AMENDMENT JANUARY 11, 2018

Clinical Protocol
CSD2017164

In-use randomized, cross over, controlled, double-blind study of four different tampons

PROTOCOL DATE	NOVEMBER 30, 2017
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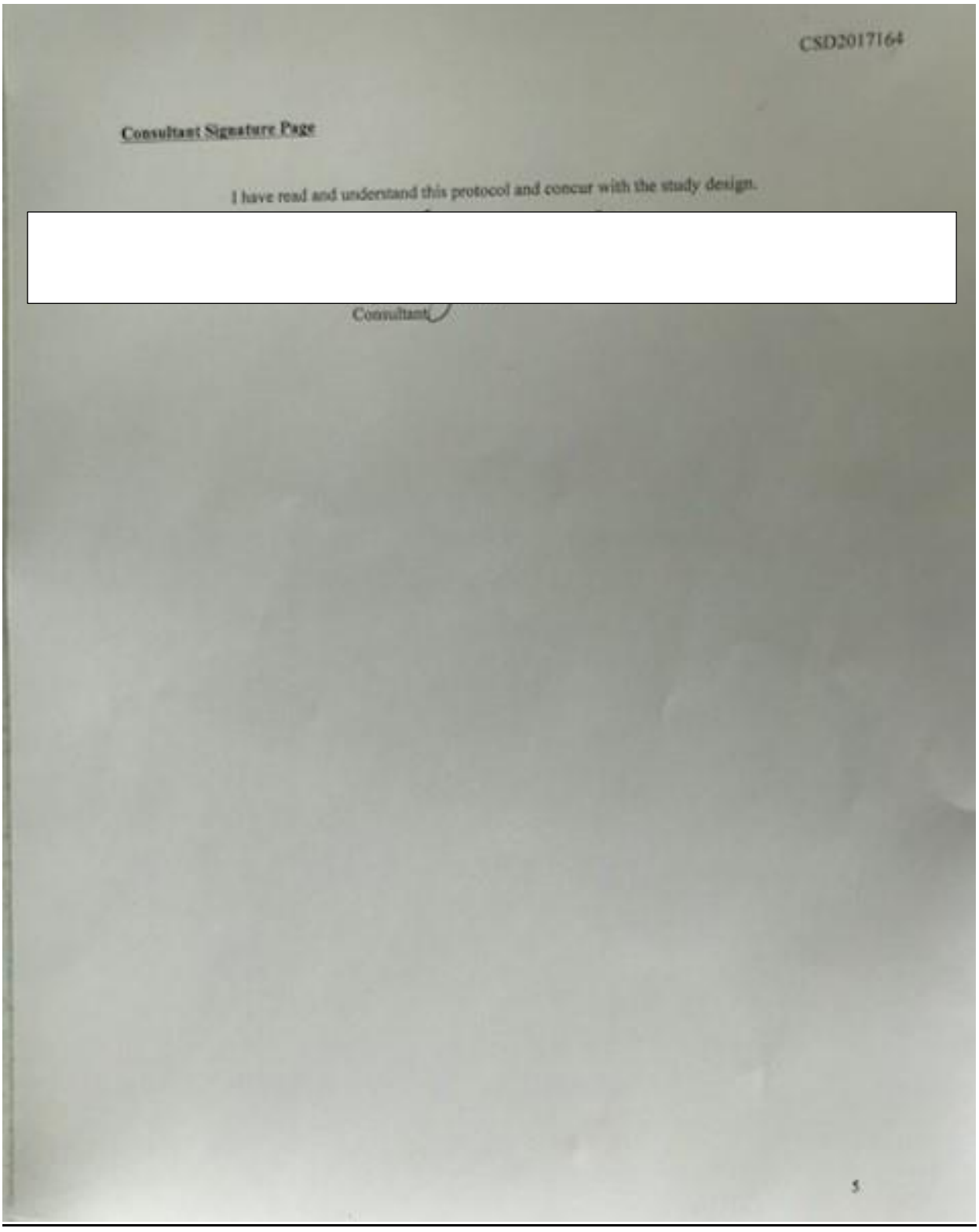
List of Abbreviations and Definition of Terms

Abbreviation	Definition
AE	Adverse Event
BMI	Body Mass Index
CDM	Clinical Data Management
CRF	Case Report Form
CEF	Closed Ended Flushable
CPK	Compak
eCRF	electronic case report form
EDC	Electronic Data Capture
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
IRB	Institutional Review Board
PAP	Papanicolaou
P&G	Procter & Gamble
SAE	Serious Adverse Event
STI	Sexually Transmitted Infections

Consultant Signature Page



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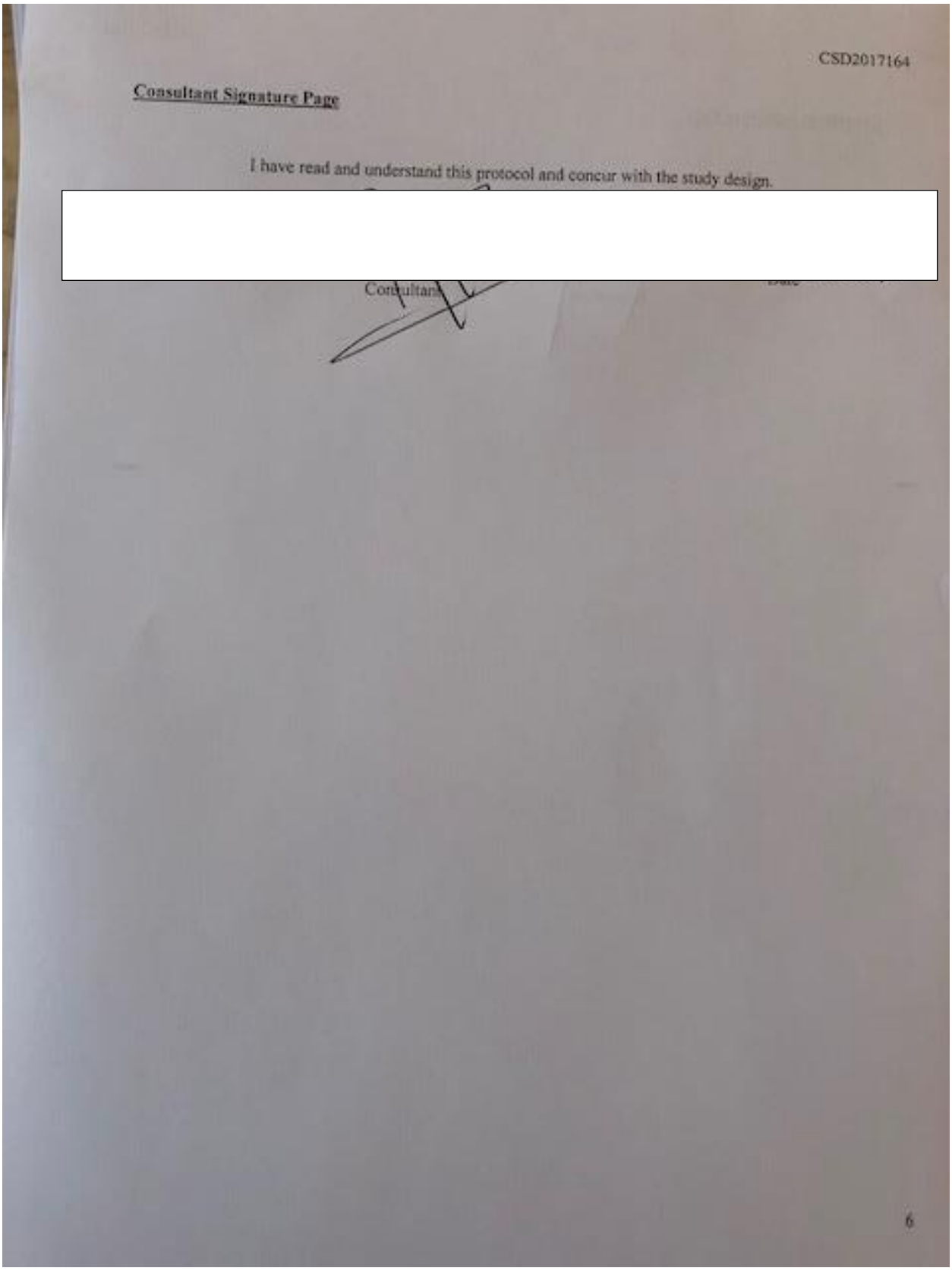


Investigator Signature Page

I have read and understand this protocol and concur with the study design. I agree to participate as an Investigator and to follow the protocol as outlined.

