

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.