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To: STN: #125596

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Sponsor: Baxalta

Subject: Addendum Review Memo for the analytical methods and their validations for lot-release methods for the Immune Globulin Subcutaneous Human), 20% Solution (CUVITRU®)

Recommendation: Approval

Summary: The quality control lot release tests for the drug product and their method validations have been reviewed. All tests other than Purity by (b) (4) test were reported to be approvable in the Primary Discipline Review memo for the drug product (memo from H. Wang et al., dated July 25, 2016). Based on the review of the additional data on the accuracy and linearity of the Purity by (b) (4) test, provided as amendments 32 and 35, it is concluded that this assay is also suitable for use as a quality control lot release test for the drug product.

Background

A new BLA was submitted by Baxalta for CUVITRU, an Immune Globulin, 20% solution to be administered subcutaneously. The Purity by (b) (4) test method used for the determination of purity of IgG in the drug product. As discussed in the Primary Discipline Review (PDR) memo (memo from H. Wang et al., dated July 25, 2016), the validation is incomplete as a quantitative method because of lacking support data for accuracy, linearity and range.

Submitted Information reviewed

125596/0.32, dated July 29, 2016

- 1.11.1: Response to Information Request
- Validation Report for “Purity determination and (b) (4) quantification in IGIV products by (b) (4)”

125596/0.35, dated August 11, 2016

– 1.11.1: Response to Information Request

Review Narrative

The response to the following Information Request was submitted after the Primary Discipline Review (PDR) memo was written.

For “Purity by (b) (4)” assay (CTP LE-13-A05001), you have demonstrated the specificity and precision in your validation report. Please provide accuracy, linearity, and range data to complete a full validation for this quantitative method.

Review of the response

The response to the IR was provided in the amendments 32 and 35 to support a complete validation of this (b) (4) assay.

The accuracy was evaluated by spiking (b) (4) with three independent sample preparations. The recoveries were 99-100%, 100% and 100% respectively, which met the acceptance criterion of (b) (4) .

The linearity was demonstrated by (b) (4) of the sample in triplicate. The correlation coefficient (R^2) is 0.99-1.00. There is no set acceptance criterion in the response. But the results are adequate for a (b) (4) .

The range of assay is (b) (4) based on the outcome of accuracy, precision and linearity.

Conclusion

The additional data provided in amendments 32 and 35 completed a full validation of this (b) (4) method. The method is adequately validated for the intended use.