Rebiotix Inc.

Protocol 2015-01

Statistical Analysis Plan

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Version 3.0, Date 01 Apr 2019

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An Open-label Efficacy and Safety Assessment of Rebiotix RBX2660 (microbiota suspension) for the Treatment of Recurrent *Clostridium difficile* Infection

Statistical Analysis Plan

Version 3.0, Date 01 Apr 2019

Revision History

Version	Date	Revision Author	Comments
[redacted]	[redacted]	[redacted]	[redacted]
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[redacted]	[redacted]	[redacted]	[redacted]

Contents

1 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
AE	adverse event(s)
ATC	anatomical therapeutic chemical
BLA	Biologics License Application
BMI	Body Mass Index (kg/m^2)
CI	confidence interval
CDI	*Clostridium difficile* infection
CSR	Clinical Study Report
eCRF	electronic case report form
FT	fecal transplant
HLGT	high level group term
HLT	high level term
IBS	irritable bowel syndrome
ICU	intensive care unit
IQR	interquartile range
LLT	lower level term
MedDRA	Medical Dictionary for Regulatory Activities
mL	milliliters
N	number of subjects
PT	preferred term
RBX2660	investigational drug product being evaluated
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
SF-36	36-item short form health survey instrument
SOC	system organ class
SOP	Standard Operating Procedure
TEAE	treatment-emergent adverse event
WHO	World Health Organization

2 INTRODUCTION

RBX2660 (microbiota suspension) is being studied for the treatment of adult subjects as an adjunct to antibiotics for the treatment of recurrent *Clostridium difficile* infection (CDI). The purpose of this study is to evaluate the efficacy and safety of RBX2660 for the treatment of recurrent CDI in subjects who have had either a) at least two recurrences after a primary episode (i.e., at least three episodes) and have completed at least two rounds of standard-of-care oral antibiotic therapy or b) have had at least two episodes of severe CDI resulting in hospitalization.

3 STUDY OBJECTIVES AND ENDPOINTS

3.1 Primary Objective

The primary objective of this study is to compare the efficacy, defined as the absence of CDI diarrhea without the need for retreatment with *C. difficile* anti-infective therapy or fecal transplant (FT) through 56 days after treatment, of one treatment with RBX2660 (one treatment consists of two enemas of RBX2660 7 ± 2 days apart) versus antibiotic-treated historical controls.

3.2 Secondary Objectives

The secondary objectives of this study are:

1. To evaluate the safety of RBX2660.
2. To evaluate the effect of RBX2660 on pre-existing conditions other than recurrent CDI.
3. To evaluate quality of life as measured by the SF-36 Health Survey.
4. To evaluate the efficacy of *C. difficile* anti-infection therapies administered to confirmed treatment failures.

3.3 Primary Endpoint

Efficacy, measured by the recurrence-free rate of CDI diarrhea without the need for retreatment with C. difficile anti-infective therapy or fecal transplant through 56 days after completion of

study treatment with RBX2660, will be evaluated by comparing the recurrence-free rate observed in the study population to the recurrence-free rate identified from antibiotic-treated historical controls.

3.4 Secondary Endpoints

The secondary endpoints for this study are:

1. The frequencies and severity grades of solicited AEs from the first day of assigned study treatment through seven days following the last enema of assigned study treatment will be collected.
2. Adverse events, including serious adverse events and the onset of new chronic diseases, will be collected at in-office visits at 1, 4, and 8 weeks and at 3-, 6-, and 12-month calls; they will be categorized by frequency, severity, seriousness, and causality.
3. Serious adverse events and new onset of chronic diseases will be collected at a telephone call at 24 months and will be categorized by frequency, severity, seriousness, and causality.
4. Frequencies of major complications of CDI including death, septic shock, toxic megacolon, colonic perforation, emergency colectomy, or ICU admission will be collected through the 24-month telephone assessment.
5. The effect of RBX2660 on pre-existing conditions other than recurrent CDI will be assessed by comparing the change in the condition throughout the course of the study.
6. SF-36 scores recorded at the Week 8 visit will be compared to scores recorded at the screening visit.
7. Efficacy of *C. difficile* anti-infection therapies administered to confirmed treatment failures will be compared to each other for the rates of success at resolving CDI diarrhea for at least 56 days after completion of the anti-infection therapy.

