

From: Do, Yu
Sent: Tuesday, June 30, 2015 3:44 PM
To: Erik.Bjornson@baxalta.com
Cc: Thompson, Edward
Subject: Information Request: Original BLA 125566/0, Anti hemophilic Factor (Recombinant), PEGylated

Dear Mr. Bjornson:

We are reviewing your original November 25, 2014 submission to BLA 125566/0 for Anti hemophilic Factor (Recombinant), PEGylated. We are providing the following comments and request additional information to continue our review:

1. In regard to method validation report (b) (4)-65-09180 "Total PEG in Bax855 (b) (4)"
 - a. The range of the assay is not properly validated. While the range of the assay is claimed to be (b) (4) of total PEG, all the studies, except specificity, were performed by (b) (4) PEG in the analyzed samples. Please perform supplemental validation of the assay range; alternatively, re-evaluate the current range and its suitability for the intended purpose of the assay.
 - b. Please provide details on how the data presented in Appendices 2 and 3 were calculated for each concentration point.
 - c. Please clarify when the PEG standard was spiked to (b) (4) - before or after the (b) (4).
2. In regard to method validation report (b) (4)-65-205Z "PEG Distribution in BAX855 (b) (4)"
 - a. Please submit the development report (b) (4)-65-20520, referenced in the validation report.
 - b. The conclusions regarding the robustness of the assay were made in the absence of pre-determined acceptance criteria. Please clarify how robustness was established.
 - c. The precision and intermediate precision of the assay were not established in regard to the (b) (4) steps. Please validate these parameters by performing the test using multiple (b) (4) of the same (b) (4) sample.
3. In regard to method validation report 2012-BAX855(b) (4)-RFPQ1 "Report of validation of the Method 'DETERMINATION DE L'ACTIVITE DU FVIII RECOMBINANT (rAHF) (b) (4) A L'AIDE DU (b) (4)' for the quantification of the BAX855 (b) (4) samples."
 - a. The data for accuracy validation presented in section 7.3 of the report demonstrate significant dependence of the assay results from (b) (4) in all matrices. Thus, the assay results may be affected by changing (b) (4) within the established range (b) (4). Please control this factor by introducing into the test instruction the system suitability criteria for sample concentration.
 - b. The data for robustness validation presented in section 7.4 of the report

demonstrate a significant (b) (4) trend for both matrices (the difference between the first and last sample in the series is (b) (4)). The acceptance criterion format (% CV from mean value) is not statistically appropriate under the circumstances. Thus, the assay results may be significantly affected by the elapsed time. Please control this factor by limiting the duration of analysis cycles in the test instruction.

c. The summary of deviation 7540 provided in the report is unclear. Please provide detailed information regarding deviation 7540.

The review of this submission is ongoing and issues may be added, expanded upon, or modified as we continue to review this submission. Please submit your response as an amendment to this file by Wednesday, July 22, 2015, referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

The action due date for this file is November 25, 2015.

Please acknowledge receipt of this request and contact me at (240) 402-8343 or Yu.Do@fda.hhs.gov if you have any questions.

Sincerely,

Yu Do, M. S.
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