you.

Regards,

Jacquelyn Smith, MA
Senior Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products
FDA/CDER/OND/OAP

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

/s/

JACQUELYN E SMITH
01/15/2014



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

IND 078227
NDA 205388

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Omeros Corporation
201 Elliott Avenue West
Seattle, WA 98119

Attention: Catherine A. Melfi, Ph.D.
Vice President, Regulatory Affairs & Quality Systems

Dear Dr. Melfi:

Please refer to:

- your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Phenylephrine HCL and Ketorolac Tromethamine, Injection Solution Concentrate, 61 mM (12.37 mg/mL) and 11 mM (4.24 mg/mL); and
- your New Drug Application (NDA), dated and received, July 30, 2013, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Phenylephrine HCL and Ketorolac Tromethamine, Injection Solution Concentrate, 61 mM (12.37 mg/mL) and 11 mM (4.24 mg/mL) .

We also refer to:

- your correspondence dated May 22, 2013, and received May 23, 2013, requesting review of your proposed proprietary name, Omidria for your IND; and
- your correspondence dated and received, September 27, 2013, requesting review of your proposed proprietary name, Omidria, for your NDA.

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

If **any** of the proposed product characteristics as stated in your September 27, 2013, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Karen Townsend, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5413. For any other information regarding this application contact Jacquelyn Smith at (301)796-1600, Office of New Drugs (OND) Regulatory Project Manager.

Sincerely,

{See appended electronic signature page}

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

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

/s/

TODD D BRIDGES on behalf of KELLIE A TAYLOR
11/15/2013



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

COMMUNICATION TRANSMITTAL SHEET

DATE: November 15, 2013

To: Catherine A. Melfi, PhD VP, Regulatory Affairs & Quality Systems	From: Jacquelyn Smith, M.A., Senior Project Manager
Company: Omeros Corp.	Division of Transplant and Ophthalmology Products
Phone Number: 206-676-5045	Phone Number: 301-796-1600
Email: cmelfi@omeros.com	Email: jacquelyn.smith@fda.hhs.gov

NDA 205388, Omidria

Total no. of pages including cover: 3

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

Dear Dr. Melfi:

Please refer to NDA 205388, Omidria (phenylephrine-ketorolac ophthalmic injection) 1% / (b) (4) received July 30, 2013.

We have the following information request from Microbiology:

Information Request

Please indicate the in-use period for the diluted drug product. Without additional microbiological data to support extended hold times, the product labeling should recommend that the post-dilution in-use period is not more than 4 hours at room temperature or 24 hours under refrigerated conditions.

Should an in-use period be required that exceeds these conditions, microbiological data should be provided in the NDA to demonstrate that the diluted product solution will not support microbial growth during the proposed period. Provide a risk assessment summarizing studies that show adventitious microbial contamination does not grow under the conditions of the in-use period. Reference is made to Guidance for Industry: ICH Q8 Pharmaceutical Development, Section II.E and Guidance for Industry: ICH Q1A(R2) Stability Testing of New Drug Substances and Products, Section 2.2.7.

Generally, "no growth" is interpreted as not more than a 0.5 log₁₀ increase from the initial count; however other evidence of growth may be significant. The test should be run at the label's recommended storage conditions, be conducted for 2 to 3-times the label's recommended storage period, and use the label-recommended fluids inoculated with low numbers (≤ 100 CFU/mL) of challenge microbes. Challenge organisms may include strains described in USP <51> plus typical skin flora or species associated with hospital-borne infections.

We are providing the above information by email for your convenience. Contact me at 301-796-1002 if you have any questions regarding the contents of this transmission. Thank you.

Regards,

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products
FDA/CDER/OND/OAP

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

/s/

JACQUELYN E SMITH
11/15/2013

Smith, Jacquelyn

From: Smith, Jacquelyn
Sent: Thursday, October 31, 2013 12:27 PM
To: Cathy Melfi-TLS (cmelfi@tls.omeross.com); cmelfi@omeross.com
Cc: Susan Sullivan-TLS
Subject: FW: Stat IR for NDA205388 (Omidria)

Hi Dr. Melfi,

We have the following information request.

Statistical Information Request for SAS Codes

For studies OMS302-ILR-003, OMS302-ILR-004, and ISE, it is still not clear to us how the primary and key efficacy analyses were performed according to the SAS program codes submitted on October 4th, 2013. Specifically, for the SAS program codes (for studies 003 and 004, and ISE) used to generate the mean area-under-the-curve analyses of both change from baseline in pupil diameter during surgery and ocular pain for 12 hours postoperatively, a SAS macro program named [REDACTED]^{(b) (4)} was used; however we cannot locate in your submission this macro program that had the details of how the protocol proposed analysis method (the generalized Cochran-Mantel-Haenszel (CMH) test stratified by the randomization strata) was utilized. As requested before, in order to help us with the review process, please submit **all** the SAS program codes used (including all the SAS macro programs used) to produce the efficacy and safety analysis results presented in the study reports for studies OMS302-ILR-003, OMS302-ILR-004, ISE, and ISS.