4 STUDY DESIGN

4.1 General Design

This is a prospective, multicenter, open-label study assessing the efficacy and safety of RBX2660 as an adjunct to antibiotics for the treatment of recurrent CDI. Up to approximately 150 subjects will be enrolled in this study and receive RBX2260. Approximately 100 historical controls will be chosen from a retrospective chart review of patients treated with antibiotics for recurrent CDI who match key inclusion/exclusion criteria from the study.

Subjects who meet all inclusion and exclusion criteria, including having a positive *C. difficile* test within 60 days prior to enrollment and experiencing either a) at least two recurrences after a primary episode (diagnosis must include at least one positive *C. difficile* test on record within 60 days prior to enrollment) and have completed at least two rounds of standard-of-care oral antibiotic therapy or b) have had at least two episodes of severe CDI resulting in hospitalization prior to enrollment, will receive open-label treatment with RBX2660. One study treatment consists of two RBX2660 enemas administered 7 ± 2 days apart; the second enema may be administered sooner if CDI diarrhea reoccurs in less than 7 days. Subjects will already be taking or will start a course of antibiotics to control recurrent CDI diarrhea at the time of enrollment, [redacted] An in-office follow-up visit will occur at 8 weeks after completing study treatment for the assessment of AEs, efficacy, collection of the Subject Diary, and blood tests. Telephone assessments for AEs including serious adverse events (SAEs) and the new onset of chronic diseases and CDI symptoms will occur at weeks 1, 2, 3, and 4 and at 3, 6, and 12 months after completing study treatment. Assessment of serious adverse events and the new onset of chronic diseases will occur via phone call at 24 months after completing study treatment. Subjects will keep a detailed Subject Diary to assess for solicited adverse events from the date of enrollment to one week after completing study treatment (second enema). Treatment

failures (as determined by the site investigator at the time of CDI recurrence) are eligible to receive another therapy deemed most appropriate by their study investigator.

[redacted]

4.1.2 Definition of CDI Diarrhea

Clostridium difficile diarrhea is defined as the passage of ≥ 3 watery stools in 24 or fewer consecutive hours for at least two consecutive days.

4.1.3 Definition of Treatment Success

Treatment success is defined as the absence of CDI diarrhea without the need for retreatment with *C. difficile* anti-infective therapy or FT through 56 days after completion of study treatment.

4.1.4 Definition of Treatment Failure (CDI Recurrence)

Treatment failure (CDI recurrence) is defined as: 1) the presence of CDI diarrhea (see Section 4.1.2), with or without other CDI symptoms, < 56 days after administration of the last assigned study enema; 2) a positive stool test for *C. difficile*; 3) need for retreatment for *C. difficile* infection; and 4) no other cause for CDI symptoms has been determined. [redacted]

[redacted]

4.1.5 Management of Treatment Failures

Treatment failures (as determined by the site investigator at the time of CDI recurrence) are to be treated with another therapy(ies) deemed most appropriate by their study investigator.

4.1.6 Determination of Treatment Success/Failure

The site investigator makes the determination of success based on the absence of CDI diarrhea without the need for retreatment with *C. difficile* anti-infective therapy or FT at less than 56 days after administration of the last assigned study enema[redacted]

[redacted]

4.2 Discussion of Study Design

Screening will be performed before treatment and will include demographics, a complete medical history, a review of inclusion/exclusion criteria, stool and blood testing, a modified physical exam, Form SF-36 completion, vital signs, Subject Diary recording, and urine pregnancy test for all females of childbearing potential.

The target population is adults (≥ 18 years old) with recurrent CDI who have had either a) at least two recurrences after a primary episode [redacted] and have completed at least two rounds of standard-of-care oral antibiotic therapy or b) have had at least two episodes of severe CDI resulting in hospitalization.

For study entry, recurrent CDI is defined as a documented diagnosis of recurrent CDI (recurrence of CDI symptoms for at least two consecutive days that begins less than 8 weeks after completion of CDI treatment) and at least one positive stool test for the presence of *C. difficile* on record within 60 days prior to enrollment.

