

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**022572Orig1s000**

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

## EXCLUSIVITY SUMMARY

NDA # 22-572

SUPPL #

HFD # 590

Trade Name Mitosol

Generic Name mitomycin for solution

Applicant Name Mobius Therapeutics, LLC

Approval Date, If Known February 7, 2012

### **PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?**

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

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

YES  NO

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

505(b)(2)

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

YES  NO

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

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

d) Did the applicant request exclusivity?

YES  NO

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

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

YES  NO

If the answer to the above question in YES is this approval a result of the studies submitted in response to the Pediatric Written Request? YES  NO

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

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

YES  NO

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

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

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES  NO

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

NDA# (b) (4) (b) (4)

NDA# 50-450 Mutamycin (mitomycin for injection)

NDA# (b) (4) (b) (4)

2. Combination product.

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

YES  NO

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

NDA#

NDA#

NDA#

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

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

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

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES  NO

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

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

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

YES  NO

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

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

YES  NO

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

YES  NO

If yes, explain:

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

YES  NO

If yes, explain:

Published clinical trials support the safety and efficacy of the drug product.

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

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

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

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

Investigation #1 YES  NO

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

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

Investigation #1 YES  NO

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"):

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 # (b) (4)      YES       ! NO   
! Explain:

Investigation #2      N/A      !  
IND #      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? N/A

Investigation #1  
YES       ! NO   
Explain:      ! Explain:

Investigation #2  
YES       ! NO

Explain:

! Explain:

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

YES  NO

If yes, explain:

=====

Name of person completing form: William M. Boyd, MD  
Title: Medical Officer  
Date: 01/30/2012

Name of Office/Division Director signing form: Wiley A Chambers  
Title: Deputy Director

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

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

/s/  
-----

JUNE GERMAIN  
02/07/2012

WILEY A CHAMBERS  
02/07/2012

# ACTION PACKAGE CHECKLIST

## APPLICATION INFORMATION<sup>1</sup>

NDA # 22-572 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Mitosol Established/Proper Name: mitomycin for solution Dosage Form: sterile lyophilized powder for reconstitution with sterile water for injection		Applicant: Mobius Therapeutics, LLC Agent for Applicant (if applicable):
RPM: June Germain		Division: Transplant and Ophthalmology Products
<p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2)</p> <p>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> Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s):</p> <p>Mutamycin</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>The dosage form of this product is topical while the dosage form of the listed drug is injection</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><b><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></b></p> <p><b><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></b></p> <p><input checked="" type="checkbox"/> No changes    <input type="checkbox"/> Updated    Date of check:</p> <p><b>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</b></p>
❖ Actions		
<ul style="list-style-type: none"> <li>• Proposed action</li> <li>• User Fee Goal Date is <u>February 8, 2012</u></li> </ul>		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> <li>• Previous actions (<i>specify type and date for each action taken</i>)</li> </ul>		<input type="checkbox"/> None    CR December 22, 2010

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

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received?                  Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a>). If not submitted, explain _____</p>	<p><input type="checkbox"/> Received</p>
<p>❖ Application Characteristics<sup>2</sup></p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority                  Chemical classification (new NDAs only):</p> <p><input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch  <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch  <input checked="" type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDAs: Subpart H <span style="margin-left: 200px;">BLAs: Subpart E</span>  <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <span style="margin-left: 100px;"><input type="checkbox"/> Accelerated approval (21 CFR 601.41)</span>  <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <span style="margin-left: 100px;"><input type="checkbox"/> Restricted distribution (21 CFR 601.42)</span></p> <p>Subpart I <span style="margin-left: 200px;">Subpart H</span>  <input type="checkbox"/> Approval based on animal studies <span style="margin-left: 100px;"><input type="checkbox"/> Approval based on animal studies</span></p> <p><input type="checkbox"/> Submitted in response to a PMR <span style="margin-left: 200px;">REMS: <input type="checkbox"/> MedGuide</span>  <input type="checkbox"/> Submitted in response to a PMC <span style="margin-left: 200px;"><input type="checkbox"/> Communication Plan</span>  <input type="checkbox"/> Submitted in response to a Pediatric Written Request <span style="margin-left: 200px;"><input type="checkbox"/> ETASU</span>  <span style="margin-left: 400px;"><input type="checkbox"/> REMS not required</span></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>	<p><input type="checkbox"/> Yes, dates</p>
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p>❖ Public communications (<i>approvals only</i>)</p>	
<p>• Office of Executive Programs (OEP) liaison has been notified of action</p>	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p>• Press Office notified of action (by OEP)</p>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
<p>• Indicate what types (if any) of information dissemination are anticipated</p>	<p><input checked="" type="checkbox"/> None  <input type="checkbox"/> HHS Press Release  <input type="checkbox"/> FDA Talk Paper  <input type="checkbox"/> CDER Q&amp;As  <input type="checkbox"/> Other</p>

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

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

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

Answer the following questions for each paragraph IV certification:

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

Yes  No

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

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

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

Yes  No

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

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

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

Yes  No

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

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

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

Yes  No

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

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

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

**CONTENTS OF ACTION PACKAGE**

❖ Copy of this Action Package Checklist <sup>3</sup>	2-8-12
<b>Officer/Employee List</b>	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list ( <i>approvals only</i> )	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s) AP February 7, 2012 CR December 22, 2010
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	January 27, 2012, January 13, 2012, November 22, 2012, June 21, 2010
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	August 8, 2011
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	

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

Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling ( <i>write submission/communication date at upper right of first page of each piece</i> )	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input checked="" type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> <li>Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	January 27, 2012, January 13, 2012, November 22, 2012
<ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>	August 8, 2011, June 21, 2012
<ul style="list-style-type: none"> <li>Example of class labeling, if applicable</li> </ul>	
❖ Labels ( <b>full color</b> carton and immediate-container labels) ( <i>write submission/communication date on upper right of first page of each submission</i> )	
<ul style="list-style-type: none"> <li>Most-recent draft labeling</li> </ul>	January 27, 2012, January 13, 2012
❖ Proprietary Name <ul style="list-style-type: none"> <li>Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>Review(s) (<i>indicate date(s)</i>)</li> <li>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.</li> </ul>	Acceptable letter-December 13, 2011 Review 12/6/11
❖ Labeling reviews ( <i>indicate dates of reviews and meetings</i> )	<input checked="" type="checkbox"/> RPM 12-6-10 <input checked="" type="checkbox"/> DMEPA 12-6-11, 12-6-10 <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC <input type="checkbox"/> SEALD <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
<b>Administrative / Regulatory Documents</b>	
❖ Administrative Reviews ( <i>e.g., RPM Filing Review<sup>4</sup>/Memo of Filing Meeting</i> ) ( <i>indicate date of each review</i> )	July 15, 2010
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte	<input type="checkbox"/> Not a (b)(2) January 6, 2012
❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment ( <i>indicate date</i> )	<input type="checkbox"/> Not a (b)(2) January 31, 2012
❖ NDAs only: Exclusivity Summary ( <i>signed by Division Director</i> )	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a>	
<ul style="list-style-type: none"> <li>Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>This application is on the AIP <ul style="list-style-type: none"> <li>If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  <input type="checkbox"/> Not an AP action
❖ Pediatrics ( <i>approvals only</i> ) <ul style="list-style-type: none"> <li>Date reviewed by PeRC _____ If PeRC review not necessary, explain: <u>orphan drug designation</u></li> <li>Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)</li> </ul>	<input type="checkbox"/> Included

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

Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent ( <i>include certification</i> )	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications ( <i>letters (except action letters), emails, faxes, telecons</i> )	December 21, 2011, December 6, 2011, 8-22-11, 12-8-10, 12-1-10, 11-22-10, 11-19-10, 11-16-10, 11-3-10, 10-27-10, 10-19-10, 10-13-10, 9-22-10, 9-20-10, 9-8-10, 9-1-10, 8-19-10, 8-13-10, 8-11-10, 8-3-10, 7-28-10, 7-13-10, 7-8-10, 6-30-10(2), 6-29-10
❖ Internal memoranda, telecons, etc.	1-21-11, 12-22-10, 11-4-10, 9-29-10, 12-10-12, 12-8-10
❖ 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 July 20, 09
• EOP2 meeting ( <i>indicate date of mtg</i> )	<input type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) ( <i>indicate dates of mtgs</i> )	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available ( <i>do not include transcript</i> )	

**Decisional and Summary Memos**

❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Division Director Summary Review ( <i>indicate date for each review</i> )	<input type="checkbox"/> None February 6, 2012, December 22, 10
Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )	<input type="checkbox"/> None February 2, 2012, December 22, 10
PMR/PMC Development Templates ( <i>indicate total number</i> )	<input checked="" type="checkbox"/> None

**Clinical Information<sup>5</sup>**

❖ Clinical Reviews	
• Clinical Team Leader Review(s) ( <i>indicate date for each review</i> )	
• Clinical review(s) ( <i>indicate date for each review</i> )	February 2, 2012, 12-22-10
• 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> )	See page 9 of clinical review dated 12-22-10
❖ 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

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

❖ Risk Management <ul style="list-style-type: none"> <li>REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>)</li> <li>REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)</li> <li>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>)</li> </ul>	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) ( <i>include copies of DSI letters to investigators</i> )	<input checked="" type="checkbox"/> None requested
<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None November 21,2011
<b>Biostatistics</b> <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Statistical Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 12-6-10
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None October 21, 201111-18-10, 7-16-10
❖ DSI Clinical Pharmacology Inspection Review Summary ( <i>include copies of DSI letters</i> )	<input type="checkbox"/> None
<b>Nonclinical</b> <input checked="" type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
<ul style="list-style-type: none"> <li>ADP/T Review(s) (<i>indicate date for each review</i>)</li> <li>Supervisory Review(s) (<i>indicate date for each review</i>)</li> <li>Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None <input checked="" type="checkbox"/> None <input type="checkbox"/> None 7-7-10, 10-28-10
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary ( <i>include copies of DSI letters</i> )	<input checked="" type="checkbox"/> None requested

<b>Product Quality</b>		<input type="checkbox"/> None
❖ Product Quality Discipline Reviews		
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>		<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>		<input checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>		<input type="checkbox"/> None 2-2-12, 12-16-10, 8-20-10
❖ Microbiology Reviews		<input type="checkbox"/> Not needed November 21, 2011, 11-23-10, 7-16-10, 7-13-10
<input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i>		
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>		
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>		<input type="checkbox"/> None CDRH 11-19-10
❖ Environmental Assessment (check one) (original and supplemental applications)		
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>		See CMC review #1 dated 8-20-10 page 77
<input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i>		
<input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i>		
❖ Facilities Review/Inspection		
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites<sup>6</sup>)</i>		Date completed: Sept. 19, 2011 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</i>		Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>		<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

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

## Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

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



NDA 22-572

**INFORMATION REQUEST**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President and CEO  
1141 South 7<sup>th</sup> street  
St. Louis, MO 63104

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mitosol (mitomycin for solution).

