CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 14-0029
Study Title:
Phase II-b Randomized Double-Blind Placebo-Controlled Trial of *Lactobacillus crispatus* CTV-05 (LACTIN-V) to Prevent the Recurrence of Bacterial Vaginosis

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Version 1.0

DATE: 11-MAY-2018

Study Title

Protocol Number Code:	DMID Protocol: 14-0029
Development Phase:	Phase 2b
Products:	LACTIN-V
Form/Route:	Intravaginally
Indication Studied:	Bacterial Vaginosis
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	28APR2018
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This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BP	Blood Pressure
BUN	Blood Urea Nitrogen
C	Celsius
CI	Confidence Interval
CRF	Case Report Form
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
EDC	Electronic Data Capture
ELISA	Enzyme-linked Immunosorbent Assay
ER	Emergency Room
F	Fahrenheit
GGT	Gamma Glutamyl Transferase
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
ITT	Intention to Treat
L	Liter
LLN	Lower Limit of Normal
mcg	Microgram
MedDRA®	Medical Dictionary for Regulatory Activities
mEq	Milliequivalent
mg	Milligram
mITT	Modified Intention to Treat
mL	Milliliter
MAR	Missing at Random
MCAR	Missing Completely at Random
MNAR	Missing Not at Random

N	Number (typically refers to subjects)
NIH	National Institutes of Health
PI	Principal Investigator
PP	Per Protocol
PT	Preferred Term
RBC	Red Blood Cell
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee
SOC	System Organ Class
SOP	Standard Operating Procedures
U	Units
ULN	Upper Limit of Normal
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "Phase II-b Randomized Double-Blind Placebo-Controlled Trial of *Lactobacillus crispatus* CTV-05 (LACTIN-V) to Prevent the Recurrence of Bacterial Vaginosis" (DMID protocol 14-0029) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for efficacy and safety outcomes, and (4) a list of proposed tables and figures. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

Bacterial vaginosis (BV), characterized by an imbalanced vaginal flora deficient in naturally occurring acid-producing lactobacilli, is one of the most frequent vaginal infections and affects about 15–50% of reproductive aged women globally [1]. Following standard antibiotic treatment of BV, 20–75% of women relapse within 1–3 months [2, 3]. The high risk of recurrence and sequelae suggests that investigational studies of new agents like live biotherapeutic products [4] may be effective for the improved treatment and prevention of BV.

Reconstituting a normal, *Lactobacillus*-predominant vaginal flora has been promoted for many years as a microbial defense against pathogens. The vaginal live biotherapeutic product *Lactobacillus (L.) crispatus* CTV-05 (LACTIN-V) was developed by Osel, Inc. in Mountain View, California, and is designed to replenish the vaginal lactobacilli population following conventional antibiotic treatment with MetroGel® (topical metronidazole gel 0.75%). The product contains a naturally occurring vaginal strain of *L. crispatus* CTV-05, preserved as a powder applied by a vaginal applicator. Since the *Lactobacillus* strain used in LACTIN-V is a commensal organism normally present in the vagina associated with vaginal health, the product has an excellent pre-clinical and clinical safety profile.

Early studies of LACTIN-V administered the product in gelatin-coated capsules. The University of California, San Francisco (UCSF) and Osel hypothesized that the efficacy of LACTIN-V to prevent BV recurrence could be improved by increasing the vaginal colonization rate of *L. crispatus* CTV-05. In order to achieve this, a vaginal applicator was developed capable of delivering a higher dose of LACTIN-V powder (up to 2×10^9 cfu/dose) directly to the vagina without the impediment of a gelatin capsule, which was found to dissolve slowly in the vaginal environment.

Collecting a larger body of data on colonization and efficacy of unmodified *Lactobacillus* strains to prevent BV recurrence will greatly contribute to the efforts of developing unmodified as well as genetically modified Lactobacillus strains as a multipurpose technology for the prevention of HIV-1 and other genital tract infections.

CTV-05 is a strain of *L. crispatus*, a gram-positive rod isolated from the vagina of a healthy woman. *L.crispatus* is found naturally in the vaginas of healthy women and is commonly found as a component of the natural human intestinal flora. Unlike most commercially available strains of *Lactobacillus*, CTV-05 adheres well to vaginal epithelial cells and is capable of colonizing the vaginal epithelium.

LACTIN-V administered as a capsule has been tested in four trials (LV 001-004) with a dose level up to 5×10^8 cfu/capsule. Since the dose of 5×10^8 cfu/capsule resulted in colonization rates lower than desired, several changes to the study product were made. The higher dose of 2×10^9 cfu/dose delivered via vaginal applicator as dried powder directly into the upper vaginal vault has been tested in a Phase 1 trial (LV-005) in 12 healthy women and subsequently in a Phase II-a trial (LV-006) in 24 women with BV.

Based on the achieved colonization rate of L. crispatus CTV-05 at 2×10^9 cfu/dose of LACTIN-V, coupled with prior data from the Phase II-a clinical trial suggesting that vaginal colonization with *L. crispatus* CTV-05 was associated with a reduced risk of BV recurrence, this Phase II-b trial is designed to provide a screening evaluation for the hypothesis that, following a 5-day course of MetroGel to treat BV, LACTIN-V administered at 2×10^9 cfu/dose using a vaginal applicator reduces the 12-week incidence of BV recurrence by ≥50% when compared to placebo. This study follows the 2015 CDC Sexually Transmitted Diseases Treatment Guidelines as well as the 2013 Food and Drug Administration (FDA) draft guidance for the use of metronidazole gel and the 2016 FDA draft guidance for BV and uses a combined requirement of at least 3 of 4 Amsel criteria and a Nugent score of 4-10.

2.1. Purpose of the Analyses

These analyses will assess the efficacy and safety of repeated doses of LACTIN-V in comparison with the placebo and will be included in the clinical study report.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Objectives

1. To estimate the efficacy of repeated doses of LACTIN-V (2 x 10^9 cfu/dose) as compared to placebo in preventing BV recurrence by 12 weeks following treatment of BV with MetroGel.
2. To assess the safety of LACTIN-V over 24 weeks by comparing the incidence of adverse events (AEs) between individuals randomized to LACTIN-V or placebo.

3.1.2. Secondary Objectives

1. To investigate the colonization of LACTIN-V (presence of *L. crispatus* CTV-05 in the vaginal specimen) and fluctuations over 12 weeks, in relation to menses and sexual intercourse.
2. To evaluate user acceptability and tolerability of LACTIN-V over 12 weeks, including perceptions around method of delivery and dosing.
3. To measure long-term colonization of LACTIN-V at 24 weeks (12 weeks after last dosing).
4. To estimate the long-term efficacy of repeated doses of LACTIN-V (2 x 10^9 cfu/dose) as compared to placebo in preventing BV recurrence at 24 weeks (12 weeks after last dosing).

3.1.3. Exploratory Objectives

1. To estimate the efficacy of repeated doses of LACTIN-V (2 x 10^9 cfu/dose) as compared to placebo in preventing repeated (more than one) episodes of BV recurrence up to 12 weeks following treatment of BV with MetroGel.

3.2. Endpoints

3.2.1. Primary Efficacy Outcome Measure

1. The proportion of subjects with a positive BV diagnosis in each study arm by Visit 4 (Week 12, Day 84).

3.2.2. Primary Safety Outcome Measure

1. The proportion of subjects reporting product-related AEs and SAEs in each study arm through Visit 7 (Week 24, Day 168).

3.2.3. Secondary Outcome Measures

1. The proportion of subjects experiencing successful colonization with L. crispatus CTV-05 following dose of study product through Visit 4 (Week 12, Day 84) in the LACTIN-V arm, overall and by occurrence of menses and intercourse.
2. *(Acceptability of LACTIN-V and the applicator):* The proportion of subjects who are compliant with the complete dose regimen in each study arm as assessed by subject reporting and applicator staining.
3. *(Tolerability of LACTIN-V and the applicator):* The proportion of subjects who discontinue study product early in each study arm due to adverse events.

4. *(Acceptability of LACTIN-V and the applicator):* Self-administered questionnaires about acceptability of the study product in each study arm.
5. The proportion of subjects experiencing successful colonization with L. crispatus CTV-05 following dose of study product at Visit 7 (Week 24, Day 168) in the LACTIN-V arm, overall and by occurrence of menses and intercourse.
6. The proportion of subjects with a positive BV diagnosis in each study arm by Visit 7 (Week 24, Day 168).

3.2.4. Exploratory Outcome Measures

1. The number of BV recurrences per 12 weeks of follow-up.
2. The probability of BV recurrence during the 12 weeks of follow-up.

3.3. Study Definitions and Derived Variables

3.3.1. BV Diagnosis

The Amsel criteria and Nugent score will be used to diagnose BV.

During a pelvic examination, presence of the following Amsel criteria will be determined:

a. Homogeneous, thin, grayish-white discharge that smoothly coats the vaginal walls
b. Vaginal pH > 4.5
c. Positive whiff-amine test, defined as the presence of a fishy odor when a drop of 10% potassium hydroxide (KOH) is added to a sample of vaginal discharge
d. Presence of clue cells (>20%) on microscopy

A vaginal swab for assessment of BV by Nugent criteria will be performed. The Nugent score utilized a 0-10-point scale for evaluation of vaginal flora. The Nugent score is interpreted as follows:

- 0-3 Normal
- 4-6 Intermediate
- 7-10 BV

A positive diagnosis of BV is defined by the presence of at least three of the Amsel criteria and a Nugent score of 4 or greater.

3.3.2. Recurrent BV

By standard definition, a treatment of BV is only considered to have failed if Amsel criteria or Nugent score on Gram stain diagnose BV to persist at 22-30 days after the initiation of the antibiotic treatment. As a result, women who continue to have BV during the enrollment visit will not be re-treated with MetroGel at the time of enrollment, as additional time is needed for BV to resolve after antibiotic treatment. Thus, they are not considered treatment failures at this time (approximately 2 days after termination of antibiotic treatment). All BV diagnoses following enrollment are considered incident, as they occur at least 22-30 days after the commencement of MetroGel treatment and consequently are treatment failures or new infections. And so, a positive diagnosis of BV at any visit after the enrollment visit will be considered a recurrence of BV (i.e. there

is no distinction between treatment failure and new infection). A positive diagnosis of BV at the enrollment visit will not be considered a recurrence of BV.

3.3.3. Successful Colonization of *L. crispatus*

Colonization of *L. crispatus* will be determined from the concentrations of *L. crispatus* species and *L. crispatus* CTV-05 obtained from qPCR. Successful colonization is defined as follows:

- If CTV-05 concentration is above the lower limit of detection (LLOD) and the *L. crispatus* is above the LLOD, then successful colonization has occurred.
- If either CTV-05 or *L. crispatus* concentration is below LLOD or indeterminate, then successful colonization has not occurred.

The LLOD for CTV-05 is 660 copies/mL and the LLOD for *L. crispatus* is 953 copies/mL.

3.3.4. Baseline Value

The baseline value for most variables will be defined as the last value obtained prior to the first dose of LACTIN-V or placebo. As noted in Section 3.3.2, for BV recurrence, the baseline BV diagnosis will be the diagnosis at the screening visit.

3.3.5. Treatment Compliance

All subjects are to receive a total of 25 doses of study product. The first dose is administered in clinic and the remaining doses will be administered by the subject at home. A subject is compliant with the assigned study product if she takes at least 75% of the scheduled doses prior to the first diagnosis of BV or through Visit 4 (Week 12, Day 84), whichever occurs first. Compliance will be assessed by applicator staining of the returned kit. If a kit is not returned, compliance will be assessed by the subject's self-report (e.g. via the memory aid). If an incomplete kit is returned or staining results are indeterminate, the subject's self-report will be used in conjunction with the count of stained applicators to determine subject compliance.

Compliance is assessed on a weekly basis, so for subjects who are not compliant per the definition above, the time (week) at which the subject became non-compliant will be determined. The time of non-compliance will be defined as the first week at which the cumulative proportion of doses taken drops below 75% of the scheduled doses up to that week.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase II-b multicenter randomized double-blind placebo-controlled trial to assess the efficacy of repeated doses of LACTIN-V compared to placebo in preventing BV recurrence in women diagnosed with BV. The study will also assess the safety of LACTIN-V by comparing the incidence of AEs between women randomized to LACTIN-V or placebo. The study plans to enroll 228 sexually-experienced, pre-menopausal women age 18 to 45 years. Women will be randomized 2:1 to receive LACTIN-V or placebo. Women will be consented and will have a history and physical examination to include a pelvic exam with STI diagnostics and testing for BV. Potentially eligible women with Amsel criteria ≥3 will have a vaginal smear sent to a central laboratory for Gram stain evaluation by Nugent score. Blood will be obtained for HIV and syphilis serologies, a vaginal swab for gonorrhea, chlamydia and trichomonas molecular testing, and urine for βhCG. Potentially eligible women will start a standard 5-day course of MetroGel. Table 1 provides the study schematic.

Women will return to the study clinic within 2 days after completing the 5-day course of MetroGel to re-evaluate eligibility criteria and review the BV test results from the screening visit. Women with Amsel criteria ≥3 and Nugent score 4-10 will be randomized and instructed to administer the LACTIN-V or placebo at home for 5 consecutive days and then twice weekly for 10 weeks.

LACTIN-V (or placebo) will be administered at 2 x 10^9 cfu/dose using a vaginal applicator. Women will complete a memory aid to record times of product application, menses, sexual intercourse, concomitant medications, condom use and any AEs. Reminders will be sent to women in order to increase adherence with all doses and prior to scheduled follow-up visits. Women will complete either a paper or electronic memory aid. If the electronic version of the memory aid is utilized by the subject, the study clinic will be alerted of any potential AEs reported by the subject for subsequent clinical evaluation, follow-up and reporting as deemed necessary.

Follow-up visits are scheduled 4, 8, 12, and 24 weeks after enrollment. A memory aid to gauge symptoms and AEs will be reviewed, a questionnaire to collect clinical, including AEs, data will be administered and a pelvic exam will be performed to detect genital tract AEs. Vaginal swabs for wet mount evaluation (Amsel criteria) and Gram stain evaluation (Nugent score) will be collected. A vaginal swab for *L. crispatus* (including CTV-05) identification will be collected. Vaginal applicators will be collected at Visits 2, 3, and 4 and stained with Trypan Blue upon return to the site as a proxy for product use. Telephone interviews will be scheduled between the 12 and 24 week visits, at 16 and 20 weeks after enrollment. Table 2 presents the schedule of events for each visit.

The DSMB met on 02JUN2017 after one-third of the 228 subjects completed Study Visit 2 (Week 4) to review aggregate safety data for increased rate of occurrence of serious suspected adverse reactions. The DSMB will also meet annually to assess safety data on each arm of the study. There are no formal planned interim analyses of efficacy.

4.2. Discussion of Study Design, Including the Choice of Control Groups

This Phase II-b trial is designed to provide a screening evaluation for the hypothesis that, following a 5-day course of MetroGel to treat BV, LACTIN-V administered at 2 x 10^9 cfu/dose using a vaginal applicator reduces the 12-week incidence of BV recurrence by ≥50% when compared to placebo. Based on the achieved colonization rate of *L. crispatus* CTV-05 at 2 x 10^9 cfu/dose of LACTIN-V, coupled with prior data from the

Phase II-a clinical trial suggesting that vaginal colonization with L. crispatus CTV-05 was associated with a reduced risk of BV recurrence, the next logical step is to perform a larger Phase II-b trial. A placebo is used since MetroGel alone is the standard antibiotic treatment.

4.3. Selection of Study Population

Subjects must meet all the inclusion criteria in order to be eligible to participate in the study:

1. Capable of reading and writing English and voluntarily provide written informed consent to participate in the study and comply with all study procedures
2. Untreated BV (asymptomatic or symptomatic) as diagnosed during the screening visit defined by ≥3 Amsel criteria

   Note: Amsel criteria include the following:

   - Homogeneous, thin, grayish-white discharge that smoothly coats the vaginal walls;
   - Vaginal pH >4.5;
   - Positive whiff-amine test, defined as the presence of a fishy odor when a drop of 10% potassium hydroxide (KOH) is added to a sample of vaginal discharge;
   - Presence of clue cells (>20% on microscopy).
3. Untreated BV (asymptomatic or symptomatic) as confirmed in the laboratory using the Nugent scoring system (Nugent Score ≥4)
4. Otherwise healthy pre-menopausal women 18–45 years of age on the day of screening
5. Regular predictable menstrual cycles or amenorrheic for at least 3 months due to use of a long-acting progestin or continuous use of oral contraceptives
6. Willing to be asked questions about personal medical health and sexual history
7. Willing to apply study agent vaginally and comply with study examinations
8. Agree to abstain from sexual intercourse during the first 5 consecutive days of study product administration, 12 hours prior to study visits and for 12 hours after each study product application
9. Agree to abstain from the use of any other intravaginal product throughout the trial period from the time of screening through Visit 7 (Week 24, Day 168)

   Note: Intravaginal products include contraceptive creams such as Gynol II, gels, foams, sponges, lubricants not approved by the study investigators, and douches. Limit use of tampons during menstruation to unscented products.
10. Must be of non-childbearing potential or if of childbearing potential, must agree to use a reliable method of birth control for the duration of the study

    Note: Reliable methods of birth control include tubal ligation, male partner with a vasectomy, a steroidal contraceptive (oral, patch, injectable or implantable), IUD, condoms or abstinence.

Subjects meeting any of the following criteria at screening, or when assessed at the enrollment visit, will be excluded from the study:

1. Urogenital infection at screening

Note**:** Urogenital infection includes urinary tract infection, *Trichomonas (T.) vaginalis, Neisseria (N.) gonorrhoeae, Chlamydia (C.) trachomatis, Treponema (T.) pallidum*, or vulvo-vaginal candidiasis.

2. Diagnosis of two or more outbreaks of *N. gonorrhoeae*, *C. trachomatis*, *T. pallidum*, *T. vaginalis,* or herpes simplex virus (herpes genitalis) within 6 months prior to screening
3. Positive for syphilis or HIV at screening
4. Current pregnancy or within 2 months of last pregnancy and/or currently breastfeeding**
5. Vaginal or systemic antibiotic or antifungal therapy (other than MetroGel given as part of study procedures) within 21 days of screening or within 30 days of enrollment**
6. Use of disulfiram within past 2 weeks or other contraindication to use of MetroGel**
7. Any condition requiring regular periodic use of systemic antibiotics during participation in the trial
8. Active genital herpes lesion (if not resolved by enrollment)**
9. Investigational drug use other than LACTIN-V within 30 days or 10 half-lives of the drug, whichever is longer, of enrollment visit**
10. Other planned participation in an investigational drug study while participating in this study**
11. Menopause defined as more than 12 consecutive months of amenorrhea without another known cause including pregnancy
12. IUD insertion or removal, pelvic surgery, cervical cryotherapy or cervical laser treatment within the last 2 months prior to screening
13. Use of vaginal ring (eg, NuvaRing) within 3 days of screening or during the course of the study**
14. Failure to complete 5 days of MetroGel with the last dose taken no later than 48 hours prior to randomization***
15. Use of new long-acting hormonal treatments. Subject may be enrolled if stable (>3 months) on existing therapy as determined by the principal investigator**
16. Known allergy to any component of LACTIN-V/placebo or MetroGel or to nitroimidazole derivatives or latex (condoms)
17. Any social, medical, or psychiatric condition, including history of drug or alcohol abuse, that in the opinion of the investigator would make it unlikely for the subject to comply with the study

** Note: Criteria will be assessed at screening and enrollment.

*** Note: Criteria will be assessed at enrollment.

Subjects may withdraw or be withdrawn for any of the reasons given below. The reason for withdrawal will be recorded on the corresponding data collection form.

- Subject withdraws consent
- Pregnancy or breastfeeding
- Adverse event which requires discontinuation of the treatment regimen or results in inability to comply with study procedures
- Discretionary decision by the site investigator

- At the discretion of the IRB, FDA, NIH, or other government agencies as part of their duties to ensure that research subjects are protected, or the industry supporter or its designee
- Study is terminated

Subjects who receive MetroGel, but do not complete the full MetroGel treatment, do not return for the Enrollment visit, or are otherwise found ineligible to be randomized to study treatment will not be enrolled into the study and will not be followed for safety or for AEs.

All randomized subjects who are discontinued from receiving further study product will continue to be followed through Visit 7 (Week 24, Day 168).

If withdrawal of consent or study product discontinuation occurs after study treatment is initiated, the subject will be asked to continue scheduled study procedures including safety evaluations, if possible, and be given appropriate care under medical supervision if symptoms of any AE related to participation in the study are continuing. The subject will be followed until the AE is resolved or until the subject's condition becomes stable.

Subjects who withdraw their consent for further participation in the study after their study treatment ends or discontinue study product early will be reminded of the importance of continuing in the study for safety evaluations. Subjects will be encouraged to complete the Early Termination evaluations if they choose not to complete the remaining study visits.

Subjects who enroll in the study but do not return for study visits after a minimum of three attempts to contact them over a 2-week period will be considered lost to follow-up.

4.4. Treatments

4.4.1. Treatments Administered

Each subject will receive one box of MetroGel vaginal gel sufficient for the 5-day course of treatment.

Women will return to the study clinic within 2 days after completing the 5-day course of MetroGel to re-evaluate eligibility criteria and review the BV test results from the screening visit. Women with Amsel criteria ≥3 and Nugent score 4-10 will be randomized.

Subjects will administer the first dose of LACTIN-V or Placebo under direct supervision by the study clinician before leaving the clinic (Day 1). Subjects will be instructed to administer one dose once a day at bedtime for the next 4 days (beginning on Day 2), and then two times a week for 10 weeks. The remaining 20 applicators will be used for the two doses each week during weeks 2 through 11.

The dates of first treatment are presented for subjects in the Safety population by site in Table 3 and actual treatment group in Table 4.

4.4.2. Method of Assigning Subjects to Treatment Groups (Randomization)

Women will be randomized at the enrollment visit (Visit 1) upon completion of the initial standardized antibiotic treatment with 0.75% topical MetroGel. Enrollment of subjects is done online using the enrollment module of AdvantageEDC^{SM}. Subjects are randomly assigned to LACTIN-V or placebo in a 2:1 ratio. The study uses a permuted blocked randomization scheme. Permuted block randomization is used to avoid the potential for serious imbalance in the number of subjects assigned to each group during the study, an imbalance that can occur in the simple randomization procedures.

The randomization is prepared by statisticians at the Statistical and Data Coordinating Center (SDCC) and included in the enrollment module for the trial. AdvantageEDC assigns each subject to a treatment group after the demographic and eligibility data have been entered into the system.

4.4.3. Selection and Timing of Dose for Each Subject

Subjects will be instructed to administer one dose of MetroGel vaginal gel once a day at bedtime for 5 days, initiated as soon as possible (ideally within 5 days of diagnosis at the screening or follow-up visit for symptomatic subjects, or within 24 days of the screening visit for asymptomatic subjects).

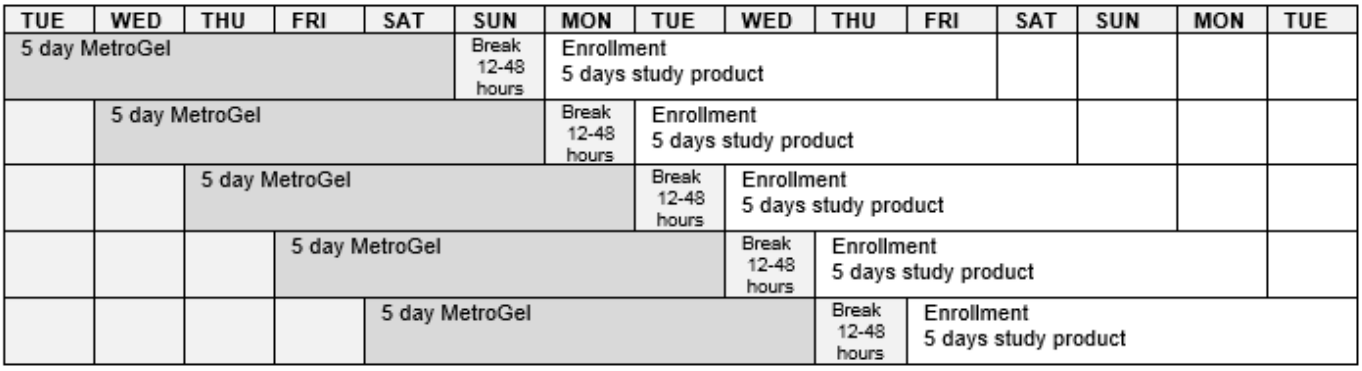
Each subject will self-administer a 5-day course of MetroGel, applied vaginally once daily in the evening for 5 consecutive days. Timing of MetroGel administration will be based on each subject's menstrual cycle.

If a subject misses a dose, she may take the missed dose on the sixth day after initiation of MetroGel treatment. A second dose may be taken on the seventh day. No more than 2 missed doses may be added. All 5 doses must be taken within 7 days after initiation of MetroGel treatment. If the duration of MetroGel treatment is longer than 5 days, the subject's enrollment visit may be rescheduled to ensure a 12-48 hour interval between completion of MetroGel treatment and the enrollment visit. At the screening visit (Visit 0), the woman's menstrual cycle history will be evaluated to ensure regular menstrual cycles (or amenorrhea due to long-acting contraceptives). Depending on the timing of her menstrual cycle, the screening procedure will be as follows:

1. If she has just finished her menstrual cycle or is within the first half of her cycle with 12 days or more expected until the onset of the next menstrual cycle, (latest screening visit on the 16th day of a regular 28-day cycle), she will proceed with screening, and will be able to complete screening, the treatment course of BV with 5 days of topical metronidazole (MetroGel), the enrollment visit (Visit 1) (in case of eligibility confirmed by the laboratory results of the screening visit) within 48 hours of her last MetroGel administration, and the 5 days of continuous treatment use starting during the enrollment visit. In this case, MetroGel treatment should be started on the evening of the screening visit.
2. If she is menstruating at the time of the screening visit, she will be asked to reschedule and return for the screening visit as soon as possible after her menstrual cycle ends.
3. If she is in the second half of her cycle with less than 12 days expected before the onset of the next menstrual bleeding, she will proceed with screening, but would be instructed to wait until after her next period before starting the 5-day course of MetroGel treatment. The screening visit must also be timed depending on her availability to return for the enrollment visit within 12-48 hours after the termination of the 5-day course of MetroGel.

MetroGel treatment for women with symptomatic BV needs to be initiated as soon as possible (ideally within 5 days of diagnosis at the screening visit). For women diagnosed with asymptomatic BV at the screening visit, MetroGel needs to be initiated according to her menstrual cycle and within 24 days of the screening visit to ensure the time window between screening and enrollment is not more than 30 days.

Women must start MetroGel treatment on a Sunday, Tuesday, Wednesday, Thursday, Friday or Saturday (NOT Monday) in order to return for enrollment within 12-48 hours after the fifth dose of her MetroGel treatment on the subsequent weekday, Monday –Friday. See the table below for a summary of the course of MetroGel treatment.



Subjects will administer the first dose under direct supervision by the study clinician before leaving the clinic (Day 1). Subjects will be instructed to administer one dose once a day at bedtime for the next 4 days (beginning on Day 2).

Should the subject forget or is not able to take the study treatment on a day within the 5-day treatment and she notices before 8 hours of the next scheduled dose, she is advised to take the missed dose as soon as she remembers. If she notices only within 8 hours of the next scheduled dose, she is advised to skip this dose. Instead, she will be instructed to apply the missed dose on Day 6 instead. A second missed dose can be taken on Day 7. No more than two missed doses can be added after the 5-day study treatment administration.
The remaining 20 doses will be self-administered twice weekly for 10 weeks (only one dose at bedtime on the first day of administration).

Subjects will choose two fixed days of the week that are 72- 96 hours apart (e.g. Mondays and Thursdays, Tuesdays and Fridays, Wednesdays and Saturdays, or Thursdays and Sundays). If the subject cannot administer a weekly dose on a scheduled day because of menstruation, she should take the missed dose as soon as the menstrual blood flow subsides and return to the schedule for the next dose. If the subject forgets to take a weekly dose on a scheduled day, wishes to have sex that particular night, or is away from home, she should take the missed dose the next day or as soon as possible and return to the schedule for the next dose.

