

From: [Riggins, Cindy](#)
To: [Giordano, Erica](#); [Patel, Manisha](#)
Cc: [Ahmed, Narin](#)
Subject: RE: BL 125646 CMC Information Request
Date: Friday, March 10, 2017 12:57:34 PM
Attachments: [7008911_ANSW_MC_840_4.pdf](#)
(b) (4)
[REDACTED]
[REDACTED]
[CCI of \(b\) \(4\)](#) - [Poster 2013.pdf](#)
Sensitivity: Confidential

Dear Erica,

Attached are the responses to the CMC information request received on March 3, 2017. There a total of 5 documents: one ANSW document and four appendices. We will follow up with a BLA submission through the gateway of these documents.

Take care,

Cindy

From: Giordano, Erica [<mailto:Erica.Giordano@fda.hhs.gov>]
Sent: Friday, March 03, 2017 3:11 PM
To: Riggins, Cindy; Patel, Manisha
Cc: Ahmed, Narin
Subject: RE: BL 125646 CMC Information Request
Sensitivity: Confidential

The CMC team has agreed to your proposed extension. Please send your response by COB on March 10, 2017.

Erica

From: Riggins, Cindy [<mailto:cindy.riggins@novartis.com>]
Sent: Friday, March 03, 2017 2:33 PM
To: Giordano, Erica; Patel, Manisha
Cc: Ahmed, Narin
Subject: RE: BL 125646 CMC Information Request
Sensitivity: Confidential

Dear Erica,

We would like to ask for an extension on the due date of response to this information request. Three business days for response is very difficult to manage from a global perspective due to time differences. In addition, Monday is a holiday in Basel, Switzerland where many of the team members are located. Could we possibly have until COB on Friday, March 10?

Thank you,

Cindy

From: Giordano, Erica [<mailto:Erica.Giordano@fda.hhs.gov>]
Sent: Friday, March 03, 2017 1:46 PM
To: Patel, Manisha
Cc: Ahmed, Narin; Riggins, Cindy
Subject: BL 125646 CMC Information Request
Sensitivity: Confidential

Good afternoon,

Please refer to the information request below and provide a response by March 8, 2017 by COB.

We have the following comments regarding the Certificate of Analyses for the Dynabeads and the antibodies used for the beads manufacturing (Section 3.2.A.2, Appendices 12-14):

Lot release specification for Dynabeads (b) (4) should not only include a low but also an upper limit to ensure that Dynabeads CD3/CD28 CTS is consistent and not (b) (4).

Lot release specifications for XR-CD3 and XR-CD28 monoclonal antibodies should include maximal acceptance criteria for amount of retrovirus-like particles in antibody (b) (4) when tested by (b) (4). The acceptance criteria should be based on the viral clearance studies and viral clearance assurance calculation.

Please provide the test reports for assay AM64150 (Determination of multiplicity of infection (MOI) of lentiviral vectors using human T cells) for vector DP lots (b) (4)

Section 3.2.S.4.2.1.6.3 (vector) regarding AM64150 describes the following formula: (b) (4). This formula seems to assume a linear relationship between the transduction percentage and the MOI. However, section 4 of validation report for this assay (VR64150A) indicates that the relationship between transduction percentage and MOI is not linear. Please explain.

VSV-G pseudotyped vectors are sensitive to (b) (4) and should be protected from (b) (4) during shipping on (b) (4). You are (b) (4) vector DP containers in (b) (4) DP (b) (4), please provide the following information:

Please describe the (b) (4) characteristics in more detail.

Please provide a risk analysis that evaluates the potential impact of an improper seal or a breach in the (b) (4)

Please confirm receipt of this request.

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

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