Please respond as soon as possible.

Regards,

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Food and Drug Administration
Division of Transplant and Ophthalmology Products
10903 New Hampshire Avenue
White Oak, Bldg. 22, Room 6114
Silver Spring, Maryland 20993
Telephone: 301-796-1002
Fax: 301-796--9881
Email: jacquelyn.smith@fda.hhs.gov

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

/s/

JACQUELYN E SMITH
11/01/2013



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

COMMUNICATION TRANSMITTAL SHEET

DATE: October 16, 2013

To: Catherine A. Melfi, PhD VP, Regulatory Affairs & Quality Systems	From: Jacquelyn Smith, M.A., Senior Project Manager
Company: Omeros Corp.	Division of Transplant and Ophthalmology Products
Phone Number: 206-676-5045	Phone Number: 301-796-1600
Email: cmelfi@omeros.com	Email: jacquelyn.smith@fda.hhs.gov

NDA 205388, Omidria

Total no. of pages including cover: 3

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

Dear Dr. Melfi:

Please refer to NDA 205388, Omidria (phenylephrine-ketorolac ophthalmic injection) 1% / (b) (4) received July 30, 2013.

We have the following information request:

Information Request

1. Provide a Letter of Authorization for the (b) (4) process for the (b) (4), (b) (4), elastomeric stopper, (b) (4) from the stopper supplier (b) (4).
2. Identify holding periods in the drug product manufacture, from (b) (4).

We are providing the above information by email for your convenience. Contact me at 301-796-1002 if you have any questions regarding the contents of this transmission. Thank you.

Regards,

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products
FDA/CDER/OND/OAP

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

/s/

JACQUELYN E SMITH
10/16/2013



NDA 205388

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

Omeros Corporation
Attention: Catherine A. Melfi, Ph.D.
Vice President, Regulatory Affairs & Quality Systems
201 Elliott Avenue West
Seattle, WA 98119

Dear Dr. Melfi:

Please refer to your New Drug Application (NDA) dated July 30, 2013, received July 30, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Omidria (phenylephrine-ketorolac ophthalmic solution) 1% / (b) (4)

We also refer to your amendments dated August 9 and 23, 2013.

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 was considered filed 60 days after the date we received your application. The review classification for this application is **Standard**.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment or requirement requests by May 2, 2014.

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

PROMOTIONAL MATERIAL

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

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

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

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

If you have any questions, call Jacquelyn Smith, M.A., Senior Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Transplant and Ophthalmology
Products
Office of Antimicrobial Products
Office of New Drugs
Center for Drug Evaluation and Research

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

/s/

RENATA ALBRECHT
09/26/2013



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

COMMUNICATION TRANSMITTAL SHEET

DATE: September 23, 2013

To: Catherine A. Melfi, PhD VP, Regulatory Affairs & Quality Systems	From: Jacquelyn Smith, M.A., Senior Project Manager
Company: Omeros Corp.	Division of Transplant and Ophthalmology Products
Phone Number: 206-676-5045	Phone Number: 301-796-1600
Email: cmelfi@omeros.com	Email: jacquelyn.smith@fda.hhs.gov

NDA 205388, Omidria

Total no. of pages including cover: 3

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

Dear Dr. Melfi:

We refer to your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Omidria (phenylephrine HCl 12.4 mg/mL and ketorolac tromethamine 4.24 mg/mL ophthalmic solution).

We have the following information request:

Information Request

Please update Section 1.9 (Pediatric Administrative Information) in your NDA based on the approved, agreed-upon Pediatric Study Plan. Please provide an estimate of when we will receive the revision.

We are providing the above information by email for your convenience. Contact me at 301-796-1002 if you have any questions regarding the contents of this transmission. Thank you.

Regards,

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products
FDA/CDER/OND/OAP

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

/s/

JACQUELYN E SMITH
09/23/2013



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

COMMUNICATION TRANSMITTAL SHEET

DATE: September 18, 2013

To: Catherine A. Melfi, PhD VP, Regulatory Affairs & Quality Systems	From: Jacquelyn Smith, M.A., Senior Project Manager
Company: Omeros Corp.	Division of Transplant and Ophthalmology Products
Phone Number: 206-676-5045	Phone Number: 301-796-1600
Email: cmelfi@omeros.com	Email: jacquelyn.smith@fda.hhs.gov

NDA 205388, Omidria

Total no. of pages including cover: 3

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

Dear Dr. Melfi:

We refer to your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Omidria (phenylephrine HCl 12.4 mg/mL and ketorolac tromethamine 4.24 mg/mL ophthalmic solution).

We have the following information request:

Information Request

It is stated on page 3 of the package insert (DOSAGE AND ADMINISTRATION) that Omidria must be diluted prior to use in standard irrigation solution. Please provide additional information regarding the storage period and conditions for the diluted drug product. Please be aware that in lieu of data supporting extended holding periods, the product labeling should recommend that the post-dilution storage period is not more than 4 hours at room temperature or 24 hours under refrigerated conditions.