If subject is unable to make up all missed doses after Week 11, leftover doses should not be taken and unused doses should be returned by the subject.

If the subject takes more than the required number of doses, she should be provided additional doses to continue dosing twice weekly through Week 11.

The minimum time gap between the applications should be about 48 hours, the maximum time gap 96 hours. No dose should be taken for at least 48 hours before each study visit.

4.4.4. Blinding

At the time of enrollment, the site pharmacist will select the next available box of study product applicators (per the kit number on the label of the box) in sequential order and will distribute to blinded study personnel with no labels that identify the product or applicators as LACTIN-V or placebo. No blinding procedures are required for the MetroGel.

The site pharmacist, subjects, study personnel who perform study assessments, data entry personnel at the sites, and laboratory personnel will be blinded to treatment assignment.

The blind was maintained when reporting results prepared for the DSMB meeting.

The protocol contains no explicit provisions for emergency unblinding. According to DMID policy, the study medical monitor responds to requests for emergency unblinding, and instructs the SDCC to release treatment codes only if necessary to ensure that the subject receives appropriate clinical care.

4.4.5. Prior and Concomitant Therapy

The following drugs and procedures are prohibited during the specified time periods as they may affect efficacy assessments:

- Vaginal or systemic antibiotic or antifungal therapy (other than MetroGel given as part of study procedures) within 21 days of screening or within 30 days of enrollment;
- Use of new long-acting hormonal treatments;
- Investigational drug use other than LACTIN-V within 30 days or 10 half-lives of the drug;
- Use of disulfiram within past 2 weeks or other contraindication to use of MetroGel;
- IUD insertion or removal, pelvic surgery, cervical cryotherapy or cervical laser treatment within the last 2 months prior to screening
- Use of vaginal ring (eg, NuvaRing) within 3 days of screening or during the course of the study.

Prior to unblinding, a blinded case review committee will review subjects with a reported concomitant infection/disease/procedure that may interfere with study product, use of concomitant medications or products that may interfere with study product, significant protocol deviations, and other events that may impact study product effectiveness or study analyses.

4.4.6. Treatment Compliance

All subjects are to receive a total of 25 doses of study product. The first dose is administered in clinic and the remaining doses will be administered by the subject at home. Compliance will be assessed by applicator staining of the returned kits. If a kit is not returned, compliance will be assessed by the subject's self-report on the memory aid. See Section 3.3.5 for a definition of treatment compliance. Treatment compliance will be part of the review of the blinded case review committee.

4.5. Efficacy and Safety Variables

For safety and efficacy analyses, multiple observations within specific visit period are accepted. In the case of multiple observations within a specific window, the assessment value that is closest to the scheduled visit window will be used in the analyses for the post-baseline records. The last observed value prior to administration of LACTIN-V or placebo will be used as the baseline value. All the recorded data will be listed. If observations have the same distance to the scheduled assessment, the latest one will be used.

4.5.1. Safety Variables

Solicited local and systemic events are captured on a memory aid starting on Day 1, the first day of dosing daily through Week 1 and then weekly, continuing through Visit 7 (Week 24, Day 168). The subject is to record the presence and intensity of solicited events on the memory aid. Any event that is present at the time that the subject is screened should be considered as baseline and not reported as a solicited urogenital AE. However, if the symptom deteriorates at any time during the study, it is recorded as an AE. If a symptom is reported that is not present at baseline, it too is recorded as an AE. Solicited local events include vaginal bleeding other than menstruation, abnormal vaginal discharge, abnormal vaginal odor, genital itching, genital

burning, external genital irritation, external genital swelling, and genital rash. Solicited systemic events include nausea, vomiting, abdominal pain/cramps, diarrhea, constipation, pain/burning with urination, frequent urination, blood in urine, and headache.

Severity of solicited events symptoms are graded according to the tables in Appendix B and Appendix C in the protocol. Symptoms not specifically mentioned will be graded using the following scale:

- Mild: Events require minimal or no treatment and do not interfere with the subject's daily activities.
- Moderate: Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- Severe: Events interrupt a subject's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually incapacitating.

Tolerability of LACTIN-V will be measured by identifying subjects who discontinue study product early due to adverse events.

4.5.2. Efficacy Variables

See Section 3.3 for efficacy variable definitions. BV recurrence is the primary efficacy variable. Amsel criteria and Nugent scores will be determined at each follow-up visit to diagnose BV according to the definition in Section 3.3.1. BV diagnosis at the screening visit will be used as the baseline BV diagnosis (see Section 3.3.2). Vaginal specimens will be analyzed for vaginal colonization with *L. crispatus* using qPCR assays and will be performed by a central laboratory. Concentrations of *L. crispatus* will be collected and used to determine the presence or absence of colonization. Acceptability of LACTIN-V will be measured by treatment compliance and responses to the self-administered questionnaire.

5. SAMPLE SIZE CONSIDERATIONS

Sample size calculations are based on the assumption of detecting a 50% reduction in the cumulative proportion of subjects who experience BV recurrence by 12 weeks post-administration of study product among subjects receiving LACTIN-V compared to those receiving placebo in a complete case analysis at the 0.05 significance level. The proportion of subjects among controls who will experience BV recurrence at 12 weeks is assumed to be 30%. We assume a LACTIN-V to placebo allocation ratio of 2:1 and 10% of subjects drop-out from the Complete Case population. Given logistical and feasibility constraints on the sample size and that this is a Phase II-b trial, which will provide screening evidence about safety and efficacy for a subsequent Phase III trial, this trial is powered at the 70% level. Given the assumptions above, a sample size of 228 subjects is required to detect a 50% reduction in the cumulative proportion of subjects experiencing recurrence in the Complete Case population with 70% power using the Pearson Chi-Square test.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Tabulations will be used extensively to summarize the data. All continuous variables will be summarized using the following descriptive statistics: n (sample size), mean, standard deviation, median, maximum, and minimum. The frequency and percentages (based on the sample size) of observed levels will be reported for all categorical measures. Wilson confidence intervals for binomial proportions and differences in binomial proportions will be computed for efficacy variables. Blaker confidence intervals for binomial proportions and differences in binomial proportions will be computed for safety variables. For the hypothesis tests comparing treatment groups with respect to safety outcomes, the two-sided Fisher's Exact test will be used. For the hypothesis tests comparing treatment groups with respect to efficacy outcomes, the two-sided Chi-Square test will be used. For all tests, a 5% two-sided significance level will be used.

For all efficacy outcome measures, the Complete Case population (see Section 6.3) will be used as the primary analysis population and the Per Protocol, modified Intent-to-Treat, and Intent-to-Treat populations will be used as secondary analysis populations. For all safety analyses, the Safety population will be used as the analysis population.

All summary tables will be structured with a column/sub-table for each treatment group (LACTIN-V, Placebo, and All Subjects). In general, all data will be listed by treatment group and/or subject, and when appropriate by visit number within subject. The total population size relevant to that table/column if applicable, including any missing observations will be displayed in the tables.

Note that in the data listings, Subject ID is the unique subject identifier, not the Study ID used on study and dates will not be included, only Study Day. Study Day 1 will be the day of the first dose of treatment.

6.1.1. Pseudo Code

The following SAS® pseudo code will be used to calculate the following:

Chi-Square test at 5% two-sided significance level and odds ratio (and 95% asymptotic CI) from 2x2 table:

```
proc freq;
      Table treatment*analysis_variable / chisq;
      ods output ChiSq=outputdsn1;
      ods output RelativeRisks=outputdsn2;
run;
```

Fisher's Exact test at 5% two-sided significance level:

```
proc freq;
      Table treatment*analysis_variable / exact;
      ods output FishersExact=outputdsn;
run;
```

95% Wilson CI for proportions/percentages:

```
proc freq;
      Table treatment*analysisvariable / binomial(wilson);
      ods output binomialcls=outputdsn;
run;
```

95% Wilson CI for difference in proportions (produces Newcombe CI):

```
proc freq;
      Table treatment*analysisvariable / riskdiff(cl=Wilson);
      Exact Riskdiff;
      ods output pdiffcls=outputdsn;
run;
```

95% Exact Blaker CI for proportions/percentages:

```
proc freq;
      Table treatment*analysisvariable / binomial(blaker);
      ods output binomialcls=outputdsn;
run;
```

Time to event analysis to estimate number of events, median (and other quartiles) time to event, and Kaplan-Meier curves:

```
ods output CensoredSummary =_censorsum Quartiles =_quartiles;
proc lifetest plots=survival;
      time studyday*eventstatus(0);
      strata treatment;
run;
```

Poisson regression analysis to estimate event rate in each treatment group and rate ratio between treatment groups (with associated 95% CIs):

```
proc genmod;
      class treatment;
      model eventcount = treatment / dist=poisson link=log offset=logfollowuptime;
      lsmeans treatment / ilink diff cl;
run;
```

Repeated measures logistic regression analysis using Generalized Estimating Equations to estimate odds of event in each treatment group and odds ratio between treatment groups (with associated 95% CIs):

```
proc genmod;
      class subjectid treatment other_covariates / param=glm;
      model outcome=treatment other_covariates / dist=bin;
      repeated subject=subjectid / type=ind/un/exch/ar(1);
      lsmeans treatment / ilink exp diff cl;
run;
```

Smoothing spline regression with different curves for each treatment group (with 95% confidence bands):

```
proc transreg;
      model identity(outcome) = class(treatment / zero=none) | spline(day / knots=0 to
      max_day by 1);
run;
```

6.2. Timing of Analyses

The final analysis will be performed after database lock when all subjects have been followed through Visit 7 (Week 24), the final study visit, at Day 168 (Window: Days 161-175).

6.3. Analysis Populations

6.3.1. Safety Analyses

All safety analyses will be performed in the safety analysis population. The safety population includes all randomized subjects who received at least one dose of study product. In the unlikely event of an error in randomization or study product administration (i.e., incorrect product), subjects will be grouped by the product they actually received.

6.3.2. Efficacy Analyses

All efficacy analyses will be performed in the Intent-to-Treat, Modified Intent-to-Treat, Complete Case, and Per Protocol analysis populations. For analyses of cumulative BV recurrence at Visit 4 or Visit 7 in all efficacy populations, subjects who withdraw or are withdrawn from study participation prior to the visit of interest and the reason for withdrawal recorded on the CRF is lack of treatment effect are included in the analysis population as experiencing recurrent BV at the point in time of the withdrawal. Likewise, for analyses of cumulative BV recurrence at Visit 4 or Visit 7 in all efficacy populations, subjects who discontinue study product prior to the visit of interest and the reason for discontinuation recorded on the CRF is lack of treatment effect or begin other treatment for BV prior to the visit of interest are included in the analysis population as experiencing recurrent BV at the point in time of the discontinuation or commencement of the other treatment.

See Section 6.5 for the imputation methods that will be used in the efficacy analyses.

6.3.2.1. Intent-to-Treat Analysis (ITT) Population

The ITT analysis population includes all randomized subjects, regardless of whether they received study treatment or were compliant with the administration procedures or schedule. In the unlikely event of an error in randomization or study product administration (i.e., incorrect product), subjects will be grouped by their intended randomized assignment.

6.3.2.2. Modified Intent-to-Treat (mITT) Population

The mITT population includes all randomized subjects who did not have any concomitant vaginal or cervical infections at screening or enrollment, received at least one dose of study product, and returned for at least one post-baseline visit prior to or including the visit of interest. In the unlikely event of an error in randomization or study product administration (i.e., incorrect product), subjects will be grouped by their intended randomized assignment.

Note this differs from what is stated in Section 11.6.2 of the protocol. See Section 13 for more details.

For efficacy analyses at Visit 4 (Week 12), subjects who discontinue prior to Visit 4, as well as subjects with a missing or non-evaluable Amsel or Nugent result at Visit 4 with no positive result at another visit, are included in the mITT population using imputation methods noted in Section 6.5.

For efficacy analyses at Visit 7 (Week 24), subjects who discontinue prior to Visit 7, as well as subjects with a missing or non-evaluable Amsel or Nugent result at Visit 7 with no positive result at another visit, are included in the mITT population using imputation methods noted in Section 6.5.

6.3.2.3. Complete Case (CC) Population

For efficacy analyses at Visit 4 (Week 12), the CC population includes all subjects who did not have any concomitant vaginal or cervical infections at screening or enrollment, received study product, and were followed up until the first diagnosis of BV or through Visit 4 (Week 12).

Note this differs from what is stated in Section 11.6.2 of the protocol. See Section 13 for more details.

For efficacy analyses at Visit 7 (Week 24), the CC population includes all subjects who did not have any concomitant vaginal or cervical infections at screening or enrollment, received study product, and were followed up until the first diagnosis of BV or through Visit 7 (Week 24).

In the unlikely event of an error in randomization or study product administration (i.e., incorrect product), subjects will be grouped by the product they actually received.

Subjects who terminate early prior to the visit of interest for reasons other than lack of treatment effect with no positive result at another visit, as well as subjects with a missing or non-evaluable Amsel or Nugent result with no positive result at another visit, are excluded from the CC population.

6.3.2.4. Per Protocol (PP) Population

For the analyses at Visit 4 (Week 12), the PP population includes all randomized subjects who met all inclusion/exclusion criteria at enrollment, complied with the assigned study product, and were followed up until the first diagnosis of BV or through Visit 4 (Week 12).

For the analyses at Visit 7 (Week 24), the PP population includes all randomized subjects who met all inclusion/exclusion criteria at enrollment, complied with the assigned study product, and were followed up until the first diagnosis of BV or through Visit 7 (Week 24).

In the unlikely event of an error in randomization or study product administration (i.e., incorrect product), subjects will be grouped by the product they actually received.

Subjects who terminate early prior to the visit of interest for reasons other than lack of treatment effect with no positive result at another visit, as well as subjects with a missing or non-evaluable Amsel or Nugent result with no positive result at another visit, are excluded from the PP population.

6.3.2.5. Blinded Review of Efficacy Analysis Population Eligibilities

Prior to unblinding, a blinded case review committee will review subjects with a reported concomitant infection/disease/procedure that may interfere with study product, use of concomitant medications or products that may interfere with study product, significant protocol deviations, and other events that may impact study product effectiveness or study analyses. On a case-by-case basis, the case review committee will determine if each subject will be included in the various efficacy analysis populations, if and when a subject should be censored or removed from any analyses, and/or any other analytical requirements for the subject. The committee will be blinded to both treatment assignment as well as BV outcome status. The protocol denotes that the committee will only review subjects for inclusion into the PP population, however all efficacy populations will be considered.

6.3.2.6. Analysis Population Summaries

Table 5 summarizes the ITT and mITT analysis population eligibilities by randomized treatment group and reasons excluded. Table 6 summarizes the Safety, CC, and PP analysis population eligibilities by actual treatment group and reasons excluded. Subjects will be included in the count for a particular reason for exclusion if they met that criterion. As subjects may meet more than one criterion for exclusion, the "Excluded from…" counts may be less than the sum of the individual reason counts. A listing of the subjects excluded from each of the analysis populations and the reasons for exclusion will be provided (Listing 1). A listing of subjects whose assigned treatment group does not match their randomized treatment group will be provided in Listing 2**.**

6.4. Covariates and Subgroups

The protocol does not define any formal subgroup hypothesis tests, and the study is not adequately powered to perform formal subgroup hypothesis testing. However, safety and enrollment summaries will be presented by clinical site. In addition, summaries of colonization will be presented by subgroups defined by menses and sexual intercourse variables (see Section 8.2).

6.5. Missing Data

The primary efficacy outcome measure of BV recurrence will be assessed in the CC population. Use of the mITT population has previously been recommended by the FDA where missing values from subjects who drop out early are imputed using Last Observation Carried Forward (LOCF) [6]. However, this includes subjects who dropped out after completing at least one-follow-up visit, and/or before their first positive diagnosis. LOCF would classify such subjects as 'not recurrent.' Thus, it is possible that the estimated proportions of treatment successes in a study arm could, in reality, be larger than expected. Thus, LOCF could result in an over-optimistic estimate of treatment effect, conflicting with the following rational for using an ITT analysis population stated in ICH E9 [7]: "[ITT analysis] tends to avoid over-optimistic estimates of efficacy resulting from a per protocol analysis, since the non-compliers included in the [ITT] analysis set will generally diminish the estimated treatment effect." In addition, simulation studies suggest that CC analysis leads to slightly less biased estimates of the difference in cure proportions (LACTIN-V vs. placebo) compared to the mITT analysis using LOCF.

To assess the effect of the choice of analysis population on the primary analysis, the analysis will be repeated as a secondary analysis in the ITT, mITT, and PP populations. The following imputation methods will be used for BV recurrence by Visit 4 and BV recurrence by Visit 7 in the ITT and mITT populations:

- LOCF
- Worst-Case Scenario – impute missing/unevaluable values in the LACTIN-V group as treatment failures and missing values in the Placebo group as treatment successes.

For summaries of recurrence in "by study day" displays, missing data will not be imputed.

For the secondary analyses of successful *L. crispatus* colonization by Visit 4 and by Visit 7, missing or unevaluable colonization data at a visit will imputed as unsuccessful colonization. For summaries of colonization in "by study day" displays, missing data will not be imputed.

6.6. Interim Analyses and Data Monitoring

The study is monitored to determine if any of the safety halting rules are met.

1. One or more subjects experience a treatment-related SAE.
2. Two or more subjects experience treatment-related vulvar and/or vaginal ulceration, abscess, or necrosis.
3. Four or more subjects experience a treatment-related severe (Grade 3) systemic adverse event.
4. An overall pattern of symptomatic, clinical, or laboratory events that the DMID, medical monitor, or DSMB consider associated with study product and that may collectively represent a serious potential concern for safety.

If any of the halting rules are met, the study will not continue with the remaining enrollments or study treatments without a review by and recommendation from the DSMB to proceed. A summary of halting rules is provided in Table 7**.**

The DSMB met to review aggregate safety data on 02JUN2017 after one third of the 228 subjects completed Study Visit 2 (Week 4). The DSMB may also review study progress and subject safety data at other specified times during the course of the study and hold a study closeout meeting, as defined in the DSMB Charter. No interim analyses of efficacy data are planned and this Statistical Analysis Plan does not cover the interim safety analyses.

6.7. Multicenter Studies

Safety and efficacy data will be pooled across all clinical sites. Center effects are not anticipated because treatment is self-administered, the sites are using standardized procedures for assessment of unsolicited adverse events, and the study relies on a central laboratory for Gram stain Nugent scoring. See Sections 8 and 9 for more details.

6.8. Multiple Comparisons/Multiplicity

As this trial is designed to provide screening evidence about safety and efficacy for a subsequent Phase III trial and is not a confirmatory trial, no adjustments for multiplicity are planned.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

The disposition of subjects in the study will be tabulated by randomized treatment group and all subjects. Table 8 shows the number of subjects who are screen failures and the number of subjects that met each inclusion/exclusion criterion. The number of enrolled subjects in the study completing study milestones will be tabulated separately by randomized treatment group. Table 9 shows the total number of subjects enrolled, randomized, treated, complying with treatment, and completing each visit (Visit 1 through Visit 7). A listing of subjects who completed the study, terminated early from study, or discontinued treatment and the reason for early termination or treatment discontinuation is included in Listing 3.

Figure 1 is a flowchart showing the disposition of study subjects in the safety and efficacy analyses, adapted from the CONSORT statement. It shows the number of subjects eligible, enrolled and randomized, lost to follow-up, and analyzed for the safety and efficacy analyses, overall and by treatment group.

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the deviation category, the type of deviation, and randomized treatment group for all enrolled subjects (Table 10). All subject-specific protocol deviations and non-subject-specific protocol deviations will be included in Appendix III as data listings (Listing 4 and Listing 5, respectively).

8. EFFICACY EVALUATION

8.1. Primary Efficacy Analysis

For the primary analysis, the cumulative proportion of BV recurrence by Visit 4 (Week 12) will be summarized by treatment group. A formal hypothesis test will be performed with null hypothesis that the cumulative proportion of BV recurrence by Visit 4 (Week 12) in the LACTIN-V group is equal to that in the placebo group and alternative hypothesis that they are not equal. Cumulative proportion of BV recurrence is defined as follows: the numerator is the number of subjects who experience recurrence at least once through Visit 4 in the particular analysis population and the denominator is the number of subjects included in the particular analysis population. Table 11 will present the cumulative proportion of BV recurrence by Visit 4 (Week 12) (and 95% Wilson confidence interval) in each treatment group along with the odds ratio of BV recurrence proportions between treatment groups (and 95% asymptotic confidence interval). The p-value from the Chi-Square test will be presented. The summaries will be calculated in the ITT, mITT, CC, and PP populations, where the ITT and mITT summaries will be replicated using the imputation methods described in Section 6.5. Listing 6 will present individual efficacy data for all subjects.

8.2. Secondary Efficacy Analyses

Table 12 will present the cumulative proportion of BV recurrence by Visit 7 (Week 24) (and 95% Wilson confidence interval) in each treatment group along with the odds ratio of BV recurrence proportions between treatment groups (and 95% asymptotic confidence interval). A formal hypothesis test will be performed with null hypothesis that the cumulative proportion of BV recurrence by Visit 7 (Week 24) in the LACTIN-V group is equal to that in the placebo group and alternative hypothesis that they are not equal. The p-value from the Chi-Square test will be presented. The summaries will be calculated in the ITT, mITT, CC, and PP populations, where the ITT and mITT summaries will be replicated using the imputation methods described in Section 6.5. Table 13, Table 14, Table 15, and Table 16 will present BV recurrence by study visit (Day 28, 56, 86, and 168). For the by-visit summaries, the proportions of subjects with BV recurrence at a visit is defined as follows: the numerator is the number of subjects who experience recurrence at the particular visit and the denominator of the proportion of subjects with BV recurrence is the number of subjects in the analysis population who returned for the visit. The 95% Wilson confidence interval for the proportion in each treatment group along with the odds ratio of BV recurrence proportions between treatment groups (and 95% asymptotic confidence interval) and the p-value from the Chi-Square test will also be presented.

As an additional analysis of the outcome measures of BV recurrence by Visit 4 and by Visit 7, the median time to BV recurrence (from randomization) will be estimated by treatment group using Kaplan-Meier estimates (Table 17 and Table 18). In addition, the median 95% confidence interval, minimum, first quartile, third quartile, and maximum estimates of time to BV recurrence will be presented. For subjects who experience BV recurrence by Visit 4 (Week 12), the time of BV recurrence will be defined as the midpoint between the earliest time point of a positive BV diagnosis (post-baseline) and the previous observed time point. For subjects without BV recurrence at or before Visit 4, the BV recurrence endpoint will be coded as censored, with time to recurrence defined as the elapsed time from the first dose of study product, to the Visit 4 time point, or to the first occurrence of loss to follow-up or the time-point at which the subject became ineligible for the particular analysis population. Time to BV recurrence by Visit 7 (Week 24) will be defined similarly. The analyses will be performed in the ITT, mITT, CC, and PP populations, where the ITT and mITT summaries will be replicated using the imputation methods described in Section 6.5. Kaplan-Meier curves for BV recurrence will also be generated for each analysis population by Visit 4 (Week 12) and by Visit 7 (Week 24), respectively (Figure 2 and Figure 3).

As a sensitivity analysis of the outcome measures of BV recurrence by Visit 4 and by Visit 7, the cumulative proportion of BV recurrence analyses will be repeated in the mITT and CC populations after removing the subjects who received additional treatment for BV as documented in the concomitant medications CRF after the beginning of administration of LACTIN-V or placebo and before Visit 4 and before Visit 7, respectively (Table 19 and Table 20).

Table 21 will present the proportion of subjects who experience successful *L. crispatus* colonization at any time post-baseline through Visit 4 (Week 12) (and 95% Wilson confidence interval) in each treatment group along with the odds ratio of *L. crispatus* colonization (and 95% asymptotic confidence interval). A formal hypothesis test will be performed with null hypothesis that the proportion subjects who experience successful *L. crispatus* colonization through Visit 4 (Week 12) in the LACTIN-V group is equal to that in the placebo group and alternative hypothesis that they are not equal. The p-value from the Chi-Square test will be presented. The analyses will be performed in the ITT, mITT, CC, and PP populations, where the ITT and mITT summaries will use the imputation methods described in Section 6.5. Table 22 presents the same summaries for successful *L. crispatus* colonization at Visit 7 (Week 24). Table 23, Table 24, Table 25, and Table 26 present *L. crispatus* colonization by study visit (and 95% Wilson confidence interval) in each treatment group along with the odds ratio of *L. crispatus* colonization (and 95% asymptotic confidence interval). A formal hypothesis test will be performed with null hypothesis that the proportion of subjects who experience successful *L. crispatus* colonization through each visit in the LACTIN-V group is equal to that in the placebo group and alternative hypothesis that they are not equal. The p-value from the Chi-Square test will be presented. Table 27, Table 28, Table 29, and Table 30 presents summary statistics of the concentration of *L. crispatus* CTV-05 by study visit.

Table 31, Table 32, Table 33, and Table 34 will present *L. crispatus* colonization by study day, treatment group, and number of condom-less sexual intercourse acts for each analysis population. The proportion of subjects with colonization along with the 95% Wilson confidence intervals will also be presented. Number of condom-less sexual intercourse acts will be broken up by quartiles from data obtained from the sexual history interview. If the distribution of sexual intercourse acts is such that the use of quartiles does not lead to distinct intervals of values, other cutpoints will be examined (e.g. tertiles, above/below median). Figure 10, Figure 11, Figure 12, and Figure 13 will present *L. crispatus* CTV-05 concentration by study visit, treatment group, number of condom-less sexual intercourse acts, and analysis population.

Table 35, Table 36, Table 37, and Table 38 will present *L. crispatus* colonization by study day, treatment group, and number of partners for each analysis population. Number of partners will be categorized as "No partners," "1 Partner," and ">1 Partner" from data obtained from the sexual history interview. Depending on the distribution of number of partners, other cutpoints may be examined. Figure 14, Figure 15, Figure 16, and Figure 17 will present *L. crispatus* CTV-05 concentration by study visit, treatment group, number of partners, and analysis population.

Summaries of days since last dose (mean, median, standard deviation, range) will be presented by *L. crispatus* colonization status will be presented in Table 39, Table 40, Table 41, and Table 42. *L. cripastus* CTV-05 concentration and time since last dose will be presented graphically for each visit, treatment group, and analysis population in Figure 6, Figure 7, Figure 8, and Figure 9. A smoothing spline regression model will be fit with treatment group as an independent variable. The fitted curves with 95% confidence bans will be included in the figures. Model fit and inference of the parameters will be commented on in the final report but not included in a table.

L. crispatus colonization will be presented by treatment compliance status in Table 43, Table 44, and Table 45. Treatment compliance will be categorized as "Compliant" or "Not compliant," and will be assessed from the start of treatment administration up until the visit listed. See Section 9.2 for measurements of

treatment compliance. Box plots of *L. crispatus* CTV-05 concentration by treatment compliance status are provided for each treatment group, visit, and analysis population in Figure 18, Figure 19, and Figure 20.

Summaries of days since the last day of the last menstrual period (mean, median, standard deviation, range) by *L. crispatus* colonization status will be presented in Table 46, Table 47, Table 48, and Table 49. Occurrence of menses will be captured on the memory aid. *L. cripastus* CTV-05 concentration and time since last day of the last menstrual period will be presented graphically for each visit, treatment group, and analysis population in Figure 21, Figure 22, Figure 23, and Figure 24. A smoothing spline regression model will be fit with treatment group as an independent variable. The fitted curves with 95% confidence bans will be included in the figures. Model fit and inference of the parameters will be commented on in the final report but not included in a table.

L. crispatus colonization will be also be presented by occurrence of menses after the last dose taken in Table 50, Table 51, Table 52, and Table 53. Subjects will be categorized as menstruating after their last dose taken before the visit presented, or not menstruating after the last dose taken before the specified visit. If there are less than three subjects in either treatment group who had menses since their last dose for a specified visit, that visit will be excluded from the table. Box plots of *L. crispatus* CTV-05 concentration by occurrence of menses are provided for each treatment group, visit, and analysis population in Figure 25, Figure 26, Figure 27, and Figure 28.

For all by-visit summaries, the proportions of subjects with colonization at a visit is defined as follows: the numerator is the number of subjects who experience recurrence at the specified visit and the denominator of the proportion of subjects with BV recurrence is the number of subjects in the analysis population and subgroup who returned for that visit.

