

Information Request Email, June 7, 2012 - Octaplas

From: Rana, Pratibha
Sent: Thursday, June 07, 2012 5:56 PM
To: Ammons, Stanley
Cc: Rangetiner, Barbara
Subject: STN 125416/0 Information Request (6/7/2012)
Our Reference: STN 125416/0
Octapharma USA, Inc.

Attention: Stanley Ammons

Dear Mr. Ammons:

We are reviewing your December 22, 2011 biologics license application (BLA) for Pooled Plasma, Solvent Detergent Treated (Human). We are providing the following comments and request for additional information to continue our review:

Chemistry, Manufacturing and Controls (CMC)

1. The OctaplasLG® manufacturing process is controlled by -----
-(b)(4)----- . Please establish in-process control limits for critical
process parameters based on evaluation of data from manufacturing
experience. Please describe the action taken should in-process limits be exceeded.

2. There was no toxicological or leachables/extractables assessment of the -----
------(b)(4)----- support for the (b)(4) ligand column. Please provide
the requested information and data.

3. Column lifetime validation for the C-18 column chromatography step was
inadequate.

a. Please provide the following information and data that were lacking from study
020VAP950/930-SPE01:

i. -----(b)(4)-----

ii. -----

iii. -----(b)(4)-----

iv. -----(b)(4)-----

v. -----(b)(4)-----

b. Please provide results from commercial scale column lifetime validation or provide
a validation protocol for concurrent validation.

4. There is no established control for ---(b)(4)--- impurity during commercial manufacture. Please comment.
5. Study report 080VRE11366.105 indicated that bag (b)(4) was controlled through - b4----- (b)(4)----- Please establish a final product fill ---(b)(4)--- limit that applies to each filled bag, independently.
6. Please establish an in-process control for HEV NAT in manufacturing plasma pools.
7. Please revise your release and shelf-life specification for the listed parameters, to reflect manufacturing capability:

Parameter	Current	Recommended
Protein S	---(b)(4)--	---(b)(4)--
a ₂ -antiplasmin (A2PI)	---(b)(4)--	---(b)(4)--
Coagulation Factors V, VIII	---(b)(4)--	---(b)(4)--
Coagulation Factor XI	---(b)(4)--	---(b)(4)--
Fibrinogen	---(b)(4)----- ---	---(b)(4)--

8. Regarding final product stability:
 - a. Although lots from study 08P010 were manufactured from non-US plasma, stability data may be supportive if extrapolation is adequately justified. Please indicate whether or not the manufacturing process and container closure system for study 08P010 lots are identical to that intended for US commercial distribution.
 - b. Similarly, data from studies 09P020, 10P026, 09P030, 10P027 may be applicable if manufactured by a process comparable to that intended for commercial distribution. Therefore, please clarify any differences between the intended commercial process and that used to manufacture lots submitted to the four cited studies.
 - c. Please submit 6 month long tem stability data from studies 11P018 and 11P029.

9. Regarding the analytical procedure for (b)(4) performed at the Stockholm facility:
 . -----

 --- (b)(4) -----

Clinical

10. Please submit all data for subjects who were screened for observational study LAS-201 but not enrolled, as well as the criteria used to exclude these subjects. Please state whether the criteria to include/exclude subjects was determined *a priori* to the known outcomes for potential study subjects.

11. Please submit additional complete clinical study reports (other than LAS201; LAS203; UNI101 and UNI110) for all studies you have cited in support of your

marketing application, including the Norway Experience. ICH E3 can be referred to for guidance for the structure and content of the clinical study reports.

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 response to this information request as an amendment to this file by June 26, 2012 referencing the date of this request.

The action due date for this file is October 22, 2012.

If you have any questions, please contact me.

Sincerely,

Pratibha Rana
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Regulatory Project Manager

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