We are providing the above information by email for your convenience. Contact me at 301-796-1002 if you have any questions regarding the contents of this transmission. Thank you.

Regards,

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products
FDA/CDER/OND/OAP

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

/s/

JACQUELYN E SMITH
09/18/2013

Smith, Jacquelyn

From: Smith, Jacquelyn
Sent: Tuesday, September 17, 2013 6:54 AM
To: 'Cathy Melfi-TLS'; Willard, Diana M
Cc: Susan Sullivan-TLS
Subject: NDA 205388/Omidria - Information Request

Hi Cathy,

Following is the response to questions Omeros sent to FDA Thursday, September 12, 2013, for a response.

- 1) The request indicates that the SAS programs used to generate the efficacy and safety results for the three primary clinical trials, the ISE, and the ISS could not be located. Module 5 includes the SAS programs used to generate the analysis datasets (with derived variables) from the SDTM files. *Please let us know if you need information on the location in Module 5 of these SAS programs.* The SAS programs used to generate the efficacy and safety results were not included in the NDA submission.

Response: We are familiar with the location in Module 5 of those SAS programs used to generate the analysis datasets. We would like you to submit the SAS programs used to generate the efficacy and safety results.

- 2) The attached document and sample of three SAS programs is the proposed format for Omeros' response to this Information Request. The PDF file represents the define document that provides information on the SAS program used (and will include a link to the SAS program) to generate the Tables and Figures in the CSRs, ISS, and ISE. It also provides information on the domain used from the analysis dataset, variable names, treatment arm used as comparison for the analysis, and any flags needed to assure appropriate subsetting of the data. In the response to the IR, there will be separate PDF files for each CSR, the ISS, and the ISE and, in addition to the information described above, the files will provide a link to the specific table or figure in the CSR/ISS/ISE, plus any explanatory comments as appropriate. The attached sample PDF file is for two tables and one figure in CSR C09-001 and uses blue text to illustrate which fields are hyperlinked. *If this format is used for all of the efficacy and safety analyses presented in the CSRs, ISS, and ISE, will this, along with the associated SAS programs, adequately provide the requested information?*

Response: The format seems adequate. During the review process, we may request additional information to be submitted if necessary.

- 3) Omeros intends to provide the requested information for the primary and key secondary efficacy analyses, and for the safety analyses presented in the CSRs, ISS, and ISE. This includes analyses presented in Tables and Figures in these documents. *Please confirm that this is the intended scope of the Information Request.*

Response: Yes, this is the intended scope of the information request. During the review process, we may request additional information to be submitted if necessary.

Regards,

Jacquelyn

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Food and Drug Administration
Division of Transplant and Ophthalmology Products
10903 New Hampshire Avenue
White Oak, Bldg. 22, Room 6114
Silver Spring, Maryland 20993
Telephone: 301-796-1002
Fax: 301-796--9881
Email: jacquelyn.smith@fda.hhs.gov

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

/s/

JACQUELYN E SMITH
09/18/2013



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products**

COMMUNICATION SHEET

DATE: September 10, 2013

To: Catherine A. Melfi, ph.D
Vice President, Regulatory Affairs &
Quality Systems

From: Diana Willard
Chief, Project Management Staff

Company: Omeros Corp.

Division of Transplant and
Ophthalmology Products

Email; cmelfi@omeros.com

Email: diana.willard@fda.hhs.gov

Telephone: 206-676-5045

Phone number: 301-796-1600

Subject: NDA 205388/Omidria

Total no. of pages including cover: 3

Comments:

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-1600. Thank you.

Dear Dr. Melfi,

We refer to your New Drug Application (NDA) submitted July 30, 2013, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Omidria (phenylephrine HCl 12.4 mg/mL and ketorolac tromethamine 4.24 mg/mL ophthalmic solution).

We have the following information request:

Statistical Information Request

We are having difficulty in reproducing the efficacy analysis results for the submitted efficacy studies (c09-001, oms302-ilr-003, and oms302-ilr-004); and we cannot locate in your NDA submission the SAS programs used to generate the efficacy and safety results for all three efficacy studies, the ISE, and the ISS.

Please submit all the SAS program codes used to produce the efficacy and safety analysis results presented in the study reports for studies c09-001, oms302-ilr-003, oms302-ilr-004, ISE, and ISS. Please provide define documents also to explain the purpose of the submitted SAS codes. These documents and the SAS codes will help us in reviewing your NDA.

We request that you submit this information by October 7, 2013.

If you have any questions regarding this communication, please contact Jacquelyn Smith at (301) 796-1600.

Sincerely,

Diana Willard
Chief, Project Management Staff
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

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

/s/

DIANA M WILLARD
09/10/2013



NDA 205388

NDA ACKNOWLEDGMENT

Omeros Corporation
Attention: Catherine A. Melfi, Ph.D.
Vice President, Regulatory Affairs & Quality Systems
201 Elliott Avenue West
Seattle, WA 98119

Dear Dr. Melfi:

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

Name of Drug Product: Omidria (phenylephrine HCl 12.4 mg/mL and ketorolac tromethamine 4.24 mg/mL ophthalmic solution)

Date of Application: July 30, 2013

Date of Receipt: July 30, 2013

Our Reference Number: NDA 205388

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 September 28, 2013, in accordance with 21 CFR 314.101(a).