As an additional analysis of the colonization analyses, the median time to colonization (from randomization) will be estimated by treatment group using Kaplan-Meier estimates (Table 54). In addition, the median 95% confidence interval, minimum, first quartile, third quartile, and maximum Kaplan-Meier estimates of time to BV recurrence will be presented. For subjects who experience colonization by Visit 4 (Week 12), the time of colonization will be defined as the midpoint between the earliest time point of colonization (post-baseline) and the previous observed time point. For subjects without colonization at or before Visit 4, the colonization endpoint will be coded as censored, with time to colonization defined as the elapsed time from the first dose of study product, to the Visit 4 time point, or to the first occurrence of loss to follow-up or the time-point at which the subject became ineligible for the particular analysis population. Time to colonization by Visit 7 (Week 24) will be defined similarly. Kaplan-Meier curves for colonization will also be generated (Figure 4 and Figure 5).

Table 55 will present the proportion of subjects who were compliant (See Section 3.3.5) with the dose regimen through their first BV recurrence or through Visit 4 (Week 12) (and 95% Wilson confidence interval) in each treatment group with difference in compliance proportions between treatment groups (and 95% Wilson confidence interval). The summaries will be presented in the ITT, mITT, and CC populations. The p-value from the Chi-Square test will also be presented. Table 56, Table 57, Table 58, Table 59, Table 60, Table 61, and Table 62 will present summaries of product administration via subject report, returned applicators, and staining for each week. Summaries will be presented by clinical site and treatment group. Listing 7 and Listing 8 will present individual dosing data.

The responses to the acceptability questionnaire at screening and at Visit 4 (Week 12) will be summarized by treatment group. For categorical responses, the proportion of subjects with the particular response and its associated 95% Wilson confidence interval will be used (Table 63 and Table 64). For continuous or discrete responses, the mean, standard deviation, median, and range of responses will be used (Table 65 and Table 66).

The analyses will be performed in the ITT, mITT, CC, and PP populations. Individual responses will be included in Listing 9.

8.3. Exploratory Efficacy Analyses

A Poisson regression model will be fit to estimate the rate of positive BV diagnoses through Visit 4 (Week 12) in each of the treatment arms and to compare the rate in the LACTIN-V arm to that in the placebo arm. The outcome of the model will be the number of positive BV diagnosis after enrollment and through Visit 4 and the model will include a covariate for treatment group and an offset term of log(follow-up time). The offset is included in the model as not all subjects will be followed up through Visit 4 (e.g. subjects who are lost to follow-up prior to Visit 4) and so subjects will have variable follow-up times. The follow-up time variable in the model will be the elapsed time (in days) from randomization to the earliest of the following: Visit 4 date, date of censoring from the particular analysis population, or the termination date. Table 67 will present the treatment group-specific rates of BV (and 95% confidence interval) along with the rate ratio between treatment groups (and 95% confidence interval).

A repeated measures logistic regression model will be fit to estimate the odds of a positive BV diagnosis through Visit 4 (Week 12) in each of the treatment arms and to compare the odds of a BV diagnosis in the LACTIN-V arm to that in the placebo arm. The marginal model to be used will have covariates for treatment group, time, and a treatment by time interaction, i.e. the model is of the form:

$$g(E[Y_{ij}]) = \beta_0 + \delta_i\beta_1 + t_{ij}\beta_2 + \delta_i t_{ij}\beta_3 + \epsilon_{ij}$$

where *g(.)* is the logit function, Y_{ij} is the BV diagnosis status of subject *i* at visit *j*, δ_i is the indicator function for the treatment group of subject *i* ($\delta_i = 1$ for LACTIN-V and $\delta_i = 0$ for Placebo), and t_{ij} is time (in study days) at which visit *j* occurred for subject *i*. The visits included in the model will be Visit 2 (Week 4) through Visit 4 (Week 12) and each subject will be included from the time of the first administration of study product to the earliest of the following: Visit 4 date, date of exclusion from the particular analysis population, or the termination date. Generalized Estimating Equations will be used to fit the model and estimate its parameters. The following working correlation structures will be explored for the assumed covariance among responses within a subject: independent, exchangeable, unstructured, and first-order autoregressive. Model estimates will be compared informally to assess robustness of the estimates with respect to choice of correlation structure. QIC will be also be used to assess model fit with regard to the correlation structure. The model with the lowest QIC will be reported. If inferential differences between the models, this will be noted in the CSR. Table 68 will present the treatment group-specific odds of BV (and 95% confidence interval) along with the odds ratio between treatment groups (and 95% confidence interval).

Select outcome measures will be further broken down by race as an exploratory analysis. Race will be categorized as Black/African American, White, and Other. The following summaries will be generated:

- BV recurrence by Visit 4 (Week 12) by analysis population, treatment group, and race (Table 69). Analyses will follow those for Table 11.
- BV recurrence by Visit 7 (Week 24) by analysis population, treatment group, and race (Table 70). Analysis will follow those for Table 12.
- *L. crispatus* colonization through Visit 4 (Week 12) by analysis population, treatment group, and race (Table 71). Analysis will follow those for Table 21.

- *L. crispatus* colonization at Visit 7 (Week 24) by analysis population, treatment group, and race (Table 72). Analyses will follow those for Table 22.
- *L. crispatus* CTV-05 concentration by study day, treatment group, and race (Table 73, Table 74, Table 75, and Table 76). Analysis will follow those for Tables 27 – 30.

Additional summaies of the *L. crispatus* colonization and CTV-05 concentration will be generated as exploratory analyses. Figures of CTV-05 concentration by *L. crispatus* concentration will be generated for each treatment group and study day (Figure 29, Figure 30, Figure 31, and Figure 32). CTV-05 concentration and *L. crispatus* colonization will be further broken down by Amsel criteria and Nugent score. Summaries *L. crispatus* colonization (Yes/No) will be presented by Amsel criteria status (Positive/Negative) (Table 77, Table 78, Table 79, and Table 80) and Nugent score category (Normal/Indeterminate/BV) (Table 81, Table 82, Table 83, and Table 84), following the analyses for Tables 23 - 26. See Section 3.3.1 for Amsel criteria and Nugent score category definitions. Similar summaries will be generated for *L. crispatus* CTV-05 concentration (Table 85, Table 86, Table 87, Table 88, Table 89, Table 90, and Table 91). Boxplots of *L. crispatus* CTV-05 concentration by Amsel Criteria/Nugent Score will be generated for each treatment group and study day (Figure 33, Figure 34, Figure 35, Figure 36, Figure 37, Figure 38, Figure 39, and Figure 40). Listing 6 will provide a listing individual efficacy data.

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Demographic and other baseline characteristics will be summarized for all randomized subjects (ITT population). Ethnicity and race will be summarized by site (Table 92) and by randomized treatment group (Table 93). Ethnicity is categorized as Hispanic or Latino, or Not Hispanic or Latino. Race is categorized as American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, Black or African American, White, Multi-Racial, or Unknown In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race (Multi-Racial) or may refuse to identify a race (Unknown), the latter reflected in the Case Report Form (CRF) as "No" to each racial option. Age will be summarized by site (Table 94) and by randomized treatment (Table 95).

Baseline sexual history will be summarized for all randomized subjects (ITT population). Categorical sexual history questions will be summarized by treatment group (Table 96) and continuous sexual history questions will be summarized by treatment group (Table 97).

Individual subject listings will be presented for all demographics, baseline and follow-up sexual history, and baseline pregnancy history (Listing 10, Listing 11, Listing 12, Listing 13, Listing 14, and Listing 15).

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and past pre-existing medical conditions will be MedDRA® coded using MedDRA dictionary version 20.1 or higher. Summaries of subjects' pre-existing and concurrent medical conditions will be presented by randomized treatment group for all sites and by each site in the ITT population (Table 98, Table 99, Table 100, Table 101, and Table 102).

Individual subject listings will be presented for all medical conditions (Listing 16).

9.1.2. Prior and Concomitant Medications

Summaries of medications that were started prior to dosing and continuing at the time of dosing as well as medications that were starting during dosing or during follow up will be presented by WHO Drug Anatomical codes (ATC) Level 1 and Level 2 and actual treatment group for subjects in the Safety population (Table 103, Table 104, Table 105, Table 106, and Table 107).

Individual subject listings will be presented for all concomitant medications (Listing 17).

9.2. Measurements of Treatment Compliance

All subjects are to receive a total of 25 doses of study product. The first dose is administered in clinic and the remaining doses will be administered by the subject at home. See Section 3.3.5 for the definition of compliance that will be used for analyses.

The number of subjects not compliant with study treatment will be presented by treatment group as part of the subject disposition table (Table 6). Treatment compliance is also a secondary outcome measure of the study; analyses and summaries are described in Section 8.2.

9.3. Adverse Events

When calculating the incidence of adverse events (i.e., on a per subject basis), each subject will only be counted once and any repetitions of adverse events within a subject will be ignored; the denominator will be the total safety population using the actual treatment group. All adverse events reported will be included in the

summaries and analyses. All analyses in Section 9.3 will be performed in the safety analysis population using the actual treatment received.

9.3.1. Solicited Events and Symptoms

Solicited local and systemic events will be captured on a memory aid starting on Day 1, the first day of therapy continuing through Visit 7 (Week 24, Day 168) and graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Solicited local events include vaginal bleeding other than menstruation, abnormal vaginal discharge, abnormal vaginal odor, genital itching, genital burning, external genital irritation, external genital swelling, and genital rash. Solicited systemic events include nausea, vomiting, abdominal pain/cramps, diarrhea, constipation, pain/burning with urination, frequent urination, blood in urine, and headache.

Any symptom that is present at the time that the subject is screened or enrolled should be considered as baseline and not reported as a solicited AE. However, if it deteriorates at any time during the study, it will be recorded as a solicited AE. If a symptom is reported that was not present at baseline, it will also be recorded as a solicited AE. Treatment-emergent solicited adverse events will be identified by comparing the severity of the baseline solicited symptoms with the severity of the post-baseline solicited symptoms. If the severity increases post-baseline or the symptoms appear post-baseline when it was 'None' at baseline, then the symptom will be considered to be treatment-emergent.

The number and percent of subjects reporting at least one treatment-emergent solicited adverse event will be summarized for each solicited adverse event and any solicited adverse event along with the 95% Blaker CI and presented in Table 108. Section 6.1 provides pseudo SAS code to use for calculating confidence intervals.

For each treatment-emergent solicited adverse event, the maximum severity over 24 weeks after the first dose will be summarized for the Safety population. The number and percentage of subjects reporting each solicited adverse event will be summarized by the maximum severity and actual treatment group along with the 95% Blaker CIs. For each event, the denominator is the number of subjects with non-missing data for the solicited adverse event being summarized. See Table 109, Table 110, Table 111, and Table 112 and Figure 41 and Figure 42.

The number of subjects reporting a solicited symptom will be summarized for each week for all subjects and separately for each treatment group (Table 113, Table 114, Table 115, Table 116, Table 117, Table 118, Table 119, Table 120, Table 121, Table 122, Table 123, and Table 124) and graphically in a bar chart (Figure 43 and Figure 44).

Solicited symptoms by subject will be presented in Listing 18 and Listing 19.

9.3.2. Unsolicited Adverse Events

The primary safety endpoint is the proportion of subjects reporting product-related AEs and SAEs in each study arm following the first dose of study product through Visit 7 (Week 24, Day 168). The number of subjects, the proportion of subjects who experienced unsolicited AEs and SAEs following the first dose of the study product through Visit 7 (Week 24, Day 168), and the 95% Blaker CIs for the proportion of subjects who experienced unsolicited AEs and SAEs related to study product through Visit 7 will be presented for the safety population and actual treatment group. In addition, the difference in proportions between the LACTIN-V arm and the Placebo arm and 95% Blaker CIs will be presented in Table 125. The proportion of subjects in each treatment group who experience product-related AEs following the first dose of the study product through Visit 7 (Week 24 Day 168) will be tested using a Fisher's exact test at the 5% two-sided level of significance level without adjustment for multiplicity in the safety analysis population. See Section 6.1 for pseudocode for calculating p-values and CIs.

The proportion of subjects reporting at least one unsolicited adverse event will be summarized by MedDRA system organ class and preferred term for all subjects and each actual treatment group. Denominators for percentages are the number of subjects who received the study product being summarized. A 95% Blaker CI will be presented for each MedDRA system organ class and preferred term (Table 126). Adverse events by subject will be presented in Listing 20.

The following summaries for unsolicited adverse events will be presented by MedDRA system organ class, preferred term, and treatment group:

- Incidence and percentage of subjects by maximum severity and maximum relationship to study product, including Frequency (Event level) of events for all subjects and by actual treatment received (Table 127 and Table 128);
- The number of adverse events occurring in 5% of subjects in any treatment group will be presented by MedDRA system organ class, preferred term, and treatment group in Table 129**;**
- The number of subjects reporting adverse events occurring in 5% of subjects in any treatment group will be presented by MedDRA system organ class, preferred term and treatment group in Table 130**;**
- Subject listing of non-serious adverse events of moderate or greater severity (Table 131);
- Bar chart of total frequency of adverse events by severity and MedDRA system organ class (Figure 45);
- Bar chart of subject incidence of adverse events by severity and MedDRA system organ class (Figure 46);
- Bar chart of total frequency of adverse events by relationship to study product and MedDRA system organ class (Figure 47);
- Bar chart of subject incidence of adverse events by relationship to study product and MedDRA system organ class (Figure 48).

9.4. Deaths, Serious Adverse Events and other Significant Adverse Events

The primary safety endpoint is the proportion of subjects reporting product-related AEs and SAEs in each study arm following the first dose of study product through Visit 7 (Week 24, Day 168). The number of subjects, the proportion of subjects who experienced product-related AEs and SAEs, and the 95% Blaker confidence interval for the proportion of subjects who experienced product-related SAEs will be presented for each analysis population, actual treatment group, and study visit. In addition, the difference in proportions between the LACTIN-V arm and the Placebo arm and 95% Blaker confidence intervals will be presented. As noted in Section 9.3.2, the proportion of subjects in each treatment group who experience product-related AEs and SAEs following the first dose of the study product through Visit 7 (Week 24 Day 168) will be tested using a Fisher's exact test at the 5% two-sided level of significance level without adjustment for multiplicity in the safety analysis population (Table 125). See Section 6.1 for pseudocode for calculating p-values and CIs.

A listing of deaths and serious adverse events will be presented, which will include Subject ID, treatment group, Adverse Event Description, Study Day the Event became Serious, Reason Reported as an SAE, Relationship to Treatment, Alternate Etiology if Not Related, Outcome, and Duration of Event in days (Table 132).

9.5. Pregnancies

For any subjects in the Safety population who became pregnant during the study, every attempt will be made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. A listing of the total pregnancies, number of live births, and number of spontaneous abortions, elective abortions or still births will be presented (Listing 21, Listing 22, Listing 23, Listing 24, and Listing 25).

9.6. Clinical Laboratory Evaluations

Various clinical laboratory parameters are collected during follow-up, if indicated. The evaluations are: clean catch urine dipstick, urinalysis, rapid urine βhCG pregnancy test, HIV and syphilis serology, and vaginal swab for *N. gonorrhoeae, C. trachomatis,* and *T. vaginalis.* Since the laboratory evaluations are only performed if indicated, subject listings of the clinical laboratory results will be provided (Listing 26 and Listing 27). Trichomoniasis and yeast vaginitis wet mount results will be provided in Listing 28.

9.7. Vital Signs and Physical Evaluations

A complete physical examination, assessment of vital signs, and a pelvic examination will be performed at screening and symptom-directed examinations will be performed at all subsequent visits. Vital sign measurements include systolic blood pressure, diastolic blood pressure, pulse, respiration, oral temperature, height, and weight. Since the evaluations are symptom-driven from enrollment to the end of follow-up, subject listings will be provided for vital signs (Listing 29), physical exam findings (Listing 30), and pelvic exam findings (Listing 31). Abnormal discharge and cervical mucus characteristics are displayed by visit and treatment group in Table 133, Table 134, and Table 135. Subject listings will be provided for abnormal discharge (Listing 32), and cervical mucus characteristics (Listing 33).

9.8. Concomitant Medications

Summaries of medications that were started prior to dosing and continuing at the time of dosing, as well as medications that were started during dosing or during follow up will be presented by WHO Drug Anatomical Codes (ATC) Level 1 and Level 2 and actual treatment group for subjects in the Safety population (See Section 9.1.2 and Table 98, Table 99, Table 100, Table 101, and Table 102).

Individual subject listings will be presented for all concomitant medications (See Section 9.1.2 and Listing 17).

10. OTHER ANALYSES

No other analyses are planned.

11. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to three decimal places; p-values less than 0.001 will be reported as "<0.001"; p-values greater than 0.999 will be reported as "> 0.999". The mean, median, standard deviation, and any other statistics other than quantiles, will be reported to one decimal place greater than the original data. Quantiles other than the median will use the same number of decimal places as the original data. Proportions will be presented to two decimal places; values <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values < 1% will be presented as "<1". Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to three significant figures.

12. TECHNICAL DETAILS

SAS version 9.4 or above will be used to generate all tables, figures, and listings.

13. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

This SAP denotes that ITT efficacy analyses will be performed, though the protocol did not specify that ITT analyses would be performed.

Section 11.6.2 of the protocol states the mITT and CC populations will include subjects who met all inclusion/exclusion criteria. Section 6.4 of this analysis plan clarifies that rather than including subjects who met all inclusion/exclusion criteria, the mITT and CC analysis populations will exclude subjects who were positive for concomitant vaginal or cervical infections at screening and enrollment to better align with the analysis population definitions in the July 2016 FDA guidance for BV.

14. REFERENCES

1. Allsworth JE and Peipert JF. Prevalence of bacterial vaginosis: 2001-2004 National Health and Nutrition Examination Survey data. Obstet Gynecol 2007;109(1):114-20.
2. Eschenbach DA, Hillier S, Critchlow C, et al. Diagnosis and clinical manifestations of bacterial vaginosis. Am J Obstet Gynecol 1988;158(4):819-28.
3. Hillier SL, Kiviat NB, Hawes SE, et al. Role of bacterial vaginosis-associated microorganisms in endometritis. Am J Obstet Gynecol 1996;175(2):435-41.
4. Watts DH, Krohn MA, Hillier SL, et al. Bacterial vaginosis as a risk factor for post-cesarean endometritis. Obstet Gynecol 1990;75(1):52-8.
5. Soper DE. Bacterial vaginosis and postoperative infections. Am J Obstet Gynecol. 1993 Aug;169(2 Pt 2):467-9.
6. FDA Draft Guidance for the Use of Metronidazole Gel. https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm345807.pdf
7. International Conference on Harmonisation (ICH) E9. http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf

15. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3, respectively.

APPENDIX 1. TABLE MOCK-UPS

Table 1: Study Design

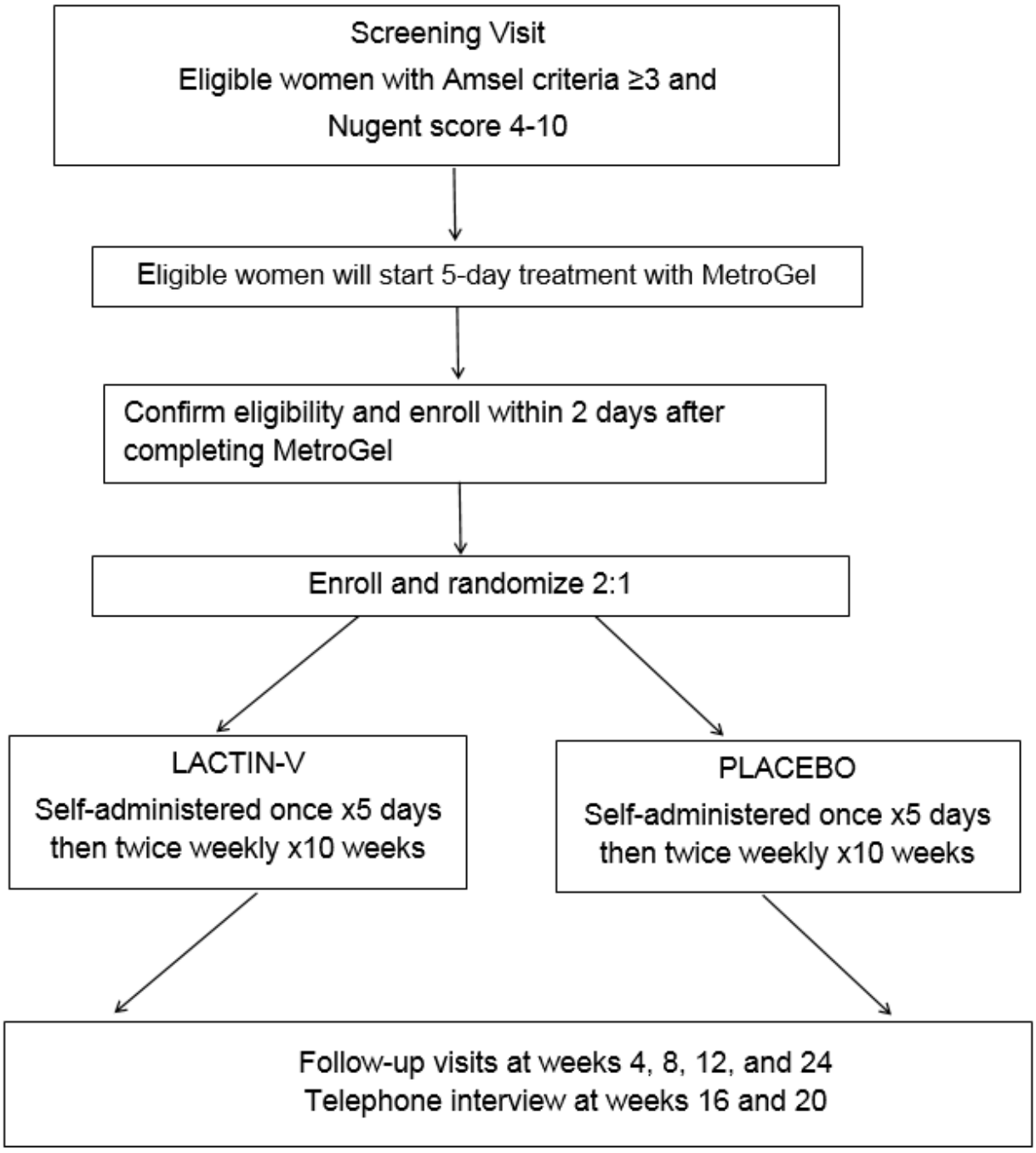


Table 2: Schedule of Study Procedures

			Study Treatment					Study Follow Up				
Evaluation		Screening Visit 0 Day -30 to -5	Enrollment Visit 1 Day 1	Study Visit 2 Day 28 (Week 4)	Study Visit 3 Day 56 (Week 8)	Study Visit 4 Day 84 (Week 12)	Phone Visit 5 Day 112 (Week 16)	Phone Visit 6 Day 140 (Week 20)	Study Visit 7 Day 168 (Week 24)	Unscheduled Visit	Study Product Discontinuation	Early Termination Visit
Visit window					± 1 week							
Signed consent form		X	X									
Assessment of eligibility criteria		X	X									
Demographics		X	X									
Randomization			X									
Detailed medical, gynecological and sexual history		X										
Dispense MetroGel		X		(X)	(X)	(X)						
Dispense LACTIN-V/placebo and applicators			X	(X)	(X)							
Dispense condoms		X	X	X	X	X				X	X	
Dispense memory aid or instructions on using web based memory aid			X									
Brief medical, gynecological and sexual history			X	X	X	X			X	X	X	X
Review of concomitant medications		X	X	X	X	X	X	X	X	X	X	X
Study intervention			X	X	X	X						
Physical Examination	Complete	X										
	Symptom-directed		X	X	X	X			X	X	X	X
	Vital signs	X	X	X	X	X			X	X	X	X
	Pelvic examination	X	X	X	X	X			X	X	X	X
Review memory aid and symptoms				X	X	X	X	X	X	X	X	X

Evaluation		Screening Visit 0 Day -30 to -5	Study Treatment: Enrollment Visit 1 Day 1	Study Visit 2 Day 28 (Week 4)	Study Visit 3 Day 56 (Week 8)	Study Visit 4 Day 84 (Week 12)	Phone Visit 5 Day 112 (Week 16)	Study Follow Up: Phone Visit 6 Day 140 (Week 20)	Study Visit 7 Day 168 (Week 24)	Unscheduled Visit	Study Product Discontinuation	Early Termination Visit
Reminder to abstain from sexual intercourse			X	X	X	X	X	X		X		
Reminder not to use vaginal products			X	X	X	X	X	X		X		
Reminder to collect and return used applicators			X	X	X	X	X	X		X	X	X
Assessment of adverse events				X	X	X	X	X	X	X	X	X
Clinical Laboratory	Clean catch urine dipstick	X	(X)	(X)	(X)	(X)			(X)	(X)	(X)	(X)
	Urinalysis	(X)	(X)	(X)	(X)	(X)			(X)	(X)	(X)	(X)
	Rapid urine βhCG pregnancy test	X	X	(X)	(X)	(X)			(X)	(X)	(X)	(X)
	HIV and syphilis serology (total blood required is approximately 15mL (3 teaspoons)	X										
	Vaginal swab for *N. gonorrhoeae, C. trachomatis, T. vaginalis*	X	(X)	(X)	(X)	(X)			(X)	(X)	(X)	(X)
Research Laboratory	Vaginal swab for pH	X	X	X	X	X			X	X	X	X
	Vaginal swab for wet mount, amine test	X	X	X	X	X			X	X	X	X
	Vaginal swab for Gram stain	X	X	X	X	X			X	X	X	X

			Study Treatment					Study Follow Up				
Evaluation		Screening Visit 0 Day -30 to -5	Enrollment Visit 1 Day 1	Study Visit 2 Day 28 (Week 4)	Study Visit 3 Day 56 (Week 8)	Study Visit 4 Day 84 (Week 12)	Phone Visit 5 Day 112 (Week 16)	Phone Visit 6 Day 140 (Week 20)	Study Visit 7 Day 168 (Week 24)	Unscheduled Visit	Study Product Discontinuation	Early Termination Visit
	Vaginal swab for storage and future identification of vaginal bacteria	X	X	X	X	X			X	X	X	X
	Vaginal swab for qPCR (*L. crispatus* identification)		X	X	X	X			X	X	X	X
Other Procedures	Acceptability questionnaire	X				X					X	X
	Staining of used applicators			X*								
	Telephone interview						X	X				

Table 3: Dates of First Treatment by Site – Safety Population

[Note: Dates will be categorized by breaking the calendar year into quarters.]

Dates of Dosing	San Francisco General Hospital (N = X)		Stroger Hospital of Cook County (N = X)		University of California, San Diego (N = X)		Washington University in St. Louis (N = X)		All Subjects (N = X)	
	n	%	n	%	n	%	n	%	n	%
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x	x	x	x	x
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x	x	x	x	x
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x	x	x	x	x
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x	x	x	x	x
Note: N=Number of subjects in the safety population										

Table 4: Dates of First Treatment by Treatment Group - Safety Population

[Note: Dates will be categorized by breaking the calendar year into quarters.]

Dates of Dosing	LACTIN-V (N = X)		Placebo (N = X)		All Subjects (N = X)	
	n	%	n	%	n	%
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x
Note: N=Number of subjects in the safety population						

Table 5: Intent-to-Treat and Modified Intent-to-Treat Analysis Populations for Primary Analysis by Treatment Group

			LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
Analysis Population	**Eligibility Category**	**Reason Subjects Excluded**	**n**	**%**	**n**	**%**	**n**	**%**
Intent-to-Treat (ITT) Analysis Population	Eligible for ITT		x	x	x	x	x	x
Modified Intent-to-Treat (mITT) Analysis	Eligible for mITT		x	x	x	x	x	x
	Excluded from mITT	Any Reason	x	x	x	x	x	x
		Did not meet inclusion/exclusion criteria	x	x	x	x	x	x
		Did not receive study product	x	x	x	x	x	x
		Did not return for at least one post-baseline visit	x	x	x	x	x	x

Notes: N=number of enrolled subjects.
Treatment group is the treatment group to which a subject was randomized.