Investigator

Sponsor's Representatives

This protocol has been approved by the Sponsor of the study.

Clinical Scientist/Project Leader

Statistician

Clinical Trial Manager

Data Manager

Clinical Study Protocol

1.0 Introduction

Tampax tampons have been used for over 80 years as an internal method of absorbing menstrual flow. Tampons are constructed of 100% cotton, 100% rayon, or blends of cotton and rayon. They are manufactured with or without an overwrap and may be provided with a cardboard or plastic applicator for inserting the tampon into the vagina.

The study involves normal menstrual use. Prior experience has indicated that the study design described below effectively detects any differences between test products with a long history of safe (as labeled) use. In addition, a questionnaire completed by the subjects, after product use, has been found to be a sensitive way of detecting any product-related sensations such as burning, stinging, irritation and comfort.

2.0 Study Objectives

2.1 Objective(s)

1. The objective of this study is to support a claim of "clinically tested" while women wear tampon(s) during their full menstrual period with medical and gynaecological assessments of vaginal health and consumer self-reported assessments of comfort.
2. To confirm the tolerability of four (4) tampon products based on a body of evidence associated with multiple assessments of vaginal health and adverse events. The primary conclusion will be derived from the clinical assessments including vaginal erythema, ulcerations, abrasions, vaginal pH, vaginal discharge, and Adverse Events (AEs).
3. Usage diaries and questionnaires are added for learning purposes regards to comfort and tolerability.

3.0 Investigational Plan

3.1 Study Design

This will be a 4-consecutive menstrual cycle, single center, randomized, controlled, double-blind, crossover study conducted with approximately 100 menstruating women to complete with 65. Women aged 18-55 who report having consistent menstrual cycles and who typically use tampons as their main source of feminine protection during their menstrual cycles. Each subject will test each of the four (4) tampon products, testing one (1) product per monthly menstrual cycle over the course of this study. The order of the products tested will be randomized for each subject. Subjects will be given a tampon use diary to be completed after the use of each tampon and a Monthly Comfort Questionnaire to be completed at the end of each menstrual cycle. Subjects will be instructed to call after the start of each period and schedule their gynecological examination visit within 72 hours after the use of their last tampon for each period. Women who choose to use a backup menstrual protection product in addition to their assigned test tampon, will be provided currently marketed Always Ultrathin, Always Pantiliners and Always Overnight pads in the product's marketed packaging. Subjects will be given instructions, including to refrain from using any douche products, sexual lubricant (except lubricated condoms), vaginal medications, suppositories, feminine deodorant spray, powder (in the perineal area), or vaginal wipes at least 48 hours prior to the screening visit and for the duration of their study

participation. Subjects will be given instructions to refrain from sexual activity for at least 48 hours prior to every gynecological examination visit. Subjects will be asked to refrain from bathing and use of antibacterial soaps while on the study, and from any vaginal hair removal 12 hours prior to the screening visit. During the tampon use phase of the study, subjects will be queried for changes in their health and medications at every visit. If during their monthly gynecological examination, a vaginal or pelvic organ associated adverse event is reported or found, if the subject wishes to continue in the study, the PI will make the continuance decision on a case by case basis after consultation with the Sponsor.

3.2 Selection of Study Population

3.2.1 Inclusion Criteria

To be considered eligible for enrollment into this study subjects must meet the following criteria:

1) signed the Informed Consent;
2) female, between 18 and 55 years of age;
3) agree to practice abstinence or use an effective form of birth control (e.g. intrauterine device, oral contraceptives, contraceptive implants or injections, diaphragm with spermicide, cervical cap, or constant use of condom) for at least the past 4 months and willing to continue throughout the study or have had a tubal ligation or your partner has had a vasectomy at least 4 months before being enrolled in the study;
4) be in generally good health without clinically significant disease as determined by investigator or designee based on medical history and vaginal exam;
5) for at least the last 4 months, have a consistent menstrual cycle lasting 21-35 days with menstrual bleeding lasting at least 3 days' duration;
6) primarily use tampons for their feminine protection needs during their periods (may use provided pads and/or pantiliners as back-up to tampon);
7) typically use Regular (6-9 grams) absorbency tampons for the majority of their period,
8) wears tampons during menstruation with no history of abnormal discomfort;
9) last pap smear was normal in the past 3 years or a normal pap with a negative HPV in the past 5 years (age 18-21 does NOT need a PAP if they have never been sexually active), per standard of care (per ACOG guidelines), (self-reported);
10) agree to refrain from vaginal intercourse within 48 hours of each vaginal exam scheduled visit;
11) agree to refrain from showering within twelve (12) hours or bathing within twenty-four (24) hours (1 day) of each visit (except Visit 2);
12) agree to refrain from using douching substances, feminine hygiene products, and to not apply powders, perfumes, wipes, lotions, creams, or emollients to their genital area 48 hours prior to **the screening visit and through the completion of the study, if accepted to participate in the study;**
13) agree to refrain from taking anti-inflammatory, antihistamine and/or, steroid systemic and/or topical, (including new hormonal contraceptives) medications until they have completed the study (e.g. Advil, Motrin, Benadryl, etc.);
14) agree to only use the tampons, pads and pantiliners supplied at each study visit for her menstrual protection while participating in this study;
15) be willing and able to comply with the study requirements;

16) agree to complete all study questionnaires;
17) agree to refrain from participation in other concurrent clinical research studies;
18) agree to refrain from genital hair removal (e.g. waxing/shaving, etc.) while on the study;
19) agree to refrain from using antibacterial body soap while on the study (e.g. safe guard)

3.2.2 Exclusion Criteria

Subjects will be excluded from the study if they meet any of the following criteria:

1) have a menstrual abnormality with in the last 4 months (such as oligomenorrhea or amenorrhea);
2) has had a vaginal delivery in the last 6 months;
3) had vaginal surgery, perineal surgery, uterine surgery, miscarriage or abortion in the last 6 months;
4) are pregnant (per urine pregnancy test at screening), or intend to become pregnant in the next 5 months;
5) have a history of Toxic Shock Syndrome (TSS);
6) have a history of heart valve replacement;
7) have had an abnormal Pap in either of your last 2 Pap Smears;
8) have taken steroids (systemic and/or topical), corticosteroids, antihistamines, and/or anti-inflammatories within the past seven days (excludes hormonal contraception);
9) have a history of immunosuppressive drug therapy, chemotherapy, or radiation therapy;
10) have uncontrolled and/or unstable diabetes *(exception...stable dose of Diabetic medication for at least 6 months prior to enrollment)* in the opinion of the Investigator;
11) have a vulvar piercing;
12) have a history of genital herpes;
13) within the last 6 months have had endometrial disease/uterine fibroids with symptoms of heavy menstrual flow (super plus tampon absorbency use) and/or severe menstrual cramping;
14) have you been diagnosed with a current medical condition which might compromise the immune system functions; including cancer, anemia, leukopenia, leukocyte function deficiency, malnutrition, or chemical dependence (e.g. opiates, marijuana etc.) (self-reported);
15) have clinically diagnosed genital warts, lesions, and/or vaginal infections (such as bacterial vaginosis (BV), *Candida spp*., *Trichomonas vaginalis*) at the screening visit;
16) have clinically diagnosed active or vaginal infections (*Chlamydia trachomatis* and/or *Neisseria gonorrhoeae*) identified through lab results from the microbiological sample obtained at the screening visit;
17) has urinary incontinence which causes subject to regularly use and saturate diapers or absorbent panties or pads more than 3 times a week over the last 4 months, or currently under treatment for a pelvic floor disorder (*i.e.,* perineal floor re-education with vaginal probe within last 6 months);
18) have history of or current diagnosis of AIDS/HIV, organ transplant, neoplasia, liver disease, renal disease, deep vein thrombosis, pulmonary embolism, haemophilia, neutropenia, autoimmune disease, major depression or any other medical condition,

which in the opinion of the Investigator would preclude study participation *(exception...stable dose of Thyroid medication for at least 6 months prior to enrollment)*;

19) currently using a vaginal probiotic therapy (self-reported);
20) have participated in a clinical study with exposure to any investigational drug product within 30 days prior to this study;
21) have a vaginal erythema grade of ≥2.0 and/or the presence of abrasions and/or ulcerations as determined by investigator, at the screening visit;
22) have taken antibiotics or antifungals within last 4 weeks (Topical use of antibiotics or antifungals outside the perineal/genitourinary area is allowed at the discretion of the Investigator);
23) have started a new hormonal birth control in the previous 4 months or plan changing hormonal birth control throughout the study period;
24) currently experiencing bladder, uterine or rectal prolapse (investigator to verify at screening visit).
25) history of led or laser vaginal therapy within last 6 months (self-reported).