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

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

Title VIII of FDAAA amended the PHS Act by adding new section 402(j) [42 USC § 282(j)], which expanded the current database known as ClinicalTrials.gov to include mandatory

registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices.

In addition to the registration and reporting requirements described above, FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) numbers [42 USC § 282(j)(5)(B)].

You did not include such certification when you submitted this application. You may use Form FDA 3674, "Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank," [42 U.S.C. § 282(j)] to comply with the certification requirement. The form may be found at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trial(s) referenced in this application. Please note that FDA published a guidance in January 2009, "Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of the Food and Drug Administration Amendments Act of 2007," that describes the Agency's current thinking regarding the types of applications and submissions that sponsors, industry, researchers, and investigators submit to the Agency and accompanying certifications. Additional information regarding the certification form is available at:

<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAAct/FoodandDrugAdministrationAmendmentsActof2007/ucm095442.htm>. Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information for registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

When submitting the certification for this application, **do not** include the certification with other submissions to the application. Submit the certification within 30 days of the date of this letter. In the cover letter of the certification submission clearly identify that it pertains to **NDA 205388** submitted on July 30, 2013, and that it contains the FDA Form 3674 that was to accompany that application.

If you have already submitted the certification for this application, please disregard the above.

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

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

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

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

If you have any questions, call me, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Jacquelyn Smith, M.A.
Senior Regulatory Project Manager
Division of Transplant and Ophthalmology
Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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

/s/

JACQUELYN E SMITH
08/06/2013



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

COMMUNICATION TRANSMITTAL SHEET

DATE: August 6, 2013

To: Catherine A. Melfi, PhD VP, Regulatory Affairs & Quality Systems	From: Jacquelyn Smith, M.A., Senior Project Manager
Company: Omeros Corp.	Division of Transplant and Ophthalmology Products
Phone Number: 206-676-5045	Phone Number: 301-796-1600
Email: cmelfi@omeros.com	Email: jacquelyn.smith@fda.hhs.gov

NDA 205388, Omidria

Total no. of pages including cover: 3

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

Dear Dr. Melfi:

We refer to your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Omidria (phenylephrine HCl 12.4 mg/mL and ketorolac tromethamine 4.24 mg/mL ophthalmic solution).

We have the following information request:

Information Request

Regarding study reports for OMS302-ILR-003, OMS302-ILR-004, and C09-001:

Please provide new tables which are similar in design to Table 1 under Appendix 16.1.4 for each of the study reports but which also contain the investigator address and number of randomized subjects. For example:

Site No.	No. Randomized	Investigator Name and Address	Sub-investigator(s) Name

We request these revised tables by September 3rd, 2013.

We are providing the above information by email for your convenience. Contact me at 301-796-1002 if you have any questions regarding the contents of this transmission. Thank you.

Regards,

Jacquelyn Smith, M.A.
Senior Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products
FDA/CDER/OND/OAP

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

/s/

JACQUELYN E SMITH
08/06/2013



IND 78227

MEETING MINUTES

Omeros Corporation
Attention: Susan Sullivan
Senior Director, Regulatory Affairs
1420 Fifth Avenue, Suite 2600
Seattle, WA 98101

Dear Ms. Sullivan:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for OMS 302 (phenylephrine HCl/ketorolac tromethamine).

We also refer to the teleconference between representatives of your firm and the FDA on February 11, 2013. The purpose of the meeting was to discuss the content and format for the upcoming NDA submission.

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

If you have any questions, call Judit Milstein, Chief, Project Management Staff at (301) 796-0763.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Deputy Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Meeting Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: B
Meeting Category: Pre-NDA

Meeting Date and Time: February 11, 2013, 2:00-10:00 AM EST
Meeting Format: Teleconference

Application Number: IND 78227
Product Name: OMS 302 Injection (phenylephrine HCl/ketorolac tromethamine)
Indication: Irrigation fluid used during surgical procedures associated with intracameral lens replacement
Sponsor/Applicant Name: Omeros Corporation
Meeting Chair: Wiley A. Chambers, MD
Meeting Recorder: Judit Milstein

FDA ATTENDEES

Renata Albrecht, Division Director
Wiley A. Chambers, Deputy Director
William Boyd, Clinical Team Leader
Jennifer Harris, Clinical Reviewer
Martin Nevitt, Clinical Reviewer
Rhea Lloyd, Clinical Reviewer
Yunfan Deng, Statistics Reviewer
Yan Wang, Statistics Team Leader
Yoriko Harigaya, Biopharmaceutics Reviewer
Philip Colangelo, Biopharmaceutics Team Leader
Balajee Shanmugam, CMC Lead, Office of New Drug Quality Assessment II
Terrance Ocheltree, Director, Office of New Drug Quality Assessment II
Judit Milstein, Chief, Project Management

SPONSOR ATTENDEES

Greg Demopulos, Chairman and CEO
Ken Ferguson, VP Development and Chief Development Officer
Paul Hamilton, Assistant Director, SAS Programming, Biometrics
Cathy Melfi, VP Regulatory Affairs & Quality Systems
Susan Sullivan, Senior Director, Regulatory Affairs
Steve Whitaker, VP Clinical Development and Chief Medical Officer
[REDACTED] (b) (4) Consultant

BACKGROUND

The sponsor requested a pre-NDA meeting (clinical) to discuss the overall format and content of an upcoming NDA, to be submitted in eCTD format.

