

From: Rivers, Katie
Sent: Wednesday, April 09, 2014 2:17 PM
To: 'Greenfeder, Scott'
Cc: Valenti, Elizabeth
Subject: Information Request - BLA125478/0

Dear Scott,

We have reviewed your responses to our CMC information request that you submitted on December 18, 2013, as an amendment to your BLA. We have the following comments and requests for additional information based on your responses:

These questions are in regards to your response to our CMC Information Request, Comment # 27

You proposed a (b) (4) expiration date for the current In-House Reference (IHR) material (b) (4) based on an on-going stability study. You initiated a stability study for a previous IHR (b) (4) in June 2009, and you provided (b) (4) worth of stability data. We note that the results for (b) (4) are within the acceptance criteria up to (b) (4) of stability. However, you do not have sufficient real-time data for a (b) (4) shelf life period.

Furthermore, during the inspection conducted by the FDA from January 29 through February 10, (b) (4) the investigator noted a deviation (deviation 4706) related to your IHR (b) (4) and cited this deviation in FDA 483 Observation 23. You initiated an investigation in to this deviation when the (b) (4) time point stability sample of the IHR (b) (4) was found contaminated with (b) (4) of mold (b) (4). In your response to of Information Requests #27 you did not mention this contaminant in the stability data table. During the investigation, your firm determined that the (b) (4) was contaminated with (b) (4). You deemed this result as out-of-trend but found this acceptable because of a specification of (b) (4) as per the (b) (4) acceptance limit of (b) (4). No microbial enumeration testing was performed at any other time point prior to the (b) (4) time point as per the protocol.

After discussion with the investigator you agreed to terminate this stability study and run a comprehensive evaluation of all procedures related to investigating out of trend microbial enumeration results that you plan on completing by March 31, 2014. The current IHR (b) (4) was placed on an ongoing stability on December 13, 2012 and 12 months stability data should be available, however you did not provide these data. With biologics, extrapolation studies are not sufficient to assign an expiry of years over actual data. We request that you assign a shelf life of (b) (4) to your IHR material based on (b) (4) stability data obtained with lot (b) (4).

We also request that you provide all stability data collected to date for IHR lot (b) (4)

Please let me know if you have any questions.

Thank you,

Katie

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