3.2.3 Continuance Criteria

Subjects will be excluded from the study if they meet any of the following criteria, and that, as determined by the investigator, would unduly influence the study or the participant's health with their continued participation:

1) Has there been any change in the subjects' health since their last visit;
2) Has subject started or stopped taking any medications since their last visit;
3) Has subject taken or applied exclusionary medications (anti-inflammatory, antihistamine, steroid) or made changes in the dosages of reported medications since the previous visit; *If **yes, record on CRF CONCOMITANT MEDS and contact the Sponsor***
4) Has subject used douche products, vaginal medications, suppositories, feminine deodorant spray, powder (in the perineal area), or vaginal wipes for the duration of your study participation; If ***yes, record on CRF COMMENTS and contact the Sponsor***
5) Has subject refrained from sexual activity for at least 48 hours prior to the examination visit; If ***no, record on CRF COMMENTS and contact the Sponsor***
6) Has subject only used supplied test products for menstrual protection; If ***no, please record on CRF COMMENTS and contact the Sponsor***
7) has subject refrained from genital hair removal (e.g. waxing/shaving, etc.)?

3.3 Study Procedures

The complete schedule of study procedures is presented in tabular form in Appendix 1.

Visit 1 (Screening)

Subjects will be initially screened at Visit 1 per the inclusion/exclusion criteria approximately 2 weeks prior to start of subject's menstrual cycle. To determine eligibility, the following will be obtained at the study site:

1. written informed consent;
2. inclusion/exclusion criteria;
3. urine pregnancy test;
4. demographics;
5. medical & gynecological history;
6. medication history;
7. weight and height;

Prior to procedures involving the vulvovaginal area, please complete the following:

8. Ask subject to empty bladder;
9. Have subject disrobe from the waist down and wear a gown or drape sheet;
10. Vaginal pH
11. Speculum insertion;
12. Vaginal assessment (Vaginal Discharge) (Appendix 7);
13. vaginal swabs for Microbiome Assessment (Appendix 9);
14. vaginal exam (Appendix 6);
15. screening STI Microbiology Screening (Appendix 8).

Order of vulvovaginal procedures is:

- Vaginal pH
- Vaginal Discharge Assessment
- Vaginal Swabs for Microbiome Assessment
- Vaginal exam
- STI Microbiology Screening (screening visit 1 only)

Following these procedures, the Investigator will determine if the subject has met the initial study eligibility requirements (pending laboratory results). Those subjects who have met the criteria, to this point, will be instructed that they will be notified of their final eligibility to participate in the study after the Investigator has received and reviewed the laboratory results. The subjects who have not met the criteria, at this point, will be informed of their ineligibility to participate and this will end their participation.

Visit 2 (at least one day prior to start of next menstrual cycle)

Subjects who have been found to be eligible to participate will be instructed to return to the study site at Visit 2 and complete the following procedures:

1. medical history update;
2. medication history update;
3. continuance criteria;
4. randomization to study product;
5. provide subjects with instructions, diary and monthly questionnaire, and monthly tampon product (per randomization) to use for their next menstrual cycle (Cycle 1) for the completion of visit. Subjects will also be given a supply of ultra-pads, overnight pads and pantiliners to use a menstrual backup for the provided tampons, if desired;

Visit(s) 3– 5 (within 72 hours after last tampon use)

Subjects will return to the study site at Visit(s) 3-5 and complete the following procedures:

1. medical history update;
2. medication history update;
3. continuance criteria;
4. collect all un-used tampons from prior visit;
5. collect tampon use diary(s);
6. collect monthly post menses questionnaire;

   Prior to procedures involving the vulvovaginal area, please complete the following:

7. Ask subject to empty her bladder.
8. Have subject disrobe from the waist down.
9. Vaginal pH
10. Speculum insertion
11. vaginal assessment (vaginal discharge) (Appendix 7);
12. vaginal swabs for Microbiome Assessment (Appendix 9)

13. vaginal exam (Appendix 6)

14. AE assessment;

15. provide subjects with instructions, questionnaires (diary and monthly) and monthly tampon product (per randomization) for the completion of visit (Cycle 2-4). Subjects will also be given a supply of ultra-pads, overnight pads and/or pantiliners to use as menstrual backup for the provided tampons, if desired.

Order of vulvovaginal procedures after above has been performed is:

- Vaginal pH
- Vaginal Discharge Assessment
- Vaginal Swabs for Microbiome Assessment
- Vaginal exam

Subjects who have abnormalities or irritation identified during their vaginal examination (including vaginal erythema grades ≥ 2.0 and/or abrasions and/or ulcerations which are severe, as determined by the Investigator) may be scheduled for an additional examination at the discretion of the Investigator. Photos maybe taken of the test site area for significant findings at the discretion of the Investigator.

Visit 6 (EXIT: within-72 hour after last tampon use)
Subjects will return to the study site at Visit 6 and complete the following procedures:

1. medical history update;

2. medication history update;

3. continuance criteria;

4. collect all un-used tampons from prior visit;

5. collect tampon use diary(s);

6. collect monthly post menses questionnaire;

Prior to procedures involving the vulvovaginal area, please complete the following:

7. Ask subject to empty her bladder;

8. Have subject disrobe from the waist down and wear a gown or drape sheet;

9. Vaginal pH

10. Speculum insertion

11. vaginal assessment (vaginal discharge) (Appendix 7);

12. vaginal swabs for Microbiome Assessment (Appendix 9)

13. vaginal exam (Appendix 6)

14. AE assessment;

15. Subjects has completed the study.

Order of vulvovaginal procedures after above has been performed is:

- Vaginal pH
- Vaginal Discharge Assessment
- Vaginal Swabs for Microbiome Assessment
- Vaginal exam

Subjects who have abnormalities or irritation identified during their vaginal examination (including vaginal erythema grades ≥ 2.0 and/or abrasions and/or ulcerations which are severe, as determined by the Investigator) may be scheduled for an additional examination at the discretion of the Investigator. Photos maybe taken of the test site area for significant findings at the discretion of the Investigator. If follow-up is needed, this examination should occur approximately 1 week following Visit 6 and will be used to confirm resolution of the identified abnormalities. At this follow-up visit, if the abnormalities or irritation have not resolved (including erythema grades ≥ 2.0 and/or abrasions and/or ulcerations which are severe, as determined by the Investigator), the Investigator may recommend further medical follow-up for the subject.

3.4 Removal of Subjects from the Study

Subjects may be withdrawn from the study by the Investigator or Sponsor for any of the following reasons:

- subject did not meet enrollment criteria (inclusion/exclusion criteria);
- subject has an AE that warrants study discontinuation;
- subject lost to follow-up during the study or voluntary withdrawals;
- significant protocol deviation (e.g., study product noncompliance);
- withdrawal at the Investigator's discretion.

If possible, any subject who is withdrawn from the study will have the reason for withdrawal documented in the subject's source documents and/or appropriate CRF and, at the time of withdrawal, all exit procedures performed (i.e., procedures for Visit 6). All subjects who do not complete the study will be required to return all un-used study products provided by the Sponsor.

3.5 Concomitant Therapy

For excluded medications prior to study start and during the study, see the inclusion/exclusion criteria (Sections 3.2.1 and 3.2.2). Subjects will be instructed to contact the study staff to report any changes in product usage during the study.

At each visit, new concomitant medications or changes to current concomitant medications will be documented.

Subjects will be instructed to only use the test products and pads and/or pantiliners which have been supplied for all of their feminine protection needs during their participation in the study. Subjects will be instructed to use their normal care practices except refrain from using douching

substances, feminine hygiene products, or applying powders, perfumes, wipes, or emollients to the genital area for at least 24 hours prior to the start of tampon use and during the study. After completion of the study, the subjects may resume using douching substances, powders, perfumes, wipes, or emollients per their normal habits and practices

3.6 Treatments

3.6.1 Method of Assigning Subjects to Treatment Groups

Subjects will be assigned a 4-digit subject number (e.g., 1001, 1002, etc) at Visit 1 (screening). At Visit 2, eligible subjects will be randomly assigned a randomization number using a balanced computer-generated randomization supplied by the Sponsor to the site. A unique randomization number (e.g., 101, 102,103, etc) will be assigned for each study product assigned to subjects.

3.6.2 Treatments Administered

At Visits 2-5, each subject who fulfilled all the entry criteria will receive one of 4 treatments along with a daily and monthly questionnaire for use until their menstruation is complete. Subject instructions will be given to each subject (Appendix 10).