On February 4, 2013, the Division sent preliminary responses on the questions posted by the sponsor in their briefing document dated January 11, 2013.

In an e-mail dated February 6, 2013, the sponsor indicated that they agreed with the Division's responses to questions 1, 2, 4, 5, 6, 8, 9, 10, 11, and 12 and therefore there was no discussion on these questions.

It is also to be noted that a pre-NDA, CMC meeting was held on January 16, 2013. On January 23, 2013, the sponsor submitted a request for reconsideration on the need to submit 12 months stability data on three registration batches at the time of their NDA submission. A letter responding to this request was sent on February 11, 2013 by the Division of New Drug Quality II in the Office of New Drug Quality Assessment (ONDQA). At the conclusion of this pre-NDA clinical meeting, the sponsor was provided an opportunity to discuss this response.

For the purposes of these minutes, the questions posted by the sponsor are reflected in **bold** format, the preliminary responses in *italics* and the discussion in normal font.

DISCUSSION

Question 1. Does the Division agree with the specification for our primary safety database?

FDA Response: The proposal to pool safety data through Day 14 postoperatively from the two Phase 3 studies (OMS302-ILR-003 and OMS302-ILR-004) and the Phase 2b study (C09-001) would be acceptable for Module 2, but complete individual study reports for these three trials should be included in Module 5 without pooling.

Meeting Discussion: None

Question 2. Does the Division agree that the pooled adverse event data through the Day 14 visit is appropriate for labeling?

FDA Response: Labeling is a review issue requiring submission and review of a complete New Drug Application; you should submit your proposal for adverse event data for your product within the application.

Meeting Discussion: None

Question 3. Does the Division agree with the plan for integration and presentation of safety data?

FDA Response: Your proposal to submit the Day 90 safety data from Study OMS302-ILR-004, the Day 30 safety data from Study C09-001, and all safety data from Study C07-005 separately

and not pool these data with the 14-day safety data from Studies OMS302-ILR-003, OMS302-ILR-004, and C09-001 would be acceptable for Module 2.

Complete individual study reports for all of these trials should be included in Module 5 without pooling.

Meeting Discussion: The sponsor requested clarification as to whether it was acceptable to include a study synopsis rather than a full CSR in Module 5, for study C07-005. The Division replied that complete study reports for each individual study (including statistical analysis plan and patient level data) should be submitted in Module 5.

The sponsor also requested confirmation that they do not need to provide any data listings, as defined in the Study Data Specifications v2, under Module 5 dataset listings since we are submitting STDM and ADaM datasets. The Division confirmed that it is acceptable to have datasets in place of data listings in Module 5.

At the meeting there were brief comments about pooled study summaries, ISS and ISE, and their location within the common technical document; however, for further details regarding the expectations and options for the location of clinical summaries (summary of clinical efficacy, summary of clinical safety), integrated summary of effectiveness and integrated summary of safety, please see: *Guidance for Industry Integrated Summaries of Effectiveness and Safety: Location within the Common Technical Document* at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM136174.pdf>.

Question 4. Does the Division agree with the plan for submission of CRFs?

FDA Response: *No. In addition to CRFs for subjects who died, experienced a serious adverse event, or discontinued due to an adverse event, you should also submit the CRFs for any subject who discontinued, regardless of the reason.*

Meeting Discussion: None

Question 5. Is the planned integration and choice of subpopulations appropriate?

FDA Response: *Your proposal to submit subpopulation analyses for Phase 3 studies (OMS302-ILR-003 and OMS302-ILR-004) to include age, gender, race, iris color, and LOCS II grade is acceptable.*

Meeting Discussion: None

Question 6. Does the Division agree with the use of existing literature for the purpose of providing the clinical pharmacology/pharmacokinetics for this 505(b)(2) application?

FDA Response: *Yes*

Meeting Discussion: None

Question 7. *Submission of videos/still images of surgical procedures:* A primary endpoint in our Phase 3 studies was pupil dilation as measured from video images captured during the surgical procedures. These images were collected on DVDs and read using software validated for this purpose. Omeros does not plan to submit videos or still images of the surgical procedures as part of our NDA. Does the Division agree?

