



Our Reference: BL125743/0  
CRMTS 14072

**MEETING SUMMARY**

Date: June 17, 2022

Green Cross Corporation

Attention: (b) (4)

Dear (b) (4)

Attached is a copy of the memorandum summarizing your May 19, 2022, Type A teleconference with CBER. This memorandum constitutes the official record of the teleconference. If your understanding of the meeting outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER as soon as possible.

Please include a reference to CRMTS #14072 or Submission BLA 125743, in your future submissions related to the subject product.

If you have any questions, please contact Nancy Skeeter at [Nancy.skeeter@fda.hhs.gov](mailto:Nancy.skeeter@fda.hhs.gov).

Sincerely,

Heather Erdman, MCPM, RAC, CQPA  
Branch Chief  
Division of Regulatory Project Management  
Office of Tissues and Advanced Therapies  
Center for Biologics Evaluation and Research

**Meeting Summary  
(Includes Preliminary Meeting Responses)**

**Meeting ID #:** CRMTS #14072  
**Submission type & #:** BLA 125743/0  
**Product name:** Immune globulin intravenous, human-stwk  
**Indication:** Treatment of primary humoral immunodeficiency (PI)  
in adults  
**Sponsor:** Green Cross Corporation  
**Meeting type:** Type A  
**Meeting category:** Teleconference  
**Meeting date & time:** May 19, 2022 15:00-16:00  
**Meeting format:** Teleconference  
**RPM:** Nancy Skeeter  
**Preliminary Meeting Responses:** May 12, 2022

**FDA Attendees:**

Rachael Anatol, PhD, CBER/OTAT  
Kimberly Benton, PhD, CBER/OTAT  
Melanie Blank, MD, CBER/OTAT/DCEPT  
Cecilia Crowley, CBER/OTAT/DRPM  
Lu Deng, PhD, CBER/OTAT/DPPT/PDB  
Parmesh Dutt, PhD, CBER/OCBQ/DBSQC  
Nancy Eller, CBER/OTAT/DPPT/PDB  
Heather Erdman, MCPM, RAC, CQPA, CBER/OTAT/DRPM  
Elizabeth Hart, MD, CBER/OTAT/DCEPT  
Jie He, CBER/OCBQ/DMPQ  
Michael Kennedy, PhD, CBER/OTAT/DPPT/PDB  
Lily Koo, PhD, CBER/OCBQ/DMPQ  
Hyesuk Kong, CBER/OCBQ/DBSQC  
Wei Liang, PhD, CBER/OTAT  
Jing Lin, CBER/OCBQ/DBSQC  
Xiuju (Sue) Lu, PhD, CBER/OCBQ/DMPQ  
Melissa Mendoza, JD, CBER/OCBQ  
Leyish Minie, MSN, RN, CBER/OTAT/DRPM  
Malgorzata Norton, CBER/OTAT/DPPT  
Lori Peters, CBER/OCBQ/DMPQ  
Carolyn Renshaw, CBER/OCBQ/DMPQ  
Anita Richardson, CBER/OCBQ  
Dorothy Scott, MD, CBER/OTAT/DPPT  
Olga Simakova, PhD CBER/OTAT/DPPT/PBD  
Ramani Sista, PhD, CBER/OTAT/DRPM  
Nancy Skeeter, MBA, CBER/OTAT/DRPM  
Million Tegenge, PhD, CBER/OTAT/DCEPT  
Maria Luisa Virata, PhD, CBER/OTAT/DPPT/PDB

Tingting Zhou, PhD, CBER/OBPB/DB

**Sponsor Attendees:**

Han Yeol Byun, Deputy General Manager

(b) (4), Team Head

(b) (4), Acting Head of IGIV TF

(b) (4), Head of Technical Operations

Chin Kim, Vice President, Head of Research and Development

(b) (4), Associate, Regulatory Affairs

Jae Woo Lee, Head of Development

Chan Woo Park, Head of Quality Management

Chun Bo Park, Team Head, Quality System

(b) (4), Associate, Regulatory Affairs

(b) (4), Head of Regulatory and Quality

**Background and Objectives:**

Green Cross Corporation submitted a meeting request on April 14, 2022:

- to discuss that the expectations and timeline for the regulatory process are aligned with the Agency;
- to obtain clarification on statements made in the Complete Response Letter (CRL) and subsequent communication between the two parties;
- to understand if the Agency has input to provide on remediation resulting from FDA's observations to the RIE;
- to agreement for GCC's proposed approaches to the PLI and the complete response submission to the CRL.

The pre-meeting materials were submitted on April 14, 2022.

FDA provided its preliminary meeting responses to Green Cross Corporation's questions on Thursday, May 12, 2022. After reviewing the preliminary meeting responses, Green Cross Corporation notified FDA on Tuesday, May 17, 2022, of its decision to limit the meeting to discuss only question numbers 5, 1, and 12.

