From:	Steve McGregor
To:	Ballica, Rabia
Cc:	Trout, Deborah; Renshaw, Carolyn
Subject:	RE: I need additional information
Date:	Wednesday, May 28, 2014 9:06:25 PM
Attachments:	image001.emz image003.png image004.png emfinfo.txt

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Dear Rabia,

The following information is provided to address the items referenced in your email of May 27th concerning BLA 125426. For ease of reference, I have copied your points for clarification below and they are followed by our responses to each of the items. Supporting stability data and a summary of the testing performed by (b)(4) have also been included.

I can be reached at 204-275-4646 to discuss this response and answer any questions you may have.

Kind regards,
Steve

Email dated May 27, 2014 "…., could you please verify the following information (that is provided in your BLA submission and its amendments):

(b)(4) performs only release testing (including sterility and other release tests listed in your BLA submission) on the (b)(4) pre-filled syringes
Cangene Response: (b)(4) conduct both release and stability testing of the (b)(4) pre-filled syringes. Section 3.2.P.8.1 (b)(4)) provides details of (b)(lots of filled and (b)(4) syringes (b)(4)) that are currently on stability. A summary of the sterility and CCI testing results from this stability program are summarized in the tables below. [Note: BLA 125426 contains two 3.2 Drug Product sections; one for rFIX Drug Product IXINITY, and one for the (b)(4) Sterile Water for Injection Syringes.]

-(b)(4) does not perform any CCIT on the (b)(4) pre-filled syringes
Cangene Response: CCIT testing is performed by (b)(4) and is conducted on the (b)(4) pre-filled syringes. The response to the FDA Information Request of October 11, 2012 (see BLA 125426 eCTD sequence 0009) indicates Container Closure Integrity (CCI) testing was added to the evaluation of production batches (b)(4). CCI testing was performed at T=9 months for Batches (b)(4), T=3 months for Batch (b)(4) and CCI testing will also be performed at the end of the stability study ((b)(4)). The positive control consists of a syringe (b)(4) (a picture of this is provided in STN 125426/0009 (response-oct11-info-request).

-(b)(4) (syringe supplier) performs (b)(4) testing on syringes (not on the (b)(4) pre-filled syringes from (b)(4)) before being shipped to (b)(4) for use in diluent manufacturing
Cangene Response: The BLA 125426/0009 response references a report (ii-103(b)(4)) which describes the testing by (b)(4). We are following up to confirm if this testing is routinely performed and will submit an updated response under separate cover.

-Cangene performs CCIT testing on the (b)(4) pre-filled syringes (b)(4))
Cangene Response: Cangene contracted (b)(4) (qualified vendor) to conduct CCI testing on (b)(4) pre-filled syringes that were shipped from (b)(4) to Cangene bioPharm (Baltimore, MD). This testing included positive controls where b)(4) . Results of this testing are included with this response.

-(b)(4) performs stability testing on diluent lots (not shipped)

Cangene Response: As indicated in 3.2.P.8.1 (b)(4) pre-filled syringes are monitored for stability by (b)(4). These syringes would not have been exposed to shipping conditions. Results for sterility testing and CITT have been summarized and included with this response. For more detailed information, please refer to the (b)(4) Drug Master File No. (b)(4) for the stability data and assessment of the primary stability studies which support the proposed shelf life of (b)(4) .

Supporting information

Stability Results of (b)(4) Syringes ((b)(4))
cid:image001.png@01CF7A87.46F9E6B0

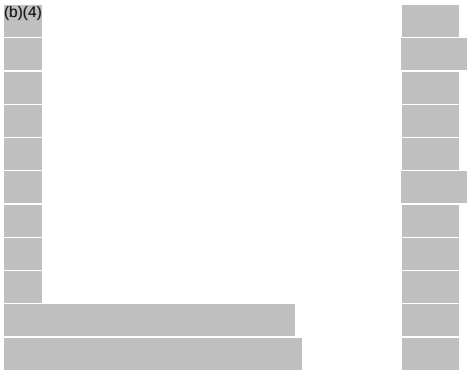
cid:image002.png@01CF7A87.46F9E6B0

Summary of Results of CCIT by (b)(4)

An overview of the(b)(4) testing was included in BLA 125426 eCTD sequence 0028 provided on May 20, 2014 and additional details on the method controls and the results have been included in this response.

Initial testing was conducted with the syringes at a qualified vendor; b)(4)

1 page determined to be not releasable: (b)(4)



From: Ballica, Rabia [mailto:Rabia.Ballica@fda.hhs.gov]
Sent: Tuesday, May 27, 2014 7:36 PM
To: Steve McGregor
Cc: Trout, Deborah; Renshaw, Carolyn
Subject: I need additional information

Hi Steve,

If I remembered correctly, you mentioned during May 1st teleconference that (b)(4) had been conducting CCIT on the diluent batches shipped from (b)(4) to US, but I cannot locate any test results from (b)(4) in any of your responses. Please provide a summary of results from the CCIT testing performed on those batches by (b)(4). I also need a summary of stability data for only sterility testing at release, expiry and other stability time points (where sterility testing is performed such as month 3 and 9 you mention in the BLA submission).

In addition, could you please verify the following information (that is provided in your BLA submission and its amendments):
-(b)(4) performs only release testing (including sterility and other release tests listed in your BLA submission) on the (b)(4) pre-filled syringes
-(b)(4) does not perform any CCIT on the (b)(4) pre-filled syringes
-(b)(4) (syringe supplier) performs (b)(4) testing on syringes (not on the (b)(4) pre-filled syringes from (b)(4)) before being shipped to (b)(4) for use in diluent manufacturing
-Cangene performs CCIT testing on the (b)(4) pre-filled syringes (b)(4))
(b)(4) performs stability testing on diluent lots (not shipped)

Please provide your response to the items listed above by the end of (b)(4). Let me know if you have any questions.

Thanks

Rabia