Table 6: Safety, Complete Case, and Per Protocol Analysis Populations for Safety and Primary Analysis by Treatment Group

			LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
Analysis Population	**Eligibility Category**	**Reason Subjects Excluded**	**n**	**%**	**n**	**%**	**n**	**%**
Safety Analysis Population	Eligible for Safety		x	x	x	x	x	x
	Excluded from Safety	Any Reason	x	x	x	x	x	x
		Did not receive study product	x	x	x	x	x	x
Complete Case (CC) Analysis Population	Eligible for CC		x	x	x	x	x	x
	Excluded from CC	Any Reason	x	x	x	x	x	x
		Did not meet inclusion/exclusion criteria	x	x	x	x	x	x
		Did not receive study product	x	x	x	x	x	x
		Was not followed up until the first diagnosis of BV or through Visit 4 (Week 12, Day 84)	x	x	x	x	x	x
Per-Protocol (PP) Analysis Population	Eligible for PP		x	x	x	x	x	x
	Excluded from PP	Any Reason	x	x	x	x	x	x
		Did not meet inclusion/exclusion criteria	x	x	x	x	x	x
		Was not compliant with study product	x	x	x	x	x	x
		Was not followed up until the first diagnosis of BV or through Visit 4 (Week 12, Day 84)	x	x	x	x	x	x

Notes: N=number of enrolled subjects.
Treatment group is the actual treatment a subject received

Table 7: Summary of Halting Rules - Safety Population

Halting Rules	Number of Subjects
One or more subjects experiences a treatment-related SAE	x
Two or more subjects experience treatment-related vulvar and/or vaginal ulceration, abscess, or necrosis	x
Four or more subjects experience a treatment-related severe (Grade 3) systemic adverse event	x
An overall pattern of symptomatic, clinical, or laboratory events that the DMID Medical Monitor or DSMB consider associated with study drug and that may appear minor in terms of individual events, but that may collectively represent a serious potential concern for safety	x

Table 8: Ineligibility Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	Number of Subjects[a]
Inclusion and Exclusion	Any Criterion	x
Inclusion	Any inclusion criterion	x
	[inclusion criterion 1]	x
	[inclusion criterion 2]	x
	[inclusion criterion 3]	x
Exclusion	Any exclusion criterion	x
	[exclusion criterion 1]	x
	[exclusion criterion 2]	x
	[exclusion criterion 3]	x
Declined Enrollment	Any Reason	x
	Time commitment	x
	Concern of potential risks	x
	Number of procedures	x
	Unable to contact subject	x
	Other	x

Note: [a]More than one criterion may be marked per subject.

Table 9: Subject Disposition by Treatment Group - All Enrolled Subjects

Subject Disposition	LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Screened	x	--	x	--	x	--
Enrolled/Randomized	x	100	x	100	x	100
Received Treatment	x	x	x	x	x	x
Complied with Treatment[a, b]	x	x	x	x	x	x
Completed Visit 2, Week 4 (Day 28 ±7)	x	x	x	x	x	x
Completed Visit 3, Week 8 (Day 56 ±7)	x	x	x	x	x	x
Completed Visit 4, Week 12 (Day 84 ±7)	x	x	x	x	x	x
Completed Visit 5, Week 16 (Day 112 ±7) – Telephone Interview*	x	x	x	x	x	x
Completed Visit 6, Week 20 (Day 140 ±7) – Telephone Interview*	x	x	x	x	x	x
Completed Visit 7, Week 24 (Study Day 168 ±7)	x	x	x	x	x	x

Notes: N=Number of enrolled subjects.
[a]Refer to Listing 16.2.1 for reasons subjects discontinued or terminated early.
[b] Refer to 16.2.5.1 and 16.2.5.2 for treatment compliance.
*Includes subjects who completed their visits in clinic.

Table 10: Distribution of Protocol Deviations by Category, Type, and Treatment Group—All Enrolled Subjects

Category	Deviation Type	LACTIN-V (N=X)			Placebo (N=X)			All Subjects (N=X)		
		# of Subj.	%	# of Dev.	# of Subj.	%	# of Dev.	# of Subj.	%	# of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x	x	x	x
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	x	x	x	x
	ICF not signed prior to study procedures	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x
Treatment administration schedule	Any type	x	x	x	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x
	Missed treatment administration	x	x	x	x	x	x	x	x	x
	Delayed treatment administration	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x
Protocol procedure/assessment	Any type	x	x	x	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x	x	x	x
	Blood not collected	x	x	x	x	x	x	x	x	x
	Urine not collected	x	x	x	x	x	x	x	x	x
	Other specimen not collected	x	x	x	x	x	x	x	x	x
	Specimen result not obtained	x	x	x	x	x	x	x	x	x
	Required procedure not conducted	x	x	x	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x

Category	Deviation Type	LACTIN-V (N=X)			Placebo (N=X)			All Subjects (N=X)		
		# of Subj.	%	# of Dev.	# of Subj.	%	# of Dev.	# of Subj.	%	# of Dev.
	Study product temperature excursion	x	x	x	x	x	x	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x	x	x	x
	Prohibited use of vaginal products	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x
Treatment administration	Any type	x	x	x	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x
Blinding policy/procedure	Any type	x	x	x	x	x	x	x	x	x
	Treatment unblinded	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x

Notes: N=Number of enrolled subjects. Treatment group is the treatment to which the subject was randomized.

Table 11: BV Recurrence by Visit 4 (Week 12) by Analysis Population and Treatment Group

Analysis Population	Treatment Group	Number of Subjects with BV Recurrence n	Number of Subjects N	Proportion of Subjects with BV Recurrence	BV Recurrence 95% CI[1]	Odds of BV Recurrence in LACTIN-V Group Compared to Placebo Group	Odds of BV Recurrence in LACTIN-V Group Compared to Placebo Group 95% CI[2]	p-value[3]
ITT (LOCF)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
mITT (LOCF)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
ITT (Worst Case)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
mITT (Worst Case)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
CC	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
PP	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Table with similar format:

Table 12: BV Recurrence by Visit 7 (Week 24) by Analysis Population and Treatment Group

Table 13: BV Recurrence by Study Day and Treatment Group – ITT Population

Study Day (Week)	Treatment Group	Number of Subjects with BV Recurrence n	Number of Subjects N	Proportion of Subjects with BV Recurrence	BV Recurrence 95% CI[1]	Odds of BV Recurrence in LACTIN-V Group Compared to Placebo Group	Odds of BV Recurrence in LACTIN-V Group Compared to Placebo Group 95% CI[2]	p-value[3]
Day 1	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
Day 28 (Week 4)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
Day 56 (Week 8)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
Day 84 (Week 12)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
Day 168 (Week 24)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population with BV diagnosis data available at the specified visit.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Tables with similar format:

Table 14: BV Recurrence by Study Day and Treatment Group – mITT Population

Table 15: BV Recurrence by Study Day and Treatment Group – CC Population

Table 16: BV Recurrence by Study Day and Treatment Group – PP Population

Table 17: Time to BV Recurrence by Analysis Population and Treatment Group – By Visit 4 (Week 12)

	ITT			mITT			CC			PP		
	LACTIN-V (N = xxx)	**Placebo (N = xxx)**	**All Subjects (N = xxx)**	**LACTIN-V (N = xxx)**	**Placebo (N = xxx)**	**All Subjects (N = xxx)**	**LACTIN-V (N = xxx)**	**Placebo (N = xxx)**	**All Subjects (N = xxx)**	**LACTIN-V (N = xxx)**	**Placebo (N = xxx)**	**All Subjects (N = xxx)**
Number (%) of subjects with BV Recurrence	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Median Time (days)	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
Median Time (days) 95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Minimum (days)	x	x	x	x	x	x	x	x	x	x	x	x
Q1 (days)	x	x	x	x	x	x	x	x	x	x	x	x
Q3 (days)	x	x	x	x	x	x	x	x	x	x	x	x
Maximum (days)	x	x	x	x	x	x	x	x	x	x	x	x
Notes: Median time and median time 95% CI comes from Kaplan-Meier estimates												

Tables with similar format:

Table 18: Time to BV Recurrence by Analysis Population and Treatment Group – By Visit 7 (Week 12)

Table 19: BV Recurrence by Visit 4 (Week 12) by Analysis Population and Treatment Group – Excluding Subjects Receiving Additional BV Treatment

Analysis Population	Treatment Group	Number of Subjects with BV Recurrence n	Number of Subjects N	Proportion of Subjects with BV Recurrence	BV Recurrence 95% CI[1]	Odds of BV Recurrence in LACTIN-V Group Compared to Placebo Group	Odds of BV Recurrence in LACTIN-V Group Compared to Placebo Group 95% CI[2]	p-value[3]
CC	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
PP	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Table with similar format:

Table 20: BV Recurrence by Visit 7 (Week 24) by Analysis Population and Treatment Group – Excluding Subjects Receiving Additional BV Treatment

Table 21: *L. crispatus* Colonization through Visit 4 (Week 12) by Analysis Population and Treatment Group

Analysis Population	Treatment Group	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI	Odds of Colonization in LACTIN-V Group Compared to Placebo Group	Odds of Colonization in LACTIN-V Group Compared to Placebo Group 95% CI	p-value[1]
ITT	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
mITT	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
CC	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
PP	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Tables with similar format:

Table 22: *L. crispatus* Colonization at Visit 7 (Week 24) by Analysis Population and Treatment Group

Table 23: *L. crispatus* Colonization by Study Day and Treatment Group – ITT Population

Study Day (Week)	Treatment Group	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI[1]	Odds of Colonization in LACTIN-V Group Compared to Placebo Group	Odds of Colonization in LACTIN-V Group Compared to Placebo Group 95% CI[2]	p-value[3]
Day 1	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
Day 28 (Week 4)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
Day 56 (Week 8)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
Day 84 (Week 12)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
Day 168 (Week 24)	LACTIN-V	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population with colonization data available at the specified visit.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Tables with similar format:

Table 24: *L. crispatus* Colonization by Study Day and Treatment Group – mITT Population

Table 25: *L. crispatus* Colonization by Study Day and Treatment Group – CC Population

Table 26: *L. crispatus* Colonization by Study Day and Treatment Group – PP Population

Table 27: *L. crispatus* CTV-05 Concentration by Study Day and Treatment Group – ITT Population

Study Day (Week)	Treatment Group	Number of Subjects[1]	Mean (SD)	Median	Range
Day 1	LACTIN-V	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Day 28 (Week 4)	LACTIN-V	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Day 56 (Week 8)	LACTIN-V	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Day 84 (Week 12)	LACTIN-V	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Day 168 (Week 24)	LACTIN-V	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	x	x.xx (x.xx)	x.xx	x.xx, x.xx

1: The number of subjects in the respective treatment group and analysis population with concentration data available at the specified visit.

Tables with similar format:

Table 28: *L. crispatus* CTV-05 Concentration by Study Day and Treatment Group – mITT Population

Table 29: *L. crispatus* CTV-05 Concentration by Study Day and Treatment Group – CC Population

Table 30: *L. crispatus* CTV-05 Concentration by Study Day and Treatment Group – PP Population

Table 31: *L. crispatus* Colonization by Study Day, Treatment Group, and Number of Condom-less Sexual Intercourse Acts – ITT Population

Study Day (Week)	Treatment Group	Number of Condom-less Sex Acts Since the Previous Visit	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI[1]
Day 1*	LACTIN-V	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	Placebo	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	All Subjects	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
Day 28 (Week 4)	LACTIN-V	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	Placebo	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	All Subjects	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
Day 56 (Week 8)	LACTIN-V	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	Placebo	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	All Subjects	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx

Study Day (Week)	Treatment Group	Number of Condom-less Sex Acts Since the Previous Visit	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI[1]
		4th Quartile	x	x	0.xx	0.xx, 0.xx
Day 84 (Week 12)	LACTIN-V	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	Placebo	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	All Subjects	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
Day 168 (Week 24)	LACTIN-V	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	Placebo	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx
	All Subjects	1st Quartile	x	x	0.xx	0.xx, 0.xx
		2nd Quartile	x	x	0.xx	0.xx, 0.xx
		3rd Quartile	x	x	0.xx	0.xx, 0.xx
		4th Quartile	x	x	0.xx	0.xx, 0.xx

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population with colonization and condomless sex act data available at the specified visit.
*Number of condom-less sexual intercourse acts in the last 30 days
1: 95% CI= 95% Wilson confidence interval

Implementation note: Quartiles will be filled in with the actual ranges

Tables with similar format:

Table 32: ***L. crispatus*** **Colonization by Study Day, Treatment Group, and Number of Condom-less Sexual Intercourse Acts – mITT**

Table 33: ***L. crispatus*** **Colonization by Study Day, Treatment Group, and Number of Condom-less Sexual Intercourse Acts – CC Population**

Table 34: ***L. crispatus*** **Colonization by Study Day, Treatment Group, and Number of Condom-less Sexual Intercourse Acts – PP Population**

Table 35: *L. crispatus* Colonization by Study Day, Treatment Group, and Number of Partners – ITT Population

Study Day (Week)	Treatment Group	Number of Partners Since the Previous Visit	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI[1]
Day 1*	LACTIN-V	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	Placebo	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	All Subjects	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
Day 28 (Week 4)	LACTIN-V	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	Placebo	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	All Subjects	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
Day 56 (Week 8)	LACTIN-V	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	Placebo	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	All Subjects	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
Day 84 (Week 12)	LACTIN-V	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	Placebo	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	All Subjects	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx

Study Day (Week)	Treatment Group	Number of Partners Since the Previous Visit	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI[1]
Day 168 (Week 24)	LACTIN-V	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	Placebo	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx
	All Subjects	No Partners	x	x	0.xx	0.xx, 0.xx
		1 Partner	x	x	0.xx	0.xx, 0.xx
		>1 Partner	x	x	0.xx	0.xx, 0.xx

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population with colonization and sexual partner data available at the specified visit.
*Number of male and female partners in the last 6 months
1: 95% CI= 95% Wilson confidence interval

Tables with similar format:

Table 36: *L. crispatus* Colonization by Study Day, Treatment Group, and Number of Partners–mITT

Table 37: *L. crispatus* Colonization by Study Day, Treatment Group, and Number of Partners – CC Population

Table 38: *L. crispatus* Colonization by Study Day, Treatment Group, and Number of Partners – PP Population

Table 39: Days Since Last Dose by Study Day, Treatment Group, and *L. crispatus* Colonization Status – ITT Population

Study Day (Week)	Treatment Group	Colonization Status	Number of Subjects[1]	Mean (SD)	Median	Range
Day 28 (Week 4)	LACTIN-V	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Day 56 (Week 8)	LACTIN-V	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Continue for Day 84 (Week 12) and Day 168 (Week 24)						
1: The number of subjects in the respective treatment group and analysis population with concentration and dosing data available at the specified visit.						

Tables with similar format:

Table 40: Days Since Last Dose by Study Day, Treatment Group, and *L. crispatus* Colonization Status – mITT Population

Table 41: Days Since Last Dose by Study Day, Treatment Group, and *L. crispatus* Colonization Status – CC Population

Table 42: Days Since Last Dose by Study Day, Treatment Group, and *L. crispatus* Colonization Status – PP Population

Table 43: *L. crispatus* Colonization by Study Day, Treatment Group, and Treatment Compliance – ITT Population

Study Day (Week)	Treatment Group	Treatment Compliance Status	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI[1]	Odds of Colonization in Compliant Group Compared to Not Compliant Group	Odds of Colonization in Compliant Group Compared to Not Compliant Group 95% CI[2]
Day 28 (Week 4)	LACTIN-V	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
	Placebo	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
	All Subjects	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
Day 56 (Week 8)	LACTIN-V	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
	Placebo	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
	All Subjects	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
Day 84 (Week 12)	LACTIN-V	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
	Placebo	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
	All Subjects	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
Day 168 (Week 24)	LACTIN-V	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
	Placebo	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--
	All Subjects	Compliant	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		Not Compliant	x	x	0.xx	0.xx, 0.xx	--	--

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population with colonization and compliance data available at the specified visit.
Treatment compliance is assessed up until the respective visit
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test

Tables with similar format:

Table 44: *L. crispatus* Colonization by Study Day, Treatment Group, and Treatment Compliance – mITT Population

Table 45: *L. crispatus* Colonization by Study Day, Treatment Group, and Treatment Compliance – CC Population

Table 46: Days Since Last Day of Last Menstrual Period by Study Day, Treatment Group, and *L. crispatus* Colonization Status – ITT Population

Study Day (Week)	Treatment Group	Colonization Status	Number of Subjects[1]	Mean (SD)	Median	Range
Day 28 (Week 4)	LACTIN-V	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Day 56 (Week 8)	LACTIN-V	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	Yes	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		No	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Continue for Day 84 (Week 12), and Day 168 (Week 24)						
1: The number of subjects in the respective treatment group and analysis population with concentration and menses data available at the specified visit.						

Tables with similar format:

Table 47: Days Since Last Day of Last Menstrual Period by Study Day, Treatment Group, and *L. crispatus* Colonization Status – mITT Population

Table 48: Days Since Last Day of Last Menstrual Period by Study Day, Treatment Group, and *L. crispatus* Colonization Status – CC Population

Table 49: Days Since Last Day of Last Menstrual Period by Study Day, Treatment Group, and *L. crispatus* Colonization Status – PP Population

Table 50: *L. crispatus* Colonization by Study Day, Treatment Group, and Occurrence of Menses After Last Dose Taken – ITT Population

Study Day (Week)	Treatment Group	Occurrence of Menses	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI[1]	Odds of Colonization in Subjects with Menses Compared to Subjects with No Menses	Odds of Colonization in Subjects with Menses Compared to Subjects with No Menses 95% CI[2]
Day 28 (Week 4)	LACTIN-V	Menses since last dose	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		No menses since last dose	x	x	0.xx	0.xx, 0.xx	--	--
	Placebo	Menses since last dose	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		No menses since last dose	x	x	0.xx	0.xx, 0.xx	--	--
Day 56 (Week 8)	LACTIN-V	Menses since last dose	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		No menses since last dose	x	x	0.xx	0.xx, 0.xx	--	--
	Placebo	Menses since last dose	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		No menses since last dose	x	x	0.xx	0.xx, 0.xx	--	--
Day 84 (Week 12)	LACTIN-V	Menses since last dose	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		No menses since last dose	x	x	0.xx	0.xx, 0.xx	--	--
	Placebo	Menses since last dose	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		No menses since last dose	x	x	0.xx	0.xx, 0.xx	--	--
Day 168 (Week 24)	LACTIN-V	Menses since last dose	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		No menses since last dose	x	x	0.xx	0.xx, 0.xx	--	--
	Placebo	Menses since last dose	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx
		No menses since last dose	x	x	0.xx	0.xx, 0.xx	--	--

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population witih colonization and menses data available at the specified visit.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test

Tables with similar format:

Table 51: *L. crispatus* Colonization by Study Day, Treatment Group, and Occurrence of Menses After Last Dose Taken – mITT Population

Table 52: *L. crispatus* Colonization by Study Day, Treatment Group, and Occurrence of Menses After Last Dose Taken – CC Population

Table 53: *L. crispatus* Colonization by Study Day, Treatment Group, and Occurrence of Menses After Last Dose Taken – PP Population

Table 54: Time to *L. crispatus* Colonization by Analysis Population and Treatment Group

	ITT			mITT			CC			PP		
	LACTIN-V (N = xxx)	**Placebo (N = xxx)**	**All Subjects (N = xxx)**	**LACTIN-V (N = xxx)**	**Placebo (N = xxx)**	**All Subjects (N = xxx)**	**LACTIN-V (N = xxx)**	**Placebo (N = xxx)**	**All Subjects (N = xxx)**	**LACTIN-V (N = xxx)**	**Placebo (N = xxx)**	**All Subjects (N = xxx)**
Number (%) of subjects with Colonization	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Median Time (days)	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
Median Time (days) 95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Minimum (days)	x	x	x	x	x	x	x	x	x	x	x	x
Q1 (days)	x	x	x	x	x	x	x	x	x	x	x	x
Q3 (days)	x	x	x	x	x	x	x	x	x	x	x	x
Maximum (days)	x	x	x	x	x	x	x	x	x	x	x	x
Notes: Median time and median time 95% CI comes from Kaplan-Meier estimates												

Table 55: Treatment Compliance by Treatment Group and Analysis Population

Analysis Population	Treatment Group	Number of Subjects Compliant with Dose Regimen n	Number of Subjects N	Proportion of Subjects Compliant with Dose Regimen	Compliant 95% CI[1]	Difference in Proportion of Subjects Compliant with Dose Regimen between LACTIN-V Group and Placebo Group	Difference in Proportion of Subjects Compliant with Dose Regimen between LACTIN-V Group and Placebo Group 95% CI[2]	p-value[3]
ITT	LACTIN-V	x	x	0.xx	0.xx, 0.xx	0.xx	0.xx, 0.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
mITT	LACTIN-V	x	x	0.xx	0.xx, 0.xx	0.xx	0.xx, 0.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	
CC	LACTIN-V	x	x	0.xx	0.xx, 0.xx	0.xx	0.xx, 0.xx	0.xxx
	Placebo	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Table 56: Product Administration by Week, Dose Number, and Method of Assessment - Safety Population

All Subjects (N=X)							
	Subject Report		Clinic Assessment of Product Accountability		Staining Results		
Dose	Dose Taken n (%)	Dose Not Taken n (%)	Used Applicators Returned Mean (Std)	Unused Applicators Returned Mean (Std)	Used Mean (Std)	Unused Mean (Std)	Indeterminate Mean (Std)
Week 1							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
3	x (x)	x (x)					
4	x (x)	x (x)					
5	x (x)	x (x)					
Week 2							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Week 3							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Week 4							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Week 5							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Week 6							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Week 7							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Week 8							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Week 9							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Week 10							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)

2	x (x)	x (x)					
Week 11							
1	x (x)	x (x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
2	x (x)	x (x)					
Note: Denominator of percentages is the number of subjects in the Safety Population.							

Tables with similar format:

Table 57: Product Administration by Site, Week, Dose Number, and Method of Assessment - Safety Population- San Francisco General Hospital

Table 58: Product Administration by Site, Week, Dose Number, and Method of Assessment - Safety Population- Stroger Hospital of Cook County

Table 59: Product Administration by Site, Week, Dose Number, and Method of Assessment - Safety Population- University of California San Diego

Table 60: Product Administration by Site, Week, Dose Number, and Method of Assessment - Safety Population- Washington University in St. Louis

Table 61: Product Administration by Treatment Group, Week, Dose Number, and Method of Assessment - Safety Population- LACTIN-V

Table 62: Product Administration by Site, Week, Dose Number, and Method of Assessment - Safety Population- Placebo

Table 63: Categorical Responses to Acceptability Questionnaire by Treatment Group – Screening Visit

Questionnaire Item	Response	LACTIN-V (N = x)				Placebo (N = x)			
		Number of Subjects with Response n	Number of Subjects Queried N	Proportion of Subjects with Response	Response 95% CI[1]	Number of Subjects with Response n	Number of Subjects Queried N	Proportion of Subjects with Response	Response 95% CI[1]
How many episodes of BV have you experienced in your life?	None	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	1-2	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	3-4	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	5 or more	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Unknown	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
If you have had BV in the past, what have you used for treatment?	Nothing	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Antibiotics	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Probiotics	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Home remedies	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Other	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Unknown	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
If you ever had BV and treated it, how would you reply to the following statement: "I believe the treatment I have previously used are effective in treating BV".	Strongly Agree	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Agree	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Neutral	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Disagree	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
	Strongly Disagree	x	x	0.xx	0.xx, 0.xx	x	x	0.xx	0.xx, 0.xx
Etc.									

Notes:
Denominator of percentages is the number of subjects in the Safety Population in the respective treatment group
1: 95% CI= 95% Wilson confidence interval

Tables with similar format:

Table 64: Categorical Responses to Acceptability Questionnaire by Treatment Group –Visit 4 (Week 12)

Table 65: Continuous/Discrete Responses to Acceptability Questionnaire by Treatment Group – Screening Visit

Questionnaire Item	Questionnaire Sub-Item	LACTIN-V (N = x)			Placebo (N = x)		
		Mean (SD)	Median	Range	Mean (SD)	Median	Range
On a scale of 0 to 10, with 0 being "not at all bothersome" to 10 being "extremely bothersome", I found the following symptoms of BV:	Increase vaginal discharge	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Vaginal odor	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Vaginal irritation and itching	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Pain with urination	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Other	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
On a scale of 0 to 10, with 0 being "not at all important" to 10 being "extremely important", I would find the following characteristics important about such a product:	Effective to treat BV	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Comfortable	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Easy to use	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Improved vaginal prescription	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Availability without prescription	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	All-natural ingredients of the product	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Partner's approval of the product	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
	Other	xx.x (xx.xx)	xx.xx	xx.x, xx.x	xx.x (xx.xx)	xx.xx	xx.x, xx.x
Etc.							
Note: N= number of subjects in the Safety Population in the respective treatment group							

Tables with similar format:

Table 66: Continuous/Discrete Responses to Acceptability Questionnaire by Treatment Group – Visit 4 (Week 12)

Table 67: Model-Based Rate of Positive BV Diagnoses by Visit 4 (Week 12) by Analysis Population and Treatment Group

Analysis Population	Treatment Group	Number of Subjects N	Rate of BV Diagnoses n	BV Diagnosis Rate 95% CI	BV Diagnosis Rate Ratio between LACTIN-V Group and Placebo Group	BV Diagnosis Rate Ratio between LACTIN-V Group and Placebo Group 95% CI
ITT	LACTIN-V	x	x.xx	x.xx, x.xx	x.xx	x.xx, x.xx
	Placebo	x	x.xx	x.xx, x.xx	--	--
	All Subjects	x	x.xx	x.xx, x.xx	--	--
mITT	LACTIN-V	x	x.xx	x.xx, x.xx	x.xx	x.xx, x.xx
	Placebo	x	x.xx	x.xx, x.xx	--	--
	All Subjects	x	x.xx	x.xx, x.xx	--	--
CC	LACTIN-V	x	x.xx	x.xx, x.xx	x.xx	x.xx, x.xx
	Placebo	x	x.xx	x.xx, x.xx	--	--
	All Subjects	x	x.xx	x.xx, x.xx	--	--
PP	LACTIN-V	x	x.xx	x.xx, x.xx	x.xx	x.xx, x.xx
	Placebo	x	x.xx	x.xx, x.xx	--	--
	All Subjects	x	x.xx	x.xx, x.xx	--	--

Table 68: Model-Based Odds of Positive BV Diagnoses by Visit 4 (Week 12) by Analysis Population and Treatment Group

Analysis Population	Treatment Group	Number of Subjects N	Odds of BV Diagnoses n	BV Diagnosis Odds 95% CI	BV Diagnosis Odds Ratio between LACTIN-V Group and Placebo Group	BV Diagnosis Odds Ratio between LACTIN-V Group and Placebo Group 95% CI
ITT	LACTIN-V	x	x.xx	x.xx, x.xx	x.xx	x.xx, x.xx
	Placebo	x	x.xx	x.xx, x.xx	--	--
	All Subjects	x	x.xx	x.xx, x.xx	--	--
mITT	LACTIN-V	x	x.xx	x.xx, x.xx	x.xx	x.xx, x.xx
	Placebo	x	x.xx	x.xx, x.xx	--	--
	All Subjects	x	x.xx	x.xx, x.xx	--	--
CC	LACTIN-V	x	x.xx	x.xx, x.xx	x.xx	x.xx, x.xx
	Placebo	x	x.xx	x.xx, x.xx	--	--
	All Subjects	x	x.xx	x.xx, x.xx	--	--
PP	LACTIN-V	x	x.xx	x.xx, x.xx	x.xx	x.xx, x.xx
	Placebo	x	x.xx	x.xx, x.xx	--	--
	All Subjects	x	x.xx	x.xx, x.xx	--	--

Table 69: BV Recurrence by Visit 4 (Week 12) by Analysis Population, Treatment Group, and Race

Analysis Population	Treatment Group	Race	Number of Subjects with BV Recurrence n	Number of Subjects N	Proportion of Subjects with BV Recurrence	BV Recurrence 95% CI[1]	Odds of BV Recurrence in LACTIN-V Group Compared to Placebo Group	Odds of BV Recurrence in LACTIN-V Group Compared to Placebo Group 95% CI[2]	p-value[3]
ITT (LOCF)	LACTIN-V	Black/African American	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
		White	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
		Other	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	Black/African American	x	x	0.xx	0.xx, 0.xx	--	--	
		White	x	x	0.xx	0.xx, 0.xx	--	--	
		Other	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	Black/African American	x	x	0.xx	0.xx, 0.xx	--	--	
		White	x	x	0.xx	0.xx, 0.xx	--	--	
		Other	x	x	0.xx	0.xx, 0.xx	--	--	
Continue for mITT (LOCF), ITT (Worst Case), mITT (Worst Case), CC, and PP populations									

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group, race group, and analysis population.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Table with similar format:

Table 70: BV Recurrence by Visit 7 (Week 24) by Analysis Population, Treatment Group, and Race

Table 71: *L. crispatus* Colonization through Visit 4 (Week 12) by Analysis Population, Treatment Group, and Race

Analysis Population	Treatment Group	Race	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI	Odds of Colonization in LACTIN-V Group Compared to Placebo Group	Odds of Colonization in LACTIN-V Group Compared to Placebo Group 95% CI	p-value[1]
ITT	LACTIN-V	Black/African American	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
		White	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
		Other	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	Black/African American	x	x	0.xx	0.xx, 0.xx	--	--	
		White	x	x	0.xx	0.xx, 0.xx	--	--	
		Other	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	Black/African American	x	x	0.xx	0.xx, 0.xx	--	--	
		White	x	x	0.xx	0.xx, 0.xx	--	--	
		Other	x	x	0.xx	0.xx, 0.xx	--	--	
Continue for mITT, CC, and PP populations									

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group, race group, and analysis population.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Tables with similar format:

Table 72: *L. crispatus* Colonization at Visit 7 (Week 24) by Analysis Population, Treatment Group, and Race

Table 73: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Race – ITT Population

Study Day (Week)	Treatment Group	Race	Number of Subjects[1]	Mean (SD)	Median	Range
Day 1	LACTIN-V	Black/African American	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		White	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		Other	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	Black/African American	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		White	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		Other	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	Black/African American	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		White	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		Other	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Continue for Day 28 (Week 4), Day 56 (Week 8), Day 84 (Week 12), and Day 168 (Week 24)						
1: The number of subjects in the respective treatment group, race group, and analysis population with concentration data available at the specified visit.						