**Sponsor Questions:**

**Sponsor Question 1:**

*Can the Agency confirm that the post-CRL issuance process will follow the flow diagram in Figure 2 above (copied below)? If not, please elaborate as to precisely what the post-CRL process will be.*

**FDA Preliminary Meeting Response to Sponsor Question 1:**

The firm's flow diagram on post CRL process appears acceptable.

**Meeting Discussion for Sponsor Question 1:** We understand your concern on the timeframe and conditions for determination of PLI readiness. To

expedite the process, GCC should submit the complete set of all relevant information on time as scheduled, and the Agency will keep communications open with GCC to facilitate the process. Your proposed timeline of conducting the PLI around November-December 2022 appears plausible. The PLI schedule will also be influenced by any potential travel restrictions due to the COVID pandemic.

**Sponsor Question Question 2:**

*Could the Agency please clarify the rationale for requiring the PLI scheduling based on the 15-day response and the subsequent CAPA updates, completion timelines, and other contributing factors to allow GCC to better prepare and respond in our quarterly updates?*

**FDA Preliminary Meeting Response to Sponsor Question 2:**

This procedure allows the Agency to effectively evaluate your implemented CAPAs and state of the associated quality system to ensure that your facility is ready for the PLI. This procedure is intended to improve mutual understanding and to facilitate the review of your resubmission.

**Meeting Discussion for Sponsor Question 2:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 3:**

*Could the Agency please clarify at what point the RIE is considered closed, and the final report will be issued? Is it before conducting the on-site facility PLI?*

**FDA Preliminary Meeting Response to Sponsor Question 3:**

The final RIE report will be issued upon approval of the BLA.

**Meeting Discussion for Sponsor Question 3:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 4:**

*Does the Agency agree with this periodic update schedule?*

*Note- GCC submitted the last CAPA update on February 14, 2022 and received the Complete Response Letter on February 25, 2022. GCC plans to submit the next update by June 30, 2022, detailing all tasks completed since the last CAPA update on February 14, 2022. GCC will submit the final update covering tasks completed from June through August by September 30, 2022.*

**FDA Preliminary Meeting Response to Sponsor Question 4:**

The proposed periodic CAPA update schedule appears acceptable.

The September submission should also include all responses sent starting from November 17, 2021.

For ease of review, please organize the submission as follows:

- The responses should be submitted to the eCTD in numerical order and categorized based on RIE observation number
  - For example, if you have provided a response last year, and amended that response recently, only the recent (final) response should be included as the response to the observation
- A detailed Table of Contents with links to each RIE response should be provided, with subheadings where needed.

**Meeting Discussion for Sponsor Question 4:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 5:**

*GCC would like clarification on how the Agency plans to communicate any questions on the requested quarterly CAPA updates, and how the Agency would like to obtain the answers from GCC.*

*Would the Agency please clarify how these communications will be handled?*

**FDA Preliminary Meeting Response to Sponsor Question 5:**

The Agency will communicate with GCC regarding your quarterly CAPA updates with email communication and information requests when necessary.

**Meeting Discussion for Sponsor Question 5:**

The Agency will communicate with GCC via email and information requests regarding the previously submitted responses to the Remote Interactive Evaluation observations. Please note that communication will be provided by CBER as appropriate in a timely manner.

GCC's response to the email communications and information requests should be submitted as amendments to the application via the gateway, meanwhile, please indicate in the cover letter that the submission(s) are not a complete response to the CRL.

The CAPAs that were submitted on January 14, 2022 (SN0048) and February 14, 2022 (SN0059) have been evaluated by the Agency. Please note that all of the CAPAs will be evaluated holistically when the last CAPA report is provided. You will be reached by the Agency via information requests should the Agency have questions on your submitted CAPAs, as well as on the future CAPAs to be submitted by June and September 2022.

**Sponsor Question 6:**

*In the email communication from the Agency on March 17, 2022, it states that CBER will review GCC's CAPA updates and will contact GCC to schedule the PLI when the Agency determines that GCC's manufacturing site is ready for inspection.*

*GCC would like to know if the Agency will determine GCC's inspection readiness based on the final CAPA update to be submitted in September 2022. If so, approximately how long will it take for the Agency to review and reply to the CAPA updates?*

**FDA Preliminary Meeting Response to Sponsor Question 6:**

We can't provide you with a specific timeline before we have received all your complete CAPA updates to the observations or concerns noted during the RIE. We will communicate with you throughout the review of your CAPA amendments, and GCC is also encouraged to update the Agency during the process on the readiness of your facility for PLI. Your proposed dates for the PLI around November and December 2022 will be taken into consideration, and we will work with you to schedule the PLI at a mutually agreed timeframe.

