



FACSIMILE TRANSMISSION RECORD
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To: -----(b)(4)-----

From: Cherie Ward-Peralta, OBRR/CBER/FDA

Date: May 3, 2010

This Fax is regarding your submission, STN 125325/0 that was submitted to the Agency on May 29, 2009 as a biologics license application for Alpha-1 Proteinase Inhibitor (Human). In order to facilitate the review of the BLA, FDA requests the following additional information:

Labeling

1. The droplet-like graphic on the labels can be interpreted in many different ways. For example, it can be seen as a glass droplet and may be used as a caller for the product name, Glassia. It can be seen as clear drop of plasma and may be used promotionally as an indication for purity. APLB feels that this graphic can be subjected to many different interpretations, and as currently presented; it is the most prominent item on the labels. We recommend removing the graphic as it is distracting and reduces the prominence of important required information, including the proper name [see 21 CFR 610.62(b)].
2. As currently presented, the product names are presented in lighter blue color font, which is less prominent to the rest of the information which is presented in black color font. Please use a more prominent text font or type-face so that the names are commensurate with the rest of the label [see 21 CFR 610.62(c)].
3. Please present the statement "Do not freeze" in conjunction with the refrigeration storage temperature of 2-8°C. For example, "Store at 2-8°C (35-46°F). Do not freeze."
4. On the carton and vial label, please add "mg α_1 -PI". This entry should be located close to the lot number and expiration. The specific amount of α_1 -PI/vial in the particular lot will be printed during packaging.
5. From the carton and vial label, please remove the sentence "Can be stored at temperatures -----(b)(4)-----." Also, from the package insert please remove the sentence "----- (b)(4) -----"

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Thank you.

Number of pages (including cover sheet) 3

----- (b)(4) -----

6. On the carton, please add the statement "This product is prepared from large pools of human plasma which may contain the causative agents of hepatitis and other viral diseases. See package insert WARNINGS." This statement is recommended for each US licensed α_1 -PI product.
7. On the carton and vial label, please add the statement "Administer product brought to room temperature within three hours of entering the vials."
8. Please do not print product labels before the product is approved. Labeling changes can be requested at any time during the review process.

CMC

9. ----- (b)(4) -----

10. Please clarify how the product was pooled into the infusion bags during the clinical study. The initial version of the package insert stated the "Vials should be pooled in an empty, sterile IV container using a sterile filter needle." Please clarify whether the product was filtered before it was pooled.

11. ----- (b)(4) -----

12. Regarding viral safety information to be provided by -(b)(4)-, please follow our email request dated 3/23/10 (Items # 1, 3, 4) and 4/20/10.

13. For the robustness study of viral clearance for -(b)(4)- for the nanofiltration step, please provide final study report as soon as it is available. Please let us know when the submission of the report is anticipated.

14. You have stated in your justification that the correction factor would not result in a more accurate assessment of RHS#1 potency and would not result in a meaningful change for patients. However none of the data you present refute the point that using an uncorrected RHS#1 standard results in a higher assessment of your product's potency. Using an uncorrected RHS#1 potency standard would result in consistently less α_1 -PI delivered to patients. Since this difference could be clinically meaningful, we request that you continue to implement the correction factor in the calculation of Kamada-API potency.

15. Please provide the following TnBP assay validation and SOP documents:
 - a. Protocol VL-100406-AM, v. 3 and its appendix VL-100406-AM/1
 - b. Report VL-100406 AM, v. 1
 - c. SOP N-1P-0001-31
16. For all analytical methods used for the final container and in-process intermediate testing, for which SOPs were not provided, please provide the SOPs.
17. For -----(b)(4)----- method, also please provide an SOP.
18. In Amendment 18, you addressed our request for -----(b)(4)-----
----- and providing arguments supporting your proposal. Your response is acceptable.
19. Please respond in writing to all our information requests, which have not been addressed yet.

Comments and recommendations in items # 1-3 are provided from a comprehension and promotional perspective to assist you in revising the proposed labeling materials. If you have any questions with regards to items # 1-3 please contact Loan Nguyen, Pharm.D, Regulatory Review Officer at 301-827-6333.

We would appreciate a response to this information request by May 13, 2010.

Please contact me if you have any questions.

Sincerely,

Cherie Ward-Peralta
Regulatory Project Manager
DBA/OBRR/CBER/FDA
Tel: (301) 827-9170