

APPROVED

By Jean Gildner at 4:41 pm, Dec 02, 2016

From: [Margarita Aguilera](#)
To: [Gildner, Jean](#)
Subject: RE: BLA125603 Information Request
Date: Friday, September 16, 2016 10:14:59 AM
Attachments: [image001.png](#)

Jean,

Good morning. This is to acknowledge receipt of the information request below. I am meeting with the team this morning and will advise on the timing as soon as possible.

Regards,
Margarita

From: Gildner, Jean [mailto:Jean.Gildner@fda.hhs.gov]
Sent: Thursday, September 15, 2016 3:26 PM
To: Margarita Aguilera
Subject: BLA125603 Information Request

Dear Margarita,

Please find below an Information Request. Please acknowledge receipt of this email and a timeline as to when you think you will be able to respond. Please submit all responses to the BLA file, to include responses sent via email.

- Please provide the maximum number of patient biopsy/cells that may be processed per shift and per day in the (b) (4) .
- Please provide the maximum number of patient biopsy/cells that may be incubated in the same equipment (incubator), and what precaution will be taken to prevent cross contamination and mix-up. Please describe routine changeover procedure for the incubators/centrifuges in the (b) (4) that will share between multiple patient cell.
- Regarding dynamic environments (viable particulate) monitoring program, your current EM procedure lacks dynamic monitoring for viable particulate during manual manipulations. Your June 2016 response states “Dynamic monitoring for MACI during final assembly include viable air (active and passive), the surface of the BSC, and non-viable air particulates are performed (b) (4) in the (b) (4) and the (b) (4) ”. The media fill protocol (GTR-753-05-01) identified and summarized following manual manipulation in (b) (4) areas:

Table 1 Summary of Process Manipulations

Procedure	Number of Manual Manipulations	Time to Complete
Cartilage Biopsy (b) (4)	(b) (4)	(4)
(b) (4)	(b) (4)	(4)
Packaging and QC Sampling		

Since (b) (4) production areas are newly renovated facility, we recommend to include adequate dynamic monitoring (for example settling plate) for all procedures listed in the above table specifically biopsy processing and all earlier steps where no dynamic monitoring performed as per current EM procedures or provide justification of your current dynamic monitoring frequencies in (b) (4) and BSC hoods.

- Regarding the container closure integrity for the validation (GTR-623-06-01) and seal integrity validation of the dish with green cover (GTR-573-03-01) , Please describe the test sensitivity (smallest integrity breach that can be detected) that was used during the container closure integrity test method validation. Please indicate locations of study protocols in the BLA or provide copy these container closure studies (GTR-623-06-01 and GTR-573-03-01).
- The BLA states that Facility surfaces are cleaned using a HEPA vacuum unit prior to disinfection steps. Please describe frequencies for the HEPA filter integrity testing for the vacuum unit.

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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