CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202514Orig1s000

OTHER ACTION LETTERS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 202514

COMPLETE RESPONSE

Merck Sharp & Dohme Corp.
Attention: Chitkala Kalidas, Ph.D.
Director, Worldwide Regulatory Affairs
P.O. Box 2000, RY33-204
Rahway, New Jersey 07065-0900

Dear Dr. Kalidas:

Please refer to your New Drug Application (NDA) dated and received January 7, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZIOPTAN (tafluprost ophthalmic solution) 0.0015%.

We acknowledge receipt of your amendments dated:

January 7, 2011 (2)	January 20, 2011	February 9, 2011
February 17, 2011	February 28, 2011	March 23, 2011
March 29, 2011	April 4, 2011	April 6, 2011
April 28, 2011	April 29, 2011	May 6, 2011
May 11, 2011	May 24, 2011	June 8, 2011
June 9, 2011	June 10, 2011	June 13, 2011
June 30, 2011	July 5, 2011	July 6, 2011
July 11, 2011	July 26, 2011	August 1, 2011
August 3, 2011	August 10, 2011	August 12, 2011
August 22, 2011	September 2, 2011	September 6, 2011
September 13, 2011	September 27, 2011	October 13, 2011
October 26, 2011	October 27, 2011	November 2, 2011 (2)
November 3, 2011	November 4, 2011	

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.

PRODUCT QUALITY MICROBIOLOGY

Your NDA does not provide assurance of the sterility of the final drug product. While you have revised your (b) (4) processing validation protocol in your submission of October 27, 2011, (b) (4)

[redacted] filling procedures using this revised validation protocol. In the absence [redacted], we cannot determine that the product is sterile and safe for use.

To address this deficiency, provide a report describing three consecutive successful [redacted] processing simulations [redacted] that you will use for manufacturing the product using the inspection and accounting procedures provided in the revised [redacted] processing validation protocol submitted in the October 27, 2011 amendment.

SAFETY UPDATE

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 non-clinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

OTHER

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, please call Constantine J. Markos, B.S., Pharm.D., R.Ph., Regulatory Health Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Edward M. Cox, M.D., M.P.H.
Director
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/

EDWARD M COX
11/07/2011