

# Information Request and PMR/PMC Request - GLASSIA, May 20, 2010

From: Ward- Peralta, Cherie

Sent: Thursday, May 20, 2010 2:53 PM

To: '-----(b)(4)-----'

Subject: RE: STN 125325 Information Request and PMR/PMC Request

Hello -(b)(4)-

After further internal discussions, we are requesting if you can provide the letter of commitments and updated PMR/PMC Milestone table by Monday, May 24, 2010 instead of May 25, 2010 as stated in the previous email request. If you have any questions, please contact me.

Thanks

Cherie Ward-Peralta, M.S.

Regulatory Project Manager

HFM-380 FDA/CBER

Office of Blood Research and Review

Division of Blood Applications

"THIS MESSAGE 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 LAW. If you are not the addressee, or a person authorized to deliver the 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 immediately notify the sender immediately by e-mail or phone."

---

From: Ward- Peralta, Cherie

Sent: Thursday, May 20, 2010 2:24 PM

To: '----(b)(4)-----'

Subject: STN 125325 Information Request and PMR/PMC Request

Hello -(b)(4)-

This email 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:

1. Regarding the BAL phase IV study:

a. FDA recommends inclusion of a small number of control subjects in the BAL study who have received a licensed A1-PI product. Should anomalous/unexpected results of any analytes be observed, the inclusion of a control will help to determine whether there was a problem with the assay or sample handling, as opposed to being indicative of a

problem with the investigational product.

b. You may consider offering BAL study subjects simultaneous participation in the immunogenicity/viral safety/safety study. If this is not done, we recommend addition of antibody testing to the BAL study.

c. The primary endpoint should be both antigenic and functional A1-PI levels in ELF after 10-12 weeks of treatment, not antigenic or functional A1-PI levels.

d. Depending on the size of the comparator group, in addition to changes in ELF analytes from baseline to 10-12 weeks, we recommend you analyze as an exploratory analysis the difference between treatment groups in 10-12 week values using the baseline value as a co-variate.

2. Regarding your synopsis of the Phase IV PMC study entitled "A Phase IV, Randomized, Placebo-Controlled, Double-Blind, Multicenter Study investigating the Safety and Efficacy of Kamada-API I.V. vs placebo and another (higher) dose of Kamada API I.V. by Weekly Administration in Alpha-1 Antitrypsin Deficient Patients with emphysema:

a. Please submit statements from your consultants discussing the proposed study duration of 18 months.

b. Please submit the power calculations used to determine the proposed sample size for the study.

c. Please justify the proposed schedule of CT exams.

3. For the immunogenicity and viral safety study (PMC to submit to the IND and cross-reference the BLA an amendment for a clinical protocol to evaluate the immunogenicity and to further evaluate the viral safety of your product following multiple repeat exposures over a period of at least 6 months of regular weekly administration):

a. Please also include design features which will permit the detection of possible adverse events (AEs) due to the presence of particulates in the product. This should be an additional objective of the study. Please provide a letter of commitment that indicates that this study will be a post-marketing requirement (PMR) rather than a PMC.

b. Please justify or omit the use of a 5-week washout period. Given that you have added a positive control group to this study, we also recommend that the study be masked rather than open-label, if possible.

c. We recommend a single licensed comparator rather than multiple comparators to be used.

d. Please clarify which type of viral safety tests will be performed at which time points.

e. Please clarify why each subject will participate in the study for ~ 64 weeks given that the planned treatment period is 12 weeks (p 4 of protocol outline).

4. For all PMC and PMR studies, please provide calendar dates (not relative dates, not calendar quarters) corresponding to estimated milestones for submission of a final protocol with which FDA is in agreement to the IND with a letter of cross reference to the BLA, start of the trial, completion of enrollment, completion of the study, and submission of the final study report to the BLA with a letter of cross reference to the IND.

5. Please add an additional PMC to provide FDA with a final anti-A1-PI antibody assay validation report prior to running stored clinical samples from the pivotal clinical trial and to submit the final results, including all raw data, of anti-A1-PI antibody assay testing

from the stored clinical samples from the pivotal clinical trial. These should be submitted as supplements to the BLA.

We would appreciate receiving your letter of commitment and updated table of PMR/PMC Milestones with calendar dates by May 25, 2010, and a response to the additional information listed in this information request by June 2, 2010.

Please contact me if you have any questions.

Sincerely,

Cherie Ward-Peralta, M.S.

Regulatory Project Manager

HFM-380 FDA/CBER

Office of Blood Research and Review

Division of Blood Applications

"THIS MESSAGE 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 LAW. If you are not the addressee, or a person authorized to deliver the 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 immediately notify the sender immediately by e-mail or phone."

Page Last Updated: 06/02/2016

Note: If you need help accessing information in different file formats, see [Instructions for Downloading Viewers and Players](#).

Language Assistance Available: [Español](#) | [繁體中文](#) | [Tiếng Việt](#) | [한국어](#) | [Tagalog](#) | [Русский](#) | [اڤيڤرغلا](#) | [Kreyòl Ayisyen](#) | [Français](#) | [Polski](#) | [Português](#) | [Italiano](#) | [Deutsch](#) | [日本語](#) | [ايسراف](#) | [English](#)