We also refer to your August 8, 2011, resubmission.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a written response by January 6, 2012 in order to continue our evaluation of your NDA.

1. The structure of mitomycin in the package insert is incorrect. Please refer to the current "USP Dictionary of USAN and International Drug Names" for the structure of mitomycin showing the correct stereochemistry. Other revisions to the labeling will be provided in a separate communication.
2. Please clarify the acceptance criterion for pH of reconstituted solution: between 5.0 and 8.0 (b) (4)
3. The updated test for related substances in the drug product (section 3.2.P.5.2a, r1; Method of Analysis - Finished Product) correctly notes that drug substance process impurities (b) (4) would not need to be reported.

However, it is noted that, (b) (4)

4. When tabulating unspecified degradants in drug product batch analyses or stability reports, please list individual impurities with the corresponding relative retention times. Those degradants that are routinely observed should be listed under specified unidentified degradation products

Recommended format for degradation products

	RRT	Acceptance Criteria
Specified identified degradation products		



If you have any questions, call Althea Cuff, Regulatory Health Project Manager, at (301) 796-4061.

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  
12/21/2011



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

---

---

**FACSIMILE TRANSMITTAL SHEET**

---

---

**DATE: December 21, 2011**

<b>To:</b> Ed Timm President and CEO	<b>From:</b> June Germain, MS Senior Regulatory Project Manager
<b>Company:</b> Mobius Therapeutics	Division of Transplant and Ophthalmology Products
<b>Fax number:</b> (314) 615-6931	<b>Fax number:</b> (301) 796-9881
<b>Phone number:</b> (314) 615-6930	<b>Phone number:</b> (301) 796-0424

**Subject:** NDA 22572 CMC information request

**Total no. of pages including cover:** 4

**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.**

NDA 22572  
Mitomycin for solution  
Mobius Therapeutics

Dear Mr. Timm,

Please refer to your new drug application (NDA), dated June 10, 2010, and received June 22, 2010. We also refer to your resubmission of the NDA dated August 8, 2011. We request you provide a response to the following CMC information by January 6, 2012.

1. The structure of mitomycin in the package insert is incorrect. Please revise. Refer to the current “USP Dictionary of USAN and International Drug Names” for the structure of mitomycin showing the correct stereochemistry. Other revisions to the labeling will be provided in a separate communication.
2. Please clarify the acceptance criterion for pH of reconstituted solution: between 5.0 and 8.0 (b) (4)  
[Redacted]
3. The updated test for related substances in the drug product (section 3.2.P.5.2a, r1; Method of Analysis - Finished Product) correctly notes that drug substance process impurities (b) (4)  
[Redacted] would not need to be reported.

However, it is noted that, [Redacted] (b) (4)

4. When tabulating unspecified degradants in drug product batch analyses or stability reports, please list individual impurities with the corresponding relative retention times. Those degradants that are routinely observed should be listed under specified unidentified degradation products.

Recommended format for degradation products

	RRT	Acceptance Criteria
Specified identified degradation products		

(b) (4)

[Redacted content] (b) (4)

5.

[Redacted content] (b) (4)

Please call me if you have any questions.

Sincerely,  
June Germain, MS  
Senior Regulatory Project Manager

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

/s/  
-----

JUNE GERMAIN

12/21/2011

CMC information request 12-21-11



NDA 022572

**PROPRIETARY NAME REQUEST  
CONDITIONALLY ACCEPTABLE**

Mobius Therapeutics, LLC  
4041 Forest Park Avenue  
St. Louis, Missouri 63108

ATTENTION: Ed Timm  
President

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) dated June 21, 2010, received June 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mitomycin for Solution, 0.2 mg per vial.

We also refer to your correspondence, dated and received, September 30, 2011, requesting review of your proposed proprietary name, Mitosol.

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

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

If any of the proposed product characteristics as stated in your September 30, 2011, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact 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 the Office of New Drugs (OND) Regulatory Project Manager June Germain at (301) 796-4024.

Sincerely,

*{See appended electronic signature page}*

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

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

/s/  
-----

CAROL A HOLQUIST  
12/13/2011



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

---



---

**FACSIMILE TRANSMITTAL SHEET**

---



---

**DATE: December 6, 2011**

<b>To:</b> Ed Timm President and CEO	<b>From:</b> June Germain, MS Regulatory Health Project Manager
<b>Sponsor:</b> Mobius Therapeutics, LLC	Division of Transplant and Ophthalmology Products
<b>Fax:</b> (314) 615-6931	<b>Fax number:</b> (301) 796-9881
<b>Phone number:</b> (314) 615-6930	<b>Phone number:</b> (301) 796-4024

**Subject:** Information request for NDA 22,572 submission dated August 8, 2011.

**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.**

NDA 22,572  
Mitomycin  
Mobius  
Information Request

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) dated June 21, 2010, received June 22, 2010 for mitomycin kit for Ophthalmic Use. We also refer to your resubmission of the NDA dated and received August 8, 2011.

We request the following be submitted by December 13, 2011, if possible.

Please provide a prototype of the Mitosol tray which you propose to introduce into the marketplace. The prototype should have the proposed label and labeling affixed to all components within the tray and include all related materials as they would appear to the user.

Please, give me a call if you need further assistance.

Sincerely,  
June Germain, M.S.  
Senior Regulatory Project Manager

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

/s/  
-----

JUNE GERMAIN  
12/06/2011



NDA 22572

**INFORMATION REQUEST**

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

Mobius Therapeutics, LLC  
4041 Forest Park Avenue  
St. Louis, MO 63108

Dear Applicant:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

<b>NDA Number</b>	<b>Product Name/Dosage Form</b>
22572	Mitomycin for solution, 0.2 mg

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

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

The impact of the data from these studies (which may include bioequivalence, bioavailability, drug-drug interaction, specific population, and others) cannot be assessed without knowing the details regarding the study and how the data in question were considered in the overall development and approval of your drug product. At this time, the Office of New Drugs is

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

searching available documentation to determine which NDAs are impacted by the above findings.

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

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

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

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

If you have any questions, call Ms. Diana Willard, Chief, Project Management Staff, at (301) 796-0833.

Sincerely,

*{See appended electronic signature page}*

Renata Albrecht, M.D.  
Director  
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/  
-----

RENATA ALBRECHT  
09/29/2011



NDA 22,572

**ACKNOWLEDGE –  
CLASS 2 RESPONSE**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President and CEO  
1141 South 7<sup>th</sup> street  
St. Louis, MO 63104

Dear Mr. Timm:

We have received your August 8, 2011 resubmission of your new drug application submitted under section 505(b) pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Mitosol (mitomycin for solution) on August 8, 2011.

We consider this a complete, class 2 response to our December 22, 2010, action letter. The PDUFA goal date is February 8, 2012.

If you have any questions, call me at (301) 796-4024.

Sincerely,

*{See appended electronic signature page}*

June Germain, M.S.  
Senior Regulatory Project Manager  
Division of Transplant and Ophthalmology  
Product  
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/  
-----

JUNE GERMAIN  
08/22/2011



NDA 22572

**MEETING MINUTES**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mitosol (mitomycin for solution).

We also refer to the teleconference between representatives of your firm and the FDA on February 8, 2011. The purpose of the teleconference was to discuss your proposal for Kit product release.

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

If you have any questions, call Alison Rodgers, Regulatory Project Manager at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Wiley A. Chambers, M.D.  
Acting Director  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosure

## MEMORANDUM OF TELECONFERENCE MINUTES

**Meeting Date and Time:** February 8, 2011, 1:30 – 2:00 PM  
**Location:** Teleconference  
**Application Number:** 22572  
**Product Name:** Mitosol (mitomycin for solution)  
**Type of Meeting:** Guidance

**Meeting Chair:** Wiley A. Chambers, M.D.  
**Meeting Recorder:** Alison Rodgers

### FDA ATTENDEES

#### Division of Anti-Infective and Ophthalmology Products

William Boyd, MD, Clinical Team Leader  
Wiley Chambers, MD, Acting Director  
Lucious Lim, MD, Medical Officer  
Rhea Lloyd, MD, Medical Officer  
Martin Nevitt, MD, Medical Officer  
Alison Rodgers, Project Manager

#### Office of New Drug Quality Assessment

Linda Ng, PhD, Pharmaceutical Assessment Lead  
Stephen Miller, PhD, Acting Branch Chief  
Mark Seggel, PhD, Chemist

#### Office of Pharmaceutical Science

Denise Miller, Microbiologist

### SPONSOR ATTENDEES

#### Mobius Therapeutics, LLC

Alan Beckman, Director, Regulatory Affairs/Quality Assurance

 (b) (4)  
Ed Timm, President

### BACKGROUND

Mobius Therapeutics, LLC (Mobius) submitted NDA 22572 on June 22, 2010. A Complete Response letter was issued on December 22, 2010. Mobius requested clarification of items in the letter and a teleconference was held on January 3, 2011. During the teleconference, the Division indicated that Mobius could place the sterile filled vial of Mitosol inside the sterile portion of the Mitosol Kit for Ophthalmic Use.