4.3 Blinding

This is an open-label study; no blinding will be employed.

4.4 Method of Assignment of Subjects to Treatment Arms

This study consists of a single prospective treatment arm, to which all eligible subjects are assigned. A historical control arm, consisting of patients treated with antibiotics for recurrent CDI, will also be used for efficacy analysis. [redacted] No randomization is employed in this study.

4.5 Determination of Sample Size

Approximately up to 150 subjects will be enrolled in this study and receive RBX2660; and another 100 historical controls with recurrent CDI diarrhea will also be included in the study based on a retrospective chart review.

The primary analysis will compare the proportion of subjects in the treatment arm who are recurrence-free to the proportion of historical controls who are recurrence-free. [redacted]

[redacted]

4.7 Treatment Arms

The open-label study consists of a single prospective treatment arm and historical control group, as described below.

- One treatment with RBX2660: one treatment consists of two enemas of RBX2660 administered 7 ± 2 days apart (the second enema may be administered sooner if CDI diarrhea reoccurs in less than 7 days). [redacted]
- Historical control group chosen from a retrospective chart review.

5 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

5.1 Changes in the Conduct of the Study

The SAP was previously updated to allow an historical control arm of approximately 100 subjects to be included in the study. These subjects were chosen from retrospective chart reviews to obtain a closely matched data set of the standard of care antibiotic treatment for recurrent CDI to the RBX2660 treated subjects based on a number of baseline factors. The historical control arm allows for efficacy comparisons to be performed.