All study products will be provided by the Sponsor in a double-blind manner.

The study product label for the treatment phase will contain the Study Number and a space where the Subject Number will be recorded by the study site prior to dispensing. The label will also contain the randomization number and a statement clearly identifying an investigational product and other information as dictated by internal regulatory requirements.

3.6.3 Identity of Study Products

During the initiation visit, the monitor will review procedures for the management of study product. Throughout the study, additional shipments of study treatments and supplies may be sent to the study center to assure a continuous supply to all study subjects.

Details regarding the study products are as follows:

Test Product(s) – Regular Absorbency (6 to 9 grams)
Tampax 91069721
100% cotton fiber tampon – 91500859
Tampax 92321409
Tampax 94522993

Back-up Pads/Liners
Always Ultrathin
Always Pantiliners
Always Overnight

3.6.4 Management of Study Products

The Investigator will have overall responsibility for the use of the study product. Under no circumstances will the Investigator allow the study products to be used other than as directed by this protocol. The Investigator or qualified study center designee(s) will provide a signed acknowledgment for receipt of the study products and a signed acknowledgment for return of study product containers and unused study product. An accurate record of the dispensing of all study products must be maintained. Upon completion or termination of the study, remaining study product and administration materials will be returned to the Sponsor, unless otherwise instructed by the Sponsor.

Qualified study center designee(s) must receive study product deliveries, record the receipt, and assure that the study product is handled and stored safely and properly. The invoice must be reconciled against the study product received. Any extra/damaged study product will be destroyed at the study center or sent to the Sponsor for destruction as instructed and documented by the Sponsor.

Copies of all invoices and dispensing records for the study product must be kept at the study center as part of required study documentation. At the end of the study, the study center must be able to reconcile delivery records with records of study product received, dispensed, and returned. Any discrepancies will be documented.

Upon receipt and until dispensed, all study product should be securely stored at controlled room temperature (20°C - 25°C or 68°F-77°F with excursions allowed between 15°C - 30°C or 59°F-86°F). Temperature excursions should be infrequent and last less than 24 hours.

3.6.5 Blinding

This is a double-blind study with limited access to the randomization code. The study product codes will be controlled by the Sponsor. The study treatment sequence each subject will receive will not be disclosed to the Investigator, other study center personnel, or other Sponsor representatives.

Bag packaging will be identical for all study products. All study products will be similar in appearance. The study will be unblinded for analysis only after the database has been locked. Study treatment assignments will be revealed to the Investigator when the final clinical report is issued.

3.6.6 Breaking the Blind

If the blind is broken (e.g. for a subject who has an AE that warrants study discontinuation) it may be broken for only the subject in question. The Sponsor must be notified immediately if the Investigator/designee is unblinded during the course of the study. Pertinent information regarding the unblinding of a subject's treatment code must be documented in the subject's source documents and the eCRF.

3.7 Measurement, Assessment, and Sample Collection

3.7.1 Evaluation Assessments

Data from this study will be collected through multiple assessments. These include:

- •Questionnaires (per use and monthly)
- •Vaginal assessment (discharge and pH)
- •Clinical Vaginal exam (vaginal exam)

3.7.2 Safety Assessments

Subject safety will be assessed with vaginal exams, at screening and at various time points throughout the study.

Safety assessments will also include the collection of AEs reported by the subjects or observed by the investigator or study center personnel. Subjects should be asked whether, since the time of the last observation or visit, they had any of the following:

- experienced any changes in well-being,
- used any new medications or supplements,
- changed medication regimens (both prescription and non-prescription), or
- been hospitalized or had any accidents.

Questions should be of a general nature and should not suggest symptoms.

When an AE is suspected, all relevant evaluations will be carried out and appropriate treatment provided. Additional follow-up will be performed as necessary, recorded in the subject's source documents, with the results provided to the Sponsor. Subjects who experience any clinically significant AE will remain under medical supervision until the Investigator deems the AE to be resolved, stabilized, or no longer serious enough to warrant follow-up. Laboratory values that are abnormal (whether or not they are assessed as AEs) may be followed at the discretion of the Investigator until resolved or stabilized.

For AE definitions and reporting requirements, refer to Section 5.6.

3.7.3 Sample Collections

pH samples for evaluations will be obtained at Visit 1(screening) and Visits 2 thru 6. These will be collected and processed according to instructions (Appendix 7)

Microbiome samples will be collected at Visit 1 (Screening) and Visits 3, 4, 5 and 6. These will be collected and processed according to instruction (Appendix 9). A vaginal microbial swab will be collected for the purpose of assessing the vaginal microbial community of the study population. Analyses will be coordinated by Procter & Gamble's Microbiology Group and is not

considered part of the clinical objectives of this study. Only microbial DNA analysis will be conducted. No human DNA analysis will be performed.

Samples will be collected using only the 4-digit subject # in keeping with Good Clinical Practices.

Samples will be stored in a -70˚Celsius freezer at the Procter & Gamble Micro Lab for a maximum of 5 years, after which, all specimens will be destroyed per P&G's policy for specimen destruction.

The results of this testing will not result in a commercially valuable product.

Subjects may withdraw their consent to participate in this testing or to have her samples used for analysis. The Microbiologist will destroy the samples collected from the subject and will delete any data collected from the analysis of the samples. The microbiologist will document this process for the Study File.

Testing does not have any clinical, diagnostic or therapeutic implications for the individual subjects. Therefore, the results will not be reported to the Investigators, the subjects or their primary care physicians. There will not be any follow-up with the subjects regarding this testing".

4.0 Statistical Methods

4.1 Analysis Population

The Intent-to-treat (ITT) population is defined as all eligible subjects who are enrolled into the study, randomized to treatment, and are given their assigned test products for use. The Per-protocol (PP) population is defined as all subjects in the ITT population who are compliant with the study protocol and complete all four months of the study. Given the duration of the study and likelihood of some panelist drop-out, analyses will be performed on both the ITT and PP populations.

4.2 Determination of Sample Size

As the prior data that is available is years old on the treatments in this study, the sample size of 65 subjects was determined using clinical results based on expert judgment related to relevant publications/past clinical studies.

4.3 Method of Assigning Subjects to Treatment

Subjects will be randomly assigned to one of 4 treatment sequences using an encoded program supplied by the Sponsor.

4.4 Statistical Analysis Plan

No formal hypothesis testing is planned. Product Acceptance will be assessed by medical/clinical with regards to the tolerability of the four treatments based on a body of evidence associated with multiple assessments of vaginal health and adverse events. The primary conclusion will be derived from the clinical assessments including vaginal erythema, ulcerations, abrasions, vaginal pH, vaginal discharge, and AE's.

Prior to statistical analysis, all data will be checked for accuracy, completeness and compliance to protocol. Analyses will be completed using PC SAS Release 9.4.

Demographic data will be summarized in tables of descriptive statistics by treatment sequence to assess overall balance between assigned sequences.

Summary descriptive statistics will be provided for all parameters. Confidence intervals (95% Confidence intervals) will be constructed for all clinical assessments for each treatment code. Any data reported as 'unable to evaluate' will be treated as missing and excluded from the analysis.

The frequencies of vaginal discharge color and consistency responses will be tabulated for each visit/treatment. Depending on the distributions, categories may be collapsed prior to statistical analysis. The frequencies for normal vs. abnormal classifications will be tabulated per visit/treatment. Ninety-five percent CIs around the proportion with abnormal classification, and corresponding odds ratios will be constructed.

The frequencies of erythema scores will be tabulated for each visit/treatment. Also per visit/treatment, 95% CIs will be constructed around: (1) the proportion of subjects with erythema, and (2) the proportion of subjects with moderate or severe erythema. CIs for the corresponding odds ratios also will be constructed.

The frequencies for abrasion and ulceration will be tabulated for each visit/treatment. For each of these parameter, 95% CIs around the proportions and odds ratios will be constructed.

Additional analyses may be conducted to further understand the data.

5.0 Investigator Obligation

This study will be conducted in accordance with the applicable GCPs, International Conference on Harmonization (ICH) Good Clinical Practice. The Principal Investigator will perform or directly supervise the performance of all the services described herein, or incidental to those described herein, in accordance with the highest standards of medical and clinical research practice. Delegation of any study responsibility will be documented in writing. The Investigator will also be required to submit a report documenting study execution.

