From:	Wonnacott, Keith
To:	Giordano, Erica
Cc:	Riggins, Cindy
Subject:	RE: BL 125646 DMPQ Information Request
Date:	Friday, March 24, 2017 1:01:26 PM
Attachments:	7008911_ANSW_MC_840_5.pdf
Sensitivity:	Confidential

Erica,
Attached are the responses to the CMC information request received on March 7, 2017. There a total of 56 documents: one ANSW document and 55 appendices. The ANSW document is attached to this email. The attachments will come in 14 separate emails to help ensure that the file size is not too large for delivery. We will follow up with a BLA submission through the gateway of these documents.

Keith Wonnacott

From: Giordano, Erica [mailto:Erica.Giordano@fda.hhs.gov]
Sent: Friday, March 24, 2017 12:07 PM
To: Wonnacott, Keith
Subject: RE: BL 125646 DMPQ Information Request
Sensitivity: Confidential

Thanks for letting me know, I will look out for it shortly.

Erica

From: Wonnacott, Keith [mailto:keith.wonnacott@novartis.com]
Sent: Friday, March 24, 2017 12:04 PM
To: Giordano, Erica
Subject: RE: BL 125646 DMPQ Information Request
Sensitivity: Confidential

Erica,
You asked for our response by noon. I figure you are a little bit flexible, but I am letting you know it is coming within the hour.

Keith

From: Giordano, Erica [mailto:Erica.Giordano@fda.hhs.gov]
Sent: Tuesday, March 07, 2017 4:41 PM
To: Patel, Manisha
Cc: Ahmed, Narin; Riggins, Cindy
Subject: BL 125646 DMPQ Information Request
Sensitivity: Confidential

Good afternoon,

Please see the information request below and provide responses by noon on March 24, 2017.

For (b) (4) Facility

Please provide environmental monitoring performance qualification (EMPQ) summary report including dynamic monitoring data and sampling locations for the (b) (4) and (b) (4) where manufacturing processes occur. Please provide EM data summary (including BSCs) during the manufacturing of the process validation lots for the vector substance.

Please provide the most recent requalification of the HVAC system for AHU Unit (b) (4) and clarify if ventilation is accomplished by single pass or recirculated air, and justify your response.

Please confirm that (b) (4) area is not utilized for CTL019 vector substance manufacturing and provide your segregation procedure or program and associated study or risk assessment for cross-contamination prevention.

Please provide the qualification summary report for the following equipment to demonstrate the functionality and suitability for their use during the vector substance manufacturing process.

Wave Mixer
Orbital shaker
Biological Safety Cabinet
Centrifuge
(b) (4)

Please provide summary report of disinfectant efficacy study for cleaning agents and disinfectants used for routine equipment and production room cleaning at the vector substance manufacturing facility.

Please provide validation summary report for the (b) (4) treatment of the manufa cturing suite during product change over.

Please provide aseptic process validation summary report for the open manipulations performed in biologic safety cabinets.

Please provide shipping validation /qualification summary report including supporting data for the vector substance shipped from (b) (4) for final processing and fill.

For (b) (4) Facility

For the filling isolator, please provide summary report of the following:

IQ, OQ and PQ (most recent requalification if applicable) including EM monitoring frequency, criteria and sampling points.

Smoke studies performed including acceptance criteria and results.

Validation study for the cleaning and decontamination of the isolator.

Sterilization of the isolator and consumables s such as tubing, (b) (4) membrane, stoppers and glass vials used inside the isolator.

. Please provide EM data summary during the manufacturing of the process validation lots for the vector product and the most recent aseptic process validation (media fill) lots.
. For equipment qualification, please provide summary report of IQ, OQ and PQ for all GMP critical equipment used in the vector product manufacturing process both in Building (b) (4) and Building (b) (4)
. Please provide summary report of disinfectant efficacy study for cleaning agents and disinfectants used for routine equipment and production room cleaning at the vector product manufacturing facility.
. Please provide a complete list of all other products handled in manufacturing Building (b) (4) and how they are segregated from the CTL019 vector product.
. Please provide a summary report of the most recent Aseptic Process Validation runs (media fills).
. Please provide shipping validation/qualification summary report including supporting data

and worst case conditions for the vector product shipped from (b) (4) to Novartis NJ plant for manufacturing of CTL019 cell product.

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

Thank you,

Erica Giordano
Regulatory Project Manager

Center for Biologics Evaluation and Research
Office of Tissues and Advanced Therapies
U.S. Food and Drug Administration
Tel: 240-402-8298
Erica.Giordano@fda.hhs.gov