6 BASELINE, EFFICACY AND SAFETY EVALUATIONS

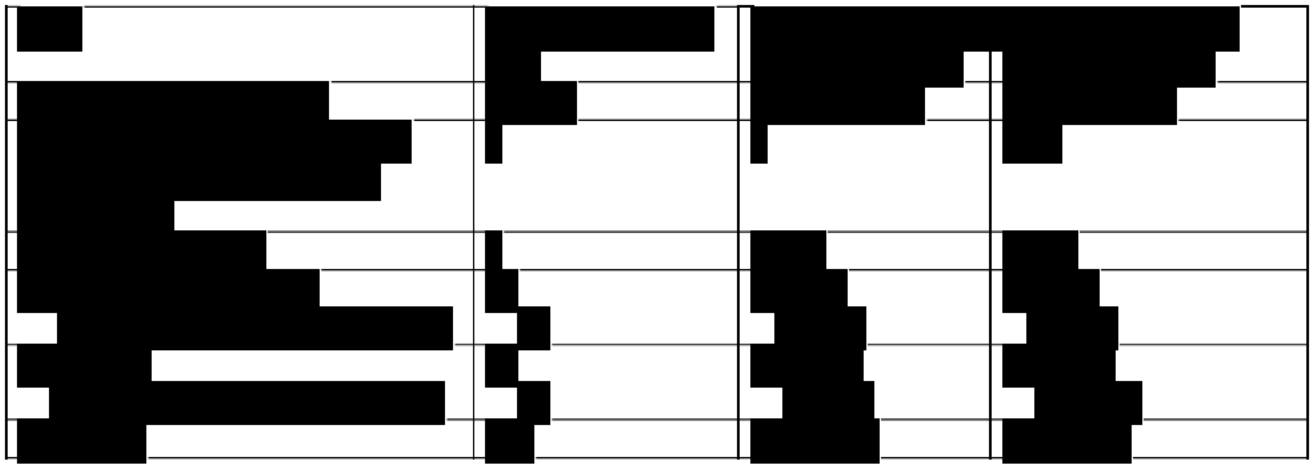
6.1 Schedule of Events

Activity	Visit 1 Screening	Visit 2 Baseline/ First Enema	Visit 3 Second Enema 7 ± 2 days after Visit 2	Visit 4 8-Week (± 7 days)	Phone Assessment (Weeks 1, 2, 3, and 4 (± 3 days))[2]	Phone Assessment at 3, 6, 12, and 24 months (± 7 days) after Visit 3[3]
Informed consent obtained	X					
Demographics, medical history	X					
Prescribe/continue antibiotics for CDI symptom control	X					
[redacted]						
Pregnancy testing performed	X	X	X			
Form SF-36 administered						
Inclusion/exclusion criteria confirmed	X	X				
[redacted]						
RBX2660 administered		X	X			
Recurrence of CDI symptoms assessed		X	X	X	X	X
Vital signs assessed	X	X	X	X		
Subject Diary reviewed and collected[1]	X[1]	X[1]	X[1]	X[1, 5]		
Concomitant medications	X	X	X	X	X	X
AEs/SAEs assessed	X	X	X	X	X	X
Review of Pre-existing Conditions				X		X

[1] Solicited AEs are collected through 7 days after last treatment with RBX2660. Review the Diary at each visit and collect completed pages at Visits 2, 3, and 4.

[redacted]

[redacted]



[redacted]

[redacted]

6.3 Analysis Populations

Enrolled Population: includes all subjects enrolled into the study, including subjects in the historical control arm.

Safety Population: includes all subjects enrolled into the study who received any study treatment with RBX2660; this does not include subjects in the historical control arm.

Full Analysis Set (FAS) Population: includes the Safety Population and subjects in the historical control arm.

Evaluable Population: includes the FAS subjects who were evaluable for treatment outcome (e.g., exclude subjects that discontinued from the study prior to determination of treatment failure and were not followed for at least 56 days (day 49 – 63) after the last treatment date).

Per Protocol Population: includes subjects from the Evaluable Population, excluding:

- Subjects from the Safety Population that did not complete 2 enemas

- Subjects that received fecal microbiota transplant before the 8-week follow-up and lacked a documented recurrence of CDI (Treatment Failure eCRF)
- Violations to the inclusion or exclusion criteria, including protocol definition of recurrent CDI two hospitalizations for CDI or 3 recurrent CDI events
- Received prohibited medication during the 8-week follow-up period

6.4 Safety Variables

Safety variables to be evaluated in the study include:

- Adverse events (AEs)
- Serious adverse events (SAEs)
- Solicited AEs
- Frequency of major complications of recurrent CDI including death, septic shock, toxic megacolon, colonic perforation, emergency colectomy, or ICU admission.

6.4.2 Adverse Events

An adverse event (AE) is any untoward medical occurrence associated with the use of RBX2660, whether or not the event is considered product-related. Pre-existing conditions that worsen in frequency, intensity or character of the condition during study participation will be recorded as an AE. Adverse events will be recorded for each subject from the day of enrollment through the 12-month phone call. Serious adverse events (SAEs) and the new onset of chronic diseases will be recorded for each subject from the day of enrollment through the duration of the study.

6.4.2.1 Adverse Event Dictionary

Adverse events and SAEs will be classified by the Medical Dictionary for Regulatory Activities (MedDRA) [redacted]

6.4.2.2 Adverse Event Severity

The severity of AEs will be graded as mild, moderate, severe, or potentially life-threatening. The severity grade of events for which the investigator does not record severity will be categorized as "Unknown" for tabular summaries and data listings, and will be considered the least severe for the purposes of sorting for data presentation. For summaries by severity grade, if a subject has multiple events occurring in the same SOC or PT, then the most severe event will be selected.

6.4.2.3 Relationship of Adverse Events to Study Treatment

Causal relationship of an AE to RBX2660, the enema procedure, *C. difficile* disease, and/or a pre-existing condition will be classified by the investigator as definite, probable, possible, or unrelated. Related events will include AEs that are classified as definitely, probably or possibly related. Events for which the investigator does not record causal relationship will be considered "Related" for tabular summaries and data listings.

