From:	Riggins, Cindy
To:	Giordano, Erica
Cc:	Ahmed, Narin; Patel, Manisha
Subject:	RE: BL 125646 CMC Information Request
Date:	Thursday, March 02, 2017 5:50:50 PM
Attachments:	B2101J.CSV B2202.csv B2205J.CSV 7008911_ANSW_MC_840_2_2_Updated_2March2017.pdf
Sensitivity:	Confidential

Dear Erica,
In our rush to deliver all the documents for the Feb 24 Information Request last night, we inadvertently missed some information.

Attached is the revised ANSW document which includes an additional description of the duration of persistence parameters (Tlast, T1/2, and Clast) in the Q6 response. This paragraph has been added to the end of the response text. In addition, the Tlast results were added to the CSV spreadsheets in a column labeled "T1/2 (days)". The updated CSV spreadsheets are also attached here.

We made a minor formatting edit to the first heading row of these spreadsheets - we added the acceptance criteria previously located in the 2nd row into the column headings in the 1st row and removed the 2nd row entirely.

Additionally, we noticed that we unintentionally left a few of the "study identifier" cells blank. We have now added that information into the updated CSV spreadsheets.

The updated ANSW document along with the SOP documents sent yesterday via email, will be submitted in a formal gateway submission within the next few days. Please note that while we will include the CSV spreadsheet attachments in the gateway submission, they will be rendered as pdf documents for submission and will no longer have the excel functionality.

Thank you and please feel free to reach out to us if you have any questions.
Cindy

From: Giordano, Erica [mailto:Erica.Giordano@fda.hhs.gov]
Sent: Friday, February 24, 2017 3:24 PM
To: Patel, Manisha
Cc: Ahmed, Narin; Riggins, Cindy
Subject: BL 125646 CMC Information Request
Sensitivity: Confidential

Good afternoon,

To facilitate our review, please provide responses to the below information requests by COB on March 1, 2017. As usual please e-mail your responses directly to me.

Please provide complete information on plasmid manufacturing at (b) (4) with sufficient details, including a summary of the manufacturing methods and quality

systems. Please include an analysis of the risk of cross-contamination of plasmids by other plasmids manufactured at this facility.

Please provide a complete list of standard operating procedures (SOPs) that are directly related to the manufacturing and testing of tisagenlecleucel–T from leukapheresis to patient infusion.

Please provide a similar list of SOPs for vector manufacturing and testing.

Please provide SOPs that cover the following processes:
Critical steps in the cell manufacturing process such as Day 0 process to determine the manufacturing pathway; positive selection for T-cells, prestimulation, vector transduction, cell expansion, cryopreservation, thawing and infusion of cells at clinical sites.
Major steps in the vector manufacturing process.
In-process and lot release test methods (assays for both the vector and tisagenlecleucel-T)
SOP-7018951: Flow cytometry daily quality control
SOP-7034323: Validation of Cell-Based and Quantitative Immunoassay Methods in CGTU

Please provide letters of authorization to the BLA to allow review of the master files for the CD3 and CD28 antibodies conjugated to the CD3/CD28 Dynabeads (Cross-referenced in Type 2 MF 11030). These are critical reagents in your manufacturing process, therefore, you must get authorization from the MF holder to reference this information to support your BLA.

To facilitate the timely review and reduce the chance of miscalculations due to transcriptional error, please provide the data from all tables in batch analyses sections 3.2.S.4.4 and 3.2.P.5.4 in an electronic format (e.g. CSV). For each product batch in 3.2.P.5.4 please include a table that lists limited clinical information. We would like the table the table to be in electronic format and include the following column headers: CTL019 batch #, highest AE score, duration of persistence, best response, and duration of response.

Please provide Patient ID for product batch (b) (4)

Please confirm receipt and let me know if you have any questions.

Thank you,

Erica Giordano
Regulatory Project Manager

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U.S. Food and Drug Administration
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