

**To: Paul Hartmann**  
**CSL Behring AG**  
**Date: February 3, 2010**

This is regarding your BLA submission STN 125350/0 for Immune Globulin Subcutaneous (Human), 20% Liquid, submitted to the Agency on April 30, 2009. FDA continues with the review of the referenced submission and requests CSL Behring AG to provide the following:

**Please make the following post-marketing commitments (PMCs):**

-----~~(b)(4)~~-----  
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2. To report all serious adverse events for IgPro20 annually, in the PMC annual report for two years following approval. This should include an executive summary, with the SAE data in tabular form. For each patient, the data reported should include the patient age, sex, indication for treatment, adverse event, and product lot number when available. Deaths should be noted.

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**Questions:**

4. Regarding Process Step CZS1500 (Formulation):
  - a. The mixing times in ----- (b)(4) -----  
--- are only defined as minimum allowable times, i.e., ---- (b)(4) ----. Please describe how the total mixing times are controlled so that ----- (b)(4) -----  
-----, and what maximum time limit, if any, is applied.
  - b. What is the time limit for the ----- (b)(4) ----- procedure used to reach the final protein concentration of 20%, and how is the duration of ----- (b)(4) ----- monitored and controlled?

Per Study Doc. No. -(b)(4)--460r (Section 3.2.S.2.5, Att. 2) the ----- (b)(4) -----  
--- ----- facility is ---- (b)(4) ----, yet the validation study only reaches addition rates as high as ---- (b)(4) ----. Please either provide additional data to validate an ----- (b)(4) ----- or set the maximum specification to ---- (b)(4) -----.

4. Your proposed Appearance specification (end-of-shelf-life) for IgPro20 does not specify ----- (b)(4) ----- . Based on the stability data of the 2 clinical lots that you submitted to us, we recommend that your Appearance specification (end-of-shelf-life) be revised as follows: "----- (b)(4) -----  
-----". Please update your list of final product specifications to include this revised specification.

3. We note that no specification for the Pyrogen Test is included in your list of final-product release testing for IgPro20; please revise this list to include the Pyrogen Test specification, and resubmit it.

Thank you.

Pratibha Rana