6.4.2.4 Treatment-Emergent Adverse Events

Adverse events will be considered treatment-emergent adverse events (TEAE) according to the following algorithm, and will be applied to the Full Analysis Set population:

- If the complete onset date of an AE is known, then:
  - If the AE onset date is prior to initial treatment date, then the AE will not be considered treatment-emergent.
  - If the AE onset date occurs on or after initial treatment date, then the AE will be considered treatment-emergent.
- If the AE onset date is partially known, then:
  - If day is unknown, and month/year occur on or after the first enema month/year, then the AE will be considered treatment-emergent. Otherwise, the AE will not be considered treatment-emergent.
  - If month/day is unknown, and year occurs on or after first enema year, then the AE will be considered treatment-emergent. Otherwise, the AE will not be considered treatment-emergent.
- If the onset date of an AE is unknown, then the following rules will apply:
  - If the AE resolution date is after the initial treatment date or ongoing, then the AE will be considered treatment-emergent.
  - If the AE resolution date is before the initial treatment date, then the AE will not be considered treatment-emergent.

- If both the onset and resolution dates are unknown, then the AE will be considered treatment-emergent.

6.4.3 Other Observations Related to Safety

6.4.3.1 Solicited Adverse Events

The following list of anticipated adverse events is solicited from subjects via the Subject Diary from the date of enrollment through the 7th day after receiving the last study treatment.

- gas (flatulence)
- abdominal distension or bloating
- rectal irritation or pain
- chills/severe shivering
- abdominal pain or cramping
- increased diarrhea
- constipation
- rectal bleeding
- nausea
- vomiting
- fever ≥ 38.0° C (100.4°F)

Frequency and severity of the solicited AEs will be recorded in the Subject Diary.

6.4.3.2 Major Complications of Recurrent CDI

The frequencies of major complications of recurrent CDI including death, septic shock, toxic megacolon, colonic perforation, emergency colectomy, or ICU admission will be collected through the 24-month telephone assessment.

6.4.3.3 Pre-existing Conditions

A pre-existing condition is one that is present at the start of the study and is to be recorded at the time of the screening or baseline visits. Pre-existing conditions are assessed at the 3-, 6-, 12-, and 24-month telephone assessments. The assessment of pre-existing conditions includes discussion with the subject to determine if the condition improved, unchanged, worsened or resolved since completion of study treatment.

6.5 Efficacy Variables

The efficacy variables include the following:

- Treatment success, defined as the absence of CDI diarrhea without the need for retreatment with *C. difficile* anti-infective therapy or fecal transplant (FT) through 56 days after administration of the last study enema.
- SF-36 scores obtained at the 8-week assessments visits as compared to those obtained at the Screening visit.

7 STATISTICAL METHODS

7.1 General Methodology

All statistical tests will be performed using SAS® [redacted]. For continuous variables, descriptive statistics (number of subjects [N], mean, standard deviation [SD], median, inter-quartile range [IQR], minimum, and maximum) will be generated. For discrete/categorical variables, the number and percentage of non-missing subjects will be generated. Descriptive statistics will be provided for all subjects. [redacted] Subject listings of all data from the eCRFs as well as any derived variables will be presented.

[redacted]

7.3 Handling of Dropouts or Missing Data

The safety assessment will be analyzed using all available data only. No imputation of missing data is planned for the safety assessment.

Efficacy assessments will also be analyzed using all available data. If there are treated subjects with missing efficacy data by 56 days [redacted] after completion of study treatment (e.g., subject discontinues study prior to evaluation of treatment outcome), the subject's treatment outcome will be listed as "missing", and for the primary analysis purpose will be handled as a treatment failure. [redacted]

7.4 Medical Monitor Adjudication

An independent Medical Monitor reviews all serious adverse events and adverse events of interest to provide an objective, qualified judgment of the events. The Medical Monitor is a physician not participating as an investigator in this study. The Medical Monitor has the responsibility to review and evaluate the information relevant to product safety throughout the development and implementation of the protocol. The Medical Monitor performs the following functions:

- Reviews and adjudicates SAEs and AEs of interest;
- Reviews the study protocol and Investigator's Brochure for adequacy of safety oversight;
- Confers with site investigators and the Rebiotix Clinical Department regarding potential safety concerns as needed;
- Provides medical surveillance and provides appropriate recommendations for the conduct of the study as needed.

7.5 Interim Analyses

Efficacy and safety analyses will be conducted when approximately 100 enrolled subjects complete their 8-week assessment. The study will not be stopped based on the efficacy results.