Subsequently, Mobius developed a proposal for Kit product release and requested a teleconference to discuss the proposal.

## DISCUSSION

- Mobius requested guidance regarding [REDACTED] (b) (4)
- The Division inquired as to why they planned to [REDACTED] (b) (4)  
[REDACTED]  
The Division requested that Mobius provide the scientific rationale for their decision to [REDACTED] (b) (4) in their complete response. Mobius agreed.
- The Division requested that Mobius obtain information from [REDACTED] (b) (4)  
[REDACTED] Mobius responded that they will provide this information.
- The Division requested that Mobius submit the report of the second label comprehension study to the IND. Mobius agreed.
- The Division reminded Mobius of the need to address the chemistry issues noted in the October 19, 2010, communication, as well as the items listed in the February 7, 2011, General Advice letter. Mobius stated that they are aware of the General Advice letter. Their testing laboratory is working to identify retention times and finding impurities. It is difficult to identify impurities. Mobius asked if they could communicate with the Division regarding this issue prior to submitting the complete response. The Division agreed.

## ISSUES REQUIRING FURTHER DISCUSSION

None

## ACTION ITEMS

- Mobius will submit the report of the second label comprehension study to the IND.
- Mobius will contact the Division as necessary to discuss retention times and impurities.

## ATTACHMENTS AND HANDOUTS

None

-----  
**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  
02/16/2011



NDA 22572

**GENERAL ADVICE**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for MitoSol (mitomycin for solution).

We also refer to the Complete Response letter issued on December 22, 2010.

The following comments are provided to facilitate your preparation of an adequate response to the deficiencies identified in the December 22, 2010 letter:

1. Please revise the acceptance criteria for related substances in the drug substance to the following ICH Q3A-recommended format:
  - Each specified identified impurity [specify by name, e.g., (b) (4) ]
  - Each specified unidentified impurity (specify by, for example, relative retention time)
  - Any unspecified impurity
  - Total impurities
  - Residual solvents
  - Inorganic impurities

Note that specifying individual identified (and unidentified) impurities in the drug substance specification may facilitate interpretation of drug substance impurity profiles and may be helpful in establishing meaningful drug product acceptance criteria.

2. Please revise the acceptance criteria for related substances in the drug product to the following ICH Q3B-recommended format:
  - Each specified identified degradation product/impurity [specify by name]
  - Each specified unidentified degradation product/impurity (specify by, for example, relative retention time)
  - Any unspecified degradation product/impurity
  - Total degradation products/impurities

3. Please explain to what specific impurities [REDACTED] (b) (4) refer (see document 3-2-p-4-4-18-c-of-a-intas-synergetics-drug-vial-mob0018.pdf).
4. Please submit a copy of the label that is to be affixed to the pre-filled sterile WFI syringe. Note that this label, including graduations, should be consistent with the intended use.

The following are preliminary comments for consideration in preparing an accurate package insert.

5. Please revise the structure of mitomycin to reflect the correct stereochemistry.
6. Please confirm that [REDACTED] (b) (4)

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Wiley A. Chambers, M.D.  
Acting Director  
Division of Anti-Infective 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/  
-----

WILEY A CHAMBERS  
02/07/2011



NDA 22572

**MEETING MINUTES**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mitosol (mitomycin for solution).

We also refer to the teleconference between representatives of your firm and the FDA on January 3, 2011. The purpose of the teleconference was to discuss the Complete Response letter.

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

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Wiley A. Chambers, M.D.  
Acting Director  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosure

## MEMORANDUM OF TELECONFERENCE MINUTES

**MEETING DATE:** January 3, 2011  
**TIME:** 3:00 – 3:30 PM  
**LOCATION:** Teleconference  
**APPLICATION:** NDA 22572  
**DRUG NAME:** Mitosol (mitomycin for solution)  
**TYPE OF MEETING:** Guidance

**MEETING CHAIR:** Wiley Chambers, M.D.

**MEETING RECORDER:** Alison Rodgers

### FDA ATTENDEES:

#### Division of Anti-Infective and Ophthalmology Products

William Boyd, MD, Clinical Team Leader

Wiley Chambers, MD, Acting Director

Leanna Kelly, Labeling Reviewer

Alison Rodgers, Project Manager

### EXTERNAL CONSTITUENT ATTENDEES:

(b) (4)  
 Ed Timm, President, Mobius Therapeutics LLC

**BACKGROUND:** Mobius Therapeutics LLC (Mobius) submitted NDA 22572 on June 21, 2010. The Division issued a Complete Response (CR) letter on December 22, 2010. On January 4, 2011, Mobius requested clarification of item number 2d (see below) in the letter. A teleconference was held to discuss the issue.

- 2d) The drug product as proposed does not comply with 21 CFR 200.50. The containers of ophthalmic preparations must be sterile at the time of filling and closing, and the container or individual carton must be so sealed that the contents cannot be used without destroying the seal. Eye cups, eye droppers, and other dispensers intended for ophthalmic use should be sterile, and may be regarded as falling below their professed standard of purity or quality if they are not sterile. These articles, which are regulated as drugs, if packaged with the drugs with which they are to be used, should be packaged so as to maintain sterility until the package is opened.”

### DISCUSSION POINTS:

- The Division explained that the regulation quoted in #2d of the CR letter states that all ophthalmic agents must be sterile. The Division requires that everything inside the kit be sterile (b) (4)

- (b) (4)
- Mobius explained that they cannot conduct (b) (4)
  - The Division stated that use of (b) (4)
  - Mobius questioned whether (b) (4)
- (b) (4)
- Mobius expressed appreciation for the Division's flexibility.

**ACTION ITEMS**

- Minutes will be issued by FDA within 30 days.
- Mobius will prepare to resubmit the NDA.

-----  
**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  
01/21/2011

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Wednesday, December 22, 2010 12:01 PM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 Complete Response Letter

We are in receipt of this letter.

Thanks and Merry Christmas,

Ed Timm  
President  
**MOBIUS THERAPEUTICS, LLC**  
**P:** +1 314-615-6930  
**F:** +1 314-615-6931  
**M:** +1 404-775-5910  
*Ed.Timm@MobiusTherapeutics.com*



**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

---

**From:** Rodgers, Alison [mailto:Alison.Rodgers@fda.hhs.gov]  
**Sent:** Wednesday, December 22, 2010 8:58 AM  
**To:** Ed Timm  
**Subject:** NDA 22572 Complete Response Letter

Hi Ed,

Please find attached the Complete Response Letter for NDA 22572.

Please let me know if you have any questions.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: alison.rodgers@fda.hhs.gov

4 Pages have been Withheld in Full as a Duplicate Copy of the Other Action Letter previously included in this Approval Package.

Reference ID: 2884053

12/28/2010

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

/s/  
-----

ALISON K RODGERS  
12/28/2010



NDA 022572

**PROPRIETARY NAME REQUEST  
CONDITIONALLY ACCEPTABLE**

Mobius Therapeutics, LLC  
4041 Forest Park Avenue  
St. Louis, Missouri 63108

ATTENTION: Ed Timm  
President

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) dated June 21, 2010, received June 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mitomycin Kit for Ophthalmic Use, 0.2 mg per vial.

We also refer to your October 22, 2010, correspondence, received October 22, 2010, requesting review of your proposed proprietary name, Mitosol. We have completed our review of the proposed proprietary name, Mitosol and have concluded that it is acceptable.

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

If **any** of the proposed product characteristics as stated in your October 22, 2010, 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 Brantley Dorch, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0150. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Alison Rodgers at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Denise P. Toyer, PharmD.  
Deputy Director  
Division of Medication Error Prevention and Analysis  
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/  
-----

DENISE P TOYER  
12/09/2010



NDA 22572

**MEETING MINUTES**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

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

We also refer to the teleconference between representatives of your firm and the FDA on December 8, 2010. The purpose of the teleconference was to discuss comments from the Center for Devices and Radiological Health.

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

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Wiley A. Chambers, M.D.  
Acting Director  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosure

## MEMORANDUM OF TELECONFERENCE MINUTES

**Date and Time:** December 8, 2010, 1:00 – 1:30 PM

**Application Number:** 22572

**Product Name:** Mitosol

**Indication:** Treatment of refractory glaucoma

**Sponsor/Applicant Name:** Mobius Therapeutics LLC

### FDA PARTICIPANTS

#### Division of Anti-Infective and Ophthalmology Products

William Boyd, MD, Clinical Team Leader

Wiley Chambers, MD, Acting Director

Jennifer Harris, MD, Medical Officer

Rhea Lloyd, MD, Medical Officer

Martin Nevitt, MD, Medical Officer

Alison Rodgers, Project Manager

Mark Seggel, PhD, Chemistry Reviewer, Office of New Drug Quality Assessment

Nikhil Thakur, PhD, Center for Devices and Radiological Health

### SPONSOR PARTICIPANTS

Ed Timm, President, Mobius Therapeutics LLC

(b) (4)

### BACKGROUND

Mobius Therapeutics LLC (Mobius) submitted NDA 22572 on June 21, 2010. On July 15, 2010, the Division notified Mobius that no information had been submitted with the NDA to demonstrate that intended users of the mitomycin for solution were able to reliably follow the directions provided and reconstitute the mitomycin product in a sterile fashion. A teleconference was held on July 16, 2010, to discuss the issue. An additional teleconference was scheduled to continue discussion of Chemistry, Manufacturing, and Controls issues.

