

125596_0_Feedback_DBSQC_062816.txt

From: Cagungun, Nannette
Sent: Tuesday, June 28, 2016 4:10 PM
To: 'ade.denloye@baxalta.com'
Cc: Thompson, Edward; Maruna, Thomas; Reed, Jennifer; Valencia, Iliana; Hooban, Christopher
Subject: RE: Follow-up: May 3. 2016 Information Request - (b) (4) Assay

Dear Ade:

Hope this finds you well.

With regard to your question, CBER finds the LOQ values in the draft response (dated June 22, 2016) are supported by experimental data and are acceptable.

Please do not hesitate to contact me if you have any questions.

Sincerely,

Nannette Cagungun, MS, PD, RAC
Regulatory Project Manager
OBRR/CBER/FDA
10903 New Hampshire Ave
W071-4258
Silver Spring, MD 20993-0002
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Email: nannette.cagungun@fda.hhs.gov

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From: Denloye, Aderonke O [mailto:Ade.Denloye@shire.com]
Sent: Monday, June 27, 2016 11:56 PM
To: Cagungun, Nannette; Hooban, Christopher
Cc: Thompson, Edward; Maruna, Thomas; Reed, Jennifer; Valencia, Iliana
Subject: FW: Follow-up: May 3. 2016 Information Request - (b) (4) Assay
Importance: High

Dear Nannette/Christopher:

Hope this finds you doing well. I understand Tom is out of the office and has indicated that you will be alternates while he is out. I am following up on below message sent last week to inquire of FDA feedback. Is there any feedback from the reviewer?

Best regards,
Aderonke Denloye, MPH
Associate Director, Global Regulatory Affairs
Shire
One Baxter Way
Westlake Village, CA 91362 USA

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From: Denloye, Aderonke O
Sent: Wednesday, June 22, 2016 11:02 AM
To: Thompson, Edward (Edward.Thompson@fda.hhs.gov); Maruna, Thomas (Thomas.Maruna@fda.hhs.gov)
Cc: Reed, Jennifer (Jennifer.Reed@fda.hhs.gov)
Subject: Follow-up: May 3, 2016 Information Request - (b) (4) Assay

Dear Thomas/Edward:

Hope this finds you both doing well. We would greatly appreciate your forwarding below e-mail along with the attached draft response to the reviewer.

Thanks for taking the time to review our draft responses and for your comments. Per your recommendations, Baxalta has revised the response to Q2 and would appreciate having a teleconference with the reviewer to ensure that our response adequately address the FDA reviewer concerns regarding Q2. Specifically, because there is no guidance for the conversion of (b) (4) for LOQ determination in (b) (4) methods, Baxalta respectfully requests a teleconference with the reviewer as we have outlined within this response our best understanding of theoretical calculation of LOQ based on available guidance.

Could you let us know what time slot works best for the reviewer so that we can make our subject matter experts available to finalize this response prior to submitting as an amendment? However, if the response has adequately addressed your concern and a conference is not needed, could you please let us know? Again thanks for accommodating our requests regarding this response.

Best regards,
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Baxalta, now part of Shire

From: Maruna, Thomas [mailto:Thomas.Maruna@fda.hhs.gov]
Sent: Friday, May 13, 2016 11:48 AM
To: Denloye, Aderonke O
Subject: Follow-up: May 3, 2016 (Clinical) Information Request

Aderonke,

We have reviewed your draft response regarding FDA information request (dated May 03, 2016). We have following comments:

1. We found the responses to question 1 and 3 are acceptable.
2. For this assay, LOQ is required for the (b) (4) [REDACTED]. We disagree with your LOQ determination for (b) (4) [REDACTED] in response to the question 2. In the table 5, you found that a sample with (b) (4) [REDACTED]. Thus you calculated that the LOQ for (b) (4) [REDACTED]. The LOQ of (b) (4) [REDACTED] is calculated using a similar approach. Please provide your justification or a scientific reference article for such approach for the LOQ determination in a (b) (4) method.

If you conclude that LOQ for (b) (4) [REDACTED] respectively, please provide data in support of your conclusion from samples, which contain (b) (4) [REDACTED], respectively. The data should show adequate accuracy, precision, and (b) (4) [REDACTED].

The figure 4 in your response is not adequate. Using ICH Q2(R1) equation $LOQ = 10\sigma/S$ to determine the LOQ of either (b) (4) [REDACTED] assay, multiple points are required for (b) (4) [REDACTED] below your specification limit. Please provide adequate data to establish LOQ of your assay for both impurities.

3. Please provide the (b) (4) [REDACTED] of lots (b) (4) [REDACTED]. Zoomed in figures may be necessary in order to clearly show the integration details of (b) (4) [REDACTED].

Please let me know if you have any questions.

Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH
Lieutenant, U.S. Public Health Service
Senior Regulatory Management Officer
FDA/CBER/OBRR/IO
thomas.maruna@fda.hhs.gov
Office: (240) 402-8454

From: Denloye, Aderonke O [mailto:Ade.Denloye@baxalta.com]
Sent: Friday, May 13, 2016 1:32 PM
To: Maruna, Thomas
Subject: RE: Follow-up: May 3, 2016 (Clinical) Information Request - BLA 125596.0 -
Page 3

Please Respond by
May 6. 2016

Yes I now have revised tables that I can submit by Monday that include the NUMBER OF SUBJECTS for 170903.

Best regards,
Aderonke Denl oye, MPH
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"A wise man learns from his own mistakes, but a genius learns from others." - Mark Twain

From: Maruna, Thomas [mailto:Thomas.Maruna@fda.hhs.gov]
Sent: Friday, May 13, 2016 10:23 AM
To: Denl oye, Aderonke O
Subject: RE: Follow-up: May 3. 2016 (Clinical) Information Request - BLA 125596.0 - Please Respond by May 6. 2016

Ade,

You appear to have addressed the NUMBER OF SUBJECTS for 160601 but I don't see the same information for 170903.

Tom

From: Denl oye, Aderonke O [mailto:Ade.Denl oye@baxalta.com]
Sent: Friday, May 13, 2016 1:12 PM
To: Maruna, Thomas
Cc: Landow, Laurence
Subject: RE: Follow-up: May 3. 2016 (Clinical) Information Request - BLA 125596.0 - Please Respond by May 6. 2016
Importance: High

Dear Lt. Maruna & Dr. Landow:

Hope this finds you doing well.

Question 1:

Baxalta submitted SEQ 0021 on Monday 9 May 2016 and I believe the table provided within that amendment addresses Q1 below, could you please verify?

Question 2:

Tables 3 & 4 from SEQ 0014 submitted on 30Mar2016 will be updated to include the number of subjects, please verify?

I will await your response prior to submitting this information as an amendment to the BLA, thanks.

Best regards,
Aderonke Denl oye, MPH
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"A wise man learns from his own mistakes, but a genius learns from others." - Mark Twain

From: Maruna, Thomas [mailto:Thomas.Maruna@fda.hhs.gov]
Sent: Thursday, May 12, 2016 3:25 PM
To: Denl oye, Aderonke O
Cc: Landow, Laurence
Subject: Follow-up: May 3, 2016 (Clinical) Information Request - BLA 125596.0 -
Please Respond by
May 6, 2016
Importance: High

Baxalta US Inc.
Attention: Ms. Aderonke Denl oye
May 12, 2016
Sent by email

Dear Ms. Denl oye:

We have just reviewed all of the March and April responses to our IRs. Most of the requests have been addressed except for the following:

1. For study 160601: Please draft a table of nonserious adverse events by absolute number of subjects (as opposed to proportion of subjects) per treatment cohort. This table should have (a) 6 columns labeled Classification, Part 1, Part 2, Part 3a, Part 3b and Extension (with appropriate sample size for each) and (b) 2 rows labeled Local adverse reactions and systemic adverse reactions. The number of subjects, Preferred Term (where applicable), and severity of each adverse reaction in each study Part should be limited to an incidence $\geq 5\%$.
2. For study 170903, Safety Analysis Set, Table 3: Please include the number of subjects (as opposed to annualized rate per subject) per treatment cohort for systemic related AEs, local related AEs, and infusional AEs.

Please respond via BLA amendment by May 16, 2016.

Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH
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Senior Regulatory Management Officer
FDA/CBER/OBRR/IO
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From: Maruna, Thomas
Sent: Tuesday, May 03, 2016 12:34 PM
To: 'Denloye, Aderonke O'
Subject: May 3, 2016 (Clinical) Information Request - BLA 125596.0 - Please Respond by May 6, 2016
Importance: High

Baxalta US Inc.
Attention: Ms. Aderonke Denloye
May 3, 2016
Sent by email

Dear Ms. Denloye:

We are reviewing your September 14, 2015 biologics license application (BLA) to treat primary immune deficiency disorders associated with defects in humoral immunity for the following:

STN	Name of Biological Products
125596/0	Immune Globulin Subcutaneous (Human), 20% Solution

We have determined the following information is required to continue our review:

1. Please specify the Integrated Summary of Safety Table number(s) from which the data for Table 3 and Table 4 in the PI were obtained.
2. For study 160601, please draft a table of nonserious adverse events by absolute number of subjects (as opposed to proportion of subjects). This table should have (a) 6 columns labeled Classification, Part 1, Part 2, Part 3a, Part 3b and Extension (with appropriate sample size for each) and (b) 2 rows labeled local adverse reactions and systemic adverse reactions. The number of subjects, Preferred Term (where applicable), and severity of each adverse reaction in each study Part should be limited to an incidence \geq 5%.

Please submit your responses as an amendment to this file by May 6, 2016 referencing the date of this request.

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

The action due date for these files is September 13, 2016.

Very Respectfully,

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