[redacted]

[redacted]

7.8 Examination of Subgroups

Subgroup analysis of age (< 65 years, ≥ 65 years), sex (Female, Male), ethnicity (Hispanic or Latino, or Not Hispanic or Latino), race group (American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, and Other, as well as White and Non-white), and number of previous episodes of CDI recurrence at baseline will be conducted on the efficacy and safety analysis.

8 STATISTICAL ANALYSIS

8.1 Disposition of Subjects

A summary table will present subject disposition for all subjects. The table will show the number of RBX2660 treated subjects enrolled and the number of enrolled subjects not treated followed by the number of subjects in the study population as well as the number of historical controls included in the study. [redacted]

Discontinuation will be categorized by reason as a percentage of the number of all subjects in study population.

[redacted]

8.3 Baseline Assessments

Baseline assessments are collected within 30 days before study treatment administration. Summaries for age (years), sex, ethnicity, and race will be provided for the Full Analysis Set. Baseline BMI and employment status will also be summarized. *C. difficile* infection history will be summarized by total number of episodes and by each episode. The following will be summarized for each episode of CDI: duration (days), treatment administered, hospitalization with duration (if applicable) and available *C. difficile* test results.

For Form SF-36, the results obtained at the Screening visit will be used for the baseline assessment.

[redacted]

8.4 Demographic and Other Baseline Characteristics

All baseline summaries will be based on the Full Analysis Set and the Enrolled populations. Descriptive statistics (number of subjects [N], mean, standard deviation [SD], median, interquartile range [IQR], minimum, and maximum for continuous variables and number of

subjects [N] and the percentage for categorical variables) will be provided for all baseline measures.

8.5 Prior and Concomitant Therapy

The World Health Organization (WHO) Drug Dictionary [redacted] will be used to classify medications by preferred term and WHO Anatomical Therapeutic Chemical (ATC) level-4 classification of ingredients. Listings of all concomitant medications will be made by WHO ATC classification of ingredients and by preferred term.

8.6 Analysis of Safety

The Full Analysis Set will be used to summarize all adverse event data, unless otherwise specified. The method of analyzing adverse event is described [redacted]. Adverse events from the historical control subjects will be summarized and will be included in listings.

8.6.1 Adverse Events

A summary of adverse events, TEAEs, non-serious TEAEs, and serious TEAEs will be summarized using counts of the number of events and frequencies (counts and percentages) of the number of subjects in the Full Analysis Set. The frequency of each preferred term (PT) within the primary system organ class (SOC) as well as overall primary SOC frequency will be presented. A subject with multiple events coded to the same PT within a primary SOC will be counted only once for the PT within the primary SOC. Likewise, a subject with multiple events coded to the same SOC will be counted only once within the SOC. Adverse events and serious adverse events will also be summarized by onset timepoint by system organ class (SOC) and preferred term (PT): [redacted] Adverse events will be counted in the interval in

which the start date of the event occurs. For subjects with multiple instances of the same event, the events will be counted once within each interval that the event starts.

An overall summary of AEs will present the frequency of all TEAEs, serious TEAEs, and TEAEs leading to death for the Full Analysis Set, as well as the frequency of the following for the RBX2660 treatment group:

- TEAEs related to RBX2660
- TEAEs related to enema procedure
- TEAEs related to *C. difficile* disease
- TEAEs related to a pre-existing condition
- Serious TEAEs related to RBX2660
- Serious TEAEs related to the enema procedure
- Serious TEAEs related to *C. difficile* disease
- Serious TEAEs related to a pre-existing condition.

Frequency of occurrence and number and percentage of subjects experiencing an event will be presented by SOC and PT using the Safety Population for the following:

- TEAEs by maximum severity
- TEAEs by relatedness to RBX2660
- TEAEs by relatedness to *C. difficile* disease
- TEAEs by relatedness to enema procedure
- TEAEs by relatedness to pre-existing condition
- Serious TEAEs
- Serious TEAEs by maximum severity
- Serious TEAEs by relatedness to RBX2660
- Serious TEAEs by relatedness to *C. difficile* disease
- Serious TEAEs by relatedness to enema procedure
- Serious TEAEs by relatedness to pre-existing condition

For the summary of AEs by maximum severity, if a subject has multiple events occurring in the same SOC or same PT, then the event with the highest severity will be counted. For AEs reported by causality, if a subject has multiple events occurring in the same SOC or same PT, the event with the highest association will be summarized.

