



Our STN: BL 125739/0

**MID-CYCLE COMMUNICATION
SUMMARY
JUNE 27, 2022**

Rebiotix, Inc
Attention: Karen Kuphal, PhD
2660 Patton Road
Roseville, MN 55113

Dear Dr. Kuphal:

Attached is a copy of the summary of your May 31, 2022, Mid-Cycle Communication Teleconference with CBER. This memorandum constitutes the official record of the Teleconference. If your understanding of the Teleconference 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 STN 125739/0 in your future submissions related to REBYOTA.

If you have any questions, please contact the Regulatory Project Managers, Margaret Dayhoff-Brannigan (margaret.dayhoff-brannigan@fda.hhs.gov), and Girish Ramachandran (girish.ramachandran@fda.hhs.gov) at (301)796-2640.

Sincerely,

Doran Fink, MD, PhD
Acting Deputy Director
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research

Mid-Cycle Communication Teleconference Summary

Application Type and Number: BLA, STN125739/0
Product Name: Fecal Microbiota, Live
Proposed Indication for Use: Reduce the recurrence of *Clostridioides difficile* infection in adults following antibiotic treatment for recurrent *Clostridioides difficile* infection
Applicant: Rebiotix, Inc.
Meeting Date & Time: May 31, 2022, 1:00PM EDT
Committee Chair: Qun Wang, PhD
RPMs: Margaret Dayhoff-Brannigan, PhD
Girish Ramachandran, PhD

FDA Attendees:

Omolara Adewuni, MD	OVRP/DVRPA
Jennifer Bridgewater	OVRP/DBPAP
Michael Brony	OCBQ/DCM/APLB
Drusilla Burns, PhD	OVRP/DBPAP
Paul Carlson, PhD	OVRP/DBPAP
Denis Cato	OCBQ/DIS/BMB
Jon Daugherty, PhD	OVRP/DVRPA
Margaret Dayhoff-Brannigan, PhD	OVRP/DVRPA
Sheila Dreher-Lesnack, PhD	OVRP/DBPAP
CDR Donald Ertel	OCBQ/DMPQ
Meghan Ferris, MD	OVRP/DVRPA
Doran Fink, MD, PhD	OVRP
Theresa Finn, PhD	OVRP/IOD
Richard Forshee	OBPV
Zhong Gao, PhD	OBPV/DB
Martin Green, PhD	OVRP/DVRPA
LCDR Kelsy Hoffman, PhD	OVRP/DVRPA
Andrea Hulse, MD	OVRP/DVRPA
Kathleen Jones, PhD	OCBQ/DMPQ
Jennifer Kirk, PhD	OBPV/DB
Loris McVittie, PhD	OVRP/DVRPA
Miriam Ngundi, PhD	OCBQ/DMPQ
Sussan Paydar	OM/DSAC
Lori Peters	OCBQ/DMPQ
Kirk Prutzman, PhD	OVRP/DVRPA
Girish Ramachandran, PhD	OVRP/DVRPA
Kanaeko Ravenell, MS	OCBQ/DIS/BMB
Rebecca Reindel, MD	OVRP/DVRPA
John Scott, PhD, MA	OBPV/DB
Jay Slater, MD	OVRP/DBPAP

Daphne Stewart	OVRP/DVRPA
Earle Scott Stibitz, PhD	OVRP/DBPAP
Lisa Stockbridge	OCBQ/DCM/APLB
Ellen Turner, MD	OVRP/DVRPA
Lihan Yan, PhD	OBPV/DB
Qun Wang, PhD	OVRP/DVRPA
Ho-Hsiang Wu, PhD	OBPV/DB

Applicant Attendees:

Lindy Bancke	Head of Clinical Development, Rebiotix
Jonas Pettersson	Senior Medical Director, Ferring
Scott Berry	Senior Statistical Scientist, Berry Consultants
Bjarke Klein	VP Biometrics, Ferring
Hari Nagaradona (Parsippany)	VP US Regulatory Affairs, Ferring
Debbora Markus	Senior Director, Quality, Rebiotix
Lene Melchiorson	VP Global Regulatory Affairs, Ferring
Karen Kuphal	Senior Director, Regulatory Affairs, Rebiotix

Agenda:

CBER issued the Mid-Cycle Communication (MCC) agenda on May 24, 2022, stating that CBER does not have any substantive review issues to discuss at this time. Rebiotix proposed several questions and topics for discussion at the MCC Teleconference by email on May 16, 2022. CBER issued a response to the proposed topics on May 24, 2022. After receiving the response to their proposed questions and MCC agenda, Rebiotix requested additional clarification on the following topics:

1. The presentation of their safety information for the Advisory Committee meeting.
2. The platform for the Advisory Committee meeting itself, to prepare their IT infrastructure accordingly.
3. BLA Transfer from Rebiotix to Ferring (the parent company of Rebiotix).
4. Their dataset architecture, especially on the clinical datasets, to facilitate some of the questions they have been receiving.

