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RESEARCH**

*APPLICATION NUMBER:*  
**022572Orig1s000**

**OTHER ACTION LETTERS**



NDA 22572

**COMPLETE RESPONSE**

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 Mitosol (mitomycin for solution).

We acknowledge receipt of your amendments dated July 9, 12, 19, 22 (2), 27, 29, and 30, August 6, 11 (4), and 12, September 8, and 22, October 7, 22, and 27, November 11, 17, and 22, and December 3 (2).

We also acknowledge receipt of your amendment dated December 7, 2010, which was not reviewed for this action. You may incorporate applicable sections of the amendment by specific reference as part of your response to the deficiencies cited in this letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

1. There is insufficient information about the drug product to determine whether the product is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling. The labeling of the product as submitted is not adequate to ensure safe and reliable reconstitution, transportation, and application of the product for the intended indication. We will continue to work with you on your labeling and packaging plans for Mitosol (mitomycin for solution) and encourage you to discuss any future protocols for labeling comprehension studies with the Division.
2. The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug substance and drug product are inadequate to preserve its identity, strength, quality, purity, and stability. Specifically,
  - a. You have not demonstrated that the proposed drug product, Mitosol (mitomycin for solution), 0.2 mg/vial, is of comparable identity, strength, quality, purity and potency to the commercially available, currently approved drug product upon

- which the clinical studies are based (e.g., cross-referenced mitomycin for injection RLD ANDA 64-144).
- b. There is insufficient justification of the drug product specification (e.g., acceptance criteria for impurities and pH).
  - c. There is insufficient justification of the expiration dating period.
  - d. 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.
3. The methods used in and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug product do not comply with the current good manufacturing practice (cGMP) regulations in parts 210 and 211. Specifically, during a recent preapproval inspection conducted at Synergetics, Inc. (FEI 1000119053), significant deviations from Current Good Manufacturing Practices (cGMP) were observed and disclosed to the firm's management. All facilities and controls will need to comply with the cGMP regulations. Please amend the application with facilities that are in compliance with current good manufacturing practice (cGMP) or notify us when all currently submitted facilities are in compliance with cGMPs.

We reserve comment on the proposed labeling until the application is otherwise adequate. If you revise labeling, your response must include updated 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>.

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have

such a meeting, submit your meeting request as described in the FDA's "Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants," May 2009 at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf>.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

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

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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WILEY A CHAMBERS  
12/22/2010