5.1 Institutional Review

The study will not begin prior to the receipt of written confirmation of approval by the IRB and any relevant regulatory authority. It is the responsibility of the Investigator to obtain the IRB approval (per the U.S. Code of Federal Regulations, Title 21, Part 56 and applicable ICH

guidelines) for the protocol, amendments, informed consent, subject information sheet, questionnaires, and advertising materials used to recruit study subjects, if appropriate. A copy of the IRB approval letter along with a list of the IRB members who acted on this protocol and a statement that the IRB is in compliance with current ICH E6 and Good Clinical Practices (GCP) guidelines will be provided to the Clinical Trial Manager.

It is the Investigator's responsibility to promptly report to the IRB all changes to the research activity and all unanticipated problems involving the risk to human subjects.

5.2 Protocol Amendment(s)

With the exception of emergency situations, implementation of any significant change in the protocol (i.e., one that affects the safety of the subjects, scope of the investigation, or the scientific quality of the study) will not be permitted until the Sponsor, the Investigator, and the IRB have reviewed, approved, and documented the protocol amendment in writing. Amendments include changes in the study procedures, Investigator or site address, change risk level, etc.

When a change is made to eliminate or reduce the risk to subjects, it may be implemented before review and approval by the IRB. The Investigator shall notify the IRB of said change in writing within 5 working days after implementation.

In the event of any emergency, the Investigator shall institute any medical procedures deemed appropriate. However, all such procedures must be documented in writing and promptly reported to the Sponsor, the IRB, or other appropriate regulatory/government authority (if appropriate).

Implementation of an administrative (minor or non-significant) change [e.g., changes in other Sponsor personnel (Clinical Data Manager, Statistician), IRB or Sponsor address, typographical errors, spelling errors, etc.] cannot be made until said change is reviewed and approved by the Sponsor and a memo communicating the change is provided to the Investigator. Forwarding of these memos to the IRB by the Investigator should be based on the individual IRB instructions.

5.3 Subject Consent

Each subject must sign and personally date a study-specific informed consent form to serve as a participant in the study. This consent form will comply with all applicable regulations governing the protection of human patients. The basic elements of informed consent are specified in the US CFR Title 21 parts 50.25, 50.27, and 50.55 and the ICH Harmonized Tripartite Guideline for GCP.

The Investigator will obtain the IRB's written approval of the written informed consent form to be provided to the subjects, including approval of all revisions. Prior to the start of the study, the Investigator or an authorized staff member will inform patients about the nature of the study. Subjects will have the opportunity to inquire about details of the study and to decide whether to participate. Subjects will be instructed that they are free to withdraw their participation in the study at any time without penalty or loss of benefits to which they are otherwise entitled. The

Investigator will inform subjects of new information that may be relevant to subjects' willingness to continue participation in the study and the Investigator's obligation to protect subject confidentiality.

The Investigator will provide each subject with a copy of the signed and dated consent form and will document in the subject's source notes that informed consent was given.

5.4 Data Collection

The Investigator has the responsibility for ensuring that all source documents (i.e., study and/or medical records) and CRFs are completed and maintained according to the study protocol. Source documents and paper CRFs, where they exist, should be available at the site during the in-life portion of the study.

5.4.1 Electronic Case Report Form(s)

This study will utilize web-based, electronic case report forms (eCRFs) developed through a validated, Electronic Records/Electronic Signatures (ERES)-compliant platform (21 CFR Part 11), and all investigator data included in the study database will be collected in these eCRFs.

Prior to the initiation of the trial, the study center will be contacted as to computer availability, hardware specifications, internet connectivity, etc., to evaluate their capacity to use this type of data capture system. Every person at the study center who will be entering data into this system will receive training on the system. Each user will be issued a unique user identification and password. For security reasons, and to be in compliance with regulatory guidelines, it is imperative that only the person who owns the user identification and password enter the system using those user names and passwords. Passwords are not transferable. In the case of a change in study center personnel, the newly assigned individuals will be trained and a personal user identification and password will be provided. They may not use the identification and password of the previous user.

Data changes, as well as the initial entry of data, into the eCRFs will be captured within the system's audit trail. Included in the audit trail will be the item, the original value, the changed value, who made the change/entry, when the change/entry was made, and a reason for the change.

During routine monitoring visits, the study center will make available to the monitor their computer and telecommunications that are suitable for Internet access so that the monitor may make a thorough crosscheck of the data entries with any source documentation.

The Investigator will be responsible for the timeliness, completeness, and accuracy of the information on the eCRFs. Electronic consistency checks and manual review will be used to identify errors or inconsistencies. Errors or inconsistencies will be posted as queries in the eCRFs or in an excel spreadsheet for resolution. The study center must answer the queries within a reasonable, mutually agreed, period of time.

5.4.2 Source Documents

The Investigator will prepare and maintain adequate and accurate source documents (medical records, raw data collection forms, etc.) designed to record all observations and other pertinent data for each patient treated with the study drug.

The Investigator will allow Sponsor representatives, contract designees, and authorized regulatory authority inspectors to have direct access to all documents pertaining to the study.

5.5 Adherence to Protocol

By signing the Investigator Signature Page of this protocol, the Investigator confirms in writing that he/she has read, understands, and will strictly adhere to the study protocol and will conduct the study in accordance with ICH Harmonized Tripartite Guidelines for Good Clinical Practice and applicable regulatory requirements.

5.6 Adverse Events

Adverse Event: Any unfavorable or unintended sign, symptom, or disease that appears or worsens in a patient or clinical investigation patient during the period of observation in a clinical study. The AE may be any of the following:

- A new illness,
- An exacerbation of a sign or symptom of the underlying condition under treatment or of a concomitant illness,
- Unrelated to participation in the clinical study or an effect of the study product or comparator drug, or
- A combination of one or more of the above factors.

No causal relationship with the study product is implied by the use of the term "adverse event." An exacerbation of a pre-existing condition/illness is defined as a more frequent occurrence or as an increase in the severity of the pre-existing condition/illness during the study. Planned or elective surgical or invasive procedures for pre-existing conditions that have not worsened are not AEs. However, any complication that occurs during a planned or elective surgery is an AE. (If the event fits the serious criteria, such as hospitalization, it will be considered a serious AE.) Conditions leading to unplanned surgical procedures may be AEs.

When an AE occurs after written informed consent has been obtained but before the first exposure of study product, the AE will be considered a nontreatment-emergent AE. Only serious nontreatment-emergent AEs that are related to study procedures will be collected. An AE that occurs from the time the patient receives her first exposure of study product until her exit from the study will be considered a treatment-emergent AE. All treatment-emergent AEs will be collected.

Serious Adverse Event (SAE): As provided by the ICH criteria, an SAE:

- results in death;
- is life threatening;

(Note: The term "life threatening" refers to any AE that, as it occurs, puts the patient at immediate risk of death. It does not refer to an AE that hypothetically might have caused death if it were more severe.)

- results in hospitalization or prolongation of current hospitalization (not including hospitalization for a pre-existing condition that has not increased in severity or frequency from the patient's underlying medical condition prior to entry into the study);
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect in the offspring of a patient; or
- is judged to be medically important.

(Note: A medically important AE is a medical event that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or require intervention to prevent one of the outcomes listed above. Medical and scientific judgment should be exercised in deciding whether AEs appropriately meet this criterion and are immediately reportable to the Sponsor. Examples of such medical events include transmission of an infectious agent via a medicinal product, allergic bronchospasm that requires intensive treatment in an emergency room or at home and blood dyspraxias or convulsions that do not result in in-patient hospitalization.)

SAEs must be reported to the Sponsor within 24 hours of the study center being informed of the AE (see Section 5.6.2). Sponsor clinical representatives are [redacted] and [redacted]

5.6.1 Adverse Event Reporting

Anticipated adverse events in this study include: mild and transient discomfort with insertion and removal of the Tampon.

Every attempt should be made to describe the AE in terms of a diagnosis. If a clear diagnosis has been made, individual signs and symptoms will not be recorded unless they represent atypical or extreme manifestations of the diagnosis, in which case they should be reported as separate events. If a clear diagnosis cannot be established, each sign and symptom must be recorded individually.

Any clinically significant abnormal laboratory finding, serious/unexpected AE, unanticipated adverse device effect, or medical event which was not present at baseline and/or which results in the withdrawal of a subject from the study must be followed to resolution with appropriate medical management unless documented as "not clinically significant" condition considered stable or the subject is lost to follow-up by the Investigator. Adverse events reported by subjects after completion or termination of study participation will not be documented in the study database after subject exit from the study.