FDA Response: No. The Agency would expect you to submit a random sampling (approximately 10%) of the video images captured and utilized in the determination of the Phase 3 pupil dilation endpoint. As part of the NDA review, these images will be evaluated to determine if the Agency can duplicate the pupil dilation results obtained by you based on the images provided.

Meeting Discussion: The sponsor explained that the sampling of video images from the Phase 3 studies will include all images captured from a random sample of approximately 10% of the subject videos from those studies, and will also include the image reading instructions used so that FDA can duplicate the pupil dilation results. They also explained that the images are in PNG, a standard graphical file format, and requested confirmation from the Division on this approach and asked if it was acceptable to submit this data in Module 5. The Division concurred with the sponsor's revised plan.

Question 8. *Submission of individual patient profiles:* With the submission of the datasets, Omeros does not plan to provide individual patient profiles. Does the Division agree?

FDA Response: Agree.

Meeting Discussion: None

Question 9. *Use of MedDRA and WHO Drug Dictionary:* Omeros plans to use MedDRA version 14.1 and WHO Drug Dictionary version June 2011 for all relevant data in the submission. Does the Division agree?

FDA Response: Yes.

Meeting Discussion: None

Question 10. *Data Definition Documents:* Omeros will use Define.pdf documents for Data Definition Documents of the SDTM and ADaM datasets. Does the Division agree?

FDA Response: Yes.

Meeting Discussion: None

Question 11. Is there any feedback on the database structure based on this data submission?

FDA Response: The data structure appears acceptable. During the NDA review process, we may request additional data to be submitted if deemed necessary.

Meeting Discussion: None

Question 12. Does the Division agree that Omeros will not be required to submit Summary Level Clinical Site Data in accordance with the new Draft Guidance?

FDA Response: No. We recommend that you follow the Agency's suggestion regarding Summary Level Clinical Site Data found in the Draft Guidance from FDA (Providing Submissions in Electronic Format — Summary Level Clinical Site Data for CDER's Inspection Planning).

Meeting Discussion: None

Question 13. Does the Division agree that a priority review may be warranted?

FDA Response: Determinations regarding the priority status of an NDA are made at the time of filing.

Meeting Discussion: The sponsor stated that their product will provide for a preservative-free phenylephrine product and asked if this fact will be taken into consideration for a priority review. The Division stated that unless Omeros' product is substantially better than other products available, it is unlikely that the NDA will receive priority review, although the final determination will be made at the time of filing.

The sponsor further asked if the possibility of having a drug shortage can affect this decision. The Division responded that it takes many factors into consideration and invited the sponsor to make their case for a priority review in their initial application.

Question 14. Does the Division agree that a request for [REDACTED] (b) (4) and deferral of assessment of OMS302 [REDACTED] (b) (4) is reasonable?

FDA Response: No. We recommend that you submit a [REDACTED] (b) (4) in the very near future. You will need to adequately justify your request for [REDACTED] (b) (4). Based on the information provided in this briefing package, the Agency is [REDACTED] (b) (4).

Meeting Discussion: The Division clarified that based on the Food and Drug Administration Safety and Innovation Act (FDASIA), sponsors are required to submit [REDACTED] (b) (4).

(b) (4) their End of Phase 2 (EOP2) meeting. However, considering that OMS302 has not requested and met with the Agency for an EOP2 meeting, this deadline is not applicable for this application at this time.

The Division also stated that it is (b) (4) indication.

DISCUSSION ON REQUEST FOR RECONSIDERATION TO ONDQA

ONDQA asked as to whether the sponsor had an opportunity to review the correspondence issued on January 11, 2013 and if they had any questions. The sponsor replied that they looked through the document and that at this time they had no additional comments.

ONDQA also stated that for submissions which qualify for priority review, adequate CMC data is still required.

ISSUES REQUIRING FURTHER DISCUSSION

None

ACTION ITEMS

The Division will issue the minutes within 30 days.

The sponsor will submit their (b) (4) by Mid March.

ADDITIONAL POST-MEETING FDA COMMENTS

1. Prescribing Information

Proposed prescribing information (PI) submitted with your application must conform to the content and format regulations found at 21 CFR 201.56 and 201.57.

Summary of the Final Rule on the Requirements for Prescribing Information for Drug and Biological Products, labeling guidances, sample tool illustrating Highlights and Table of Contents, an educational module concerning prescription drug labeling, and fictitious prototypes of prescribing information are available at:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm>. We encourage you to review the information at this website and use it as you draft prescribing information for your application.

2. Manufacturing Facilities

To facilitate our inspectional process, the Office of Manufacturing and Product Quality in CDER's Office of Compliance requests that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

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

/s/

WILEY A CHAMBERS
02/28/2013



MEETING MINUTES

IND 78227

Omeros Corporation
Attn: Susan Sullivan
Senior Director, Regulatory Affairs
1420 Fifth Avenue, Suite 2600
Seattle, WA 98101

Dear Ms. Sullivan:

Please refer to the End-of-Phase 2 meeting between representatives of your firm and FDA on July 15, 2011. The purpose of the meeting was to discuss the clinical development of OMS302 (phenylephrine HCl and ketorolac tromethamine) Injection for surgical irrigation for the (b) (4) and the reduction of pain in the early postoperative period in lens replacement surgery with phacoemulsification.