**Meeting Discussion for Sponsor Question 6:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 7:**

*GCC would like to propose having a discussion of the PLI schedule once the June 2022 CAPA update is submitted to the Agency. As the manufacture of PLI lots will be part of a production campaign, GCC requires sufficient lead time for planning the campaign and would like to propose that the PLI take place between November 28, 2022 and December 9, 2022. Would the Agency consider this proposal in determining the PLI schedule?*

**FDA Preliminary Meeting Response to Sponsor Question 7:**

See response to #6.

**Meeting Discussion for Sponsor Question 7:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 8:**

*As the above-listed documents are critical to ensuring and demonstrating compliance with the commitments established in the BLA, for the purpose of the PLI GCC proposes to submit the revised documents and relevant sections of the CTD in the final RIE CAPA update (September 2022) as amendments that are not the complete responses to the CRL. After the PLI, the sections will be included in the complete responses to the CRL. Does the Agency agree with this strategy?*

**FDA Preliminary Meeting Response to Sponsor Question 8:**

The above plan is acceptable. Please submit only the documents that have been updated and redline all the changes from the September 2022 versions to the document version submitted in the CRL response. Please do not remove any documents that are already in the eCTD. We reserve our final decision on the

documents submitted in September 2022 when they are submitted in the CRL resubmission.

**Meeting Discussion for Sponsor Question 8:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 9:**

*Does the Agency agree that this resubmission could be categorized as a Class 1 resubmission, given that the PLI will precede the resubmission?*

**FDA Preliminary Meeting Response to Sponsor Question 9:**

The resubmission categorization will be determined upon the receipt of the resubmission.

**Meeting Discussion for Sponsor Question 9:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 10:**

*In the event the CAPA actions to the RIE observations are acceptable to the Agency and no significant findings are observed as an outcome of the PLI, GCC would like to resubmit the application or abbreviated application within 2 months post PLI. Does the Agency agree with this proposal?*

**FDA Preliminary Meeting Response to Sponsor Question 10:**

This appears to be acceptable.

**Meeting Discussion for Sponsor Question 10:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 11:**

*GCC currently assigns source plasma a shelf life of (b) (4) from bleed date, although 21 CFR section 610.53 specifies a dating time of 10 years for frozen source plasma, and the original shelf life assigned to the source plasma from the plasma centers is 10 years. The (b) (4) shelf life was established based on a previous version of the (b) (4). GCC accordingly plans on extending the shelf-life of source plasma from (b) (4) to 10 years from the bleed date. Does the Agency agree with this proposal?*

**FDA Preliminary Meeting Response to Sponsor Question 11:**

The proposal to change the frozen Source Plasma shelf life to no more than 10 years, at –20°C or colder, as stated in 21 CFR section 610.53 is acceptable.

**Meeting Discussion for Sponsor Question 11:**

There was no discussion of this FDA question/comment during the meeting.

**Sponsor Question 12:**

*Could the Agency please clarify what additional (b) (4) study is required for the manufacturing process?*

**FDA Preliminary Meeting Response to Sponsor Question 12:**

To fully understand the kinetics and robustness of the (b) (4) process (to align with (b) (4) guidelines), when performing the (b) (4) study, especially at critical (b) (4) steps, it is recommended to take samples not only at the (b) (4), but also at (b) (4). Samples should be taken from (b) (4).

**Meeting Discussion for Sponsor Question 12:**

Your studies did not give a full profile of your (b) (4) steps which is required for a well-controlled manufacturing process and for being able to consistently make drug product. This is particularly important for the critical (b) (4) steps. You need to identify which (b) (4) steps are critical; after the (b) (4) how long does it take to see (b) (4).

In the meeting agenda, you stated that you performed range-finding studies and (b) (4) studies. For the range-finding studies, the report OB-PV-0044-16-01 was for your 5% IGIV product. The study was done in 2017. Since then, you have implemented many changes. You did not submit any analysis to show that the implemented changes have no impact on (b) (4) studies. Therefore, this study is not representative for the 10% IGIV manufacturing process at commercial scale. The small-scale studies can be used to design but not to replace the (b) (4) study at commercial scale. No comments can be provided for the report GC5107-QMR-147 because it was not submitted to the eCTD.

For the (b) (4) studies, as it has been communicated through IRs and in meetings, the study for the worst-case condition (b) (4) was incorrectly validated. One of the deficiencies was that you do not have data for the samples taken (b) (4) (b) (4). In the case of Worst-case condition (b) (4) resulting in total of (b) (4) valid (b) (4) for this condition. However, for the Worst-case condition (b) (4) can be considered valid which is insufficient for this condition. We also want to emphasize that all samples should be taken from (b) (4).