Tables with similar format:

Table 74: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Race – mITT Population

Table 75: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Race – CC Population

Table 76: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Race – PP Population

Table 77: *L. crispatus* Colonization by Study Day, Treatment Group, and Amsel Critera – ITT Population

Study Day (Week)	Treatment Group	Amsel Criteria	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI	Odds of Colonization in LACTIN-V Group Compared to Placebo Group	Odds of Colonization in LACTIN-V Group Compared to Placebo Group 95% CI	p-value[1]
Day 1	LACTIN-V	Positive	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
		Negative	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	Positive	x	x	0.xx	0.xx, 0.xx	--	--	
		Negative	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	Positive	x	x	0.xx	0.xx, 0.xx	--	--	
		Negative	x	x	0.xx	0.xx, 0.xx	--	--	
Continue for Day 28 (Week 4), Day 56 (Week 8), Day 84 (Week 12), and Day 168 (Week 24)									

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Tables with similar format:

Table 78: *L. crispatus* Colonization by Study Day, Treatment Group, and Amsel Critera – mITT Population

Table 79: *L. crispatus* Colonization by Study Day, Treatment Group, and Amsel Critera – CC Population

Table 80: *L. crispatus* Colonization by Study Day, Treatment Group, and Amsel Critera – PP Population

Table 81: *L. crispatus* Colonization by Study Day, Treatment Group, and Nugent Score – ITT Population

Study Day (Week)	Treatment Group	Nugent Score Category	Number of Subjects with Colonization n	Number of Subjects N	Proportion of Subjects with Colonization	Colonization 95% CI	Odds of Colonization in LACTIN-V Group Compared to Placebo Group	Odds of Colonization in LACTIN-V Group Compared to Placebo Group 95% CI	p-value[1]
Day 1	LACTIN-V	Normal	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
		Intermediate	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
		BV	x	x	0.xx	0.xx, 0.xx	x.xx	x.xx, x.xx	0.xxx
	Placebo	Normal	x	x	0.xx	0.xx, 0.xx	--	--	
		Intermediate	x	x	0.xx	0.xx, 0.xx	--	--	
		BV	x	x	0.xx	0.xx, 0.xx	--	--	
	All Subjects	Normal	x	x	0.xx	0.xx, 0.xx	--	--	
		Intermediate	x	x	0.xx	0.xx, 0.xx	--	--	
		BV	x	x	0.xx	0.xx, 0.xx	--	--	
Continue for Day 28 (Week 4), Day 56 (Week 8), Day 84 (Week 12), and Day 168 (Week 24)									

Note: The denominator for rate estimates is based on the number of subjects in the respective treatment group and analysis population.
1: 95% CI= 95% Wilson confidence interval
2: Difference in 95% CI=asymptotic 95% CI from a Chi-Square test
3: p-value calculated from the Chi Square Test.

Tables with similar format:

Table 82: *L. crispatus* Colonization by Study Day, Treatment Group, and Nugent Score – mITT Population

Table 83: *L. crispatus* Colonization by Study Day, Treatment Group, and Nugent Score – CC Population

Table 84: *L. crispatus* Colonization by Study Day, Treatment Group, and Nugent Score – PP Population

Table 85: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Amsel Criteria – ITT Population

Study Day (Week)	Treatment Group	Amsel Criteria	Number of Subjects[1]	Mean (SD)	Median	Range
Day 1	LACTIN-V	Positive	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		Negative	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	Placebo	Positive	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		Negative	x	x.xx (x.xx)	x.xx	x.xx, x.xx
	All Subjects	Positive	x	x.xx (x.xx)	x.xx	x.xx, x.xx
		Negative	x	x.xx (x.xx)	x.xx	x.xx, x.xx
Continue for Day 28 (Week 4), Day 56 (Week 8), Day 84 (Week 12), and Day 168 (Week 24)						
1: The number of subjects in the respective treatment group and analysis population with concentration and Amsel data available at the specified visit.						

Tables with similar format:

Table 86: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Amsel Criteria – mITT Population

Table 87: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Amsel Criteria – CC Population

Table 88: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Amsel Criteria – PP Population

Table 89: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Nugent Score – mITT Population

Table 90: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Nugent Score – CC Population

Table 91: *L. crispatus* CTV-05 Concentration by Study Day, Treatment Group, and Nugent Score – PP Population

Table 92: Summary of Categorical Demographic and Baseline Characteristics by Site - All Enrolled Subjects

Variable	Characteristic	San Francisco General Hospital (N = X)		Stroger Hospital of Cook County (N = X)		University of California, San Diego (N = X)		Washington University in St. Louis (N = X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
Sex	Female	x	x	x	x	x	x	x	x	x	x
Ethnicity	Not Hispanic or Latino	x	x	x	x	x	x	x	x	x	x
	Hispanic or Latino	x	x	x	x	x	x	x	x	x	x
	Not Reported	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x
Race	American Indian or Alaska Native	x	x	x	x	x	x	x	x	x	x
	Asian	x	x	x	x	x	x	x	x	x	x
	Native Hawaiian or Other Pacific Islander	x	x	x	x	x	x	x	x	x	x
	Black or African American	x	x	x	x	x	x	x	x	x	x
	White	x	x	x	x	x	x	x	x	x	x
	Multi-Racial	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x
Notes: N=number of enrolled subjects											

Table 93: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group—ITT Population

Variable	Characteristic	LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Sex	Female	x	x	x	x	x	x
Ethnicity	Not Hispanic or Latino	x	x	x	x	x	x
	Hispanic or Latino	x	x	x	x	x	x
	Not Reported	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x
Race	American Indian or Alaska Native	x	x	x	x	x	x
	Asian	x	x	x	x	x	x
	Native Hawaiian or Other Pacific Islander	x	x	x	x	x	x
	Black or African American	x	x	x	x	x	x
	White	x	x	x	x	x	x
	Multi-Racial	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x

Note: N=Number of Subjects in the ITT population

Table 94: Summary of Continuous Demographic and Baseline Characteristics by Site—All Enrolled Subjects

Variable	Statistic	San Francisco General Hospital (N = X)	Stroger Hospital of Cook County (N = X)	University of California, San Diego (N = X)	Washington University in St. Louis (N=X)	All Subjects (N=X)
Age	Mean	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x
	Maximum	x	x	x	x	x
Notes: N=number of enrolled subjects						

Table 95: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group - ITT Population

Variable	Statistic	LACTIN-V (N=X)	Placebo (N=X)	All Subjects (N=X)
Age	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x.x	x.x	x.x
	Minimum	x	x	x
	Maximum	x	x	x
Note: N=Number of subjects in the ITT population				

Table 96: Summary of Baseline* Categorical Sexual History by Treatment Group - ITT Population

Gynecological and Sexual History Interview Question	Value	LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Have you been amenorrheic for at least 3 months due to use of a long-acting progestin or continuous use of oral contraceptives?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x
In the past 3 months, have you had any abnormal menstrual cycles?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x
Cycle length less than 21 days?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x
Cycle length less than 35 days?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x
Intermenstrual bleeding/spotting?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x
What sanitary products do you use during your period?	Pads	x	x	x	x	x	x
	Cups	x	x	x	x	x	x
	Tampons	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Have you ever douched or used vaginal preparations or drying agents?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x
Do you have any children born with congenital anomalies?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x
What is your current relationship status?	Married	x	x	x	x	x	x
	Divorced/Separated	x	x	x	x	x	x
	Single (never married)	x	x	x	x	x	x
	Widowed	x	x	x	x	x	x
	Steady partner, cohabitating	x	x	x	x	x	x
	Steady partner, not cohabitating	x	x	x	x	x	x
	Casual partner	x	x	x	x	x	x
Have you had sex in the past 30 days?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x
If you had sex with a man, did your partner use a condom each time?	Yes	x	x	x	x	x	x
	No	x	x	x	x	x	x

Notes: N=Number of subjects in the ITT population
*Visit 1 Day 1

Table 97: Summary of Baseline* Continuous Sexual History by Treatment Group - ITT Population

Gynecological and Sexual History Interview Question	Value	LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
How many days does your period last?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
In the last 30 days how many times have you douched or used vaginal preparations or drying agents?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many days has it been since you last douched or vaginally inserted anything other than the study applicator or MetroGel	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many times have you douched or vaginally inserted anything other than the study applicator or MetroGel?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many times have you been pregnant?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many pregnancies resulted in live birth?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many pregnancies resulted in stillborn birth?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many pregnancies resulted in spontaneous abortion?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many pregnancies resulted in elective abortion?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many pregnancies resulted in ectopic pregnancy?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x

Gynecological and Sexual History Interview Question	Value	LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
How many male partners have you had in the past 6 months?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many female partners have you had in the past 6 months?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many times did you have sex since the last visit?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many times did you have unprotected sex since the last visit?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many times did you have unprotected sex since the last visit?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many new partners did you have?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x
How many days has it been since the last time you had sex?	Mean (Standard Deviation)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)	x.x (x.x)	x x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x	x, x

Notes: N=Number of subjects in the ITT population

*Visit 1 Day 1

Table 98: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group - ITT Population – All Sites

MedDRA System Organ Class	LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Any SOC	x	x	x	x	x	x
[SOC 1]	x	x	x	x	x	x
[SOC 2]	x	x	x	x	x	x

Notes: N=number of subjects in the ITT population.
n = Number of subjects reporting medical history within the specified SOC.
A subject is only counted once per SOC.

Tables with Similar Format:

Table 99: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group - ITT Population – San Francisco General Hospital

Table 100: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group - ITT Population – Stroger Hospital of Cook County

Table 101: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group - ITT Population – University of California, San Diego

Table 102: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group - ITT Population – Washington University in St. Louis

Table 103: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group - Safety Population - All Subjects

All Subjects (N=X)							
WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	LACTIN-V (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	x	x	x	x	x
[ATC Level 1 - 1]	Any	x	x	x	x	x	x
	[ATC 2 - 1]	x	x	x	x	x	x
	[ATC 2 - 2]	x	x	x	x	x	x
	[ATC 2 - 3]	x	x	x	x	x	x
[ATC Level 1 – 2]	Any	x	x	x	x	x	x
	[ATC 2 - 1]	x	x	x	x	x	x
	[ATC 2 - 2]	x	x	x	x	x	x
	[ATC 2 - 3]	x	x	x	x	x	x

Notes: N= Number of subjects in the Safety population
n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

Tables with Similar Format:

Table 104: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group-Safety Population-San Francisco General Hospital

Table 105: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group-Safety Population-Stroger Hospital of Cook County

Table 106: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group-Safety Population-University of California, San Diego

Table 107: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group-Safety Population-Washington University in St. Louis

Table 108: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group—Safety Population

Category	Solicited Adverse Event	LACTIN-V (N=X)			Placebo (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
Solicited Adverse Events	Any Solicited Adverse Event	x	x	x, x	x	x	x, x	x	x	x, x
Solicited Local Adverse Events	Any Local Adverse Event	x	x	x, x	x	x	x, x	x	x	x, x
	Vaginal Bleeding	x	x	x, x	x	x	x, x	x	x	x, x
	Abnormal Vaginal Discharge	x	x	x, x	x	x	x, x	x	x	x, x
	Abnormal Vaginal Odor	x	x	x, x	x	x	x, x	x	x	x, x
	Genital Itching	x	x	x, x	x	x	x, x	x	x	x, x
	Genital Burning	x	x	x, x	x	x	x, x	x	x	x, x
	External Genital Irritation	x	x	x, x	x	x	x, x	x	x	x, x
	External Genital Swelling	x	x	x, x	x	x	x, x	x	x	x, x
	Genital Rash	x	x	x, x	x	x	x, x	x	x	x, x
Solicited Systemic Adverse Events	Any Systemic Adverse Event	x	x	x, x	x	x	x, x	x	x	x, x
	Nausea	x	x	x, x	x	x	x, x	x	x	x, x
	Vomiting	x	x	x, x	x	x	x, x	x	x	x, x
	Abdominal Pain/Cramps	x	x	x, x	x	x	x, x	x	x	x, x
	Diarrhea	x	x	x, x	x	x	x, x	x	x	x, x
	Constipation	x	x	x, x	x	x	x, x	x	x	x, x
	Pain/Burning with Urination	x	x	x, x	x	x	x, x	x	x	x, x
	Blood in Urine	x	x	x, x	x	x	x, x	x	x	x, x
	Headache	x	x	x, x	x	x	x, x	x	x	x, x

Notes: N = number of subjects in the Safety Analysis Population who received the specified treatment.
This table presents number and percentage of subjects.
A subject is only counted once per solicited adverse event.
95% CI= 95% Blaker Confidence Interval

Table 109: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom and Maximum Severity - Safety Population - All Subjects

		All Subjects (N=X)		
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**95% CI**
Any Solicited Local Event	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Vaginal bleeding other than menstruation	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Abnormal vaginal discharge	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Abnormal vaginal odor	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Genital itching	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Genital burning	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
External genital irritation	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
External genital swelling	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x

		All Subjects (N=X)		
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**95% CI**
Genital rash	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x

Notes: Denominator for percentages is the number of subjects in the Safety Population (N) with solicited adverse event data available after the first dose of study product.
[1]Each subject's maximum severity is reported for each solicited adverse event across all doses.
95% CI= 95% Blaker Confidence Interval

Table 110: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Maximum Severity, and Treatment Group - Safety Population

		LACTIN-V (N=X)			Placebo (N=X)		
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Solicited Local Event	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Vaginal bleeding other than menstruation	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Abnormal vaginal discharge	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Abnormal vaginal odor	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Genital itching	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Genital burning	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
External genital irritation	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
External genital swelling	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x

		LACTIN-V (N=X)			Placebo (N=X)		
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Genital rash	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x

Notes: Denominator for percentages is the number of subjects in the Safety Population (N) with solicited adverse event data available after the first dose of study product.
[1]Each subject's maximum severity is reported for each solicited adverse event across all doses.
95% CI= 95% Blaker Confidence Interval

Table 111: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Symptom and Maximum Severity—Safety Population—All Subjects

		All Subjects (N=X)		
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**95% CI**
Any Solicited Systemic Event	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Nausea	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Vomiting	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Abdominal pain/cramps	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Diarrhea	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Constipation	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Pain/burning with urination	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x
Frequent urination	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x

		All Subjects (N=X)		
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**95% CI**
Blood in urine	None	x	x	x,x
	Mild	x	x	x,x
	Moderate	x	x	x,x
	Severe	x	x	x,x

Notes: Denominator for percentages is the number of subjects in the Safety Population (N) with solicited adverse event data available after the first dose of study product.
[1]Each subject's maximum severity is reported for each solicited adverse event across all doses.
95% CI= 95% Blaker Confidence Interval

Table 112: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Maximum Severity, and Treatment Group—Safety Population

		LACTIN-V (N=X)			Placebo (N=X)		
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Solicited Systemic Event	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Nausea	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Vomiting	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Abdominal pain/cramps	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Diarrhea	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Constipation	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Pain/burning with urination	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x
Frequent urination	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x

		LACTIN-V (N=X)			Placebo (N=X)		
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Blood in urine	None	x	x	x,x	x	x	x,x
	Mild	x	x	x,x	x	x	x,x
	Moderate	x	x	x,x	x	x	x,x
	Severe	x	x	x,x	x	x	x,x

Notes: Denominator for percentages is the number of subjects in the Safety Population (N) with solicited adverse event data available after the first dose of study product.
[1]Each subject's maximum severity is reported for each solicited adverse event across all doses.
95% CI= 95% Blaker Confidence Interval

Table 113: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group - Safety Population - All Subjects - Weeks 1-6

Treatment Group=All (N=X)													
		Week 1 (N=X)		Week 2 (N=X)		Week 3 (N=X)		Week 4 (N=X)		Week 5 (N=X)		Week 6 (N=X)	
Solicited Adverse Event	Severity[1]	n	%	n	%	n	%	n	%	n	%	n	%
Any Solicited Local Event	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Vaginal bleeding other than menstruation	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Abnormal vaginal discharge	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Abnormal vaginal odor	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Genital itching	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x

Treatment Group=All (N=X)													
		Week 1 (N=X)		Week 2 (N=X)		Week 3 (N=X)		Week 4 (N=X)		Week 5 (N=X)		Week 6 (N=X)	
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Genital burning	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
External genital irritation	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
External genital swelling	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Genital rash	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x

Notes: Denominator for percentages is the number of subjects in the Safety Population (N) completing memory aid that week.
[1]The maximum severity of any solicited adverse event is summarized. A subject is only counted once at the maximum severity.

Table 114: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group - Safety Population - All Subjects - Weeks 7-24

Treatment Group=All (N=X)															
		Week 7 (N=X)		Week 8 (N=X)		Week 9 (N=X)		Week 10 (N=X)		Week 11 (N=X)		Weeks 12-18 (N=X)		Weeks 19-24 (N=X)	
Solicited Adverse Event	Severity[1]	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Solicited Local Event	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Vaginal bleeding other than menstruation	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Abnormal vaginal discharge	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Abnormal vaginal odor	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Genital itching	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Treatment Group=All (N=X)														
		Week 7 (N=X)		Week 8 (N=X)		Week 9 (N=X)		Week 10 (N=X)		Week 11 (N=X)		Weeks 12-18 (N=X)		Weeks 19-24 (N=X)	
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Genital burning	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
External genital irritation	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
External genital swelling	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Genital rash	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Notes: Denominator for percentages is the number of subjects in the Safety Population (N) completing memory aid that week.
[1]The maximum severity of any solicited adverse event is summarized. A subject is only counted once at the maximum severity.

Tables with Similar Format:

Table 115: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group—Safety Population—LACTIN-V—Weeks 1-6

Table 116: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group—Safety Population—LACTIN-V—Weeks 7-24

Table 117: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group—Safety Population—Placebo—Weeks 1-6

Table 118: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group—Safety Population—Placebo—Weeks 7-24

Table 119: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Symptom, Severity, Week, and Treatment Group - Safety Population - All Subjects - Weeks 1-6

Treatment Group= All (N=X)													
		Week 1 (N=X)		Week 2 (N=X)		Week 3 (N=X)		Week 4 (N=X)		Week 5 (N=X)		Week 6 (N=X)	
Solicited Adverse Event	Severity[1]	n	%	n	%	n	%	n	%	n	%	n	%
Any Solicited Systemic Event	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Nausea*	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Vomiting*	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Abdominal pain/cramps*	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Diarrhea*	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x

Treatment Group= All (N=X)													
		Week 1 (N=X)		Week 2 (N=X)		Week 3 (N=X)		Week 4 (N=X)		Week 5 (N=X)		Week 6 (N=X)	
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Constipation*	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Pain/burning with urination	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Frequent urination	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Blood in urine*	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x
Headache*	None	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x

Notes: Denominator for percentages is the number of subjects in the Safety Population (N) completing memory aid that week.
*Symptom not collected during weeks 12-24.
[1]The maximum severity of any solicited adverse event is summarized. A subject is only counted once at the maximum severity.

Table 120: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Symptom, Severity, Week, and Treatment Group—Safety Population—All Subjects—Weeks 7-24

Treatment Group=All (N=X)															
		Week 7 (N=X)		Week 8 (N=X)		Week 9 (N=X)		Week 10 (N=X)		Week 11 (N=X)		Weeks 12-18 (N=X)		Weeks 19-24 (N=X)	
Solicited Adverse Event	Severity[1]	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Solicited Systemic Event	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Nausea*	None	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Mild	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Moderate	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Severe	x	x	x	x	x	x	x	x	x	x	-	-	-	-
Vomiting*	None	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Mild	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Moderate	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Severe	x	x	x	x	x	x	x	x	x	x	-	-	-	-
Abdominal pain/cramps*	None	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Mild	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Moderate	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Severe	x	x	x	x	x	x	x	x	x	x	-	-	-	-
Diarrhea*	None	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Mild	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Moderate	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Severe	x	x	x	x	x	x	x	x	x	x	-	-	-	-

Treatment Group=All (N=X)															
		Week 7 (N=X)		Week 8 (N=X)		Week 9 (N=X)		Week 10 (N=X)		Week 11 (N=X)		Weeks 12-18 (N=X)		Weeks 19-24 (N=X)	
Solicited Adverse Event	**Severity[1]**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Constipation*	None	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Mild	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Moderate	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Severe	x	x	x	x	x	x	x	x	x	x	-	-	-	-
Pain/burning with urination	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Frequent urination	None	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Mild	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Severe	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Blood in urine*	None	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Mild	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Moderate	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Severe	x	x	x	x	x	x	x	x	x	x	-	-	-	-
Headache*	None	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Mild	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Moderate	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	Severe	x	x	x	x	x	x	x	x	x	x	-	-	-	-

Notes: Denominator for percentages is the number of subjects in the Safety Population (N) completing memory aid that week.
*Symptom not collected during weeks 12-24.
[1]The maximum severity of any solicited adverse event is summarized. A subject is only counted once at the maximum severity.

Tables with Similar Format:

Table 121: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group—Safety Population—LACTIN-V—Weeks 1-6

Table 122: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group—Safety Population—LACTIN-V—Weeks 7-24

Table 123: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group—Safety Population—Placebo—Weeks 1-6

Table 124: Number and Percentage of Subjects Experiencing Solicited Local Events by Symptom, Severity, Week, and Treatment Group—Safety Population—Placebo—Weeks 7-24

Table 125: Proportion of Subjects Reporting Product Related Unsolicited Adverse Events Following the First Dose of Study Product through Visit 7 by Treatment Group – Safety Population

Treatment Group	Number of Subjects with AEs n	Number of Subjects N	Proportion of Subjects with AEs	Proportion of Subjects with AEs 95% CI	Difference in Proportion of Subjects with AEs between LACTIN-V and Placebo	Difference in Proportion of Subjects with AEs between LACTIN-V and Placebo 95% CI	P-value*
LACTIN-V	x	x	0.xx	0.xx, 0.xx	0.xx	0.xx, 0.xx	0.xxx
Placebo	x	x	0.xx	0.xx, 0.xx	--	--	--
All Subjects	x	x	0.xx	0.xx, 0.xx	--	--	--

Notes: The denominator for proportions is based on the number of subjects enrolled in the respective treatment group and analysis population.
*P-value from the Fisher's exact two-sided test at the .05 level of significance.
95% CI= 95% Blaker Confidence Interval

Table 126: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events with 95% Confidence Intervals by MedDRA System Organ Class and Preferred Term, Dose Number, and Treatment Group - Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	LACTIN-V (N=X)			Placebo (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
Any SOC	Any PT	x	x	x, x	x	x	x, x	x	x	x, x
[SOC 1]	Any PT	x	x	x, x	x	x	x, x	x	x	x, x
	[PT 1]	x	x	x, x	x	x	x, x	x	x	x, x
	[PT 2]	x	x	x, x	x	x	x, x	x	x	x, x
[SOC 2]	Any PT	x	x	x, x	x	x	x, x	x	x	x, x
	[PT 1]	x	x	x, x	x	x	x, x	x	x	x, x
	[PT 2]	x	x	x, x	x	x	x, x	x	x	x, x

Notes: N = number of subjects in the Safety Analysis Population who received the specified treatment.
This table presents number and percentage of subjects.
A subject is only counted once per PT/timepoint.
95% CI= 95% Blaker Confidence Interval

Table 127: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity and Relationship—Safety Population

			All Subjects (N = X)								
			Related			Not Related			Total		
			n	%	Freq	n	%	Freq	n	%	Freq
Any SOC	Any PT	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x
[SOC 1]	Any PT	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x
	[PT 1]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x

Notes: N = Number of subjects in the Safety Analysis Population
This table presents number and percentage of subjects as well as number of events.
For severity, a subject is counted once per preferred term and is summarized according to their highest severity.

Table 128: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group - Safety Population

			LACTIN-V (N = X)									Placebo (N = X)								
			Related			Not Related			Total			Related			Not Related			Total		
			n	%	Freq	n	%	Freq	n	%	Freq	n	%	Freq	n	%	Freq	n	%	Freq
Any SOC	Any PT	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
[SOC 1]	Any PT	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	[PT 1]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Notes: N = Number of subjects in the Safety Analysis Population
This table presents number and percentage of subjects as well as number of events.
For severity, a subject is counted once per preferred term and is summarized according to their highest severity.

