

From: Morris, Nevitt  
To: Jennifer.Wellman@sparktx.com  
Cc: Morris, Nevitt  
Subject: BLA 125610, CMC Information Request  
Date: Wednesday, July 05, 2017 4:21:32 PM  
Attachments:  
(File Attachment comment)  
image001.png

Hello Ms. Wellman:

Please provide responses to the following information requested by our review team:

1.

Please provide the data and the accompanying analysis that was used to support

justification of Drug Substance and Drug Product specifications

(3.2.S.4.5 and

3.2.P.5.6). Specifically, please provide the following individual values separately for

the CHOP lots, Spark lots and all (Spark and CHOP) combined lots:

i.

Mean

ii.

Standard Deviation (SD)

iii.

(b) (4)

iv.

(b) (4); upper and lower

v.

Specifications used for lot release earlier (in IND phase)

vi.

Specification proposed for release in BLA.

In that table, please also provide the actual lot release value (for each data point) that

were considered in your analysis.

2.

Please provide your rationale for the proposed lot release acceptance criteria, based on

the tolerance interval limits, for the DS and DP submitted to the BLA. We note that

during previous discussions with the agency (e.g. your type C meeting packaged

submitted on September 22, 2015 and FDA response of October 28, 2015), you

proposed to set lot release acceptance criteria for the DS and DP based on the "(b) (4)

values". We indicated that this may not reflect your accumulated data, and we also

suggested that (b) (4) may not be appropriate for assays with very high variability. In

your BLA, you have set the lot release acceptance criteria for the DS and DP based on

(b) (4), which are much wider than the previously proposed

(b) (4). We note that setting acceptance criteria based on (b) (4) already

encompasses the (b) (4), so it is not clear what is the origin or

rational for the proposed tolerance interval limits.

3.

Please also provide the justification used for "rounding up and rounding down"

acceptance criteria. For instance, you noted that the (b) (4)

acceptance

criterion is (b) (4) and the Drug Substance (b) (4) acceptance criterion cannot be

(Unsigned signature field (Click to sign)) Signature field is unsigned

narrower than the (b) (4) range; therefore, the Drug Substance acceptance criterion range must be (b) (4) units. However, you state that the tolerance interval lower limit was rounded-down and the tolerance interval upper limit was rounded-up to give an acceptance criterion of (b) (4), which is outside the limit for the (b) (4). criterion range must be (b) (4) units. However, you state that the tolerance interval lower limit was rounded-down and the tolerance interval upper limit was rounded-up to give an acceptance criterion of (b) (4), which is outside the limit for the (b) (4).

4.

We note that you are using (b) (4) test for Drug Product release (in reference to the information provided under Section 3.2.P.5.2 and Section 3.2.P.5.1). We informed you previously that you must have an assay for subvisible particles according to (b) (4) (see FDA responses of October 1, 2014). The release criteria for particulate matter (b) (4) should be revised accordingly to (b) (4). , in accordance with (b) (4). If you could provide responses by the end of next week, that would be great.

Thanks,

Nevitt

Nevitt Morris

Nevitt  
Morris,  
RN,  
BSN,  
BS  
Consumer  
Safety  
Officer  
Office  
of

Tissues  
and  
Advanced  
Therapies  
Center  
for  
Biologics  
Evaluation  
and  
Research  
(CBER)

U.S.  
Food  
and  
Drug  
Administration  
Building  
71,  
Room  
4207  
10903  
New  
Hampshire  
Avenue  
Silver  
Spring,  
MD 20993  
Phone: (240)  
402-8269  
Fax: (301)  
595-1303  
Nevitt.Morris@fda.hhs.gov

THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS  
ADDRESSED  
AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND  
PROTECTED  
FROM DISCLOSURE UNDER LAW. If you are not the addressee, or a person  
authorized to deliver  
the document to the addressee, you are hereby notified that any review,  
disclosure,  
dissemination, copying, or other action based on the content of this  
communication is not  
authorized. If you have received this document in error, please  
immediately notify the sender  
immediately by e-mail or phone.