Mobius conducted a Label Comprehension Study (LCS) in September 2010. Based on the results of the study, the Division requested that Mobius conduct a second LCS. The Division and the Center for Devices and Radiological Health (CDRH) sent comments and recommendations to Mobius based on the findings of the first study. Mobius requested a teleconference to discuss the CDRH comments.

### DISCUSSION

- Mobius requested clarification of the CDRH comments regarding Human Factors. The Division responded that the product is a drug so the application must meet requirements for a New Drug Application. CDRH normally uses a Human Factors approach while the Center for Drug Evaluation and Research may use a variety of different approaches. The

Division thought that the CDRH comments might be helpful to Mobius in developing their label, but the comments are not absolute requirements. The Division also clarified that Mobius' product is not a combination product.

- Mobius expects to submit the results of their second LCS next week.
- In response to Mobius' inquiry, the Division explained that applications are expected to be complete at the time of original submission. In order to facilitate the coordination of the reviews, the Division may not review information that is submitted within the last 30 days of the NDA review cycle.
- The Division will issue an action letter either approving the drug product or listing all of the deficiencies when all of the reviews have been completed. Comments issued prior to the action letter are often incomplete because the final review has not been completed.

-----  
**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  
12/22/2010



NDA 022572

**PROPRIETARY NAME REQUEST  
WITHDRAWN**

Mobius Therapeutics, LLC  
4041 Forest Park Avenue  
St. Louis, Missouri 63108

ATTENTION: Ed Timm  
President

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) dated June 21, 2010, received June 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mitomycin Kit for Ophthalmic Use, 0.2 mg per vial.

We acknowledge receipt of your October 22, 2010, correspondence, on October 22, 2010, notifying us that you are withdrawing your request for a review of the proposed proprietary name, (b) (4). This proposed proprietary name request is considered withdrawn as of October 22, 2010.

We also acknowledge that you have proposed an alternate proprietary name, Mitosol, in your submission dated October 22, 2010.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Brantley Dorch, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0150. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Alison Rodgers at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

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

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

/s/  
-----

CAROL A HOLQUIST  
12/08/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Wednesday, December 01, 2010 9:54 AM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 Safety Update

This process has been engaged with UBC - I will come back to you with the ETA.

Ed Timm  
President

**MOBIUS THERAPEUTICS, LLC**

**P:** +1 314-615-6930

**F:** +1 314-615-6931

**M:** +1 404-775-5910

*Ed.Timm@MobiusTherapeutics.com*



**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

---

**From:** Rodgers, Alison [mailto:Alison.Rodgers@fda.hhs.gov]  
**Sent:** Wednesday, December 01, 2010 8:53 AM  
**To:** Ed Timm  
**Subject:** NDA 22572 Safety Update

Hi Ed,

We still need your safety update for the NDA. Again, it can be just a page stating that there are no adverse events to report. Please submit this by Friday, 12/3.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: alison.rodgers@fda.hhs.gov

Reference ID: 2870670

12/1/2010

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

/s/  
-----

ALISON K RODGERS  
12/01/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Monday, November 22, 2010 10:24 AM  
**To:** Rodgers, Alison  
**Subject:** Re: NDA 22572 - Additional Comments

Many thanks - amendment 0020 w-the updated PI coming in today.

Ed Timm  
President  
MOBIUS THERAPEUTICS, LLC

4041 Forest Park Avenue  
St. Louis, MO 63108

P: +1 314-615-6930  
F: +1 314-615-6931  
M: +1 404-775-5910  
[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)

Sent from my iPad  
Please excuse any typos

On Nov 22, 2010, at 9:20 AM, "Rodgers, Alison" <[Alison.Rodgers@fda.hhs.gov](mailto:Alison.Rodgers@fda.hhs.gov)> wrote:

Hi Ed,

As promised, attached are comments from the Center for Devices and Radiological Health.

Please let me know if you have any questions.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

<CDRH Comments for Mobius.pdf>

Device Performance:

Regarding the 1 mL Syringe Containing SWFI with the (b) (4) Connector:

1. Your combination product contains a 1 mL syringe that is prefilled with Sterile Water for Injection, and mated to a (b) (4) connector. You referenced DMF (b) (4) in your submission with respect to this syringe. DMF (b) (4) states that the (b) (4) syringe is utilized by (b) (4) in manufacturing syringes prefilled with Sterile WFI. We note that the DMF states that these syringes conform to ISO 7886 and ISO 594.

Although this syringe claims to conform to ISO 7886-1, FDA notes that it contains

(b) (4)

(b) (4)

2. (b) (4)

(b) (4)

3. (b) (4)

4. (b) (4)

Human Factors:

5. Your submission contains an "Instruction for Use Testing" report dated September 2010 (eCTD Sequence 15, Section 1.14.1.4.3). However, this test does not satisfy CDRH's requirement regarding Human Factors / Usability testing for devices. As a drug product, the device components are not required to satisfy CDRH's requirement regarding Human Factors, but the concepts should be incorporated into the testing of the overall product.

*The intent of a human factors validation study is to demonstrate that the device can be used by representative users under simulated conditions without patterns of failures that could result in clinical impact to patients or, in some cases, to users themselves. To the extent that failures with use do occur, the study should collect sufficient and appropriate data such that these failures can be described in terms of their cause from the perspective of the representative users. The test report should present a summary of these results within a discussion with respect to failures and whether they may be related to device design, labeling, or the content or proximity of training. The test report should also state if modifications are indicated. The Agency may agree or disagree with your analyses. If a design flaw could result in a risk to health, we do not agree that deferred modifications are acceptable.*

*If you have not conducted human factors validation testing, we recommend that you first develop a study protocol and then submit it to receive Agency feedback prior to initiating a study.*

*Please provide a summative validation study, which addresses the following items:*

- a. *Relative priority of tasks: The Agency needs to understand the relative priority of the tasks selected for testing in terms of the potential results of inadequate performance on these tasks. The rationale applied to their priority should be clearly provided.*
- b. *Comprehensiveness of task set: The Agency needs to understand that the tasks you chose to test represent the extent of the tasks that could lead to use-related problems (as defined). Please provide a rationale for the group of tasks you include in your Summarative testing.*
- c. *Number of study participants: The Agency's expectations for the number of study participants to be used in Human Factors/Usability Validation (or "Summative Test") include a minimum of 15 or more. The user groups should represent the United States population.*
- d. *Realism of simulated use: The testing environment and realism of the simulated use should be described in sufficient detail to determine if it is reasonable for a validation study of the subject device. Please describe the conditions under which the testing was undertaken.*

- e. *Performance criteria: Please describe the performance criteria and clearly state what the results mean in terms of failures that could correspond to potential harm to patients. Please provide study results that contain comprehensive assessment of test results particularly for high-priority use problems and failures.*
- f. *Objective and Subjective data: Please describe the objective and subjective data that will be collected during the study and discuss how variability in the data will be analyzed. Please provide study results that clarify use difficulties and failures.*
- g. *Training: The training you provide users should equate to your best assessment of the extent of training actual users will receive. Please clarify your description of the training provided to the participants in this test with respect to the extent to which it corresponds to realistic training levels.*
- h. *Unexpected failures: Your test plan should address how unexpected failures will be identified, recorded and reported.*

*For additional guidance on Medical Device Use-Safety and Human Factors, please go to the CDRH's guidance at:*

*<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm094461.pdf>*

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

/s/  
-----

ALISON K RODGERS  
11/22/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Tuesday, November 16, 2010 11:48 AM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 - Safety Update

Confirmed receipt - this will be easy to do.

Thanks for the communication,

Ed Timm  
President  
**MOBIUS THERAPEUTICS, LLC**  
**P:** +1 314-615-6930  
**F:** +1 314-615-6931  
**M:** +1 404-775-5910  
[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)



**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

---

**From:** Rodgers, Alison [mailto:Alison.Rodgers@fda.hhs.gov]  
**Sent:** Tuesday, November 16, 2010 10:25 AM  
**To:** Ed Timm  
**Subject:** NDA 22572 - Safety Update

Hi Ed,

Even though NDA 22572 is a 505(b)(2) application, you are required to submit a safety update. It may be as simple as a statement along the lines of, "There is no new safety information to report."

Please submit this to the NDA at your earliest convenience.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Reference ID: 2864510

11/16/2010

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

/s/  
-----

ALISON K RODGERS  
11/16/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Wednesday, November 03, 2010 11:19 AM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 Comments re 10-27-10 Labeling Submission

Sorry for not replying yesterday. Yes - we are in receipt.

Thanks,

Ed Timm  
President  
**MOBIUS THERAPEUTICS, LLC**  
**P:** +1 314-615-6930  
**F:** +1 314-615-6931  
**M:** +1 404-775-5910  
*Ed.Timm@MobiusTherapeutics.com*



**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

---

**From:** Rodgers, Alison [mailto:Alison.Rodgers@fda.hhs.gov]  
**Sent:** Wednesday, November 03, 2010 10:08 AM  
**To:** Ed Timm  
**Subject:** FW: NDA 22572 Comments re 10-27-10 Labeling Submission

Hi Ed,

Please confirm receipt of the email below.

Thanks,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: alison.rodgers@fda.hhs.gov

Reference ID: 2859417

11/3/2010

---

son  
ember 02, 2010 2:05 PM

2572 Comments re 10-27-10 Labeling Submission

Hi Ed,

As promised, attached are our comments regarding your labeling submission of 10-27-10, for NDA 22572.

As we discussed, we need to have the new Label Comprehension Study completed and results submitted as soon as possible. Please let me know when you plan to conduct the study.

