

APPROVED

By Jean Gildner at 1:38 pm, Jul 19, 2016

From: [Lorien Armour](#)
To: [Gildner, Jean](#)
Cc: [Margarita Aguilera](#); [Riggins, Patrick](#)
Subject: Response to BLA 125603 May 27th Information Request
Date: Friday, June 10, 2016 2:56:44 PM
Attachments: [1-11-1 Quality Information Amendment for May 27 Questions.pdf](#)

Dear Jean,

Vericel is providing a response to the Quality/Facility information request received via email on May 27th. I have attached the 1.11.1 Quality Information Amendment document, which lists FDA's questions, followed by Vericel's responses. Please note that due to file size, a protocol and report GTR-897-06-01 "Installation and Operational Qualification of the (b) (4) HVAC System" referenced in 1.11.1 is not attached to this email, but will be submitted in the BLA amendment next week.

An amendment to the BLA will be submitted next week (week of June 13th) and will include the response documents (1.11.1) for both the May 26th and May 27th sets of questions (also sent by email response to FDA), as well as updates to the respective Module 2.3/Module 3 documents, as detailed in the responses.

If you have any questions please feel free to contact me.

Kind Regards,

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

From: Lorien Armour
Sent: Tuesday, May 31, 2016 1:10 PM
To: Gildner, Jean
Cc: Margarita Aguilera
Subject: RE: BLA 125603 Information Request

Hi Jean,

I hope you had a nice holiday weekend. Vericel will provide responses to the facility questions posed below by next Friday, June 10th.

Kind Regards,

Lorien Armour, RAC
CMC Regulatory Consultant

Vericel Corporation
Office: 919-450-0802
Fax: 734-239-7401

From: Margarita Aguilera
Sent: Friday, May 27, 2016 1:15 PM
To: Gildner, Jean
Cc: Lorien Armour
Subject: RE: BLA 125603 Information Request

Hi Jean,

This to acknowledge receipt of the Information Request below. Please note that I will be out of the office starting this afternoon and returning on June 1, 2016.

Lorien Armour is the CMC Regulatory representative and will be liaising in regards to this request. In my absence, please include Lorien in any additional requests for information.

Many thanks in advance for your consideration.

Regards,
Margarita

Margarita Aguilera, M.Sc.
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From: Gildner, Jean [<mailto:Jean.Gildner@fda.hhs.gov>]
Sent: Friday, May 27, 2016 12:15 PM
To: Margarita Aguilera
Subject: BLA 125603 Information Request

Dear Margarita,

Please find the following requests for information regarding Facility Section 3.2.A. Please respond as soon as possible. Please acknowledge receipt of this email.

Question #1

Section 1.7 describe the prevention of contamination and cross contamination. Please provide following additional information:

- **Please provide a description of the sanitizer effectiveness assessment performed for (b) (4) used in (b) (4) areas.**
- **Please describe room clearance and changeover procedure in place to prevent cross contamination.**
- **Please provide a narrative summary of how the manufacturing operations and storage of other licensed products are segregated from MACI production and storage areas.**
- **Please describe equipment cleaning/sanitization procedures used in (b) (4) for product contact equipment.**

Question #2

Section 1.1.6 describes Environmental monitoring program. Please provide following additional information for MACI production areas:

- **Please provide a description of your routine monitoring program including the testing performed, frequency of testing, alert and action limits and sampling locations.**
- **Please provide the environmental monitoring qualification data for the new cell therapy suite (b) (4) including BSC hoods.**
- **Please provide summary of the most recent three months routine environmental monitoring data.**

Question #3

Section 1.3.1(product contact equipment) states that (b) (4) validation and routine (b) (4) verification audits are performed to confirm the custom made membrane loading units are suitable for use. The materials are sourced from approved vendors and (b) (4) or (b) (4). Please provide following information for (b) (4), membrane loading unit, forceps, scalpel and primary container and (b) (4) :

- **Name of approved vendors and summary of vendor qualification completed**
- **How (b) (4) data provided in the certificate of analysis were validated**
- **Describe acceptance criteria for the product contact equipment**
- **Describe your dose verification audit and current status of these audit**

Question #4

Section 1.2.3 (b) (4) and section 1.2.4 (b) (4) describe (b) (4) system. Please provide following additional information:

- **Describe approved vendor name and vendor qualification summary (brief)**
- **Copy of certificate of analysis (vendor provided)**
- **Please explain why you did not established acceptance criteria for (b) (4) system and clarify if you routinely monitor (b) (4)**

Question #5

Section 1.2.1 describe Heating Ventilation and Air Conditioning (HVAC). Please provide following additional information:

- **Please provide a diagram that shows the location of air handling unites and rooms they service, locations of the terminal HEPA filters, and an enlargement of the area. classification diagram for the (b) (4) production areas.**
- **Please describe total number of air handling units that serve (b) (4) including clarification if air is recirculated or once through.**
- **Please provide an enlargement of the area pressurization diagram that shows the production areas on (b) (4).**
- **Please provide HVAC qualification protocol and report (OQ/PQ) for the MACI production areas.**
- **Please provide the clean room (cell therapy suite- (b) (4)) qualification summary.**
- **Please provide Biological safety hood (BSC) qualification summary for the (b) (4)**

Question #6

Section 1.2.2 describes (b) (4) purified water system. Please provide following additional information:

- **Briefly summarized the purified water system description and qualification/requalification**
- **Summary of validated acceptance criteria**
- **Routine monitoring frequencies, acceptance criteria**

If you have any questions please feel free to contact me.

Sincerely, Jean

Jean F. Gildner MSHS, MT (ASCP), CQA (ASQ)

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