

From: Morris, Nevitt
To: jim.wang@sparktx.com; paul.gil@sparktx.com
Cc: Morris, Nevitt
Subject: BLA 125610 CMC Information Request dated 8/4/17
Date: Friday, August 04, 2017 11:43:35 AM
Attachments:
(File Attachment comment)
image001.png

Hi Jim and Paul:

We have a CMC Information Request that we are asking for responses by August 11, 2017. Please let us know if this is not possible.

Spark BLA 125610, CMC Information Requests:

Please provide the responses to the following Information Requests by August 11, 2017.

Shipping

1.

In module 3.2.S.2.5 Drug Substance Shipping Validation, you describe a general plan for Drug Substance Shipping Validation. Please provide a complete Drug Substance Shipping Validation study report to your BLA.

2.

In module 3.2.P.3.5.7 Validation of the Shipping Process, you indicate plans for validation of shipping to the secondary packaging and labeling site and shipping to distribution centers. The focus will be on transportation hazards such as temperature, shock, vibration and pressure that the DP and Diluent may encounter. However, we did not find the study reports for the Validation of the Shipping Processes. Please provide comprehensive study reports, that include the following details to the BLA:

a.

Please include shipping to all sites appropriate to your distribution including clinical sites. Please consider worst case scenarios.

b.

Please indicate if actual shipments or simulations were used. If simulations were used, please provide a strong justification as to how they relate to real world experience.

c.

Please discuss any changes to the configuration of the DP material (e.g., boxes/pouches) relative to that used for shipment of the DS, and whether configuration changes might affect the results of previous studies.

d.

Please indicate which quality attributes you assessed.

e.

We recommend that you evaluate the (b) (4) during shipping under hazardous conditions or deviations such as those you have investigated.

f.

Please indicate if the same shipping container was used that is described for the DS.

Stability

3.

The PPQ lots ((b) (4) DP) were put on stability in Nov of 2016, and 3 month data were submitted to the BLA. Please submit the six month data. Please note that the expiration date of your product may be based on the available real time stability data at the time of approval, if approved. Please also note that expiry date may be extended through BLA supplements with additional stability data.

4.

Please clarify if "CCIT", found in module 3.2.P.8.1.2.1 for the DP, Table 3 and Table 4, means

Container Closure Integrity Testing.

(Document certified by Nevitt V. Morris -S <nevitt.morris@fda.hhs.gov>)

Signed by Nevitt V. Morris -S <nevitt.morris@fda.hhs.gov> Time:

2017.08.04 12:33:54 -04'00'

Control of Materials for DS manufacturing

5.

Please provide additional information regarding the Characterization of CHOP HEK293 MCB

(b) (4) in Table 2 of section 3.2.S.2.3 Control of Materials. Please include:

a.

Limit of detection for each of the tests listed

b.

Name of each (b) (4) tested for

c.

Name of each (b) (4) tested for

d.

Brief description of how the in vitro assay for the presence of (b) (4) (9CFR) was performed

e.

Brief description of how the in vitro assay for the presence of (b) (4) (9CFR) was performed

6.

Please provide a brief description of the (b) (4) analysis assay used for cell identification referenced in Table 3 of section 3.2.S.2.3. Please include a description of the qualification of this assay.

Thanks,

Nevitt

Nevitt Morris

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