Please let me know if you have any questions.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Clinical Comments:

- 1) Mobius should submit a revised package insert and vial labeling. The revised package insert should contain the additional information found in the "Instructions for Use" pages from the kit, including diagrams.
- 2) Recommend a second labeling comprehension study using the new, revised labeling.
  - a) The new, revised labeling should replace the name Optomycin with Mitosol.
  - b) [REDACTED] (b) (4); should be removed from the carton and packaging. The carton and packaging are part of the product's labeling, [REDACTED] (b) (4); [REDACTED]
  - c) [REDACTED] (b) (4); should be removed from the packaging.
  - d) [REDACTED] (b) (4); [REDACTED]
  - e) There was confusion during the first comprehension study regarding [REDACTED] (b) (4); [REDACTED]

DMEPA Comments:

A. Study Participants

1. Ensure that the study participants are naïve and have not participated in the previous Mitosol label comprehension study.
2. We recommend the number of participants be increased to 20.
3. We request the observer record all failures in the procedure. Once the participant has completed all steps in the procedure, the observer should ask open ended questions concerning all failures. The observer needs to record the participants responses as to why they didn't complete the step in preparation as described in the labeling and record all comments with respect to what was confusing and why it was confusing. [REDACTED] (b) (4); [REDACTED]

B. Carton and Kit labeling

1. The drug vial does not have a label. The drug vial should be labeled to identify its contents just as it would appear in the market.
2. [REDACTED] (b) (4); [REDACTED]
3. [REDACTED] (b) (4); [REDACTED]

C. Instructions for use

1. [REDACTED] (b) (4); [REDACTED]

[Redacted] (b) (4)

2. [Redacted] (b) (4)

3. [Redacted] (b) (4)

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

/s/  
-----

ALISON K RODGERS  
11/03/2010

## Rodgers, Alison

---

**From:** Rodgers, Alison  
**Sent:** Friday, October 22, 2010 9:20 AM  
**To:** (b) (4)  
**Subject:** Information Request for DMF (b) (4)

**Importance:** High

Dear Mr. Horton,

Information Request for DMF (b) (4)

DMF Holder: (b) (4)  
Contact Person: (b) (4)

Review of DMF (b) (4) in support of Mobius Therapeutics NDA 22-572 authorized per LOA dated 23 Feb 2010. Quality microbiology review of updated DMF (dated 09 Jan 2009 and received 12 Jan 2009).

The container closure report provided in your response of 13 September 2010 was not the report of the container closure study that was summarized in your DMF.

- 1) Provide the container closure test protocol and final report for the microbial ingress container closure report on the media filled syringes.
- 2) Concerning the dye ingress container closure report that was provided in your response, provide the following:
  - a) provide the information on positive controls used in the study and describe how they were generated.
  - b) what is the sensitivity of the assay
  - c) what is the method for detecting the presence of the dye

Please provide the requested information no later than Friday, October 29, 2010.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: alison.rodgers@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/

---

ALISON K RODGERS  
10/27/2010

## MEMORANDUM OF MEETING MINUTES

**Meeting Type:** FDA-Initiated Teleconference Meeting  
**Time:** October 21, 2010; 11:00 AM – 11:30 AM EST  
**Meeting Location:** WO Bldg 22, RM 4440  
**Application Type and Number:** NDA 22572  
**Product Name:** Optomycin  
**Indication:** Treatment of refractory glaucoma  
**Sponsor/Applicant Name:** Mobius Therapeutics, LLC

**Meeting Chair:** Melina Griffis  
**Meeting Recorder:** Brantley Dorch

### FDA ATTENDEES

Office of Surveillance and Epidemiology (OSE)  
Melina Griffis, Team Leader, DMEPA  
Lubna Najam, Safety Evaluator, DMEPA

### SPONSOR PARTICIPANT

Mobius Therapeutics, LLC  
Ed Timm, President

**BACKGROUND:**

NDA 22572 is a new NDA with Priority review status in OND. The OND PDUFA date is December 22, 2010. The Applicant submitted a request for proprietary name review on July 19, 2010, proposing the name, Optomycin. The Division of Medication Error Prevention and Analysis (DMEPA) evaluated the proposed name and found it unacceptable [REDACTED] (b) (4). The Applicant's proposed alternate proprietary name, [REDACTED] (b) (4) [REDACTED] (b) (4).

On September 8, 2010, the Applicant withdrew their proposed proprietary name, Optomycin, and submitted a new request for proposed proprietary name, [REDACTED] (b) (4) and alternate name, Mitosol. DMEPA's preliminary evaluation indicates the proposed name, [REDACTED] (b) (4). DMEPA's preliminary review of the proposed alternate name, Mitosol, did not identify any orthographic or phonetic similarities that would render the name unacceptable.

**MEETING OBJECTIVES:**

- Discuss DMEPA's objection to the proposed proprietary name, [REDACTED] (b) (4)
- Discuss the Applicant's options regarding their proposed proprietary name.

**DISCUSSION POINTS:**

- DMEPA indicated that the proposed proprietary name, [REDACTED] (b) (4) is unacceptable for the following reason:  
[REDACTED] (b) (4)
- DMEPA explained that the proposed alternate name, Mitosol, did not identify any look-alike or sound-alike names that would render the name unacceptable.
- FDA informed company of their options which are
  - to wait for the full review to be completed in which case a subsequent denial letter will be issued or
  - withdraw the proposed name, [REDACTED] (b) (4) and submit a new request for proposed name, Mitosol.

**ACTION ITEMS:**

- The Applicant will withdraw the proposed name, [REDACTED] (b) (4) and submit a new request for proposed name, Mitosol.

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

/s/  
-----

BRANTLEY H DORCH  
11/04/2010



NDA 22572

**INFORMATION REQUEST**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Optomyacin (mitomycin for solution).

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 in order to continue our evaluation of your NDA.

Reference is made to NDA 22-572 and in particular the proposed specification for Mitomycin for Ophthalmic Solution, 0.2 mg /Vial (Section 3.2.P.5.1a).

1. The test for Related Substances in the Drug Product lists (b) (4)

[Redacted]

The Method Validation Report - Forced Degradation provided in Module 3.2.R12 indicates that

[Redacted] (b) (4)

[REDACTED] (b) (4)

a. Please identify the origin of each of the specified impurities in Mitomycin for Ophthalmic Solution, 0.2 mg/Vial. If they are process impurities (by-products) in the drug substance, and are not also degradation products, they may be best controlled to appropriate levels at the drug substance stage.

b. As references standards for [REDACTED] (b) (4) are not available, it is advisable to establish the identities of [REDACTED] (b) (4) by, for example, LC-MS.

c. [REDACTED] (b) (4)

2. [REDACTED] (b) (4)

We also note that the levels of [REDACTED] (b) (4) observed in the drug product stability studies are quite variable.

a. Please propose acceptance criteria for Related Substances that are consistent with the observed product release and stability data.

b. Note that the acceptance criteria for Related Substances in the drug product should not exceed the acceptance criteria established for the FDA-approved mitomycin drug products that would have been used in the clinical studies upon which your NDA is based. The [REDACTED] (b) (4) may require additional Pharmacology /Toxicology impurity qualification testing.

c. Please explain the variability in the levels of [REDACTED] (b) (4) on stability.

3. Please explain the relevance of U.S. Patent [REDACTED] (b) (4) of Mitomycin for Ophthalmic Solution, 0.2 mg / Vial.

4. Please revise the acceptance criterion for moisture in the drug product from [REDACTED] (b) (4)

We highly recommend that you discuss these issues with your contract drug product manufacturer, Accord Healthcare Inc. /INTAS. Note that we have referred to ANDA 64-144 as authorized in their 26-JUL-2010 correspondence.

If you have any questions, call Althea Cuff, Regulatory Health Project Manager, at (301) 796-4061.

Sincerely,

*{See appended electronic signature page}*

Stephen Miller, Ph.D.  
Acting 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/

---

ALTHEA CUFF  
10/19/2010



NDA 022572

**PROPRIETARY NAME REQUEST  
WITHDRAWN**

Mobius Therapeutics, LLC  
4041 Forest Park Avenue  
St. Louis, Missouri 63108

ATTENTION: Ed Timm  
President

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) dated June 21, 2010, received June 22, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mitomycin Kit for Ophthalmic Use, 0.2 mg per vial.

We acknowledge receipt of your September 8, 2010, correspondence, on September 8, 2010, notifying us that you are withdrawing your request for a review of the proposed proprietary name, Optomycin. This proposed proprietary name request is considered withdrawn as of September 8, 2010.

We also acknowledge that you have proposed an alternate proprietary name, (b) (4) in your submission dated September 8, 2010.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Brantley Dorch, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0150. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Alison Rodgers at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

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

---

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

---

/s/

---

DENISE P TOYER on behalf of CAROL A HOLQUIST  
10/13/2010

**From:** Cuff, Althea  
**Sent:** Tuesday, September 21, 2010 5:14 PM  
**To:** 'ed.timm@mobiustherapeutics.com'  
**Subject:** Information request NDA 22-572  
Dear Ed,

I have the following request from our CMC reviewer.

Reference is made to our July 13, 2010 request, "For the stability data, provide actual data for each time point rather than summary data for a) the accelerated study of lyophilized mitomycin, []. If already included in the NDA, provide the section and page reference."

Although on July 29, 2010 you identified the location for these data, we cannot locate this information. We note that Drug Vial Module 3.2.P.8.3a includes Intas' report covering only 12-month stability data at 25°C/60% RH. Please resubmit the accelerated vial stability data.

In addition please submit any stability updates (i.e., 6-months accelerated data for the drug vial, 18-24 months long term data for the drug vial, and long term kit stability).