When completing appropriate forms for reporting the AE, the Investigator will be asked to assess the AE as follows:

Severity of Adverse Event: Refers to the extent to which an AE affects the subject's daily activities. Severity will be categorized according to the following criteria:

-- mild - normal activities unaltered, AE is annoying, but AE is tolerable
-- moderate - normal activities altered or AE requires intervention
-- severe - unable to undertake normal activities or is incapacitated

The term "severity" is used to describe the intensity of an event (as in mild, moderate, severe); the event itself may be of relatively minor medical significance, such as a severe headache. This is not the same as "serious." Seriousness, not severity, serves as the guide for defining regulatory reporting obligations.

- Investigator's Opinion of Test Product Relationship
-- not related - there is no medical evidence to suggest that the AE may be related to investigational product usage
-- doubtful - there is no medical evidence to suggest that the AE may be related to investigational product usage, or there is another more probable medical explanation
-- possible - there is possible evidence to suggest that the AE could possibly be related to investigational product usage
-- probable - there is probable evidence to suggest that the AE is probably related to investigational product usage

- Action Taken Regarding Test Product
-- none - no change in test product usage
-- reduced/interrupted - test product usage will be reduced or temporarily interrupted
-- discontinued - test product usage will be discontinued

The Investigator(s) will decide on a case-by-case basis as to whether any subject should be dropped from the study. If the Investigator(s) or subject decides to discontinue study participation, this should be documented and filed with the Sponsor within 72 hours. All adverse events will be followed until resolution or until the Investigator deems it safe to discharge the subject.

5.6.2 Serious or Unexpected Adverse Event Reporting

All Serious Adverse Events will be recorded (on a Detailed Adverse Event Report) and tracked in this study. A Serious Adverse Event (SAE) is "any unexpected medical occurrence that at any exposure: 1) Results in death; 2) Is life-threatening; 3) Requires in-patient hospitalization or prolongation of existing hospitalizations; 4) Results in persistent or significant disability/incapacity; 5) Is a congenital anomaly/birth defect, or 6) Is medically significant. The Investigator will notify the Sponsor within 24 hours of any Serious Adverse Events.

Medical and scientific judgment should be exercised in deciding whether 24-hour sponsor notification is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in this definition of a Serious Adverse Event. These should also be considered serious.

The Study Site should contact the Sponsor within 24 hours at the following numbers to answer questions regarding potentially serious or unexpected Adverse Events.

During normal business hours or after hours:

The Clinical site will be responsible for notifying the IRB of any reportable AEs in keeping with the site SOPs and IRB SOPs. Any notifications to the IRB also require notifications to the Sponsor's reps within 24 hrs per the above.

5.7 Records Retention

The Investigator(s) must retain the subject identification codes, informed consent documentation, and disposition of the test product, CRFs, medical records, and other source data for a minimum of 5 years after study completion. The Investigator(s) must receive written authorization from the Sponsor before destroying any study document.

The Investigator(s) will make the records available for inspection and copying upon the request of an authorized employee of a government authority or the Sponsor, at reasonable times.
In the event the Investigator(s) retires, relocates, or for any other reason withdraws from the responsibility for maintaining records for the period of time required, custody of the records may be transferred to another person who will accept responsibility for the records. Notice of such a transfer must be given in writing to the Sponsor.

The sponsor will maintain clinical records according to P&G Records Management Guidelines.

5.8 Publications

All data collected during this study is the sole responsibility of the Sponsor. No publication by the site or any of the non-employees of the sponsor is allowed from the results of this study. The Sponsor reserves the right to withhold consent for publications due to the confidential nature of the data. Subjects will be identified only by the assigned four-digit code and no identifiable personal information will be included.

6.0 Study Management

6.1 Data Quality Assurance

The following steps will be taken to ensure the accuracy, consistency, completeness, and reliability of the data:

- Routine site monitoring,
- Source/CRF review, and
- Data management quality control checks

In addition, a representative from the Sponsor may conduct periodic audits of study processes, including, but not limited to, a review of the Investigator's Trial Master File (TMF), Standard

Operating Procedures (SOPs) pertaining to the clinical study, and training records of staff involved.

6.1.1 Monitoring

Prior to the commencement of the study, an initiation meeting will be held with the appropriate study site personnel to review the objectives and procedures of the clinical trial. To assure accurate, complete, consistent, and reliable data, the study site(s) and study procedures will be monitored by a representative of the Sponsor according to the US CFR Title 21 Part 312 and ICH Guideline for GCP (Section 5.18). The investigator will permit Sponsor's representative(s) to make consistent site visits during the study. The frequency of monitoring visits will be agreed upon as to the most appropriate intervals as determined by the Sponsor and the study site.

6.2 Study Termination

The study may be terminated at any time at the request of the Sponsor or a regulatory authority. In addition, individual study centers may be suspended or withdrawn by the Sponsor or may choose to withdraw from participation in the study. In such cases, all parties will be notified in a proper and timely fashion. The IRB will be informed promptly and the Sponsor or the Investigator will supply reason(s) for the termination or suspension, as specified by the applicable regulatory requirements. Otherwise, the study is considered terminated upon completion of all patient treatments and evaluations.

6.3 Investigator(s) Final Report

The Investigator or designee will submit a study report to the Sponsor within 4 weeks following study completion or termination. This report should include:

- Investigator's designee of authority statement for specific tasks, e.g., designation by investigator to a qualified staff person to enroll subjects.
- Personnel list of responsibilities (including any non-Test Site Facility personnel)
- Number of subjects screened for eligibility
- Number of subjects entering and completing the study
- Number of subjects that withdrew from the study and reasons for withdrawal
- Any deviations or changes/amendments to the protocol
- Summary of adverse events
- Clinical judgments relative to any significant adverse events and their disposition; any alterations in treatment due to adverse events
- Records of the study site visits by the Sponsor
- Notes to file
- Data transfer
- Forms disposition
- Signed and dated quality assurance statement ensuring protocol compliance

Appendix 1

Schedule of Study Procedures

STUDY ACTIVITIES	SCREENING, VISIT 1 (~2 WEEKS BEFORE START OF MENSES)	LAB RESULTS REVIEW FOR QUAL (NOT A VISIT)	VISIT 2, AT LEAST 1 DAY PRIOR TO START OF MENSES	VISIT 3 WITHIN 72 HRS AFTER LAST TAMPON USE	VISIT 4 WITHIN 72 HRS AFTER LAST TAMPON USE	VISIT 5 WITHIN 72 HRS AFTER LAST TAMPON USE	VISIT 6 WITHIN 72 HRS AFTER LAST TAMPON USE –FINAL EXAM
INFORMED CONSENT	X						
INCL./EXCL./DEMOGRAPHICS	X						
VAGINAL DISCHARGE, VAGINAL EXAM, STI VAGINAL SWABS & VAGINAL PH, PREG TEST	X						
VAGINAL MICROBIOME SWABS	X			X	X	X	X
STI SCREEN LAB (BV, CANDIDA,TRIC, GONO, CHLAMYDIA,) RESULTS REVIEW FOR EXCLUSIONARY CRITIERA		X					
CONTINUANCE CRITERIA			X	X	X	X	X
CONCOMITANT MEDICATIONS (CON_MED)			X	X	X	X	X
GYN HISTORY QUESTIONNAIRE	X						
VAGINAL EXAM + VAGINAL PH & VAGINAL DISCHARGE ASSESSMENT				X	X	X	X
DISTRIBUTE TEST PRODUCTS ACCORDING TO RANDOMIZATION, INCLUDING BACK UP PANTY LINER/PAD PROTECTION IF DESIRED			X Distrib Unit 1	X Collect Unit 1, Distrib Unit 2	X Collect Unit 2, Distrib Unit 3	X Collect Unit 3, Distrib Unit 4	X Collect Unit 4
DISTRIBUTE/COLLECT MONTHLY COMFORT AND PRODUCT USE QUESTIONNAIRE AND REVIEW FOR PROPER COMPLETION			X Distrib Unit 1	X Collect Unit 1, Distrib Unit 2	X Collect Unit 2, Distrib Unit 3	X Collect Unit 3, Distrib Unit 4	X Collect Unit 4

Appendix 2

Risk Assessment

This study is a four month in use randomized, cross over, controlled, double blind study to assess the tolerability and comfort of four tampon products. The study will be conducted at Radiant Research (Cincinnati, OH) under the direction of Michael Noss, MD. The study will include up to 100 women ages 18-55 years who currently use tampons as their primary source for menstrual protection and hygiene.

The test products and test methods along with the study design described in this protocol for CSD2017164 are assessed as minimal risk based on the probability and magnitude of harm or discomfort anticipated in the study not being greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. This assessment is based on study design, appropriate inclusion/exclusion criteria for eligibility, physician oversight, properly trained study personnel, safe history of use of these tampons and/or similar tampon products, proper usage instructions and controlled product use.

