

From: Paul Gil  
To: Morris, Nevitt  
Subject: RE: BLA 125610 Information Request CMC/November 3, 2017  
Date: Friday, November 03, 2017 10:14:14 AM  
Attachments: image002.png

image003.png

(File Attachment comment)  
(File Attachment comment)  
Thanks, Nevitt. I acknowledge receipt.  
Regards,  
Paul

Paul J. Gil, Ph.D.

Regulatory CMC Lead

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From: Morris, Nevitt [mailto:Nevitt.Morris@fda.hhs.gov]  
Sent: Friday, November 3, 2017 10:05 AM  
To: Jim Wang <jim.wang@sparktx.com>  
Cc: Paul Gil <Paul.gil@sparktx.com>; Morris, Nevitt <Nevitt.Morris@fda.hhs.gov>  
Subject: BLA 125610 Information Request CMC/November 3, 2017  
Importance: High

BLA 125610 CMC Information Request. Please respond to this Information Request by Friday, November 10, 2017.

Regarding your lot release specifications for Drug Substance and Drug Product:

1.

The acceptance criteria for (b) (4) should be set to (b) (4)

. This takes into consideration the (b) (4)

that was determined to be (b) (4), and also that the (b) (4)

of

(b) (4) Spark lots, the Spark PPQ lot and the CHOP clinical lot (b) (4)

(assessed

during comparability) lie well within this limit (b) (4). Please

note that

(b) (4) is a CQA. The (b) (4) should be tightened for commercial manufacturing (from that set for IND studies, (b) (4) ) based on the clinical/manufacturing experience to date.

2.

The lower limit of the acceptance criteria for (b) (4) ratio should be set to (b) (4)

which is the (b) (4) value determined for the (b) (4) Spark lots.

(b) (4) is

a CQA and the manufacturing (data from Spark) and the clinical experience ((b) (4) value of the CHOP clinical lots) supports tightening this limit.

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3.

Please plan to retest and verify the (b) (4) of the primary working standard; the reported value is unusually high ((b) (4) ) and not consistent with the other measures of potency ((b) (4) ) for that lot. Regarding your proposed "BLA ranges" for crude cell harvest hold time and (b) (4) cell lysate hold time:

4.

In your BLA submission section "3.2.S.2.5.3 IN-PROCESS HOLDS EVALUATION, Supporting Studies", you proposed to extend the crude cell harvest hold time and (b) (4) cell lysate hold time from the established "(b) (4) " to "(b) (4) " (as BLA ranges) based on published literature only. We don't agree with the proposed "BLA ranges" as "(b) (4) " for the crude cell harvest hold time and (b) (4) cell lysate hold time, till you provide study data to support the hold time extension using products manufactured by Spark. Thanks, and please acknowledge receipt of the email Information Request.

Nevitt

Nevitt Morris

Nevitt  
Morris,  
RN,  
BSN,  
BS  
Consumer  
Safety  
Officer  
Office  
of  
Tissues  
and  
Advanced  
Therapies  
Center  
for  
Biologics  
Evaluation  
and  
Research  
(CBER)

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and  
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