*Althea M. Cuff*  
*Regulatory Health Project Manager*  
*FDA/CDER/OPS/ONDQA*  
*Division of Post-Marketing Evaluation*  
*Phone (301) 796-4061*

---

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

---

/s/

---

ALTHEA CUFF  
09/22/2010

**Rodgers, Alison**

---

**From:** (b) (4)  
**Sent:** Monday, September 20, 2010 10:42 AM  
**To:** Rodgers, Alison  
**Cc:** (b) (4)  
**Subject:** Re: FW: DMF (b) (4) and (b) (4) - Request for Information  
**Importance:** High

Dear Alison,

This email notification confirms receipt of the inquiry from the U.S FDA (CDER).

Regards,

(b) (4)

(b) (4)



Please consider the environment before printing this email.

**From:** "Rodgers, Alison" <Alison.Rodgers@fda.hhs.gov>  
**To:** (b) (4)  
**Date:** 09/20/2010 09:29 AM  
**Subject:** FW: DMF (b) (4) and (b) (4) - Request for Information

---

Hi (b) (4)

Also, please confirm receipt of the email below.

Thank you,

9/20/2010

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: alison.rodgers@fda.hhs.gov

---

**From:** Rodgers, Alison  
**Sent:** Monday, September 20, 2010 9:29 AM  
**To:** (b) (4)  
**Subject:** DMF (b) (4) and (b) (4) - Request for Information

Hi (b) (4)

As we discussed on the telephone this morning, please see our request for information regarding DMF numbers (b) (4) and (b) (4) listed below. Please provide a response no later than October 15, 2010. Please send the response directly to me via email and submit it to the Central Document Room as well.

Please let me know if you have any questions.

DMF (b) (4) submission dated 18-June 2010 is being reviewed in support of DMF (b) (4) Letter Of Authorization dated 12 DEC 2008.

DMF (b) (4) review is in support of NDA 22-572 as authorized per LOA dated 23 Feb 2010.

Microbiology questions:



Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)



(b) (4)

---

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

---

/s/

---

ALISON K RODGERS  
09/20/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Wednesday, September 08, 2010 9:20 AM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 Preliminary Labeling Deficiencies

Thank you for the direction and yes, we are in receipt of this message. To my reading, there are no major deficiencies here, correct?

Thanks and best regards,

Ed Timm  
President  
**MOBIUS THERAPEUTICS, LLC**  
**P:** +1 314-615-6930  
**F:** +1 314-615-6931  
**M:** +1 404-775-5910  
[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)

**MOBIUS THERAPEUTICS HAS MOVED**

**Effective 1 July 2010, our new "Ship to" address is:**

**4041 Forest Park Avenue  
St. Louis, MO 63108 USA**

**Mobile, E-Mail, and URL to remain the same.**

**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

---

**From:** Rodgers, Alison [mailto:Alison.Rodgers@fda.hhs.gov]  
**Sent:** Wednesday, September 08, 2010 8:19 AM  
**To:** Ed Timm  
**Subject:** NDA 22572 Preliminary Labeling Deficiencies

Hi Ed,

The following preliminary labeling deficiencies have been identified for NDA 22572. Please plan to incorporate these changes into the label along with any revisions required upon completion of the label comprehension

9/8/2010

study. This updated version of labeling will be used for further labeling discussions.

#### **HIGHLIGHTS OF PRESCRIBING INFORMATION:**

- The new rule [21 CFR 201.57(a)(6)] requires that if a product is a member of an established pharmacologic class, the following statement must appear under the Indications and Usage heading in the Highlights: “(Drug Product) is a (name of class) indicated for (indication(s)).”
- Do not include the pregnancy category (e.g., A, B, C, D, X) in Highlights.
- The Patient Counseling Information statement must appear in Highlights and must read See 17 for PATIENT COUNSELING INFORMATION. [See 21 CFR 201.57(a)(14)]
- A revision (i.e., Revised: month/year) must appear at the end of Highlights. [See 21 CFR 201.57(a)(15)]. For a new NDA, BLA, or supplement, the revision date should be left blank at the time of submission and will be edited to the month/year of application or supplement approval.

#### **Contents (Table of Contents)**

- Create subsection headings that identify the content. Avoid using the word General, Other, or Miscellaneous for a subsection heading.

#### **FULL PRESCRIBING INFORMATION: DETAILS**

- Only section and subsection headings should be numbered. Do not number headings within a subsection (e.g., 12.2.1 Central Nervous System). Use headings without numbering (e.g., Central Nervous System).
- Do not refer to adverse reactions as “adverse events.” Please refer to the “Guidance for Industry: Adverse Reactions Sections of Labeling for Human Prescription Drug and Biological Products – Content and Format,” available at <http://www.fda.gov/cder/guidance>.
- The preferred presentation of cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. For example, [see *Use in Specific Populations (8.4)*] not See Pediatric Use (8.4). The cross-reference should be in brackets. Because cross-references are embedded in the text in the FPI, the use of italics to achieve emphasis is encouraged. Do not use all capital letters or bold print.
- Patient Counseling Information must follow after How Supplied/Storage and Handling section. [See 21 CFR 201.456(d)(1)] This section must not be written for the patient but rather for the prescriber so that important information is conveyed to the patient to use the drug safely and effectively [See 21 CFR 201.57(c)(18)].
- If the “Rx only” statement appears anywhere in labeling, delete it. This statement is not required for the prescribing information, only container and carton labels. [See Guidance for Industry: Implementation of Section 126 of the Food and Drug Administration Modernization Act of 1997 – Elimination of Certain Labeling Requirements]. The same applies to Patient Package Inserts and Medication Guides.

Please let me know if you have any questions.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products

Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

ALISON K RODGERS  
09/08/2010

## Rodgers, Alison

---

**From:** Rodgers, Alison  
**Sent:** Wednesday, September 01, 2010 10:50 AM  
**To:** (b) (4)  
**Subject:** DMF (b) (4) - NDA 22572 - Mobius Therapeutics

Dear (b) (4)

Review of DMF (b) (4) in support of Mobius Therapeutics NDA 22-572 authorized per LOA dated 23 Feb 2010. A review of the updated DMF (dated 09 Jan 2009 and received 12 Jan 2009) was done and the following information is requested:

(b) (4)

Please provide the requested information by September 9, 2010. Please send the information to the address listed below and a copy to me via email, if possible:

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

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

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: alison.rodgers@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

ALISON K RODGERS  
09/01/2010

**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** FDA-Initiated Teleconference Meeting  
**Time:** September 1, 2010; 1:00 PM – 1:30 PM EST  
**Meeting Location:** WO Bldg 22, RM 6396  
**Application Type and Number:** NDA 22572  
**Product Name:** Optomycin  
**Indication:** Treatment of refractory glaucoma  
**Sponsor/Applicant Name:** Mobius Therapeutics, LLC

**Meeting Chair:** Melina Griffis  
**Meeting Recorder:** Brantley Dorch

**FDA ATTENDEES**

Office of Surveillance and Epidemiology (OSE)  
Melina Griffis, Team Leader, DMEPA  
Lubna Najam, Safety Evaluator, DMEPA  
Doris Bates, Team Leader, Project Management Staff

Office of New Drugs (OND)  
Wiley Chambers, Acting Director, DAIOP  
William Boyd, Medical Officer, DAIOP  
Alison Rodgers, Project Manager, DAIOP

**SPONSOR PARTICIPANTS**

Mobius Therapeutics, LLC  
Ed Timm, President

(b) (4)

**BACKGROUND:**

NDA 22572 is a new NDA with Priority review status in OND. The OND PDUFA date is December 22, 2010. The Applicant submitted a request for proprietary name review on July 19, 2010, proposing the name, Optomycin. The Division of Medication Error Prevention and Analysis (DMEPA) evaluated the proposed name and found it unacceptable [REDACTED] (b) (4). The Applicant's proposed alternate proprietary name, [REDACTED] (b) (4), [REDACTED] (b) (4).

**MEETING OBJECTIVES:**

- Discuss DMEPA's objection to the proposed proprietary names.
- Discuss the Applicant's options regarding their proposed proprietary names.

**DISCUSSION POINTS:**

- FDA indicated that the proposed proprietary names, Optomycin and [REDACTED] (b) (4) were unacceptable for the following reasons:  
[REDACTED] (b) (4)
- Applicant inquired about not changing their proposed proprietary name, Optomycin.
- The FDA indicated that is an option; however, supporting data would have to be submitted [REDACTED] (b) (4).
- FDA informed company of other options which are
  - to wait for the full review to be completed in which case a subsequent denial letter will be issued or
  - withdraw the proposed name and submit a new request for a proprietary name review.
- The Applicant will withdraw the proposed name and submit a new proprietary name.
- FDA explained that both actions can be taken in the same submission, but the cover letter should clearly indicate that both actions are being taken.

- Applicant inquired about a reference for Approved USAN Stems to avoid incorporating one in new proposed proprietary name.
- FDA informed the applicant that there is an Approved USAN Stems website that can be referenced prior to submitting their new name proposals and FDA would send link via email.
- Applicant inquired about a guidance for developing new proprietary names prior to submitting to FDA.
- FDA explained that there is a Proprietary Name Review Concept Paper located on the FDA website which can be used as a reference, as well as The Orange Book.

**ACTION ITEMS:**

- Applicant will take all of their options into consideration before determining their path moving forward.

---

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

---

/s/

---

BRANTLEY H DORCH  
09/29/2010



NDA 22572

**FILING COMMUNICATION**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

Please refer to your new drug application (NDA) dated June 21, 2010, received June 22, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Optomycin (mitomycin for solution).

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Priority**. Therefore, the user fee goal date is December 22, 2010.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by December 1, 2010.

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

An evaluation of the ability of intended users of the kit to reliably follow the directions provided and reconstitute the mitomycin product in a sterile fashion has not been submitted.