The study procedures will include non-invasive measurements of the labia minora, vagina and introitus as detailed above. During study conduct, subjects will be asked to participate in the following procedures at various time points: speculum insertion, vaginal assessment, and/or vaginal sampling. Assessment may include non-invasive measurements for vaginal discharge, pH, visual grading for erythema, abrasions, ulcerations, and superficial tissue/cell collection. The study site staff will have sufficient training and experience with each of these minimal risk procedures. The side effects associated with this examination and technical measures are expected to be minimal.

Safety

Regulatory

Appendix 3

Gynecological History (sample)

1.	Number of vaginal births.			☐	
2.	Number of cesarean births.			☐	
3.	Are you currently breastfeeding?	☐	Yes	☐	No
4.	What is the average duration of your period/discharge? (i.e. 5 days)	_____		☐	Days
5.	What is the heaviest flow day (after start of flow) during your period? (Example: Day 2)		Day	☐	
6.	What is the average time between the end of your period and the start of your next period?			☐	Days
7.	How old were you when you first started to menstruate?			☐	Years
8.	How old were you when you first started to use tampons?			☐	Years
9.	Have you ever had pelvic or perineal surgery? (e.g. episiotomies, etc.)	☐	Yes*	☐	No

*If yes, describe surgery:

_____

_____

10. Are you currently using a birth control method? ☐ Yes ☐ No
If yes, please answer question #11. If no, do not answer question #11.

11. If currently using a birth control method, check type and list length of time used:

Contraceptive Methods	**Using?** (check all applicable)	**Length of Time Used** (ex. 04 yrs., 03 mths) years	months
Oral Contraceptive	☐	☐☐	☐☐
Norplant	☐	☐☐	☐☐
Contraceptive Injection (i.e. Lunelle, Depo Provera)	☐	☐☐	☐☐
Hormonal Ring (i.e. NuVa)	☐	☐☐	☐☐
Contraceptive Patch	☐	☐☐	☐☐
Spermicide	☐	☐☐	☐☐
Condoms	☐	☐☐	☐☐
IUD	☐	☐☐	☐☐
Tubal Sterilization	☐	☐☐	☐☐
Vasectomy (partner)	☐	☐☐	☐☐
Other: Describe_____	☐	☐☐	☐☐

12. In the past 12 months, have you had a genital infection? ☐ Yes ☐ No
(If yes, complete the table below)

Type of infection (check all that apply)		Number of infections in last 12 months	Date of most recent infection of this type	How was the infection treated
Yeast				
Genital Herpes				
Gonorrhea				
Trichomonas				
(Human Papilloma Virus) HPV				
Genital Warts				
Cytomegalovirus				
Chlamydia				
Other (_____)				

13. Do you have any known allergies? ☐ Yes* ☐ No
*If yes, list the allergies:
_____
_____
_____

14. Are you currently taking any medications to treat your allergies? ☐ Yes* ☐ No
*If yes, record medications on medication log

Appendix 4

Vaginal Health General Procedures

In General

A physician will conduct all vaginal exams on all subjects at the time points indicated in the Study Events table of the protocol.

At the Screening visit, Vaginal swabs will be collected to rule out positive results Trichomonas, BV and Yeast, Chlamydia, and Gonorrhea (STI).

Supplies:

- Plastic, clear speculums should be used
- Sterile saline
- Appropriate lighting such as a gooseneck lamp or a headlamp; same lighting should be used at all examination intervals
- Aptima Swabs

Vaginal Assessments, Documentation of Findings, and Follow Up PRN

The study Physician of record will conduct the procedures and vaginal exam/assessments appearing below. Any potential confounding activities will also be assessed during the vaginal exam i.e., sexual activity within the past 48 hours or intra-vaginal product use other than study supplied tampons.

All findings either normal and abnormal, will be documented in the eCRF Form, noting score (for erythema) and absence or presence of abrasion, ulceration, laceration, and color and character of vaginal discharge and any evidence of sexually transmitted disease. Document the location, extent, and detailed description of any findings in comments.

Study subjects who have abnormalities or irritation noted on their gynecological examination form may be scheduled for a follow up examination. The Study Physician will determine whether follow-up is necessary. Follow up examinations will occur 1-2 weeks before the start of the subject's next menstrual period.

Procedure Order:

- Subjects will be placed in the dorsal lithotomy position.
- Observe external genitalia and record any findings on eCRF Form;
- A speculum will be inserted into the vagina to visualize the upper 1/3 of the vagina;
- Using the scales and descriptors outlined in the protocol and Appendices, record all findings on eCRF Form;

Appendix 5

ERYTHEMA GRADING SCALE

0 No apparent cutaneous involvement.

0.5 Greater than 0, less than 1.

1 Faint but definite erythema, no eruptions or broken skin or no erythema but definite dryness; may have epidermal fissuring.

1.5 Greater than 1, less than 2.

2 Moderate erythema, may have a few papules or deep fissures, moderate-to-severe erythema in the cracks.

2.5 Greater than 2, less than 3.

3 Severe erythema (beet redness), may have generalized papules or moderate-to-severe erythema with slight edema.

3.5 Greater than 3, less than 4.

4 Generalized vesicles or eschar formations or moderate-to-severe erythema and/or edema.

NOTE: The degree of reaction expressed by such descriptive terms as "moderate" and "severe" is, in itself, subjective. Such terminology can be accurately understood only through experience.

Any reaction of greater severity than Grade 4 should be described in detail. Unusual reactions not described by the scale should also be described.

TYPICAL EXAMPLES OF HALF-GRADE SCORES

0.5 Faint, barely perceptible erythema or slight dryness (glazed appearance).

1.5 Well-defined erythema or faint erythema with definite dryness, may have epidermal fissuring.

2.5 Moderate erythema with barely perceptible edema or severe erythema, may have a few papules or moderate-to-severe erythema.

3.5 Moderate-to-severe erythema with moderate edema or moderate-to-severe erythema with isolated eschar formations or vesicles.

Appendix 6

Vaginal Examination (sample)

Ulceration/Abrasion These lesions will be noted as either No (absent) or Yes (present) only.

	Erythema[1]		Abrasion[2]		Ulceration[3]	
			Yes	No	Yes	No
Labia Minora:	☐ . ☐		☐	☐	☐	☐
Introitus:	☐ . ☐		☐	☐	☐	☐
Lower Vaginal Walls:	☐ . ☐		☐	☐	☐	☐
Middle Vaginal Walls:	☐ . ☐		☐	☐	☐	☐
Upper Vagina (incl. Fornices):	☐ . ☐		☐	☐	☐	☐
Cervix:	☐ . ☐		☐	☐	☐	☐

Prolapse Present: Bladder [ ] Yes [ ] No Uterine [ ] Yes [ ] No Rectal [ ] Yes [ ] No

Based on this Examination:

Is a follow-up visit indicated? Yes* ☐ No ☐

*If yes, state reason: _____

Does the subject meet (continue to meet) study eligibility? Yes ☐ No* ☐

*If no, state reason: _____

[1] Erythema Scale. Record scores as: 0.0, 0.5, 1.0, 1.5, etc.
[2] Abrasion – 'yes' indicates partially disrupted epithelium, blood vessels may be intact or disrupted. Diffuse area of demarcation.
[3] Ulceration – 'yes' indicates tear in or sloughing of epithelium, blood vessels may be intact or disrupted. Sharp demarcation.

Appendix 7

Vaginal Assessment

Vaginal pH

1) Use appropriate personal protective equipment.
2) Vaginal pH is measured before the insertion of a speculum.
3) A pH test strip (2.0-9.0 range) is grasped at the end and either held by hand or a sterile hemostat (long tool capable of reaching into the vagina thru the speculum) and carefully brought to the vagina.
4) The strip is moistened with the "fluid" from the middle to upper third of the lateral wall of the vagina. It is held in place for 30 sec.
5) The strip is carefully removed and the colour change should be "read" immediately after removal.
6) The corresponding pH value is recorded on the eCRF Database

Materials

BDH Cat No. 83930.601; gradation in 0.5 units between 2.0 and 9.0.

VAGINAL DISCHARGE:

Discharge: ☐ Normal ☐ Abnormal

If Abnormal, please indicate color and consistency below:

Color		Consistency
☐ White	☐ Red	☐ Flocculent
☐ Gray	☐ Green	☐ Frothy
☐ Yellow	☐ Brown	☐ Cheesy
☐ Other		☐ Other

If Other, please describe:

_____

Evidence of sexually transmitted diseases or other infections? Yes No

If yes, describe:

Appendix 8

STI Microbiology Screening (Visit 1 Only)

Vaginal swab samples will be collected at the screening visit (Visit 1). In keeping with GCP's, subject's specimens will be identified only by their 4-digit subject number.