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

If you have any questions, call Raphael R. Rodriguez, Regulatory Project Manager, at (301) 796-0798.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Deputy Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure:

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type B
Meeting Category: End-of-Phase 2

Meeting Date and Time: July 15, 2011, Start: 1:10, End: 2:00
Meeting Location: Bldg 22, Room 1313

Application Number: IND 78,227
Product Name: OMS302 Injection for surgical irrigation (phenylephrine HCl and ketorolac tromethamine)
Indication: [REDACTED] (b) (4) and reduction of pain in the early postoperative period in lens replacement surgery with phacoemulsification.

Sponsor/Applicant Name: Omeros Corporation

Meeting Chair: Renata Albrecht, M.D.
Meeting Recorder: Raphael R. Rodriguez

FDA ATTENDEES

Renata Albrecht, M.D. Director, DTOP
Wiley Chambers, M.D., Deputy Director, DTOP
William Boyd, M.D., Clinical Team Leader
Martin Nevitt, M.D., Clinical Reviewer
Philip Colangelo, Pharm. D., Ph.D., Clinical Pharmacology Team Leader
Yoriko Harigaya, Ph. D., Clinical Pharmacology Reviewer
Yunfan Deng, Ph.D., Statistical Reviewer
Yan Wang Ph. D., Statistical Team Leader
Raphael Rodriguez, Regulatory Project Manager

SPONSOR ATTENDEES

Gregory Demopulos, M.D., CEO
Steve Whitaker, M.D., VP, Clinical Development
Ken Ferguson, VP, Development
Allan Crandall, M.D., Senior VP and Professor of University of Utah School of Medicine
Paul Flyer, Statistician
Susan Sullivan, Senior Director, Regulatory Affairs

BACKGROUND

Omeros Corporation is developing OMS302, a combination drug product containing phenylephrine HCl (PE) and ketorolac tromethamine (KE) for use during intraocular lens replacement (ILR) surgery with phacoemulsification. Three nonclinical efficacy, one nonclinical safety and two clinical studies have been completed.

The sponsor submitted a meeting request on April 29, 2011. Preliminary responses to the questions posted in the briefing document dated June 14, 2011 were provided via email July 11, 2011. This meeting served to clarify responses to questions 6, 7, and 9. The sponsor's questions are described in **BOLD** format, the preliminary responses are in *italics* and the meeting discussions are in normal font.

Pharmacology and Toxicology

Question 1: Does the Division agree that the pharmacology and toxicology studies performed by Omeros combined with historical nonclinical and clinical experience with topical ophthalmic phenylephrine (PE) and ketorolac (KE) provide adequate support for the Phase 3 program, subsequent NDA review, and approval?

FDA Response: Yes the Division agrees that the pharmacology and toxicology studies conducted by Omeros are sufficient to support the phase 3 program and subsequent NDA review. No additional nonclinical studies are needed at this time. Any decision on approval for OMS302 will be determined upon review of the NDA application.

Clinical

Question 2: Omeros will seek agreement on the proposed indication of prevention of intraoperative miosis and reduction of postoperative pain associated with lens replacement surgery with phacoemulsification.

FDA Response: Final determination of the labeling requires review of a New Drug application; we will need to review the final protocol and statistical analysis plan. It is recommended that consideration be given to measuring the time to pain relief as opposed to reduction of postoperative pain.

Combination Drug Policy

Question 3: Based on the statistically significant treatment effect of OMS302 over vehicle, ketorolac and phenylephrine on co-primary endpoints in a full-factorial Phase 2b clinical study and the well-documented distinct pharmacological actions of ketorolac and phenylephrine, Omeros will seek agreement that these data demonstrate the independent contribution of phenylephrine and of ketorolac to the proposed indication and satisfy the Combination Drug Policy.

FDA Response: The Agency would expect to see replication of the contribution of phenylephrine and of ketorolac to the proposed indication.

Phase 3 Development Plan and Study Designs

The Phase 3 program will include two studies. The design of these studies will be identical with the exception of sample size as described in Question 11 below and measurement of pharmacokinetics as described in Question 13.

Question 4: Does the Division agree that the co-primary endpoints of change in mean intraoperative pupil diameter and mean postoperative pain as measured by VAS are appropriate endpoints to support the proposed indication?

FDA Response: The endpoints are potentially acceptable; although we recommend evaluation of the time to postoperative pain relief instead of a change in mean pain and we will need to review the final protocol and statistical analysis plan.

Question 5: Omeros will seek agreement that two Phase 3 studies including both cataract extraction and lens replacement (CELR) surgery patients and refractive lens exchange (RLE) patients would provide the basis for an indication of lens replacement surgery if both studies meet the co-primary endpoints.

