

APPROVED

By Jean Gildner at 11:26 am, Aug 18, 2016

From: [Lorien Armour](#)
To: [Moos, Malcolm](#)
Cc: [Margarita Aguilera](#); [John Duguid](#); [Riggins, Patrick](#); [Gildner, Jean](#)
Subject: RE: Follow up to June 17th Teleconference MACI BL 125603
Date: Friday, June 17, 2016 7:07:58 PM

Dear Malcolm,

To address your concerns detailed in your email below, the following criteria are currently included in the (b) (4) test method SOP. Note: "No test" is an internal term for an invalid test result due to failure of assay acceptance criteria or controls.

Please confirm this addresses your concern and we will then formally amend the description of the Potency method in 3.2.P.5.2. in the BLA to include these criteria.

(b) (4)

Independent of the (b) (4) results, the (b) (4) determines whether the sample is a (b) (4) according to the table below.

(b) (4)

Kind Regards,

Lorien Armour, RAC
CMC Regulatory Consultant
Vericel Corporation
Office: 919-450-0802
Fax: 734-239-7401

From: Moos, Malcolm [<mailto:Malcolm.Moos@fda.hhs.gov>]
Sent: Friday, June 17, 2016 5:45 PM
To: Margarita Aguilera
Subject: the email in question

If this is the one, I found it—one of countless messages from Ron Chamrin. It explains Figure 1, which I had trouble with initially. However, the issue I was referring to today is separate. The current (b) (4) is a big improvement over an acceptance criterion of (b) (4) for (b) (4) in that it is (b) (4) that is pretty good as (b) (4) go. However, (b) (4) cells could have low (b) (4) levels—giving a (b) (4), for example—and the (b) (4) could pass without meaning much. Is your rationale that in such a case, (b) (4) would always be above (b) (4)? I think you might nevertheless want an internal control for the (b) (4). Moreover, when I look at the (b) (4) data vs. the (b) (4) data, it seems to me that the former are considerably tighter, so eventually both the (b) (4) and (b) (4) limits would be adjusted to reflect this. Then there would be even more rationale for an additional limit on (b) (4).

Let me know where I'm off base.

Thanks again for the short notice discussion—very helpful.

Best,

Malcolm

Malcolm Moos Jr., M.D., Ph.D.
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From: Lorien Armour
Sent: Friday, June 17, 2016 6:07 PM
To: 'moos@cber.fda.gov'
Cc: Margarita Aguilera; John Duguid; Riggins, Patrick (Patrick.Riggins@fda.hhs.gov); Gildner, Jean <Jean.Gildner@fda.hhs.gov> (Jean.Gildner@fda.hhs.gov)
Subject: RE: Follow up to June 17th Teleconference MACI BL 125603

Dear Malcolm,

I understand from an email you just sent Margarita, you are already aware of this document I just sent and that your question was a separate issue. We will review the issue expressed in the email to Margarita internally and respond accordingly.

Kind Regards,

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From: Lorien Armour
Sent: Friday, June 17, 2016 6:03 PM
To: 'moos@cber.fda.gov'
Cc: Margarita Aguilera; John Duguid; Riggins, Patrick (Patrick.Riggins@fda.hhs.gov); Gildner, Jean
<Jean.Gildner@fda.hhs.gov> (Jean.Gildner@fda.hhs.gov)
Subject: Follow up to June 17th Teleconference MACI BL 125603

Dear Malcolm,

We appreciate the time you took this afternoon to address outstanding questions/comments you had regarding the comparability protocol in 3.2.R as well as (b) (4), which was previously discussed during a March 9th teleconference.

As agreed, Vericel will formally withdraw 3.2.R Comparability Protocol from the BLA next week.

The attached document is the response follow up we sent via email to FDA regarding outstanding questions from the March 9th teleconference, which discusses (b) (4). Please do not hesitate to contact us if this response does not answer your question. As agreed, Vericel will include this response in a formal amendment to the BLA.

Kind Regards,

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