Aptima swabs will be used for wet mount samples.

All subjects will be screened for the microflora exclusion criteria BV (bacterial vaginosis), *Candida spp*., *Trichomonas vaginalis*, *Chlamydia trachomatis*, and *Neisseria gonorrhoeae*. The presence of three of the four following criteria is diagnostic of BV: (1) non-viscous homogenous milky Vaginal Discharge, (2) vaginal pH > 4.5, (3) the presence of a fishy amine odor or the production of the odor upon the addition of potassium hydroxide (KOH) to the vaginal discharge, and (4), the presence of clue cells (> 20 % clue cells). All subjects will be tested for *Candida spp*., *Trichomonas vaginalis*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae* using suitable diagnostic methods. Subjects testing positive for any of the microbial vaginal exclusion criteria will be dismissed from further study participation.

Tests for Bacterial Vaginosis, *Candida spp*., *Trichomonas vaginalis*: Vaginal samples are treated as follows. Gently agitate the vaginal swab suspension and place one drop on a glass slide. Apply a cover slip and examine under low- and high-power magnifications, looking for clue cells (vaginal epithelial cells with indistinct cell borders obscured by large numbers of attached microorganisms). The presence of clue cells (> 20 % clue cells) is consistent with the diagnosis of nonspecific vaginosis (BV); pseudohyphae is consistent with *Candida spp*.; and motile trichomonads is consistent with *Trichomonas vaginalis*. Add a drop of 10% KOH for detection of yeast pseudohyphae and presence of a fishy amine odor.

Tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*: A nucleic acid probe-based method is recommended, e.g. the PACE 2 System (Gen-Probe, Inc., San Diego, CA). Endocervical samples will be handled per manufacturer's instructions.

Results for all microbiological screening will be captured in the eCRF Database.

Appendix 9

Vaginal Swab for Microbiome Assessment

Microbiome swab sample will be collected at Visit 1 (Screening), 3, 4, 5 and 6. In keeping with GCP's, subject's specimens will be identified only by their 4-digit subject number.

Materials Needed for the Sampling:

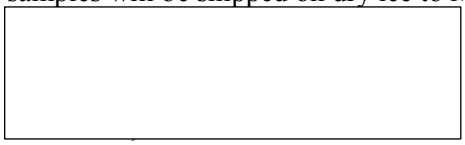
1. COPAN ESwab™ (COPAN Diagnostics Inc.)
   A Sterile Peel Pouch Package with:
   - A Nylon Flocked Swab
   - A Screw Cap Tube with 1 ml of liquid Amies
2. Sterile Saline

Prior to sampling:

1. Note whether subject has used antibiotics within 1 week prior to this sampling procedure on their case report form. Subjects will need to undress below the waist and be provided appropriate covering while waiting for the procedure.
2. Subjects will be positioned appropriately for sampling (*i.e.;* feet in stirrups of gynaecologic exam table).
3. This vaginal swabbing procedure will be conducted following the visual vaginal exam and prior to subsequent vaginal swabbing for vaginal infections or sexually transmitted diseases.

During Sampling (Aseptic technique must be followed with regard to swab handling; minimize open tubes, use sterile solutions etc.)

1. Use appropriate hand hygiene and apply gloves.
2. Open the peel pouch and remove the swab from the pouch with care (must not touch the area below the marked breakpoint indication line and avoid touching the swab tips to any unintended surface to avoid contamination).
3. Pre-moisten the swab by dipping it into the sterile saline tube for 5 seconds.
4. Insert speculum by wetting with saline or lubricant (if not already done).
5. When swabbing: insert the moist swab beyond the tip of the speculum, in the posterior fornix, being careful not to touch the tip of swab to any unintended surface to avoid contamination. Note, the sample should be obtained from an area of the posterior fornix that has not been in contact with the speculum.
6. Rotate the swab 5 times (clockwise 2 times and counter clockwise 3 times), pressing lightly against the vaginal wall.
7. Carefully remove the swab without touching any unintended surface.
8. Remove the ESwab tube from the pouch and uncap.
9. Insert the swab all the way to the bottom of the tube.
10. Holding the swab shaft close to the rim of the tube, break the swab shaft at the colored breakpoint line while holding the tube opening away from your face.
11. Screw the cap on tightly to prevent leakage.
12. Apply a label to the tube and then store the samples at -20C until shipping.
13. Visually assess the fornix region after all swabs are collected and note any new visual findings.
14. The samples will be shipped on dry ice to MBC micro lab to the below address:



Appendix 10

SUBJECTS INSTRUCTIONS
SITE TO PROVIDE

Appendix 11

INFORMED CONSENT
Site to Provide

Appendix 12

Subject Number | | | | | Subject Initials | | |

TAMPON USE DIARY 2017164

Product Code: _____

First Day of Menstrual Cycle: Date _____ /_____ /_____ **Last Day of Menstrual Cycle**: Date _____ / _____ / _____ **VISIT**: _____

Instructions: Fill in table below for **each tampon use**: place an X in column for 'YES', leave column blank for 'NO'

TAMPON		**DATE Tampon Inserted**	**Time of Insertion**	**DATE of Removal**	**Time of Removal**	**Insertion Discomfort**	**Wearing Discomfort**	**Removal Discomfort**	**Sensation During Use?**			**How would you rate this tampon's overall comfort?**				
#	Code								Itching	Burning	Stinging	1	2	3	4	5
Ex.	D	10-1-17	**10:10 am**	10-1-17	**12:30 am**			X						X		
1			:		:											
2			:		:											
3			:		:											
4			:		:											
5			:		:											
6			:		:											
7			:		:											
8			:		:											
19			:		:											
10			:		:											
11			:		:											
12			:		:											
13			:		:											
14			:		:											
15			:		:											

How would you rate this tampon's overall comfort? Place 'X' in appropriate column above	**Very Comfortable**	**Comfortable**	**Neither Comfortable nor**	**Uncomfortable**	**Very Uncomfortable**
	1	**2**	**3**	**4**	**5**

Subject Signature Date

Subject Number | | | | | Subject Initials | | | |

TAMPON USE DIARY 2017164

Product Code: _____

First Day of Menstrual Cycle: Date _____ /_____ /_____ **Last Day of Menstrual Cycle**: Date _____ / _____ / _____ **VISIT**: _____

Instructions: Fill in table below for **each tampon use**: place an X in column for 'YES', leave column blank for 'NO'

TAMPON		**DATE Tampon Inserted**	**Time of Insertion**	**DATE of Removal**	**Time of Removal**	**Insertion Discomfort**	**Wearing Discomfort**	**Removal Discomfort**	**Sensation During Use?**			**How would you rate this tampon's overall comfort?**				
#	Code								Itching	Burning	Stinging	1	2	3	4	5
Ex.	DS	10-1-17	**10:10 am**	10-1-17	**12:30 am**			X						X		
16			:		:											
17			:		:											
18			:		:											
19			:		:											
20			:		:											
21			:		:											
22			:		:											
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28			:		:											
29			:		:											
30			:		:											

How would you rate this tampon's overall comfort? Place 'X' in appropriate column above	**Very Comfortable**	**Comfortable**	**Neither Comfortable nor**	**Uncomfortable**	**Very Uncomfortable**
	1	**2**	**3**	**4**	**5**

ubject Signature Date

Appendix 13

Subject Identification Number Subject Initials (mm) (dd) (yyyy)

Product Code _____

POST-USE QUESTIONNAIRE

Please, completely fill in ovals: ● Do not mark ovals: ∅ ⊗ ⊙ √

Thank you for taking a few minutes of your time to complete this survey. The reason we are conducting this research is to understand your opinions and your experience while on this study. Therefore, it is very important that you answer each question candidly and thoughtfully

1. Considering everything about your experience with the tampon you used, please indicate the one word or phrase which best describes your overall satisfaction with your experience with the tampon:
   - o Very satisfied
   - o Somewhat satisfied
   - o Neutral
   - o Somewhat dissatisfied
   - o Very dissatisfied

2. Please **RATE** the tampon over the use period for each of the following characteristics.
(Select one answer for each row)

	Excellent	Very Good	Good	Fair	Poor
Overall comfort	O	O	O	O	O
Overall protection	O	O	O	O	O
Overall quality	O	O	O	O	O
Providing me with protection I trust	O	O	O	O	O
Providing me with comfort I trust	O	O	O	O	O
Being so comfortable I can't feel it	O	O	O	O	O