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

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

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

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Wiley A. Chambers, M.D.  
Acting Director  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

**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  
08/19/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Friday, August 13, 2010 9:16 AM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 Label Comprehension Study

You have just (officially) made my week.

This serves as confirmation of receipt of your message. Further, by way of this message, we confirm that the study respondents will be provided a sealed kit and nothing more.

Thanks and have a great weekend,

Ed Timm  
President  
MOBIUS THERAPEUTICS, LLC  
P: +1 314-615-6930  
F: +1 314-615-6931  
M: +1 404-775-5910  
Ed.Timm@MobiusTherapeutics.com  
By way of remote access

**MOBIUS THERAPEUTICS HAS MOVED**

Effective 1 July 2010, our new "Ship to" address is:

4041 Forest Park Avenue  
St. Louis, MO 63108 USA

Mobile, E-Mail, and URL to remain the same.

-----Original Message-----

From: Rodgers, Alison [<mailto:Alison.Rodgers@fda.hhs.gov>]  
Sent: Fri 8/13/2010 8:07 AM  
To: Ed Timm  
Subject: NDA 22572 Label Comprehension Study

Hi Ed,

Provided the label comprehension study will give the participants a sealed Optomycin kit with no other instructions, the submissions are acceptable.

Please let me know if you have any questions.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER

8/13/2010

Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

ALISON K RODGERS  
08/13/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Wednesday, August 11, 2010 10:55 AM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 Label Comprehension Study

We will be submitting our response no later than tomorrow. This time, we believe we will assuredly hit the mark.

Best,

Ed Timm  
President  
**MOBIUS THERAPEUTICS, LLC**  
**P:** +1 314-615-6930  
**F:** +1 314-615-6931  
**M:** +1 404-775-5910  
[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)

**MOBIUS THERAPEUTICS HAS MOVED**

**Effective 1 July 2010, our new "Ship to" address is:**

**4041 Forest Park Avenue  
St. Louis, MO 63108 USA**

**Mobile, E-Mail, and URL to remain the same.**

**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

---

**From:** Rodgers, Alison [mailto:Alison.Rodgers@fda.hhs.gov]  
**Sent:** Tuesday, August 10, 2010 7:33 AM  
**To:** Ed Timm  
**Subject:** NDA 22572 Label Comprehension Study

Hi Ed,

Please see our comments below regarding the Label Comprehension Study and the August 6, 2010 amendment. Please let me know if you have any questions.

8/11/2010

*Our prior comments regarding Items 1 and 2 on the Observer Form are unchanged. Both items are far too broad. These items should be modified to include specific evaluated tasks and components. We do not consider Items 1 and 2 to be useful assessments as currently written.*

Please submit your response by August 16, 2010, or sooner.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

ALISON K RODGERS  
08/11/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Tuesday, August 03, 2010 2:19 PM  
**To:** Rodgers, Alison  
**Cc:** (b) (4)  
**Subject:** Fwd: NDA 22572 Label Comprehension Study

We are in receipt of your message and will easily meet your timeline as defined in it's text. (b) (4) and I have spoken and will do a deeper dive on these issues tomorrow.

Thank tour for the detailed comments and the open communication.

Thanks and best regards,

Ed Timm  
President  
MOBIUS THERAPEUTICS, LLC

MOBIUS THERAPEUTICS HAS MOVED  
Effective 1 July 2010, our new address is:

4041 Forest Park Avenue  
St. Louis, MO 63108 USA

P: +1 314-615-6930  
F: +1 314-615-6931  
M: +1 404-775-5910  
[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)  
Mobile, E-Mail and URL to remain the same.  
From my iPhone  
Please excuse any typos

Begin forwarded message:

**From:** "Ed Timm" <[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)>  
**Date:** August 3, 2010 12:19:05 PM CDT  
**To:** (b) (4)  
**Subject:** Fwd: NDA 22572 Label Comprehension Study

FYI - let's speak live today.

Ed Timm  
President  
MOBIUS THERAPEUTICS, LLC

MOBIUS THERAPEUTICS HAS MOVED  
Effective 1 July 2010, our new address is:

4041 Forest Park Avenue  
St. Louis, MO 63108 USA

P: +1 314-615-6930

F: +1 314-615-6931

M: +1 404-775-5910

[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)

Mobile, E-Mail and URL to remain the same.

From my iPhone

Please excuse any typos

Begin forwarded message:

**From:** "Rodgers, Alison" <[Alison.Rodgers@fda.hhs.gov](mailto:Alison.Rodgers@fda.hhs.gov)>

**Date:** August 3, 2010 7:37:15 AM CDT

**To:** Ed Timm <[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)>

**Subject:** NDA 22572 Label Comprehension Study

Hi Ed,

Please note the following comments regarding your proposed label comprehension study for NDA 22572:

- 1) The label comprehension study should be using the to-be-marketed kit, otherwise the study is of no value.
- 2) The study participants should NOT be handed the instructions for use if they are found inside the sealed tray; they should be handed a sealed tray. We are interested in whether the current labeling of the kit as it will be marketed is adequate for use.
- 3) Mobius should make sure all printed instructions for use for the Optomycin kit have been formally submitted to the NDA.
- 4) Items 1 and 2 on the Observer Form imply the study personnel have been given the instructions for use prior to receiving a kit. They are very broad. These items should be modified. The personnel should be handed a sealed kit and observed for technique.

Please respond by August 9, 2010, or sooner.

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

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

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

/s/

ALISON K RODGERS  
08/03/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Wednesday, July 28, 2010 12:12 PM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 Label Comprehension Protocol

We just internally approved a written IFU for inclusion within this protocol. We will get this to you ASAP. I will get the recording form as well.

Best,

Ed Timm  
President  
**MOBIUS THERAPEUTICS, LLC**  
**P:** +1 314-615-6930  
**F:** +1 314-615-6931  
**M:** +1 404-775-5910  
[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)

**MOBIUS THERAPEUTICS HAS MOVED**

**Effective 1 July 2010, our new "Ship to" address is:**

**4041 Forest Park Avenue  
St. Louis, MO 63108 USA**

**Mobile, E-Mail, and URL to remain the same.**

**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

---

**From:** Rodgers, Alison [mailto:Alison.Rodgers@fda.hhs.gov]  
**Sent:** Wednesday, July 28, 2010 11:09 AM  
**To:** Ed Timm  
**Subject:** NDA 22572 Label Comprehension Protocol

Hi Ed,

7/28/2010

Please see our comments regarding your proposed Label Comprehension Study listed below. Please respond as soon as possible.

- 1) *We will need to see a copy of the independent observer's recording form (i.e. we need to see what is actually recorded in the OR as the nurses/technicians prepare the Optomycin).*
- 2) *The overview should clarify what is meant by the "printed IFU" given to technicians and nurses. The kits as submitted to the NDA have pictographic instructions INSIDE the sealed kit. The draft package insert states the PI will be in the kit, but it is not in the kits submitted to the NDA.*

Please let me know if you have any questions.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

ALISON K RODGERS  
07/28/2010



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 22572

**MEETING MINUTES**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Optomydin™ Kit for Ophthalmic Use.

We also refer to the telecon between representatives of your firm and the FDA on July 19, 2010. The purpose of the telecon was to discuss Chemistry, Manufacturing, and Controls issues.

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

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Wiley A. Chambers, M.D.  
Acting Director  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosure

## MEMORANDUM OF TELECONFERENCE MINUTES

**Teleconference Date and Time:** July 19, 2010, 3:00 – 4:00 PM

**Application Number:** 22572  
**Product Name:** Optomycin  
**Indication:** Treatment of refractory glaucoma  
**Sponsor/Applicant Name:** Mobius Therapeutics LLC

### FDA PARTICIPANTS

#### Division of Anti-Infective and Ophthalmology Products

William Boyd, MD, Clinical Team Leader

Wiley Chambers, MD, Acting Director

Denise Miller, Microbiologist, Office of Pharmaceutical Science

Alison Rodgers, Project Manager

Mark Seggel, PhD, Chemistry Reviewer, Office of New Drug Quality Assessment

### SPONSOR PARTICIPANTS

Ed Timm, President, Mobius Therapeutics LLC

(b) (4)

### BACKGROUND

Mobius Therapeutics LLC (Mobius) submitted NDA 22572 on June 21, 2010. On July 15, 2010, the Division notified Mobius that no information had been submitted with the NDA to demonstrate that intended users of the Optomycin kit were able to reliably follow the directions provided and reconstitute the mitomycin product in a sterile fashion. A teleconference was held on July 16, 2010, to discuss the issue. An additional teleconference was scheduled to continue discussion of Chemistry, Manufacturing, and Controls issues.

### DISCUSSION

- The Division reminded Mobius that they need to make the link between the sponges used in their kit and those used in the clinical trials. Mobius stated that it has done an analysis of the sponges used in clinical trials and the materials are the same as those used in the Mobius kit. Most of the sponges are manufactured by (b) (4). Mobius will submit an amendment to the NDA with the information regarding sponges.
- Mobius will submit a protocol for the label comprehension study this week.
- Mobius noted that they are unable to find a lab willing to (b) (4). (b) (4) Intas does not have the methodology to do the test within the required time frame. Mobius also stated that according to the American Society of Operating Room Nurses, the technique Mobius has utilized for (b) (4) is a safe technique.

-----  
**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  
12/10/2010



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 22572

**MEETING MINUTES**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Optomyacin Kit for Ophthalmic Use.

We also refer to the telecon between representatives of your firm and the FDA on July 16, 2010. The purpose of the meeting was to discuss the Instructions for Use provided in the NDA.

