



Our Reference: BLA 125668/o

Octapharma Pharmazeutika Produktionsges.m.b.H.

Attention: Mr. Stanley Ammons

May 22, 2018

Sent by email

Dear Mr. Ammons:

We are reviewing your December 28, 2017, biologics license application (BLA), for Immune Globulin Subcutaneous (Human). We determined that the following information is necessary to continue our review:

1. For analytical procedure validation report “Determination of Maltose by (b) (4) [REDACTED]
[REDACTED]” (000VAL169 FC 81x)
 - a. Please explain how the theoretical value of Cutaquig sample ((b) (4) [REDACTED]) was obtained in the accuracy evaluation in section 5.4.4.
 - b. You determined that the LOQ of the assay is (b) (4) [REDACTED]. However, the spike-recovery data at this level was not provided in the specificity study (section 5.2). Please provide spike-recovery data to support the decision. We accept LOQ of (b) (4) [REDACTED] based on data in the current report.
2. For analytical procedure validation report “Determination of the Molecular Size Distribution in Cutaquig Final Container using (b) (4) [REDACTED]” (000VAL071 FC 81x)
 - a. The linear plot of peak area versus %(Monomer+Dimer) has a correlation coefficient (r) of (b) (4) [REDACTED] in section 6.3.4.5. This value met the acceptance criterion of (b) (4) [REDACTED] while the acceptance criteria of r for (b) (4) [REDACTED] and %Fragments are both (b) (4) [REDACTED]. It seems to be unusual that acceptance criterion of correlation coefficient for the active component is lower than those for impurities ((b) (4) [REDACTED] and fragments) in a (b) (4) [REDACTED] assay. Please provide justification for setting acceptance criterion of an active component lower than those of impurities.
 - b. Please provide appropriate data to show that the molecular forms larger than the dimer in Cutaquig final container are not (b) (4) [REDACTED] by the (b) (4) [REDACTED] under the proposed (b) (4) [REDACTED] condition.
3. For analytical procedure “Determination of Sodium (b) (4) [REDACTED] by (b) (4) [REDACTED]
[REDACTED]” (13oSOP029)

- a. Please define a calibration range of the standard curve in the SOP for Cutaquig product.
 - b. Please add a calculation section for sodium concentration of the test sample in the SOP.
 - c. Please set acceptance criteria for the calibration curve and drift of the control sample in an appropriate section of the SOP.
4. For analytical procedure validation report “Determination of Sodium in Cutaquig Final Container Samples by (b) (4)” (138VAL029FC 81x)
- a. Please use plot of instrumental response versus sodium concentration with linear regression result (at confidence interval of (b) (4)) to demonstrate the linearity and applicable assay range in sections 6.1.4 and 6.2.4, respectively.
 - b. Please provide statistical outcome at (b) (4) confidence interval for parallelism plot in section 6.2.4 (specificity).
 - c. LOQ estimation should use the slope and the standard deviation of the response from the plot mentioned in 4a, not the values from parallelism plot in page 19 because the parallelism plot is to demonstrate the accuracy of the proposed assay. Please re-evaluate and submit for review.
5. For analytical procedure validation report “Determination of Residual Tri-n-butylphosphate (TnBP) in Cutaquig FC by means of (b) (4)” (000VAL153FC 81x)

The parallelism plot of found TnBP versus theoretical TnBP has a slope value of (b) (4) in section 6.4.4.2.4. This value is too low compared to the ideal value of (b) (4). Please justify this low slope value with appropriate supporting data or narrow down the linear range of the method.

6. For analytical procedure validation report “Determination of Octoxynol (Triton X-100) with (b) (4)” (130SOP090)
- a. Please provide a (b) (4) of typical Cutaquig FC sample showed on page 16 of the SOP with (b) (4) for octoxynol (b) (4).
 - b. Please provide identifications of the (b) (4) supported by data, which are (b) (4) with the octoxynol around the (b) (4) in the (b) (4) of Cutaquig FC (page 16 of 23).

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

Please submit your response to this information request as an amendment to this file by June 11, 2018, 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 December 29, 2018.

Please send an email message acknowledging receipt of this request.

If you have any questions, please contact me.

Sincerely,
Edward Thompson
Regulatory Project Manager
FDA/CBER/OBRR/RPMS

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Thank you