FDA Response: It is unclear how many subjects will undergo CELR and how many subjects will undergo RLE. The protocol(s) should specify. It is not clear why these two procedures are being considered together in the same protocol. It is not clear that the amount of pain attributed to each procedure is the same or that the amount of pupil dilation needed to safely complete the procedure is the same. We will need to review the final protocol and statistical analysis plan.

Question 6: Does the Division agree with the populations defined by the inclusion and exclusion criteria in the proposed Phase 3 studies?

FDA Response: The entry criteria are potentially acceptable; we will need to review the final protocol and statistical analysis plan.

(b) (4)

Meeting Discussion: The Division recommended a pediatric plan in an age population that is appropriate for the product. Regarding the pain endpoint, the Division recommends setting an age limit at which pain data can be reliably collected. The number of pediatric patients studied should be representative of the relative percentage of pediatric patients within the total patient population undergoing intraocular lens replacement.

Question 7: Does the Division agree with the 14-day follow-up period of the proposed Phase 3 studies?

FDA Response: Yes, but safety evaluations are recommended to be continued for at least 3 months after the end of treatment.

Meeting Discussion: The recommendation for a 3-month follow-up period is based on the postoperative period currently covered by Medicare for cataract surgery. A shorter follow-up

period is acceptable provided that Omeros can establish that previous studies have adequately demonstrated the safety of each of OMS302's active agents for at least a 3-month period.

Question 8: Does the Division agree that pupil size only needs to be measured in a subset of subjects in the proposed Phase 3 studies?

FDA Response: A subset-only evaluation of pupil size is not recommended. Clinical trials evaluating the inhibition of miosis even with known effective therapies can fail to demonstrate efficacy.

Question 9: Does the Division agree with the proposed process for measuring pupil size in the proposed Phase 3 studies?

FDA Response: It is recommended that there be a demonstration of a statistically significant difference between the test treatment group and the vehicle group in the number of patients who have a pupillary diameter of at least 6 millimeters while being stimulated with a prespecified light stimulus (i.e., specific light level on the operating microscope).

Randomization should include stratification for baseline factors which can significantly impact the outcome. Typically, in pupillary dilation or constriction, iris pigmentation can influence the outcome.

Meeting Discussion: The Division defines 6 mm as a clinically relevant pupil diameter based on an earlier study conducted in India demonstrating an increase in the number of surgical complications in eyes dilated less than 6 mm. The proposed endpoint needs to be clinically relevant. Consideration should be given to the critical times that the pupil must be well dilated during intraocular lens replacement.

Question 10: Does the Division agree with the proposed design and statistical analyses of the proposed Phase 3 studies?

FDA Response: The Agency would expect to see replication of the contribution of phenylephrine and of ketorolac to the proposed indication.

The protocol should provide details and references for the generalized CMH method used in the primary analysis of the co-primary efficacy endpoints.

The protocol should clearly specify the details of the models used in the repeated measures analyses of variance for the supportive efficacy analysis. The details should include the dependent and independent variables, the fixed and random effects, and the covariance structures. SAS sample codes of these analyses should be provided to help us in reviewing the appropriateness of your proposed analysis methods.

As part of the sensitivity analyses, please compare the treatment arms using t-test for both change from baseline of pupil diameter and average ocular pain after surgery (within 12 hours) as defined in the protocol.

As part of the sensitivity analyses, please analyze the co-primary endpoint by imputing missing data using multiple imputation methods.

We may have further comments once the statistical analysis plan (SAP) is submitted for review.

Question 11: Does the Division agree that the proposed exposure of approximately 350 subjects treated with OMS302 would support approval?

FDA Response: It is recommended that the topical clinical program include enough patients to identify adverse events that occur at a rate of 1% or greater. To accomplish this, it is recommended that approximately 500 or more subjects using the test drug product complete treatment with a concentration of the test drug product at least as high as proposed for marketing with a frequency at least as frequent as proposed for marketing. Safety should be demonstrated in at least 300 patients who have completed 3 months of follow-up after the initiation of treatment using the proposed dosing regimen (including concentration).

Question 12: Does the Division agree with Omeros' plan for adverse event collection?

FDA Response: The adverse event collection plan is potentially acceptable; we will need to review the final protocol and statistical analysis plan.

Pharmacokinetics

Question 13: Does the Division agree that a pharmacokinetic substudy on approximately 12 patients in one of the Phase 3 studies is sufficient for NDA review and approval?

FDA Response: We agree that a pharmacokinetic (PK) analysis in a subset of 12 patients in one of the proposed Phase 3 studies is sufficient for NDA review. In protocols OMS302-ILR-003 or OMS302-ILR-003R, we note that no description of a PK substudy is included. Please add the proposed PK substudy in a revised version of either of these protocols for our review.

In your PK analysis, we recommend that you obtain sufficient PK samples to allow you to determine plasma Tmax, Cmax and AUC for both phenylephrine and ketorolac if levels are above the limit of detection.

Action Items:

The Division agreed to review the final protocol prior to initiating the Phase 3 studies. The statistical analysis plan will be submitted at the same time.

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

/s/

WILEY A CHAMBERS
12/07/2011