Table 129: Number of Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - Safety Population

Preferred Term	MedDRA System Organ Class	MedDRA Version	LACTIN-V (N=X)	Placebo (N=X)	All Subjects (N=X)
xxxxxx	xxxxxxxxxx	xx.x	xx	xx	xx
Notes: N = Number of subjects in the Safety Analysis Population					

Table 130: Subjects Reporting Adverse Events Occurring in 5% Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - Safety Population

Preferred Term	MedDRA System Organ Class	MedDRA Version	LACTIN-V (N=X)	Placebo (N=X)	All Subjects (N=X)
xxxxxx	xxxxxxxxxx	xx.x	xx	xx	xx
Notes: N = Number of subjects in the Safety Analysis Population					

Table 131: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

Adverse Event	Study Day	Severity	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Treatment Group: , AE Number:									
xxxxxxx	xx	xxxxxx	xxxxxx	xxxxx	xxxxxx	Y/N	xxxxx	xxxxx	xxxxx
Comments:xxxxxxxxxxx									
Subject ID: , Treatment Group: , AE Number:									
xxxxxxx	xx	xxxxxx	xxxxxx	xxxxx	xxxxxx	Y/N	xxxxx	xxxxx	xxxxx
Comments:xxxxxxxxxxx									

Table 132: Listing of Serious Adverse Events

Adverse Event	Study Day the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Treatment Group: , AE Number:										
xxxxxxx	**xx**	**xxxxxx**	**xxxxxx**	**xxxxxx**	**xxxxx**	**xxxxxx**	**Y/N**	**xxxxx**	**xxxxx**	**xxxxx**
Comments: xxxxxxxxxxxxx										
Subject ID: , Treatment Group: , AE Number:										
xxxxxxx	**xx**	**xxxxxx**	**xxxxxx**	**xxxxxx**	**xxxxx**	**xxxxxx**	**Y/N**	**xxxxx**	**xxxxx**	**xxxxx**
Comments: xxxxxxxxxxxxx										

Narratives of Deaths, Other Serious and Significant Adverse Events (not included in SAP, but will be included in the CSR)

Table 133: Abnormal Discharge and Cervical Mucus Characteristics by Visit and Treatment Group - Safety Population

All Subjects (N=X)									
		Visit 1 (N=X)		Visit 2 (N=X)		Visit 3 (N=X)		Visit 4 (N=X)	
Category	Value	n	%	n	%	n	%	n	%
Abnormal Discharge									
Source	Vagina	x	x	x	x	x	x	x	x
	Cervix/vagina	x	x	x	x	x	x	x	x
Amount	Minimal	x	x	x	x	x	x	x	x
	Moderate	x	x	x	x	x	x	x	x
	Profuse	x	x	x	x	x	x	x	x
Character	Thin/watery	x	x	x	x	x	x	x	x
	Normal	x	x	x	x	x	x	x	x
	Thicker than normal	x	x	x	x	x	x	x	x
Color	White	x	x	x	x	x	x	x	x
	Clear	x	x	x	x	x	x	x	x
	Yellow	x	x	x	x	x	x	x	x
	Brown	x	x	x	x	x	x	x	x
	Bloody	x	x	x	x	x	x	x	x
Consistency	Non-homogenous (normal)	x	x	x	x	x	x	x	x
	Homogenous	x	x	x	x	x	x	x	x
	Curdy/Plaques	x	x	x	x	x	x	x	x
	Frothy	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x
Distribution	Pooled	x	x	x	x	x	x	x	x
	Diffuse	x	x	x	x	x	x	x	x
	Patches	x	x	x	x	x	x	x	x
Odor	None	x	x	x	x	x	x	x	x
	Foul	x	x	x	x	x	x	x	x
	Fishy	x	x	x	x	x	x	x	x
Cervical Mucus									
Amount	Minimal (to os)	x	x	x	x	x	x	x	x
	Moderate (on face)	x	x	x	x	x	x	x	x
	Profuse (pools)	x	x	x	x	x	x	x	x
Color	Clear	x	x	x	x	x	x	x	x
	Opaque White	x	x	x	x	x	x	x	x
	Translucent White	x	x	x	x	x	x	x	x
	Yellow	x	x	x	x	x	x	x	x
	Brown	x	x	x	x	x	x	x	x

All Subjects (N=X)									
Category	Value	Visit 1 (N=X)		Visit 2 (N=X)		Visit 3 (N=X)		Visit 4 (N=X)	
		n	%	n	%	n	%	n	%
	Bloody	x	x	x	x	x	x	x	x
Viscosity	Thin	x	x	x	x	x	x	x	x
	Average	x	x	x	x	x	x	x	x
	Thick	x	x	x	x	x	x	x	x
Note: Denominator for percentages are the number of subjects with abnormal discharge that can be evaluated at the respective visit									

Tables with similar format:

Table 134: Abnormal Discharge and Cervical Mucus Characteristics by Visit and Treatment Group - Safety Population - LACTIN-V

Table 135: Abnormal Discharge and Cervical Mucus Characteristics by Visit and Treatment Group - Safety Population - Placebo

APPENDIX 2. FIGURE MOCK-UPS

This document includes example mock-ups of figures to present efficacy and safety data.

Figure 1: CONSORT Flow Diagram

Implementation notes: The actual diagram will match the design of this study.

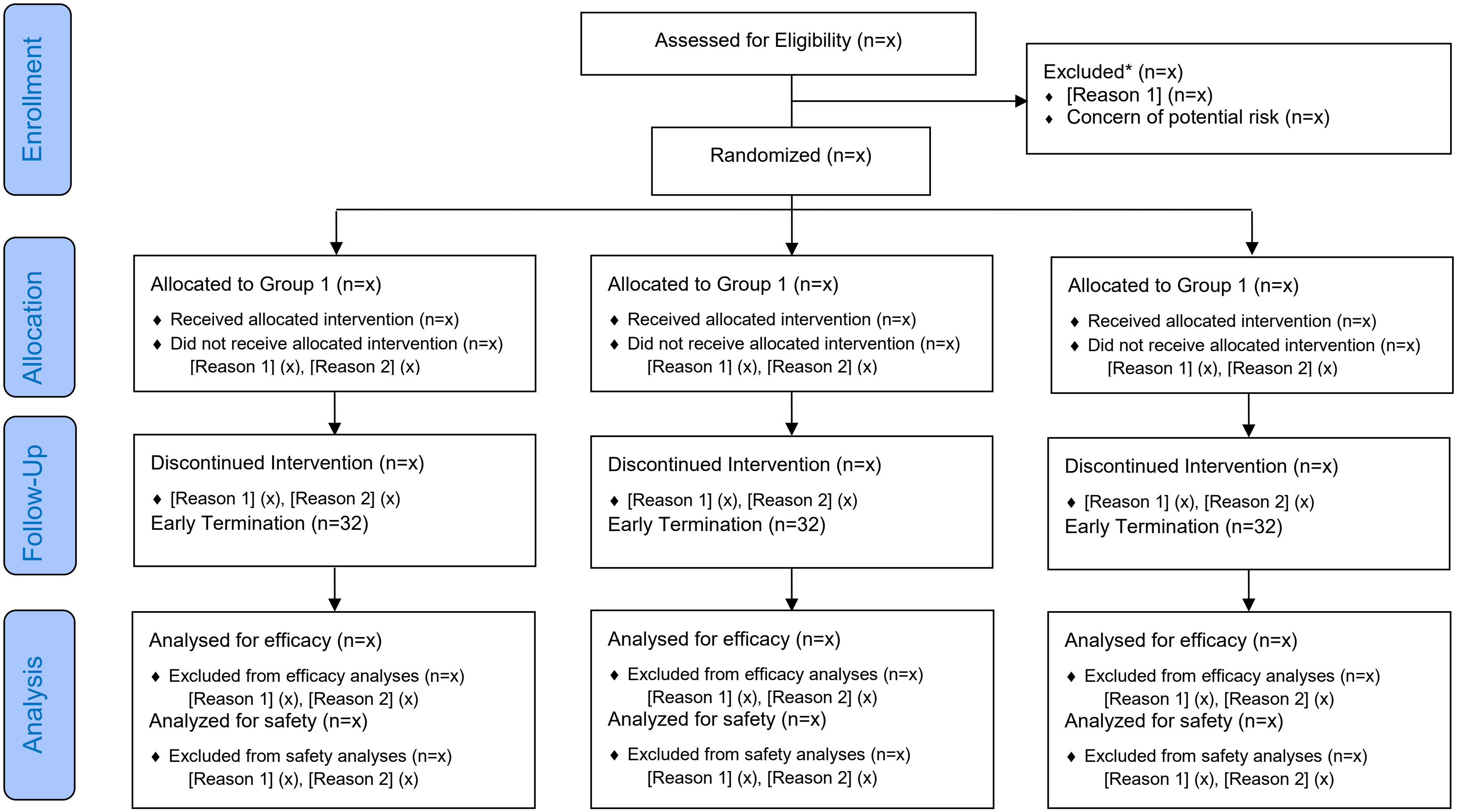


Figure 2: Time to BV Recurrence by Visit 4 (Week 12) by Treatment Group

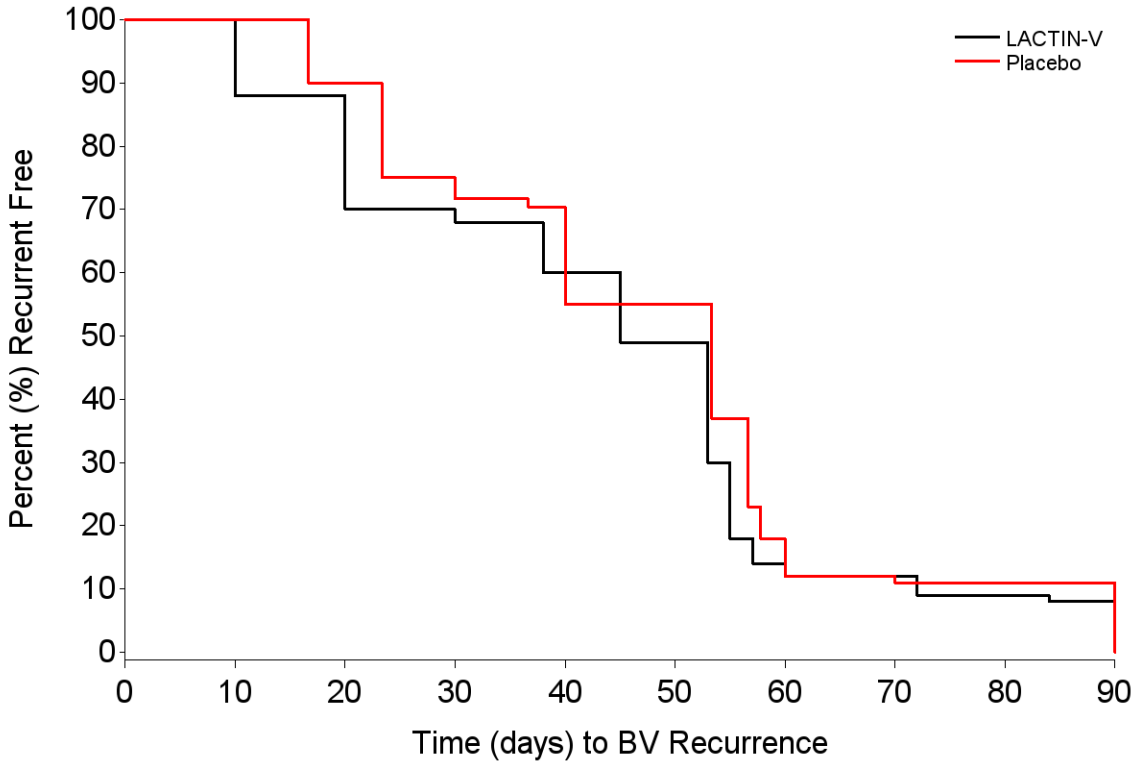


Figure will be a 2x2 panel plot with each panel displaying one of the analysis populations: ITT, mITT, CC, and PP.

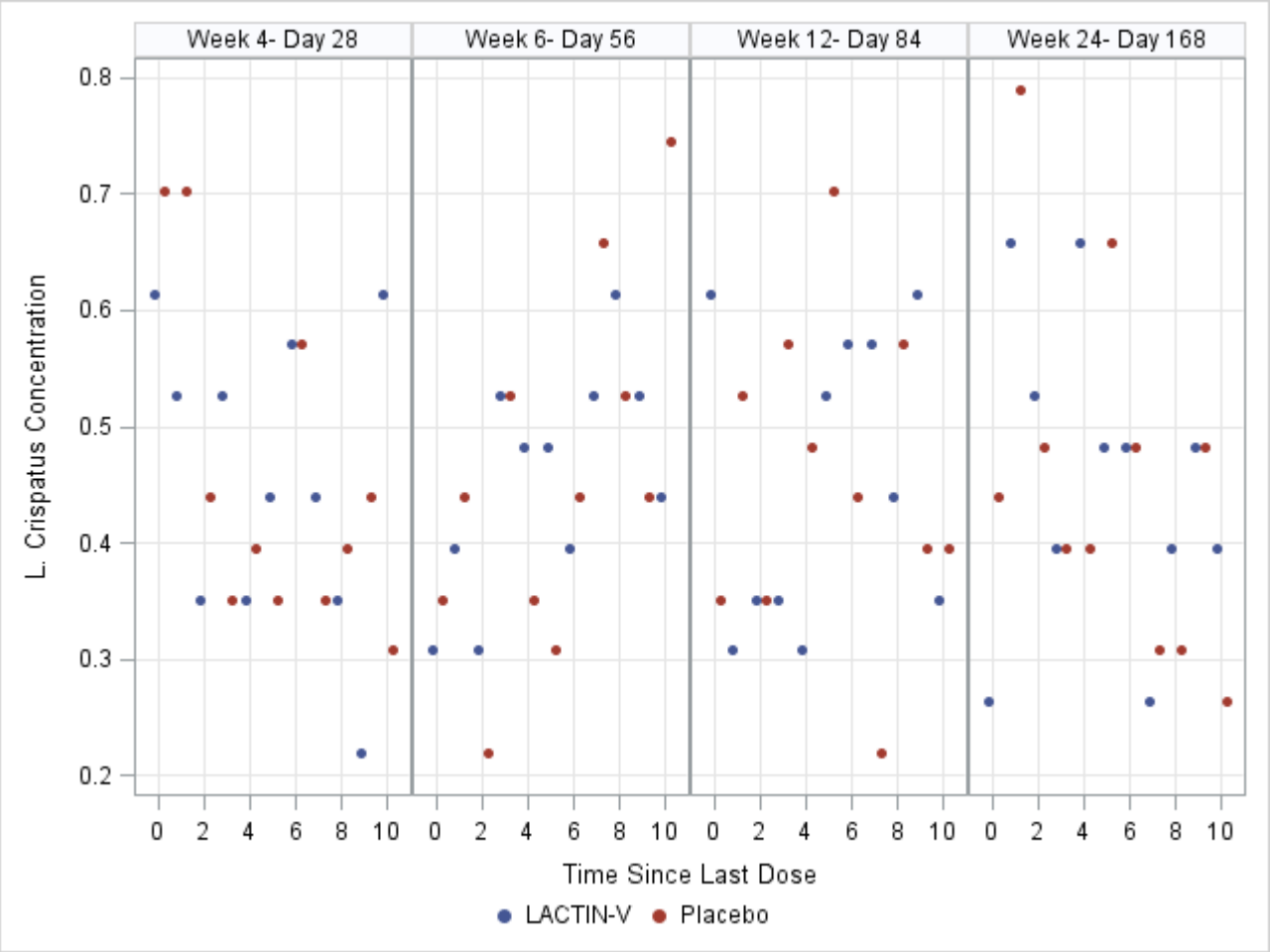
Figures with similar format:

Figure 3: Time to BV Recurrence by Visit 7 (Week 24) by Treatment Group

Figure 4: Time to *L. crispatus* Colonization by Visit 4 (Week 12) by Treatment Group

Figure 5: Time to *L. crispatus* Colonization by Visit 7 (Week 24) by Treatment Group

Figure 6: *L. crispatus* CTV-05 Concentration by Time Since Last Dose, Week, and Treatment Group-ITT Population



Figures with similar format:

Figure 7: ***L. crispatus*** **CTV-05 Concentration by Time Since Last Dose, Week, and Treatment Group-mITT Population**

Figure 8: ***L. crispatus*** **CTV-05 Concentration by Time Since Last Dose, Week, and Treatment Group-CC Population**

Figure 9: ***L. crispatus*** **CTV-05 Concentration by Time Since Last Dose, Week, and Treatment Group-PP Population**

Figure 10: ***L. crispatus*** **CTV-05 Concentration by Number of Condom-less Sexual Intercourse Acts, Week, and Treatment Group-ITT Population**

Figure 11: ***L. crispatus*** **CTV-05 Concentration by Number of Condom-less Sexual Intercourse Acts, Week, and Treatment Group-mITT Population**

Figure 12: ***L. crispatus*** **CTV-05 Concentration by Number of Condom-less Sexual Intercourse Acts, Week, and Treatment Group-CC Population**

Figure 13: ***L. crispatus*** **CTV-05 Concentration by Number of Condom-less Sexual Intercourse Acts, Week, and Treatment Group-PP Population**

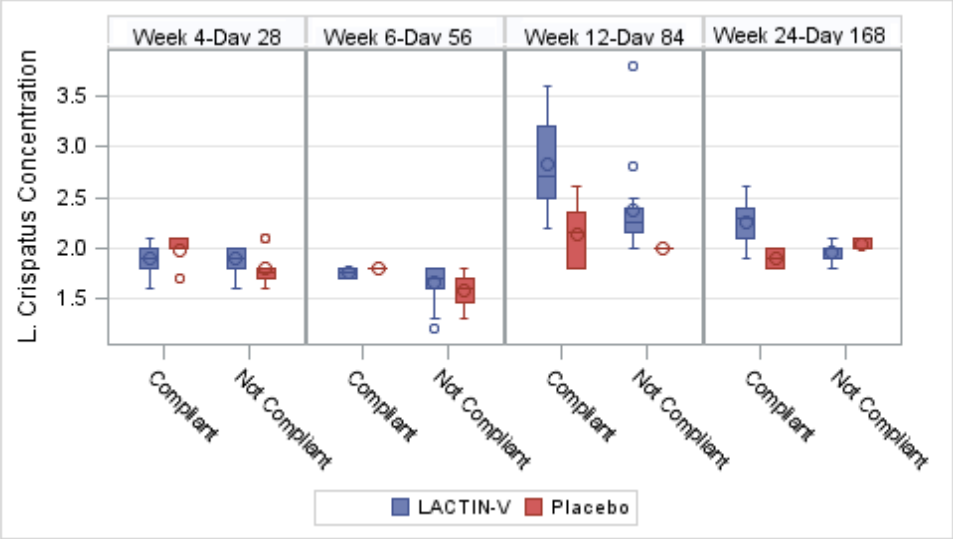
Figure 14: ***L. crispatus*** **CTV-05 Concentration by Number of Partners, Week, and Treatment Group-ITT Population**

Figure 15: ***L. crispatus*** **CTV-05 Concentration by Number of Partners, Week, and Treatment Group-mITT Population**

Figure 16: ***L. crispatus*** **CTV-05 Concentration by Number of Partners, Week, and Treatment Group-CC Population**

Figure 17: ***L. crispatus*** **CTV-05 Concentration by Number of Partners, Week, and Treatment Group-PP Population**

Figure 18: *L. crispatus* CTV-05 Concentration by Compliance Status, Week, and Treatment Group-ITT Population

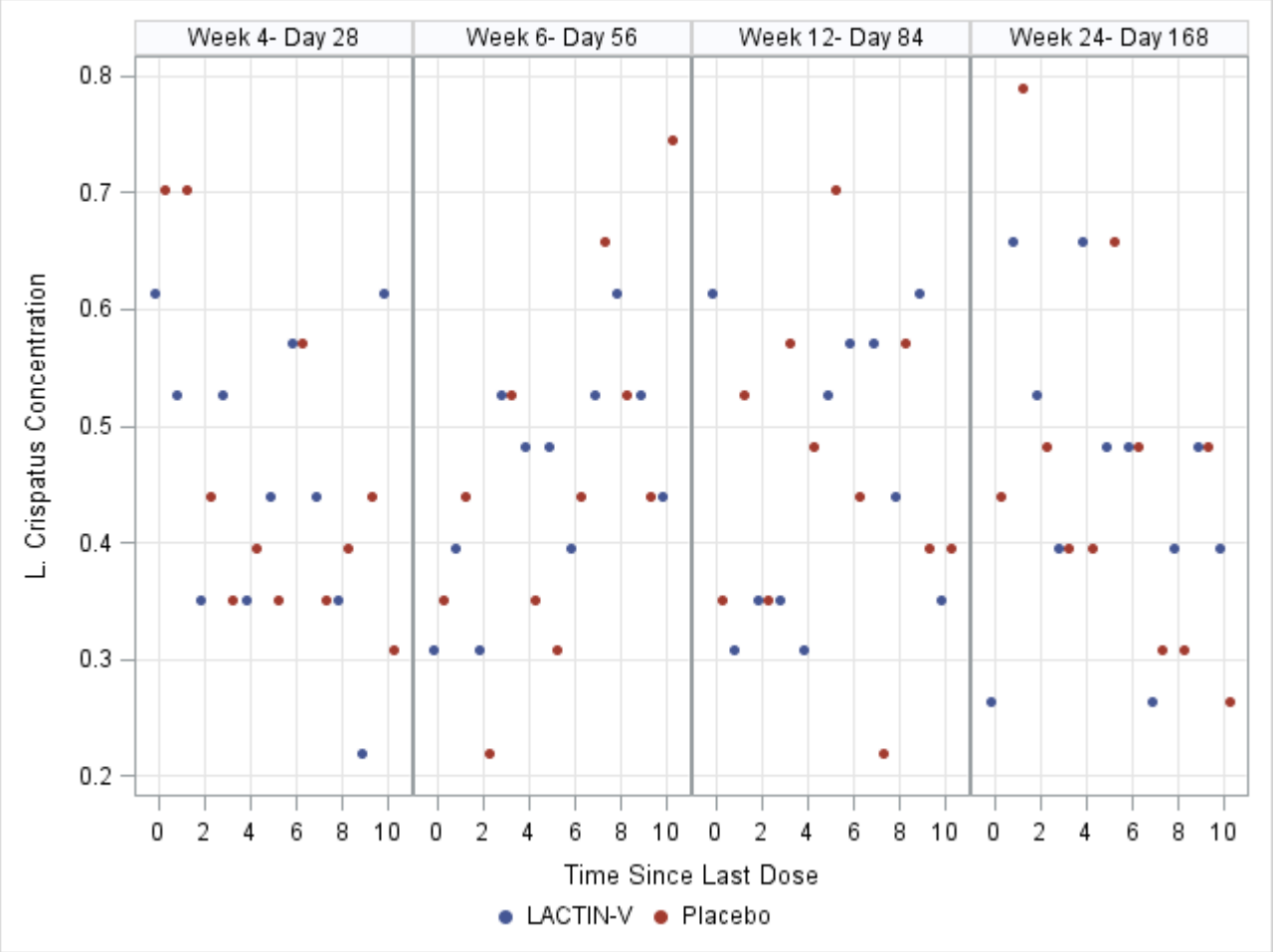


Figures with similar format:

Figure 19: *L. crispatus* CTV-05 Concentration by Compliance Status, Week, and Treatment Group-mITT Population

Figure 20: *L. crispatus* CTV-05 Concentration by Compliance Status, Week, and Treatment Group-CC Population

Figure 21: *L. crispatus* CTV-05 Concentration by Day Since Last Day of Last Menstrual Period, Week, and Treatment Group - ITT Population



Implementation Note:

X-axis labels will read "Days Since Last Day of Last Menstrual Period"

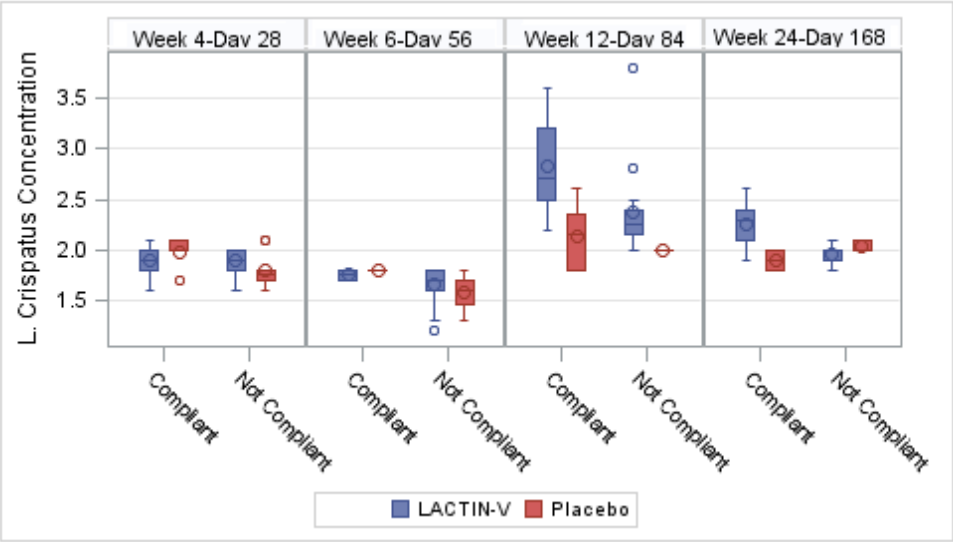
Figures with similar format:

Figure 22: *L. crispatus* CTV-05 Concentration by Day Since Last Day of Last Menstrual Period, Week, and Treatment Group - mITT Population

Figure 23: *L. crispatus* CTV-05 Concentration by Day Since Last Day of Last Menstrual Period, Week, and Treatment Group - CC Population

Figure 24: *L. crispatus* CTV-05 Concentration by Day Since Last Day of Last Menstrual Period, Week, and Treatment Group - PP Population

Figure 25: *L. crispatus* CTV-05 Concentration by Menses After Last Dose Taken, Week, and Treatment Group-ITT Population



Implementation Note:

X-axis groups will be "Menses" and "No Menses"

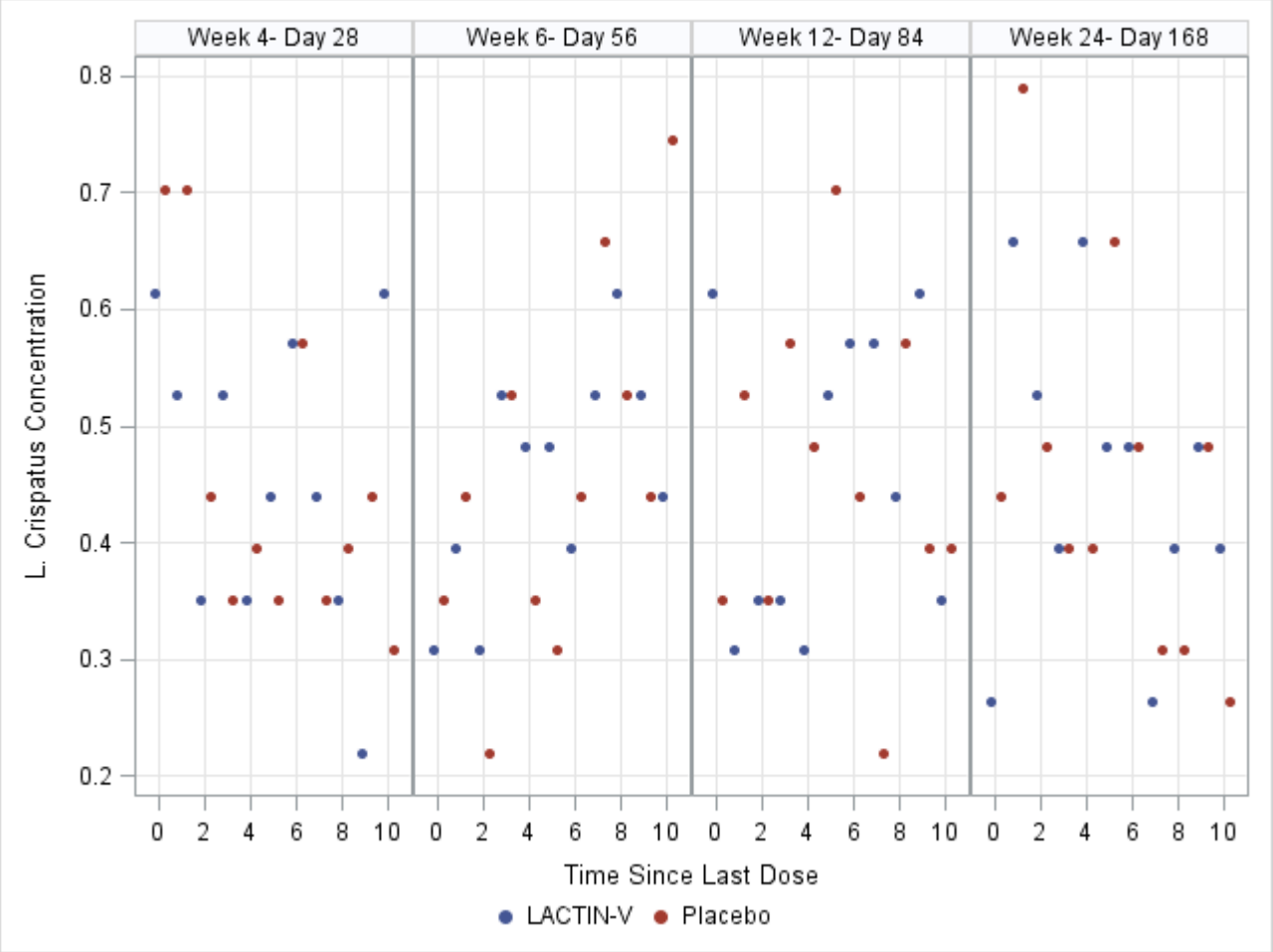
Figures with similar format:

Figure 26: *L. crispatus* CTV-05 Concentration by Menses After Last Dose Taken, Week, and Treatment Group-mITT Population

Figure 27: *L. crispatus* CTV-05 Concentration by Menses After Last Dose Taken, Week, and Treatment Group-CC Population

Figure 28: *L. crispatus* CTV-05 Concentration by Menses After Last Dose Taken, Week, and Treatment Group-PP Population

Figure 29: CTV-05 Concentration by *L. crispatus* Concentration, Week, and Treatment Group - ITT Population



Implementation Note:

Y-axis labels will read "CTV-05 concentration", X-axis labels will read "*L. crispatus* concentration".