A summary of TEAE and serious TEAE characteristics (severity, relatedness to RBX2660, relatedness to *C. difficile* disease, relatedness to enema procedure, and relatedness to pre-existing condition by outcome) will be presented for the Safety Population.

A summary of TEAE and serious TEAE characteristics (severity, relatedness to RBX2660, relatedness to *C. difficile* disease, relatedness to enema procedure, and relatedness to pre-existing condition by outcome) by SOC will also be presented for the Safety Population.

For data presentation, SOC will be ordered alphabetically, with PT sorted by decreasing total frequency. No inferential statistics will be provided for the AE data.

Subject listings will be presented for all AEs and for SAEs.

8.6.2 Other Analyses Related to Safety

8.6.2.1 Subject Diary including Solicited Adverse Events and Compliance

All solicited adverse events recorded in the Subject Diary will be summarized utilizing frequencies, proportions and 95% CIs for categorical variables and using the descriptive statistics as listed in Section 7.1 for continuous variables.

For each solicited event, severity scores will be summarized as both categorical and continuous values. For continuous summaries, severity scores will be identified as either pre-treatment or post-treatment, and the average for each period will be calculated across individual subjects.

Baseline for continuous summaries will be considered the average during the pre-treatment period. For categorical summaries, if a subject reports more than one severity score on the same date, the maximum severity will be used. Baseline for categorical summaries will be considered the last non-missing assessment prior to the first enema.

For each categorical summary of event frequency, a two-sided 95% CI will be calculated using the normal approximation of the binomial.

The following summaries will be produced relative to both the first and second enema:

- Frequency of severity scores on day of enema administration
- Frequency of severity scores on day 1 through day 7 post-treatment
- Frequency of maximum post-treatment severity score

The following summaries will be produced:

- Summary of average severity score and change from baseline
- Shift from baseline to 7-day post-treatment severity score
- Shift from baseline to maximum post-treatment severity score

Compliance in returning the Subject Diary will be calculated by dividing the number of diaries turned in, whether complete or not, by the number of diaries expected to be turned in. Furthermore, compliance will be summarized by calculating the proportion of subjects who turned in "complete" diaries, where complete is defined as answering all 14 daily questions for at least 80% of the expected number of diaries.

8.6.2.2 Major Complications of Recurrent CDI

Major complications of recurrent CDI include death, septic shock, toxic megacolon, colonic perforation, emergency colectomy, or ICU admission collected through the 24-month telephone assessment. Incidence of major complications of recurrent CDI will be summarized in a table.

A listing of all major complications recurrent CDI throughout the study will be generated.

[redacted]

8.7 Analysis of Efficacy

8.7.1 Treatment Success

Treatment success is the primary efficacy endpoint and the analyses will be performed on the Evaluable Population. The primary endpoint will be summarized by frequencies and percentages [redacted] The analysis of efficacy will be repeated using the Full Analysis Set and Per Protocol populations. Sensitivity analyses will also be conducted using the Full Analysis Set where missing responses are imputed using a best-case scenario where missing responses are treated as successes.

[redacted]

8.7.2 Change from Baseline SF-36 scores at 8-week assessment visit

Eight subscales of the SF-36 (PF: Physical Functioning, RP: Role Physical, BP: Bodily Pain, GH: General Health, VT: Vitality, SF: Social Functioning, RE: Role Emotional, MH: Mental Health) and two summary component measures (PCS: Physical Component Summary, MCS: Mental Component Summary), and their changes from the baseline values collected at the Screening visit will be summarized using descriptive statistics for the Safety Population. Change from baseline of SF-36 scores will summarized at the scheduled 8-week visit using the Safety Population.

[redacted]

9 COMPUTER SOFTWARE

All analyses will be performed [redacted] All summary tables and data listings will be prepared utilizing SAS® software.