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

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Wiley A. Chambers, M.D.  
Acting Director  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosure

## MEMORANDUM OF TELECONFERENCE MINUTES

**Date and Time:** July 16, 2010, 9:30 – 10:00 AM  
**Application Number:** 22572  
**Product Name:** Optomycin Kit  
**Indication:** Treatment of refractory glaucoma  
**Sponsor/Applicant Name:** Mobius Therapeutics LLC

**Meeting Chair:** Wiley Chambers, MD  
**Meeting Recorder:** Alison Rodgers

### FDA ATTENDEES

#### Division of Anti-Infective and Ophthalmology Products

William Boyd, MD, Clinical Team Leader  
Wiley Chambers, MD, Acting Director  
Jennifer Harris, MD, Medical Officer  
Lucious Lim, MD, Medical Officer  
Rhea Lloyd, MD, Medical Officer  
Linda Ng, PhD, Pharmaceutical Assessment Lead, Office of New Drug Quality Assessment  
Alison Rodgers, Project Manager  
Mark Seggel, PhD, Chemistry Reviewer, Office of New Drug Quality Assessment

### SPONSOR ATTENDEES

Ed Timm, President, Mobius Therapeutics LLC

(b) (4)

### BACKGROUND

Mobius Therapeutics LLC (Mobius) submitted NDA 22572 on June 21, 2010. On July 15, 2010, the Division notified Mobius that no information had been submitted in the NDA to demonstrate that intended users of the Optomycin kit were able to reliably follow the directions provided and reconstitute the mitomycin product in a sterile fashion. A teleconference was scheduled to discuss the issue.

### DISCUSSION

- The Division opened the teleconference by asking if Mobius had information demonstrating that people who use the kit can reliably open and reproduce sterile Mitomycin according to the directions provided. The Division was concerned that individuals would not be able to follow the instructions provided for reconstituting the product without contaminating it. The Division requested that a study be conducted to demonstrate that the product can be reproducibly reconstituted and used in the operating room as intended.
- Mobius inquired as to how they should demonstrate the ability to follow the Instructions for Use. The Division responded that Mobius should have an observer watch and

document what happens with the critical elements of the process. Mobius will develop a protocol and submit it for the Division's review.

- The Division requested that Mobius submit information showing that the material used in the sponges in the kit is the same as that used by other ophthalmologists in the operating room. Mobius should identify the material used for sponges in the majority of trials and the material in their sponges. Mobius will conduct a literature search to determine the material that is utilized most often for sponges in the operating room.
- The Division inquired as to why the entire kit is not sterilized. Mobius stated that they could not find any lab willing to

(b) (4)



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

/s/  
-----

WILEY A CHAMBERS  
12/08/2010

## Cuff, Althea

---

**From:** Cuff, Althea  
**Sent:** Tuesday, July 13, 2010 9:36 AM  
**To:** 'ed.timm@mobiustherapeutics.com'  
**Subject:** Information Request NDA 22-572

Good Morning Ed,

I have the following request from our CMC reviewer.

1. Please provide the device approval references or regulatory status of the components in the Optomycin kit as described on pp 21-22, section 3.2.P.2. If these components are contained in a DMF/MAF, provide letter of authorization, DMF/MAF number, submission date and page number. If no reference is available for the component, provide detail information on the material and the specification:



2. Please provide the LOA for ANDA 64-144 claimed to be included in section 3.2.P.2, p. 4, or provide the section # with page reference.
3. For the stability data, provide actual data for each time point rather than summary data for a) the accelerated study of lyophilized mitomycin, and b) accelerated and room temperature data for the kit (sterility and appearance of each component). If already included in the NDA, provide the section and page reference.

Please submit your response by July 19, 2010.

Thanks,  
*Althea M. Cuff*  
*Regulatory Health Project Manager*  
*FDA/CDER/OPS/ONDQA*  
*Division of Post-Marketing Evaluation*  
*Phone (301) 796-4061*

APPEARS THIS WAY ON ORIGINAL.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

STEPHEN P MILLER  
07/13/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Wednesday, July 07, 2010 4:43 PM  
**To:** Rodgers, Alison  
**Subject:** RE: NDA 22572 Request for Information 07-07-10

I have just returned to the office after being off-site all afternoon. We are on this immediately.

Did you have a good 4th?

Best,

Ed Timm  
President

**MOBIUS THERAPEUTICS, LLC**

**P:** +1 314-615-6930

**F:** +1 314-615-6931

**M:** +1 404-775-5910

*Ed.Timm@MobiusTherapeutics.com*

**MOBIUS THERAPEUTICS HAS MOVED**

**Effective 1 July 2010, our new "Ship to" address is:**

**4041 Forest Park Avenue  
St. Louis, MO 63108 USA**

**Mobile, E-Mail, and URL to remain the same.**

**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

---

**From:** Rodgers, Alison [mailto:Alison.Rodgers@fda.hhs.gov]  
**Sent:** Wednesday, July 07, 2010 12:53 PM  
**To:** Ed Timm  
**Subject:** NDA 22572 Request for Information 07-07-10

Hi Ed,

7/8/2010

Please note the following requests for information:

Clinical:

1. Which, if any, of your literature references specifically cite the name, Mutamycin?
2. Please submit an annotated draft label.

Pharmacology/Toxicology:

Nonclinical references 4.3.1.37 and 4.3.1.38 are not provided in the electronic submission. Please be sure to provide the abstract, if not the whole article, in English.

Chemistry, Manufacturing, and Controls:

Please provide two (2) samples of the complete product kit (with placebo vials).

Please submit the requested information by July 14th, if possible.

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

ALISON K RODGERS  
07/08/2010



NDA 22572

**NDA ACKNOWLEDGMENT**

Mobius Therapeutics, LLC  
Attention: Ed Timm  
President  
1141 South 7<sup>th</sup> Street  
St. Louis, MO 63104

Dear Mr. Timm:

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: Optomycin (mitomycin) Kit for Ophthalmic Use (Rx Only)

Date of Application: June 21, 2010

Date of Receipt: June 22, 2010

Our Reference Number: NDA 22572

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

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

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

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Anti-Infective 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>

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

*{See appended electronic signature page}*

Maureen P. Dillon-Parker  
Chief, Project Management Staff  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

MAUREEN P DILLON PARKER  
06/30/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Tuesday, June 29, 2010 9:18 AM  
**To:** Rodgers, Alison  
**Subject:** Re: NDA 22572 - Error in Labeling

I forwarded on to (b) (4) He will correct and review for additional errors.

Ed Timm  
President  
MOBIUS THERAPEUTICS, LLC  
P: +1 314-571-6205  
F: +1 314-450-5933  
M: +1 404-775-5910  
[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)  
From my iPhone  
Please excuse any typos

**MOBIUS THERAPEUTICS IS MOVING.**

Effective 1 July 2010, our new address will be:

4041 Forest Park Avenue  
St. Louis, MO 63108 USA

P: +1 314-615-6930  
F: +1 314-615-6931

Mobile, E-Mail and URL to remain the same.

**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

On Jun 29, 2010, at 8:56 AM, "Rodgers, Alison" <[Alison.Rodgers@fda.hhs.gov](mailto:Alison.Rodgers@fda.hhs.gov)> wrote:

Hi Ed,

Please note that (b) (4) is cited in headers in section 1.14.3.1, annotated comparison with listed drug. This needs to be corrected and the section replaced. Also, please be sure that (b) (4) is not listed incorrectly anywhere else in the submission.

Please let me know when you plan to respond to this request.

6/29/2010

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

---

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

---

/s/

---

ALISON K RODGERS  
06/30/2010

**Rodgers, Alison**

---

**From:** Ed Timm [Ed.Timm@MobiusTherapeutics.com]  
**Sent:** Tuesday, June 29, 2010 9:18 AM  
**To:** Rodgers, Alison  
**Subject:** Re: NDA 22572 - Error in Labeling

I forwarded on to (b) (4) He will correct and review for additional errors.

Ed Timm  
President  
MOBIUS THERAPEUTICS, LLC  
P: +1 314-571-6205  
F: +1 314-450-5933  
M: +1 404-775-5910  
[Ed.Timm@MobiusTherapeutics.com](mailto:Ed.Timm@MobiusTherapeutics.com)  
From my iPhone  
Please excuse any typos

**MOBIUS THERAPEUTICS IS MOVING.**

Effective 1 July 2010, our new address will be:

4041 Forest Park Avenue  
St. Louis, MO 63108 USA

P: +1 314-615-6930  
F: +1 314-615-6931

Mobile, E-Mail and URL to remain the same.

**CONFIDENTIALITY NOTE:** This electronic message is intended solely for the use of the recipient(s) to whom it is addressed and might contain information that is privileged, confidential, or otherwise exempt from disclosure under applicable law. If the reader of this message is not an intended recipient, any dissemination, distribution or copying of this communication (including any attachments) is strictly prohibited. If you have received this communication in error, please delete it (including any attachments) from your system without copying or forwarding it, and notify the sender of the error by reply e-mail.

On Jun 29, 2010, at 8:56 AM, "Rodgers, Alison" <[Alison.Rodgers@fda.hhs.gov](mailto:Alison.Rodgers@fda.hhs.gov)> wrote:

Hi Ed,

Please note that (b) (4) is cited in headers in section 1.14.3.1, annotated comparison with listed drug. This needs to be corrected and the section replaced. Also, please be sure that (b) (4) is not listed incorrectly anywhere else in the submission.

Please let me know when you plan to respond to this request.

6/29/2010

Please confirm receipt of this email.

Thank you,

Alison

Alison K. Rodgers  
Regulatory Health Project Manager  
FDA/CDER  
Division of Anti-Infective and Ophthalmology Products  
Phone: 301-796-0797  
Fax: 301-796-9882  
Email: [alison.rodgers@fda.hhs.gov](mailto:alison.rodgers@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	TRABOMY(MITOMYCIN)KIT FOR OPHTHALMIC USE

---

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

---

/s/

---

ALISON K RODGERS  
06/29/2010