

From: Maruna, Thomas
Sent: Friday, May 13, 2016 2:48 PM
To: 'Denloye, Aderonke O'
Subject: Follow-up: May 3. 2016 (Clinical) Information Request
Attachments: 0020-response-to2016may03-cmc-rfi_Draft.docx

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) which include (b) (4). We disagree with your LOQ determination for (b) (4) in response to the question 2. In the table 5, you found that a sample with (b) (4). Thus you calculated that the LOQ for (b) (4). The LOQ of (b) (4) 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) respectively, please provide data in support of your conclusion from samples, which contain (b) (4), respectively. The data should show adequate accuracy, precision, and (b) (4).

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) in a (b) (4) assay, multiple points are required for (b) (4) below your specification limit. Please provide adequate data to establish LOQ of your assay for both impurities.

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

Please let me know if you have any questions.

Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH
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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 - 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 Denloye, 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: Denloye, 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: Denloye, Aderonke O [mailto:Ade.Denloye@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,
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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: Denloye, 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 Denloye
May 12, 2016
Sent by email

Dear Ms. Denloye:

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 infusion related AEs.

Please respond via BLA amendment by May 16, 2016.

Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH
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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 Solution	Immune Globulin Subcutaneous (Human), 20%

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,

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