DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203510

INFORMATION REQUEST

Paragon BioTeck, Inc.
c/o Point Guard Partners LLC
Attention: Jeremy Brace, B.Sc. (Hons)
400 N. Ashley Street, Suite 1950
Tampa, FL 33602

Dear Mr. Brace:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for phenylephrine hydrochloride ophthalmic solution, 2.5% and 10%.

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.

1. Please describe how the drug product manufacturer assures the quality of the in-coming drug substance and which tests are conducted in house. If the assay and impurities are determined by HPLC testing please describe how the drug product manufacturer has validated the method or verified that it is suitable for use.

2. Provide a description of the HPLC method used for SOP SAS-037 (the UV 210 nm method) described in extract-migration-study. How is the reporting limit of 1 ppm defined? 1 ppm with reference to what?

3. Conduct extraction and migration studies (in a similar fashion to those already carried out) for 1-3 batches after storage at 25°C/60% RH (accelerated) for 6 months and after storage refrigerated (long-term) through expiration. We recommend that the control be a sealed glass vial containing the drug product solution.

4. In the description of the manufacturing Process (3.2.P.3.3) you state "Compounding and mixing of Phenylephrine HCl Ophthalmic Solution 2.5% (457.2 kg batch size) will occur in a 600 liter mixing tank equipped with a simple propeller-style mixer." Additionally a 600 L sterile holding tank is used. However Figures 2 and 3 show only 50 gallon mixing tanks. Are these 50 gallon tanks replaced with 600 L tanks when necessary and, if so, how does this impact on the cleanliness of the various rooms? Alternatively, is a different facility used? Please provide information on the validation of the holding times

of product in the mixing and sterile holding tanks. Please indicate if metal from the holding or mixing tanks has been found to contaminate the product.

5. In 3.2.P.3.4.1 the in-process control is given as 450-550 mOsm/Kg H_2O. However in the specification the 10% solution is 950-1050 mOsm/Kg H_2O. Please reconcile.

6. Provide a description of the sampling plan and representative analyses for the Water for Injection.

7. Specify if the light obscuration or the microscopic particle test method is used to determine particulates. Please provide a report verifying that it is suitable for its intended purpose.

8. Please change the phenylephrine hydrochloride assay acceptance criterion to 90.0-110.0% of label claim.

9. We note that the highest observed Total Impurities value is 0.02%. Please consider reducing the Total Impurities acceptance criterion from ≤ 1.5% to ≤ 0.5%.

10. Consider adding a chiral purity test to the dug product specification or provide a justification for not doing so.

11. Please supply batch numbers, expiration dates, and assigned purities for all the reference standards.

12. Provide specifications for the in-coming container-closure system components.

13. Provide a description (including brand, type, and composition, as far as is known) of the labeling materials and inks that may be used for this product. Please note that these should not be changed without notifying the Agency.

14. Provide a Methods Validation Package. This should consist of a list of samples that could be supplied and links to the various analytical methods.

15. You state in 3.2.P.2.5 Microbiological Attributes that "The validation of the sterilizing filter (Pall Fluorodyne II 0.2 µm) used in the production of Phenylephrine HCl Ophthalmic Solution, 2.5.% and 10% has been conducted and can be found in Sterilizing Filter Validation." However the report on the Sterilizing Filter Validation appears to describe only the use of the 2.5% solution. Please provide a similar report using the 10% solution or a justification for not providing such a report.

16. Test the sterilizing filter for extractables.

17. Test the drug product for endotoxins on stability, at least annually.

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

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/s/

RAPTI D MADURAWE
12/05/2012