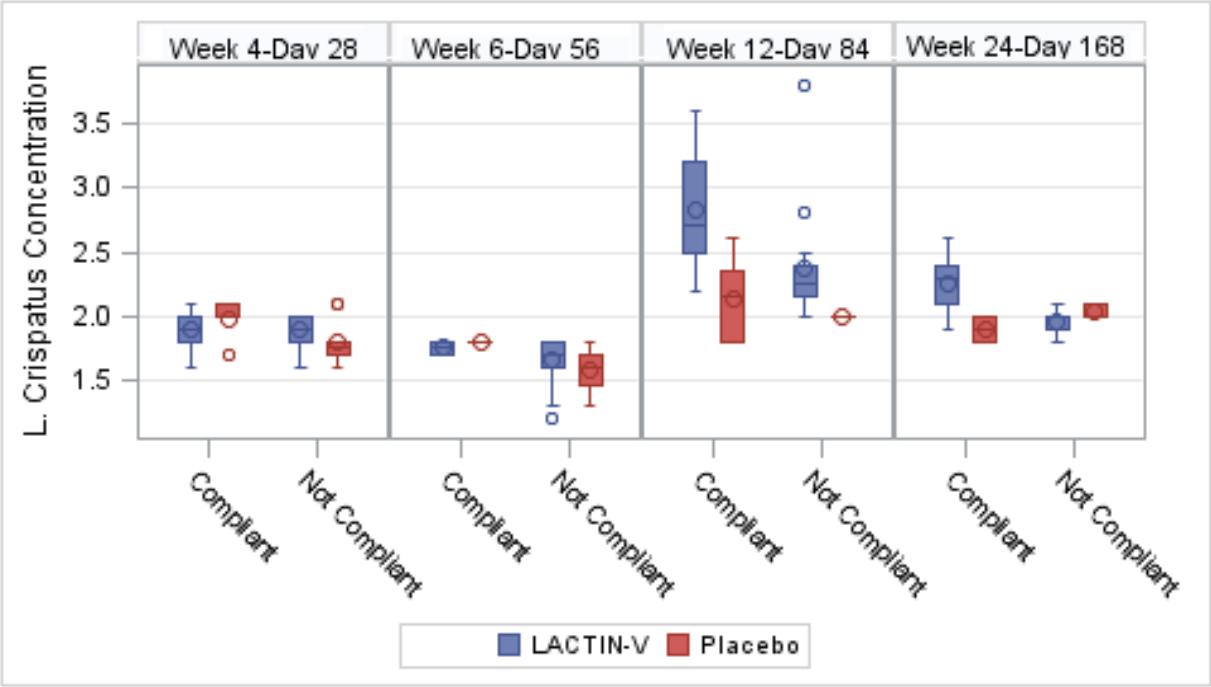
Figures with similar format:

Figure 30: CTV-05 Concentration by *L. crispatus* Concentration, Week, and Treatment Group - mITT Population

Figure 31: CTV-05 Concentration by *L. crispatus* Concentration, Week, and Treatment Group - CC Population

Figure 32: CTV-05 Concentration by *L. crispatus* Concentration, Week, and Treatment Group - PP Population

Figure 33: *L. crispatus* CTV-05 Concentration by Amsel Criteria, Week, and Treatment Group-ITT Population



Implementation Note:

X-axis groups will be "Positive" and "Negative"

Figures with similar format:

Figure 34: *L. crispatus* CTV-05 Concentration by Amsel Criteria, Week, and Treatment Group-mITT Population

Figure 35: *L. crispatus* CTV-05 Concentration by Amsel Criteria, Week, and Treatment Group-CC Population

Figure 36: *L. crispatus* CTV-05 Concentration by Amsel Criteria, Week, and Treatment Group-PP Population

Figure 37: *L. crispatus* CTV-05 Concentration by Nugent Score, Week, and Treatment Group-ITT Population

Figure 38: *L. crispatus* CTV-05 Concentration by Nugent Score, Week, and Treatment Group-mITT Population

Figure 39: *L. crispatus* CTV-05 Concentration by Nugent Score, Week, and Treatment Group-CC Population

Figure 40: *L. crispatus* CTV-05 Concentration by Nugent Score, Week, and Treatment Group-PP Population

Figure 41: Maximum Severity of Solicited Local Adverse Events by Symptom and Treatment Group - Safety Population

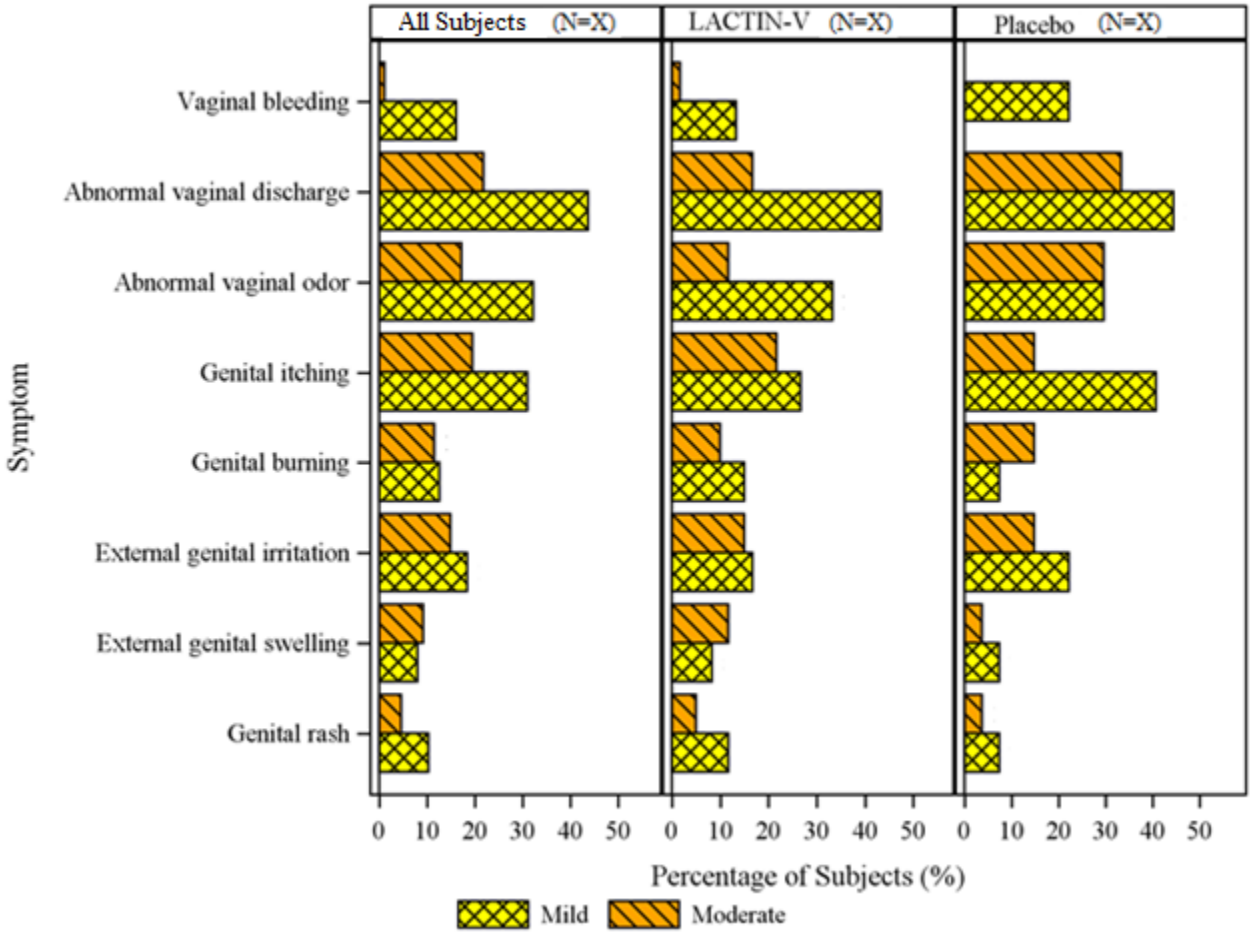


Figure 42: Maximum Severity of Solicited Systemic Adverse Events by Symptom and Treatment Group - Safety Population

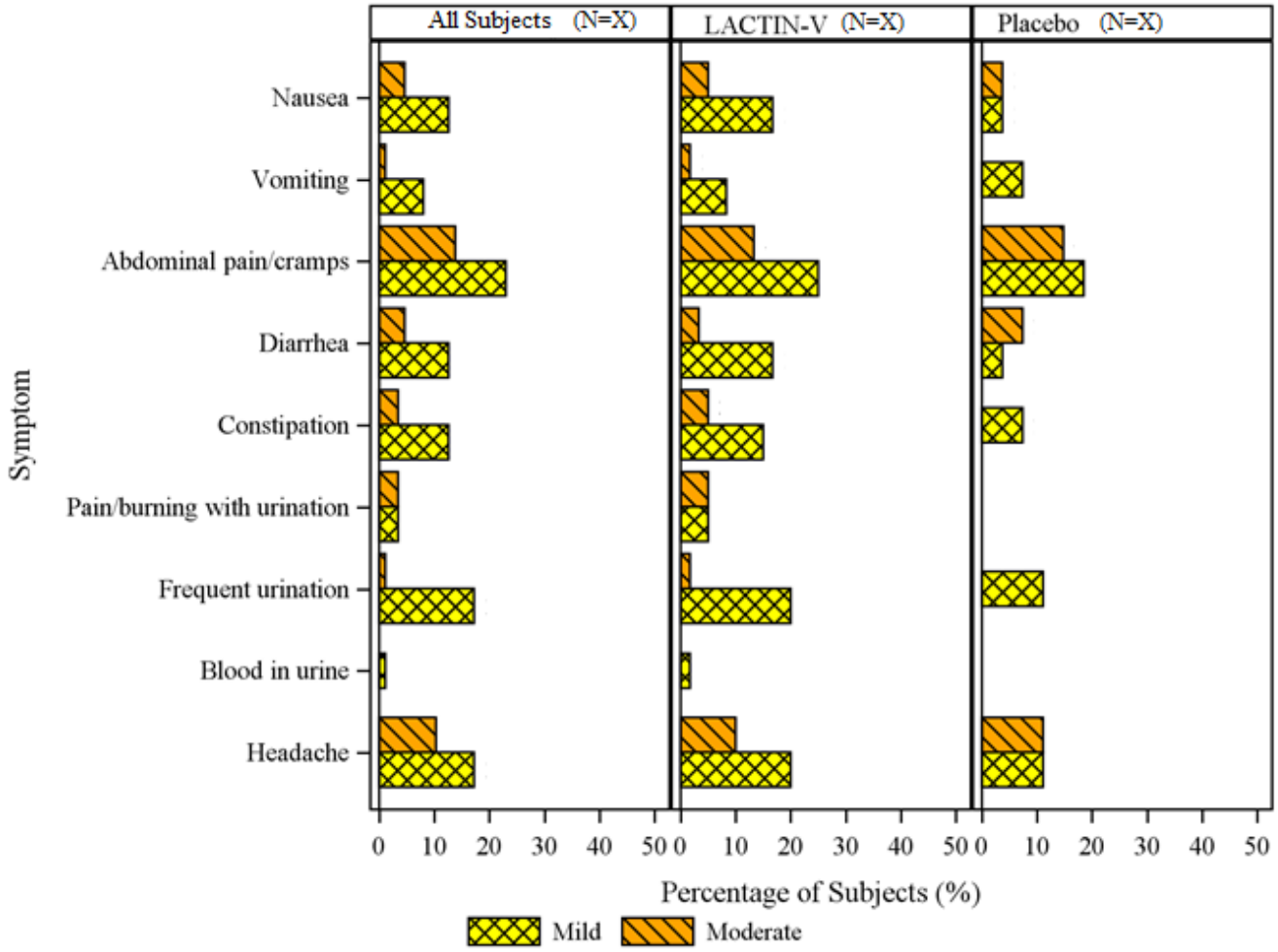
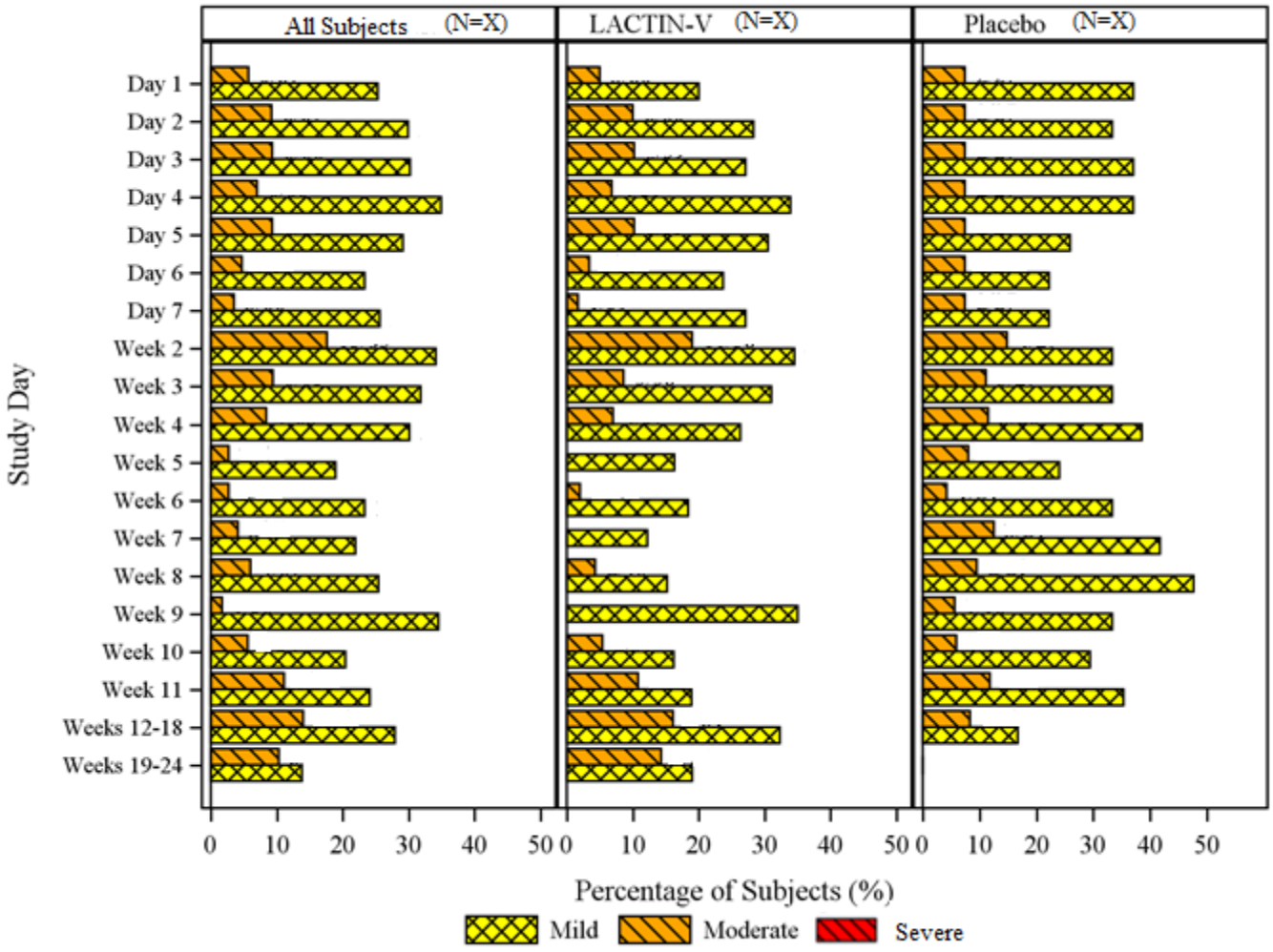


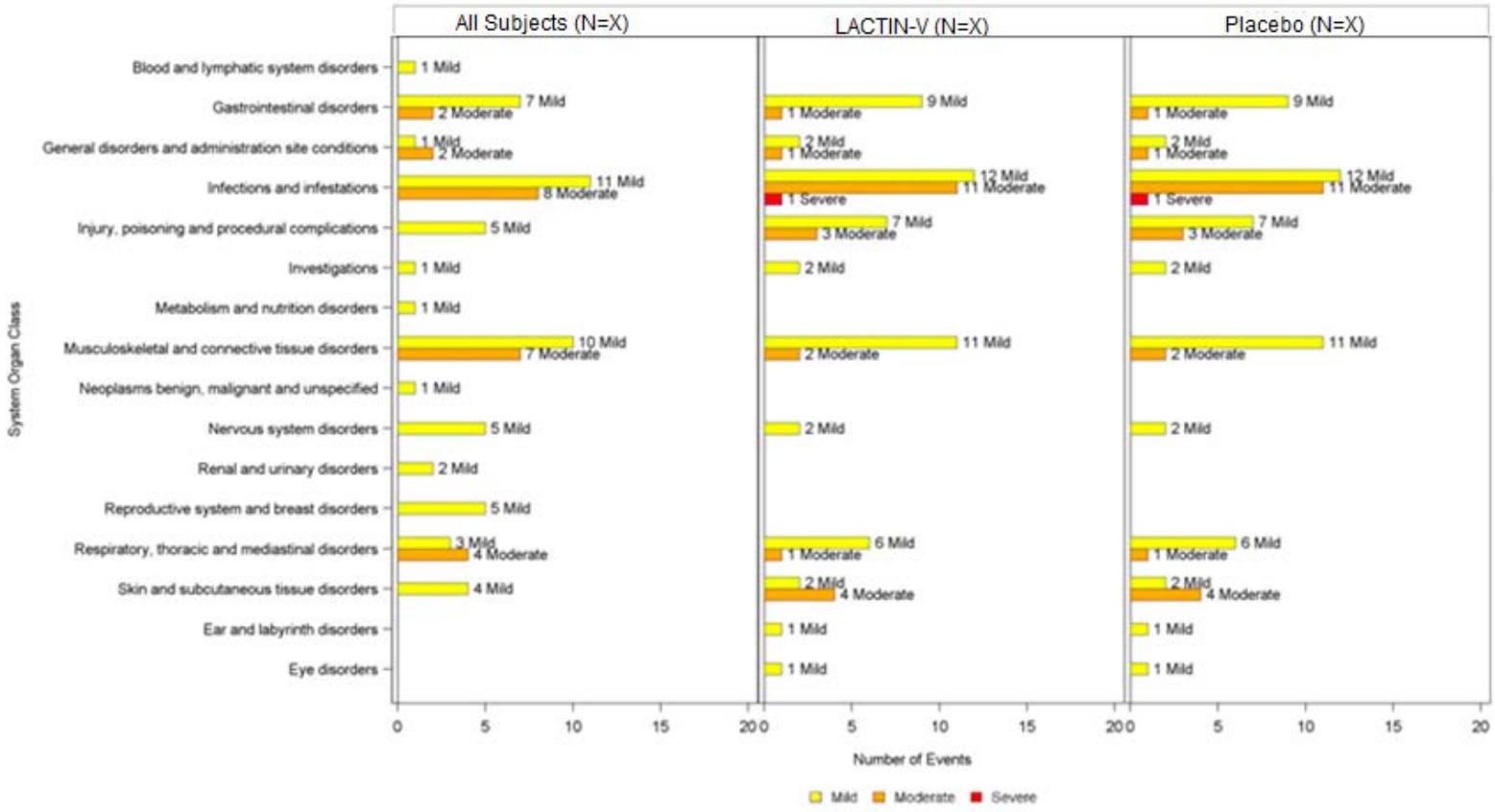
Figure 43: Maximum Severity of Solicited Local Adverse Events by Day and Treatment Group—Safety Population



Figures with Similar Format:

Figure 44: Maximum Severity of Solicited Systemic Adverse Events by Day and Treatment Group—Safety Population

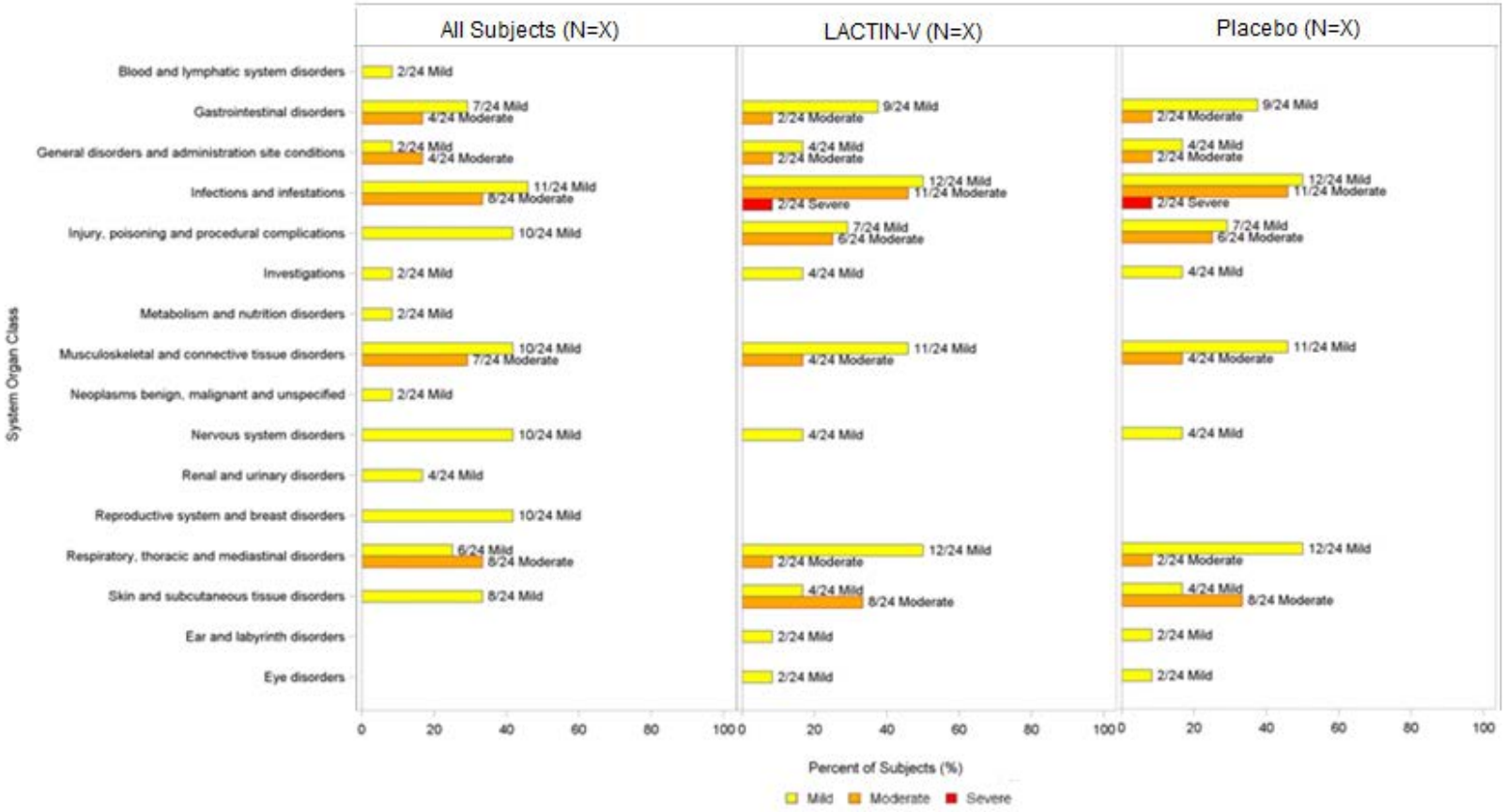
Figure 45: Frequency of Adverse Events by MedDRA System Organ Class and Severity



Implementation Note:

- Include “Any SOC” bars

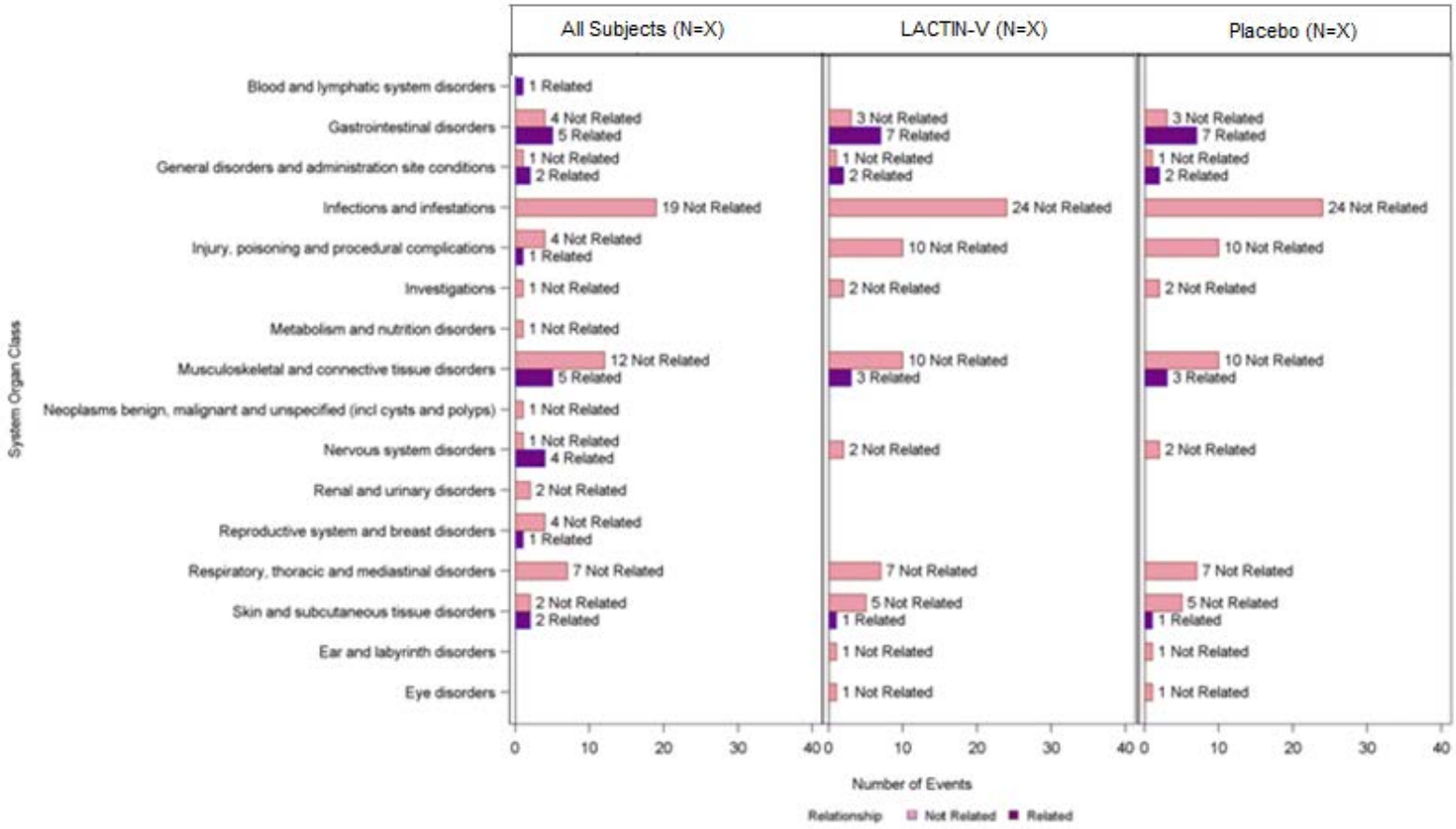
Figure 46: Incidence of Adverse Events by MedDRA System Organ Class and Maximum Severity



Implementation Note:

- Include “Any SOC” bars

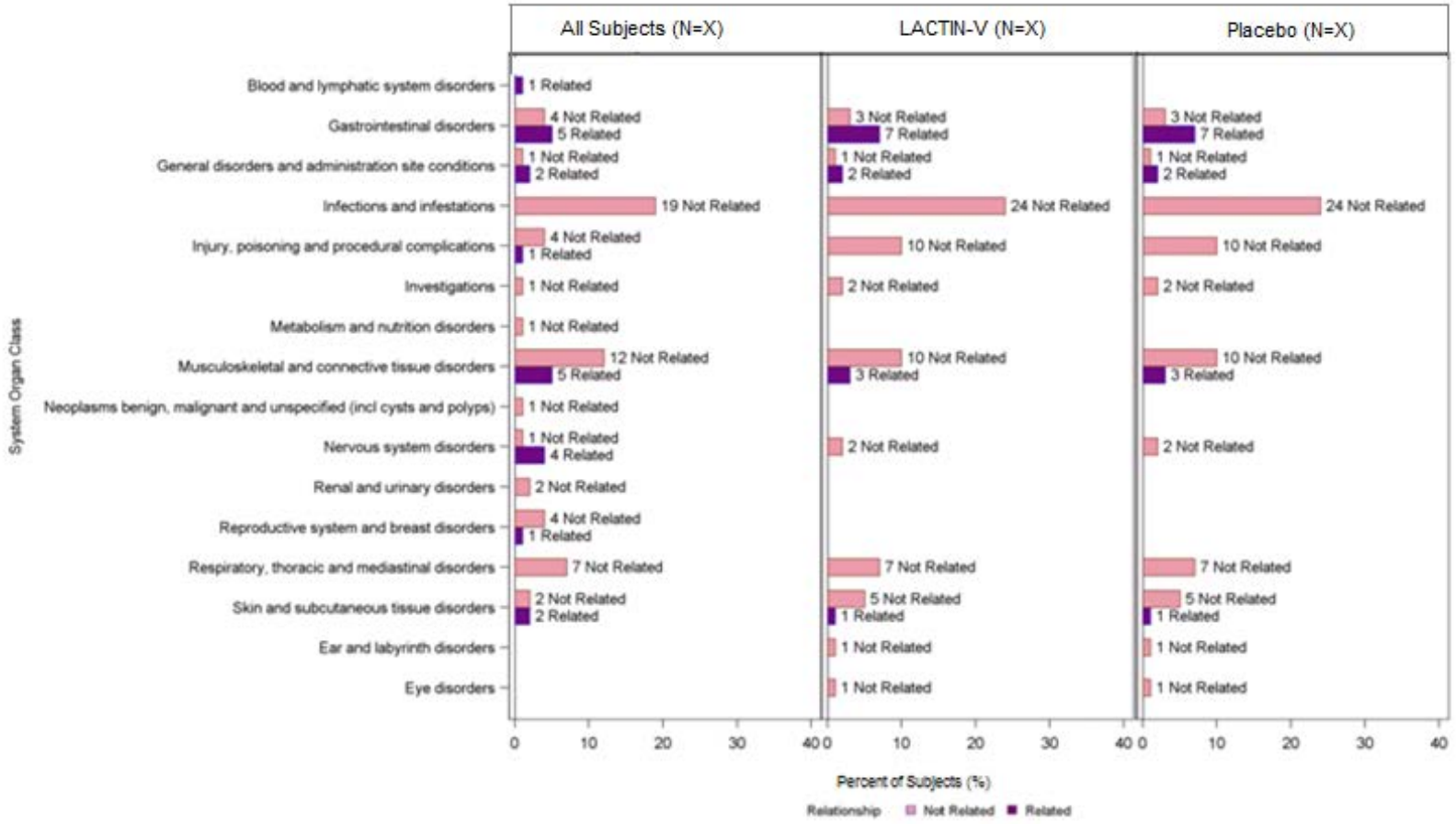
Figure 47: Frequency of Adverse Events by MedDRA System Organ Class and Relationship to Treatment



Implementation Note:

- Include “Any SOC” bars

Figure 48: Incidence of Adverse Events by MedDRA System Organ Class and Relationship to Treatment



Implementation Note:

- Include “Any SOC” bars

APPENDIX 3. LISTINGS MOCK-UPS

This document includes example mock-ups of listings to present subject-level data.

