

From: [Giordano, Erica](#)
To: [Patel, Manisha \(manisha.patel@novartis.com\)](#)
Cc: [Riggins, Cindy](#); [narin.ahmed@novartis.com](#)
Subject: BL 125646 CMC Information Request
Date: Friday, July 07, 2017 11:44:47 AM
Attachments: [image001.png](#)

Good afternoon,

Please see the information request below and provide a response by 4 pm on July 18, 2017. As usual please provide a response directly to this e-mail and follow up by submitting the information as a formal amendment to the BLA.

Regarding your MOI assay, point 2.a.v in your CMC response #21 that was emailed on 6/21/17:

During future qualification of a new healthy donor cell bank for the MOI assay, you propose to perform (b) (4). If we understand correctly, you will then pool the data and calculate the mean and CV of these (b) (4) data points. If the CV of the pooled data exceeds (b) (4), this will be taken to indicate that the (b) (4) are not equivalent, and a conversion factor will be established by dividing the means from the (b) (4).

We are not familiar with this approach to evaluating equivalence of two reagents, and if this approach is to be used we will require additional explanation regarding the appropriateness of this approach, the sensitivity of this approach (equivalence margin and power), and the likely accuracy of the resulting conversion factor. Our initial analysis suggests that the proposed approach has limited ability to detect major differences between the banks due to the small number of runs, the variance of the assay (intermediate precision roughly (b) (4) CV), and the questionable approach to evaluating equivalence.

Please provide a revised proposal that uses an appropriate number of independent replicates and an appropriate method to evaluate equivalence of the (b) (4). We suggest an equivalence margin of (b) (4). Please justify your approach and include an analysis of the statistical power.

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
Tel: 240-402-8298
Erica.Giordano@fda.hhs.gov



"THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER

LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify the sender by e-mail or phone."