

From: Jim Wang
To: Morris, Nevitt
Subject: RE: BLA 125610 Information Requests DMPQ 9//5/17
Date: Tuesday, September 05, 2017 9:31:02 AM
Attachments: image001.png

(File Attachment comment)

Good morning Newitt. I got the DMPQ information request.
Best Regards,
Jim

From: Morris, Nevitt [mailto:Nevitt.Morris@fda.hhs.gov]
Sent: Tuesday, September 05, 2017 9:08 AM
To: Jim Wang <jim.wang@sparktx.com>
Cc: Morris, Nevitt <Nevitt.Morris@fda.hhs.gov>
Subject: BLA 125610 Information Requests DMPQ 9//5/17

Hi Jim:

We have the following two Information Requests for Spark Therapeutics that need to be addressed by the two different due dates as outlined and highlighted in yellow in the email:

DMPQ Information Request

1st set of IR due by November 12, 2017

1.
Please provide data (results of EM and media fill) from the media fill run being executed September 26 through October 10, 2017. Please ensure that nonviable particle monitoring in operation (as you agreed in the e-mails dated August 29 -August 31, 2017) will be performed during this media fill run.
2nd set of IR due by October 5, 2017

1.
Regarding drug product and diluent shipping validation:
1.1.
We note from the information provided in your BLA 125610 that no shipping validation was conducted for the drug product and diluent -filled into their primary container closure systems at (b) (4). Please provide a shipping validation protocol for voretigene neparvovec (AAV2-hRPE65v2) drug product and the diluent along with associated validation data. Shipping validation should be performed with the actual primary container closure system used in PPQ lot and (Unsigned signature field (Click to sign)) Signature field is unsigned

commercial manufacturing. Because the diluent primary container closure system is the same as that of the drug product (2 ml (b) (4) vial, 13 mm (b) (4) chlorobutyl stopper with (b) (4) seal), shipping validation can be performed with the diluent in its primary container closure system if there is no sufficient drug product at this time (by information request due date). Shipping validation protocol for the diluent should include at least the following:

container closure system is the same as that of the drug product (2 ml (b) (4) vial, 13 mm (b) (4) chlorobutyl stopper with (b) (4) seal), shipping validation can be performed with the diluent in its primary container closure system if there is no sufficient drug product at this time (by information request due date). Shipping validation protocol for the diluent should include at least the following:

1.1.1. Detailed description of the diluent primary container closure system and contents of the shipping container (e.g., number of diluent vials, dimensions of the shipping container, amount of (b) (4), temperature monitoring device, and others if any).

1.1.2. Detailed description of shipping conditions (e.g., shipping by air in cabin, frozen diluent at <65o C, and shipping temperature, pressure and duration) and monitoring. We recommend that three shipments be considered for the validation studies and actual and worst case shipping conditions be challenged in the shipments.

1.1.3. Detailed description of inspection and testing being performed upon delivery of the shipping container. For the diluent shipping validation, testing should include for, but not limited to, primary container closure system integrity, pH and appearance. Container closure system integrity (CCIT) can be evaluated (b) (4)

1.2.

Please also provide a shipping validation protocol with the same information above for voretigene neparvovec drug product along with product testing plan. If associated data is not available, please provide a date for submitting validation data. Alternatively, if the diluent and product are shipped in the same shipping container, you may combine the protocols.

1.3.

If secondary packaging and labeling will be performed at (b) (4) and then shipped to US, your shipping protocol may also need to include transport for secondary packaging. For example, it should include type of transport (ground or air) and transport time and conditions from (b) (4) to (b) (4). In this case, the primary container closure system in its secondary package will be shipped from (b) (4) to US. If there

is any additional transport in US, then that may also need to be included in the shipping validation. If any of these additional transports are not incorporated in your shipping validation, please provide a rationale /justification.

2.

Regarding the information provided in the August 22nd Amendment:

2.1.

Please provide a detailed description of the equipment present in (b) (4) during voretigene neparvovec drug product and diluent filling (in Filling Suite (b) (4)).

2.2.

We note that (b) (4) decontamination qualification report is provided only for (b) (4) in response to July 31st information request, not for (b) (4). Please provide a copy of the qualification report (including protocol and data) for (b) (4) decontamination, which was conducted with (b) (4) spores/ Biological Indicator (summarized under 3.2.A.1.1.3 Equipment in 3.2.A.1 Facilities and Equipment - (b) (4)).

3.

We note from the information provided in the BLA submission that (b) (4) are also manufactured in (b) (4) (in Filling Suite, (b) (4)). Please provide a copy of qualification reports for cleaning and decontamination of (b) (4) after manufacturing these (b) (4). If qualification reports are the same as the ones provided for AAV2-hRPE65v2, please provide a scientific rationale/justification for using the same validation protocols/procedures.

4.

We note from the information provided in your August 22nd Amendment that a sterilization validation report is provided for (b) (4) of 20mm stoppers. Please provide a justification/rationale for not providing a validation report specific for 13 mm (b) (4) stoppers used for voretigene neparvovec drug product and the diluent.

5.

During the pre-license inspection of your drug substance manufacturing site from August 21 to August 25, 2017, for commercial manufacturing, you initiated a change for the filter used in the final filtration of the drug substance to (b) (4). You indicated that the new filter was the same as the one used in the sterile filtration of voretigene neparvovec drug product at (b) (4).

Please provide the following information for this change:

5.1. A copy of the document created per your change control SOP for the filter change from (b) (4) filter to (b) (4) filter ((b) (4))

5.2. A copy of COA for the new (b) (4) filter

5.3.

Established operating conditions/ranges for the new (b) (4) filter (e.g., for pre-use flushing volume with appropriate solution, filtration flow rate or pressure, filtration time) along with their

justifications

5.4.

A copy of the revised batch record for the final (b) (4) filtration of the drug substance using the new (b) (4) filter at Spark Therapeutics, Inc.

5.5.

Available data from currently ongoing commercial drug substance manufacturing

Thanks Jim. Please acknowledge receipt of these two Information Requests.

Nevitt

Nevitt Morris

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RN,
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