

**From:** Maruna, Thomas  
**Sent:** Monday, April 11, 2016 10:15 AM  
**To:** KevinDarryl.White@csllbehring.com; 'Angela.Azzara@csllbehring.com'  
**Subject:** April 11. 2016 Information Request - BLA 125591.0 - Please Respond By Dates Noted Below

**Importance:** High

CSL Behring Recombinant Facility AG  
Attention: Mr. Kevin Darryl White  
April 11, 2016  
Sent by email

Dear Mr. White:

We are reviewing your May 29, 2015 biologics license application (BLA) for the following:

<b>STN</b>	<b>Name of Biological Products</b>
125591/0	Antihemophilic Factor (Recombinant), Single Chain

We have determined that the following information is necessary to continue review:

CLINICAL – Please respond by April 15, 2016

1. In the Final Study Report for CSL627\_3002 74 of the 80 subjects were assigned to an initial dose between 15 and 50 IU/kg, with only 1 subject assigned a dose less than 20 IU/kg. The remaining prophylaxis subjects assigned to an initial dose outside of the 15 to 50 IU/kg range used Afstyla doses no higher than 57 IU/kg. The current draft label indicates a pediatric prophylaxis dose of 20 to 50 IU per kg 2 to 3 times per week. Please indicate what the final prophylaxis doses were for the children were in this trial, i.e. were the doses changed during the trial?

CMC – Please respond by April 20, 2016

1. With reference to section 3.2.P.8.1 Stability, to support 36 months shelf life for all dosage strengths of AFSTYLA Drug Product please provide updated stability report on ongoing stability studies and studies completed after submission of this BLA.
2. With reference to sections 3.2.S.5 and 3.2.P.6 Reference Standards or Materials:
  - a. Please provide the Certificate of Analysis for product-specific standard used for measuring FVIII activity in chromogenic substrate assay.
  - b. Please provide the information regarding the date when product-specific standard was introduced for release testing and the list of released batches specifying what potency standard was used for potency assignment.

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

Please submit your responses as an amendment to this file by the dates noted above, referencing the date of this request.

The action due date for this file is May 28, 2016.

If you have any questions, please contact me.

Very Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH

Lieutenant, U.S. Public Health Service

Senior Regulatory Management Officer

Food and Drug Administration

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