Discussion Summary:

1. Any significant issues/major deficiencies, categorized by discipline, identified by the Review Committee to date.

There are no significant issues or major deficiencies identified at this time.

2. Information regarding major safety concerns.

There are no major safety concerns identified at this time.

3. Preliminary Review Committee thinking regarding risk management.

At this time, a REMS is not anticipated for this product.

4. Any information requests sent, and responses not received.
 - **IR#13 dated May 18, 2022: Request for CMC information regarding donor screening/testing protocols, product manufacturing/labeling protocol, potency assay, batch report information, storage condition, etc.**
 - **IR#15 dated June 17, 2022: additional analyses on Study 2014-01, 2017-01, and the integrated Bayesian analyses on the primary efficacy endpoint, etc.**

5. Any new information requests to be communicated.

None at this time.

6. Proposed date(s) for the Late-Cycle meeting (LCM).

- **The Late-Cycle Meeting (LCM) with the Applicant is scheduled for August 30, 2021.**
- **The LCM Materials are intended to be sent to the Applicant 10 days prior to the LCM.**

7. Updates regarding plans for the AC meeting.

The tentative advisory committee meeting date will be September 15 or 22, 2022. It will be a virtual meeting, and we will follow the timelines described in the *Guidance for Industry Advisory Committee Meetings – Preparation and Public Availability of Information Given to Advisory Committee Members* <https://www.fda.gov/media/75436/download>

8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates.

- **Labeling Comments: we intend to send our labeling comments no later than October 28, 2022.**
- **Action Due Date: we intend to take action on this application no later than November 30, 2022.**

9. Additional questions from the Applicant:

Applicant Question #1:

The Applicant requested clarification on the presentation of their safety information for the advisory committee meeting, as advised from Former FDA (external experts).

Meeting Discussion:

The Applicant stated that they would like to supplement the safety information in the Advisory Committee briefing package with additional safety information. They plan to add additional analysis of the safety data to include blinded and unblinded data from both controlled trials and open label studies. CBER advised the Applicant to submit this information as an amendment to the BLA. The Applicant agreed to submit the information for review.

Applicant Question #2:

The Applicant requested clarification on the platform for the Advisory Committee meeting itself, to prepare their IT infrastructure accordingly.

Meeting Discussion:

CBER stated that the Advisory Committee meeting would be a virtual format using Adobe Connect Platform. The presenters will use their camera during presentations and for follow-up questions. CBER advised the Applicant that they will provide training and assistance on the use of the software and platform prior to the advisory committee meeting. CBER also indicated that a communication will be sent closer to the date of the meeting.

Applicant Question #3:

BLA Transfer from Rebiotix to Ferring (the parent company of Rebiotix), we would like to clarify that Ferring already has a License number (and they are marketing some of the products under that license number). In this scenario, we would to clarify how long it takes for FDA to take action on the transfer BLA under the existing License number of Ferring.

Meeting Discussion:

CBER acknowledges that Ferring owns Rebiotix and has a license number for marketed products. However, a license transfer consists of multiple elements including but not limited to review of new labeling and facility compliance check. The review activities involve considerable work by multiple Offices in CBER, even when transferring to a company that already has other licensed products. CBER indicated that this request may

be submitted as a product correspondence after the original BLA is approved. CBER also informed the Applicant that there is no PDUFA timeline for this type of product correspondence and it may take up to several months. CBER/DMPQ indicated that they will provide a direct contact to assist with this transfer.

Applicant Question #4:

The Applicant asked for clarification on their dataset architecture, especially on the clinical datasets, to facilitate some of the questions they have been receiving (Biometrics/Statistics representative)

Meeting Discussion:

The Applicant stated that they have responded to Information Requests dated (#11 and #12). However, the revised tables created in response to these requests complicate the dataset. CBER stated that the review of these amendments is ongoing, and there are no further requests for clarification at this time.