Listing of Subjects Receiving Investigational Product (not included in SAP, but will be included in the CSR)

Listing 1 Subjects Excluded from Analysis Populations

Actual Treatment Group	Randomized Treatment Group	Subject ID	Analyses in which Subject is Included	Analyses from which Subject is Excluded	Results Available?	Reason(s) Subject Excluded
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	[e.g., Safety, ITT, mITT, CC, PP]	[e.g., Safety, ITT, mITT, CC, PP, Visit x]	Yes/No	xxxxx
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	[e.g., Safety, ITT, mITT, CC, PP]	[e.g., Safety, ITT, mITT, CC, PP, Visit x]	Yes/No	xxxxx
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	[e.g., Safety, ITT, mITT, CC, PP]	[e.g., Safety, ITT, mITT, CC, PP, Visit x]	Yes/No	xxxxx

Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. If "Yes" the population in which data were removed will be listed in parenthesis. "No" indicates that no data were available for inclusion in the analysis.

Implementation Notes:

1. Sort order will be actual treatment group, Subject ID
2. Reasons Subject Excluded should match the same verbiage that is used on the Analysis population tables
3. If all subjects received the correct treatment, only display "Treatment Group".

Listing 2 Subjects Whose Assigned Treatment Group Does Not Match Their Randomized Treatment Group

Subject ID	Treatment Group at Randomization	Treatment Actually Received
xxxxxx	LACTIN-V/Placebo	LACTIN-V/Placebo
xxxxxx	LACTIN-V/Placebo	LACTIN-V/Placebo

Implementation Note:

1. Sort order is Subject ID.

Listing 3 Early Terminations or Discontinued Subjects-All Enrolled Subjects

Actual Treatment Group	Randomized Treatment Group	Subject ID	Category	Study Day Corresponding to Early Termination/Treatment Discontinuation/Completion	Reason for Early Termination/ Treatment Discontinuation
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxxx	Early Termination/Treatment Discontinuation/Completion	xx	xxxxxxxxxxxxxxxx
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxxx	Early Termination/Treatment Discontinuation/Completion	xx	---

Implementation Notes:

1. Sort order will be by Actual Treatment Group, Subject ID, Category

2. Category will be "Early Termination", "Completion" or "Treatment Discontinuation". If a subject discontinued treatment, they will have two records.

3. In the “Reason” column, concatenate any “specify” fields, including AE number and DV number.

Listing 4 Subject-Specific Protocol Deviations-All Enrolled Subjects

Deviation Number	Study Day	Deviation Description	Deviation Category	Reason for Deviation	Deviation Affected Product Stability?	Deviation Resulted in AE?	Deviation Resulted in Subject Termination?	Deviation Resolution	Comments
Actual Treatment Group: , Randomized Treatment Group: , Subject ID:									
xx	xx	xxxxxxx	xxxxxxxxxxx	xxxxxxx	Yes/No	Yes/No	Yes/No	Yes/No	xxxxxxxxxxx
xx	xx	xxxxxxx	xxxxxxxxxxx	xxxxxxx	Yes/No	Yes/No	Yes/No	Yes/No	--

Note: Deviation description column will contain all subfields concatenated together

Implementation Notes:

1. Sort order will be by Actual Treatment Group, Subject ID, Deviation Number
2. In the Deviation Category column concatenate any specify fields
3. In the Reason for Deviation column concatenate any specify fields.

Listing 5 Non-Subject-Specific Protocol Deviations

Site	Deviation	Start Day	End Day	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Category	Deviation Resolution	Comments
xxxx	xxxx	xx	xx	xxxx	Yes/No	Yes/No/NA	xxxx	xxxx	xxxx
xxxx	xxxx	xx	xx	xxxx	Yes/No	Yes/No/NA	xxxx	xxxx	xxxx

Note: Deviation column will contain all subfields concatenated together

Implementation Notes:

1. Sort order will be by Site Name, Start Date
2. In the Deviation Category column concatenate any specify fields
3. In the Reason for Deviation column concatenate any specify fields.

Listing 6 Individual Efficacy Response Data

Study Day (Week)	Homogeneous, thin, grayish-white discharge	Vaginal pH	Amine ("whiff") test on KOH wet mount	Clue Cells on wet mount (%)	Amsel Criteria	Nugent Score	BV Diagnosis	*L. crispatus* Concentration (copies/mL)	CTV-05 Concentration (copies/mL)	*Lactobacillus spp.* Concentration (copies/mL)	Total Bacteria Concentration (copies/mL)	*L. crispatus* Colonization Status
Actual Treatment Group: , Randomized Treatment Group: Subject ID:												
x (x)	Present/ Absent/ Not Assessed	xx.x	Negative/ Positive/ Not Assessed	xx	x	x	Positive/ Negative/ Indeterminate	x.x E x	x.x E x	x.x E x	x.x E x	Successful/ No colonization

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.
2. If all subjects received the correct treatment, only display "Treatment Group".

Listing 7 Compliance Data- All Treated Subjects

Actual Treatment Group	Subject ID	Week	Dose	Dose Taken? (Subject Report)	Study Day of Administration (Subject Report)	Time of Administration (Subject Report)	Number of Applicators Returned (Used / Unused)	Staining Assessment (Used / Unused / Indeterminate)	Compliance Status
xxxxxx	xxxxxx	1	1	Yes/No	xx	xx:xx	x / x	x / x / x	Compliant/Non-compliant
			2	Yes/No	xx	xx:xx			
			3	Yes/No	xx	xx:xx			
			4	Yes/No	xx	xx:xx			
			5	Yes/No	xx	xx:xx			
		2	1	Yes/No	xx	xx:xx	x / x	x / x / x	
			2	Yes/No	xx	xx:xx			
		3	1	Yes/No	xx	xx:xx	x / x	x / x / x	
			2	Yes/No	xx	xx:xx			
Etc.									

Implementation Notes:

1. Sort order is actual treatment Group, Subject ID.

2. Total number of doses is 25. Number of doses not taken will be calculated as 25 - Number of doses taken as scheduled - Number of doses taken out of window.

3. If a subject does not have a record for 'Returned Used Applicators' or 'Returned Unused Applicators', then an 'Unknown' will be placed in those columns.

Listing 8 Missed Dose Data- All Treated Subjects

Actual Treatment Group	Randomized Treatment Group	Subject ID	Dose(s) Missed
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	[e.g., Week 2 Dose 1, Week Dose 2, etc.]

Implementation Notes:

1. Sort order is Treatment Group, Subject ID.

Listing 9 Individual Acceptability Questionnaire Responses

Actual Treatment Group	Subject ID	Questionnaire Item	Questionnaire Sub-Item	Screening		Follow-up	
				Study Day (Week)	Response	Study Day (Week)	Response
LACTIN-V/Placebo	xxxxxx	1	-	x (x)	xxx	x (x)	xxx
		2	A	x (x)	Yes/No	x (x)	Yes/No
			B	x (x)	Yes/No	x (x)	Yes/No
			C	x (x)	Yes/No	x (x)	Yes/No
			D	x (x)	Yes/No	x (x)	Yes/No
			E	x (x)	Yes/No	x (x)	Yes/No
			F	x (x)	Yes/No	x (x)	Yes/No
		3	-	x (x)	xxx	x (x)	xxx
		4	-	x (x)	xxx	x (x)	xxx
		5	-	x (x)	xxx	x (x)	xxx
Etc.							

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.
2. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 10 Demographic Data-All Enrolled Subjects

Actual Treatment Group	Randomized Treatment Group	Subject ID	Age at Enrollment (years)	Ethnicity	Race
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	xx	xxxxxx	xxxxxx
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	xx	xxxxxx	xxxxxx
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	xx	xxxxxx	xxxxxx

Implementation Notes:

1. Sort order will be by Actual Treatment Group, Subject ID

2. For the Race column, if a subject is Multi-Racial, all races will be listed, separated by a comma

Listing 11 Screening Gynecological History Interview-All Enrolled Subjects

Study Day	Have you been amenorrheic for at least 3 months due to use of a long-acting progestin or continuous use of oral contraceptives?	First Day of your last menstrual period (Study Day)	How many days is your average menstrual cycle?	How many days does your period last?	In the past 3 months, have you had any abnormal menstrual cycles?	What sanitary products do you use during your period?	Have you ever douched or used vaginal preparations or drying agents?	In the last 30 days how many times have you douched or used vaginal preparations or drying agents?
Actual Treatment Group: , Randomized Treatment Group: Subject ID:								
xx	Yes/No	xx	xx	xx	Yes/No [cycle length less than 21 days/cycle length more than 35 days/Intermenstrual bleeding/spotting]	Pads/Cups/Tampons/Other	Yes/No [Specify]	xx/NA

Implementation Notes:

1. Sort order will be by Actual treatment group, Subject ID

2. For questions that are parented, if the parent question is "No" and the subsequent fields are not required, fill the cell with "—"

3. Includes data from Visit 00

4. If answer to 'In the past 3 months, have you had any abnormal menstrual cycles?' is "Yes," then concatenate the answer to the abnormal cycles that were experienced

5. If answer to 'Have you ever douched or used vaginal preparations or drying agents?' is "Yes," then concatenate answer to the 'specify' field. If the answer is "No" then there will be no answer.

Listing 12 Screening Sexual History Interview-All Enrolled Subjects

Study Day	How many male partners have you had in the past 6 months?	How many female partners have you had in the past 6 months?	Have you had sex in the past 30 days?	How many times did you have sex?	How many times did you have protected sex?	How many times did you have unprotected sex?	How many days has it been since the last time you had sex?
Actual Treatment Group: , Randomized Treatment Group: Subject ID:							
xx	xx	xx	Yes/No	xx	xx	xx	xx

Implementation Notes:

1. Sort order will be by actual treatment group, Subject ID
2. For questions that are parented, if the parent question is "No" and the subsequent fields are not required, fill the cell with "—"
3. Includes data from Visit 00

Listing 13 Follow-up Gynecological History Interview-All Enrolled Subjects

Study Day	Have you menstruated since your last visit?	First Day of your last menstrual period (Study Day)	Since your last visit, have you experienced any spotting or bleeding other than menstrual bleeding?	Since your last visit, have you used scented tampons?	Since your last visit, have you douched or vaginally inserted anything other than the study applicator or MetroGel?	How many days has it been since you last douched or vaginally inserted anything other than the study applicator or MetroGel?	Since your last visit, how many times have you douched or vaginally inserted anything other than the study applicator or MetroGel?	Have you changed birth control methods or started a new method since the last visit?
Actual Treatment Group: , Randomized Treatment Group: Subject ID:								
xx	Yes/No	xx	Yes/No	Yes/No/NA	Yes/No [specify]	xx	xx	Yes/No/NA

Implementation Notes:

1. Sort order will be by actual treatment group, subject ID

2. For questions that are parented, if the parent question is "No" and the subsequent fields are not required, fill the cell with "—"

3. Includes data from Visit 0, 02, 03, 04,07

4. If answer to 'Since your last visit, have you douched or vaginally inserted anything other than the study applicator or MetroGel?' is "Yes," concatenate answer to 'Specify' field. If the answer is "No" then there will be no answer.

Listing 14 Follow-up Sexual History Interview-All Enrolled Subjects

Study Day	Have you had sex since the last visit?	How many times did you have sex?	How many new partners did you have?	How many days has it been since the last time you had sex?	If you had sex with a man, did your partner use a condom each time?
Actual Treatment Group: , Randomized Treatment Group: Subject ID:					
xx	Yes/No	xx	xx	xx	Yes/No/NA

Implementation Notes:

1. Sort order will be by Subject ID
2. For questions that are parented, if the parent question is "No" and the subsequent fields are not required, fill the cell with "—"
3. Includes data from Visit 0, 02, 03, 04,07

Listing 15 Screening Pregnancy History Interview-All Enrolled Subjects

Study Day	How many times have you been pregnant?	Number of Live Births	Number of Stillborn Births	Number of Spontaneous Abortions	Number of Elective Abortions	Number of Ectopic Pregnancies	Do you have any children born with congenital anomalies?	What is your current Relationship Status?
Actual Treatment Group: , Randomized Treatment Group: Subject ID:								
xx	xx	xx	xx	xx	xx	xx	Yes/No [Specify]	Married/Divorced/Separated/Single (never married)/Widowed/Steads partner, cohabitating/Steady partner, not cohabitating/Casual partner

Implementation Notes:

1. Sort order will be by Actual treatment group, Subject ID

2. For questions that are parented, if the parent question is "No" and the subsequent fields are not required, fill the cell with "—"

3. Includes data from Visit 00

4. If answer to 'Do you have any children born with congenital anomalies?' is yes, then concatenate answer to 'Describe.' If the answer is "No" then there will be no answer.

Listing 16 Pre-Existing Medical Conditions- All Enrolled Subjects

Actual Treatment Group	Randomized Treatment Group	Subject ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	xxx	xxxxxx	xx	xx	xxxxxx	xxxxxx
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxx	xxx	xxxxxx	xx	xx	xxxxxx	xxxxxx

Implementation Notes:

1. Sort order is Actual Treatment Group, Subject ID, MH Number.

2. "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). Rather than use exact study days, categorize as follows:

- > 5 years prior to enrollment

- 1-5 years prior to enrollment

-1-12 months prior to enrollment

-Within 1 month of enrollment

-During Study

-If Ongoing at the end of the study, display "Ongoing' in the "Condition End Day" column.

-If ending is unknown at the end of the study, display "Unknown" in the "Condition End Day" column.

Listing 17 Concomitant Medications

Actual Treatment Group	Randomized Treatment Group	Subject ID	Concomitant Medication Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; AE Number)	Taken for a condition on Medical History? (MH Description; MH Number)
LACTIN-V/Placebo	LACTIN-V/Placebo	LACTIN-V/Placebo	xx	xxxxxx	xx	xx	xxxxxx	Yes/No xxxxx; xx	Yes/No xxxxx; xx
LACTIN-V/Placebo	LACTIN-V/Placebo	LACTIN-V/Placebo	xx	xxxxxx	xx	xx	xxxxxx	Yes/No xxxxx; xx	Yes/No xxxxx; xx

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, concomitant medication number.

2. 'Medication Start Day' and 'Medication End Day' are relative to enrollment (which is Day 1, day before enrollment is Day -1). For medication start dates that are > 30 days prior to enrollment, rather than use exact days, categorize as follows:

- > 5 years prior to enrollment

- 1- 5 years prior to enrollment

- 1-12 months prior to enrollment.

- For 'Medication End Day', if medication is Ongoing, display 'Ongoing' in the Medication End Day' column.

- For 'Medication End Day', if end of medication is unknown, display 'Unknown' in the 'Medication End Day' column.

3. If a Medication is taken for an AE, then concatenate the conmed with the Advere Events by AENUM and report the AETERM, plus the AE Number.

4. If a Medication is taken for an MH, then concatenate the conmed with the Medical History event by MHNUM and report the MHTERM, plus the MH Number.

5. Include the birth control information in this dataset. The birth control information is coming from the RP/SUPPRP or BC1 dataset.

6. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 18 Solicited Local Events –All Treated Subjects

Week	Study Day	Vaginal Bleeding Other than Menstruation	Abnormal Vaginal Discharge	Abnormal Vaginal Odor	Genital Itching	Genital Burning	External Genital Irritation	External Genital Swelling	Genital Rash
Actual Treatment Group: , Randomized Treatment Group: Subject ID:									
x	x	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]
x	x	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.

2. If a symptom is ongoing after day 5, add a row for Day 6 and for each day until the end date of the symptom. The severity will be the maximum severity reported for that symptom.

3. Mark all severities with a +, that are considered treatment emergent solicited adverse events.

4. Severity will be color coded

5. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 19 Solicited Systemic Events – Safety Population

Week	Study Day	Nausea*	Vomiting*	Abdominal Pain/Cramps*	Diarrhea*	Constipation*	Pain/Burning with Urination	Frequent Urination	Blood in Urine*	Headache*
Actual Treatment Group: , Randomized Treatment Group: Subject ID:										
x	x	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]
x	x	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]	[severity]
Note: *Symptom not collected during weeks 12-24.										

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.

2. If a symptom is ongoing after day 5, add a row for Day 6 and for each day until the end date of the symptom. The severity will be the maximum severity reported for that symptom.

3. Mark all severities with a +, that are considered treatment emergent solicited adverse events.

4. Severity will be color coded

5. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 20 Unsolicited Adverse Events

Adverse Event	Study Day	Severity	SAE?	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Actual Treatment Group: , Randomized Treatment Group: , Subject ID: , AE Number:										
xxxxxxx	**xx**	**xxxxxx**	**xxxxxx**	**xxxxxx**	**xxxxx**	**xxxxxx**	**Y/N**	**xxxxx**	**xxxxx**	**xxxxx**
Comments: xxxxxxxxxxxxx										
Actual Treatment Group: , Randomized Treatment Group: , Subject ID: , AE Number:										
xxxxxxx	**xx**	**xxxxxx**	**xxxxxx**	**xxxxxx**	**xxxxx**	**xxxxxx**	**Y/N**	**xxxxx**	**xxxxx**	**xxxxx**
Comments: xxxxxxxxxxxxx										
Note: For additional details about SAEs, see Table X.										

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, AE Number.
2. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 21 Pregnancy Reports – Maternal Information

Actual Treatment Group	Actual Treatment Group	Subject ID	Pregnancy Number	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxxxx	xx	xx	xxx	xxx	xxx	xxx	Y/N	Y/N	Y/N	Y Y/N /N
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxxxx	xx	xx	xxx	xxx	xxx	xxx	Y/N	Y/N	Y/N	Y Y/N /N
Note: Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.												

Implementation Notes:

1. Sort order is actual treatment group, Subject ID
2. If all subjects received the correct treatment, only display "Treatment Group".

Listing 22 Pregnancy Reports – Gravida and Para

			Live Births												
Subject ID	**Pregnancy Number**	**Gravida**	**Extremely Preterm Births**	**Very Preterm Births**	**Early Preterm Births**	**Late Preterm Births**	**Early Term Births**	**Full Term Births**	**Late Term Births**	**Post Term Births**	**Still Births**	**Spontaneous Abortion/ Miscarriage**	**Elective Abortions**	**Therapeutic Abortions**	**Major Congenital Anomaly with Previous Pregnancy?**
xxxxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	Y/N
xxxxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	Y/N
Note: Gravida includes the current pregnancy, para events do not.															

Listing 23 Pregnancy Reports – Live Birth Outcomes

Subject ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score, 1 minute	Apgar Score, 5 minutes	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?
xxxxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	Y/N	xxx
xxxxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	Y/N	xxx
Note: Congenital Anomalies are included in the Adverse Event listing.												

Listing 24 Pregnancy Reports – Still Birth Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?
xxxxxx	xx	xxx	xxxxxxx	Y/N	xxxxxxx	xxx	xxx	xx	Y/N	Y/N	xxxxxxx

Listing 25 Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion
xxxxxx	xx	xxx	xxxxx	xxxx	Y/N	xxxxxxx

Listing 26 Clinical Laboratory Results – Urinalysis

Study Visit	Study Day of Assessment	Collection Day	Was Urine assessed by dipstick?	UTI Testing Result	Are clean catch urine dipstick results acceptable and do not warrant a full urinalysis and urine culture to be completed?	Are urinalysis and urine culture results acceptable and not clinically significant?	Was a urine pregnancy test performed?	Result
Actual Treatment Group: , Randomized Treatment Group: , Subject ID:								
Screening Visit (Day -30)	xx	xx	No/Yes/NA	Negative/Positive	Yes/No	Yes/No	No/Yes/NA	Negative/Positive
Visit 1 (Day 1)	xx	xx	No/Yes/NA	Negative/Positive	Yes/No	Yes/No	No/Yes/NA	Negative/Positive
Visit 2, Week 4 (Day 28)	xx	xx	No/Yes/NA	Negative/Positive	Yes/No	Yes/No	No/Yes/NA	Negative/Positive
Visit 3, Week 8 (Day 56)	xx	xx	No/Yes/NA	Negative/Positive	Yes/No	Yes/No	No/Yes/NA	Negative/Positive
Visit 4, Week 12 (Day 84)	xx	xx	No/Yes/NA	Negative/Positive	Yes/No	Yes/No	No/Yes/NA	Negative/Positive
Visit 7, Week 24 (Day 168)	xx	xx	No/Yes/NA	Negative/Positive	Yes/No	Yes/No	No/Yes/NA	Negative/Positive

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.
2. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 27 Clinical Laboratory Results – Serology and STI Testing

Study Day of Assessment	HIV Result	Syphilis Result	Gonorrhea NAAT Result	Chlamydia NAAT Result	Trichomoniasis NAAT Result
Actual Treatment Group: , Randomized Treatment Group: , Subject ID:					
xx	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive
xx	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive
xx	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive
xx	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive
xx	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive
xx	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive	Negative/Positive

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.

2. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 28 Additional Gynecological Test Results

Actual Treatment Group	Randomized Treatment Group	Subject ID	Study Day	Trichomoniasis Present on Wet Mount?	Yeast Vaginitis Present on Wet Mount?
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxxxx	xx	Absent/Present/Not Assessed	Absent/Present/Not Assessed

Implementation Notes:

1. Sort order is Actual treatment group, Subject ID, Study Day.
2. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 29 Vital Signs

Study Visit	Study Day of Assessment	Temperature (°F)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Pulse (beats/min)	Respiratory Rate (breaths/min)
Subject ID: , Randomized Treatment Group: , Actual Treatment Group:						
Screening Visit (Day -30)	xx	xx	xx	xx	xx	xx
Visit 1 (Day 1)	xx	xx	xx	xx	xx	xx
Visit 2, Week 4 (Day 28)	xx	xx	xx	xx	xx	xx
Visit 3, Week 8 (Day 56)	xx	xx	xx	xx	xx	xx
Visit 4, Week 12 (Day 84)	xx	xx	xx	xx	xx	xx
Visit 7, Week 24 (Day 168)	xx	xx	xx	xx	xx	xx

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.

2. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 30 Physical Exam Findings

Actual Treatment Group	Randomized Treatment Group	Subject ID	Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; AE Number)
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxxx	xxx	xxxxxxxx	xxxxxxxx	Yes/No xxxxxx; xx

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.
2. If all subjects received the correct treatment, only display “Treatment Group”.
3. Only abnormal findings will be presented.
4. If the physical exam was reported as an AE, then concatenate the Physical exam with the Adverse Events by AENUM and report the AETERM, plus the AE Number

Listing 31 Pelvic Exam Findings

Actual Treatment Group	Randomized Treatment Group	Subject ID	Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; AE Number)
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxxxx	xxx	xxxxxxxx	xxxxxxxx	Yes/No xxxxxx; xx

Implementation Notes:

1. Sort order is actual treatment group, Subject ID, Study Day.

2. Only abnormal findings will be presented.

3. If the pelvic exam was reported as an AE, then concatenate the Pelvic exam with the Adverse Events by AENUM and report the AETERM, plus the AE Number

4. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 32 Abnormal Discharge

Study Day	Does the subject have abnormal discharge that can be evaluated?	Source of Discharge	Amount of Discharge	Discharge Character	Discharge Color	Discharge Consistency	Discharge Distribution	Discharge Odor
Actual Treatment Group: , Randomized Treatment Group: , Subject ID:								
xx	Yes/No	Vagina/Cervix	Minimal/Moderate/Profuse	Thin watery/ Normal/Thicker than normal	White/Clear/Yellow/Brown/Bloody	Non-homogenous (normal/homogenous/ Curdy plaques/Frothy/Other	Pooled/Diffuse/Patches	None/foul/fishy

Implementation Notes:

1. Sort order is Actual treatment group, Subject ID, Study Day.
2. If all subjects received the correct treatment, only display “Treatment Group”.

Listing 33 Cervical Mucus

Actual Treatment Group	Randomized Treatment Group	Subject ID	Study Day	Amount	Color	Viscosity
LACTIN-V/Placebo	LACTIN-V/Placebo	xxxxxxxx	xx	Minimal (to os)/Moderate (on face)/Profuse (pools)	Clear/Opaque White/ Translucent White/Yellow/Brown/Bloody	Thin/Average/Thick

Implementation Notes:

1. Sort order is Actual treatment group, Subject ID, Study Day.
2. If all subjects received the correct treatment, only display “Treatment Group”.