

From: Morris, Nevitt
To: Jennifer.Wellman@sparktx.com
Cc: Morris, Nevitt; jim.wang@sparktx.com; paul.gil@sparktx.com
Subject: BLA 125610 Information Request CMC (7.17.17)
Date: Friday, July 21, 2017 4:12:28 PM
Attachments:
(File Attachment comment)
image001.png

Hi Jennifer:

1.

Please provide the detailed manufacturing and testing information of the "Diluent" (180 mM NaCl, 10 mM sodium phosphate, 0.001% (b) (4) P188, pH (b) (4), (b) (4)), used to dilute (b) (4)

Filtration step. Please clarify if there is any difference in source/supplier, composition, preparation, formulation and qualification of the buffer used as the "Diluent" to formulate the drug substance at Spark and that used for manufacturing the "Drug Product Diluent" at (b) (4).

2.

Please provide the following testing data with pictures in figures for the (b) (4)

(b) (4) and Drug Product Lot (b) (4) :

a.

Purity by (b) (4) ;

b.

(b) (4) Protein Identification by (b) (4) ;

c.

Gene Product Expression by (b) (4) Assay.

3.

Please provide the SOPs for qualification of your key starting materials/reagents, including but not limited to the following:

a. Cell banks

b. Plasmid DNAs

c. FBS

The information should describe how each of these materials are received in your

GMP facility, quarantined, tested, and stored at your site. Please specify the in-house

testing that is performed at your site to confirm the identity, purity and potency of these materials.

4.

Please clarify if there are any animal-derived reagents/ materials besides the Fetal

Bovine Serum, used for drug substance or drug product manufacturing.

5.

Please specify the CTD section that contains the table of all raw materials used in manufacturing of the drug substance and drug product. If this is not in the BLA please provide a table that lists all raw materials/ reagents used to in manufacture of the drug substance and drug product. This table should include:

- a. Reagent name
- b. Vendor/Supplier
- c. Source (human, bovine, recombinant, etc.);
- d. If animal-derived, identify source organism and country of origin

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- e. Grade (licensed product, clinical grade, research grade, etc.)
- f. Final concentration
- g. Certificate of Analysis (CoA)
- h. Purpose or step used in manufacturing

6.

Please describe the purification process for the plasmids from (b) (4) .

Specify which

materials are dedicated to your product vs repeat use, and validation of any cleaning

procedures for columns and other materials that are used for multiple products.

Additionally, please specify which identity test for the plasmids are completed by

(b) (4) , which are completed by Spark and or other contracted sites and describe the

ability of each test to detect contaminating plasmids present at low concentrations and

the limit of detection for each test.

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)

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