CLINICAL RESEARCH IN INFECTIOUS DISEASES

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STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 18-0024

Study Title:

Pivotal Study of a Single-Use, Point-of-Care Molecular Diagnostic Device for the Detection of *Neisseria gonorrhoeae* (NG), *Trichomonas vaginalis* (TV), and *Chlamydia trachomatis* (CT) in Women

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Study Title

Protocol Number Code:	DMID Protocol: 18-0024
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Indication Studied:	Neisseria gonorrhoeae, Trichomonas vaginalis, and Chlamydia trachomatis
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	
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This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ATC	Anatomical Code
CI	Confidence Interval
CLIA	Clinical Laboratory Improvement Amendments of 1988
CRF	Case Report Form
CT	*Chlamydia trachomatis*
DMID	Division of Microbiology and Infectious Diseases
FN	False Negative
FP	False Positive
HCP	Health Care Professional
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
N	Number (of subjects or devices)
NAAT	Nucleic Acid Amplification Test
NG	*Neisseria gonorrhoeae*
NIH	National Institutes of Health
NPV	Negative Predictive Value
PI	Principal Investigator
PIS	Patient Infected Status
POC	Point of Care
PPV	Positive Predictive Value
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SDCC	Statistical and Data Coordinating Center
STD	Standard Deviation
STI	Sexually Transmitted Infection
TN	True Negative
TP	True Positive
TV	*Trichomonas vaginalis*
UADE	Unanticipated Adverse Device Effect
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "Pivotal Study of a Single-Use, Point-of-Care Molecular Diagnostic Device for the Detection of *Neisseria gonorrhoeae* (NG), *Trichomonas vaginalis* (TV), and *Chlamydia trachomatis* (CT) in Women" (DMID protocol 18-0024) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses for the final report and provides reasons and justifications for these analyses. It also includes sample tables and listings planned for the final analyses. Regarding the analyses and reports, this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E9 (Statistical Principles for Clinical Trials) [1]. In addition, this SAP follows 21 CFR Section 807.92, the FDA statistical guidance on Reporting Results from Studies Evaluating Diagnostic Tests, and the FDA guidance on Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices [2,3,4]. 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 SAP amendments and/or in the report, 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 study assessments.

2. INTRODUCTION

2.1. Study Background

Diagnostic testing for pathogens of Chlamydia (*Chlamydia trachomatis* [CT]), gonorrhea (*Neisseria gonorrhoeae*, [NG]), and trichomoniasis (*Trichomonas vaginalis*, [TV]) is currently performed at a variety of sites: public health, private, and hospital laboratories, physician's offices/physician office laboratories, and some pharmacies. Sample collection is performed at the physician's office. The sample is then transported and processed in a qualified laboratory. After testing, the results are transferred by a laboratory information system, or manually entered into patient records. Competition in these sectors ranges from very high-quality testing and large test menus in the laboratories to a very limited menu of low quality rapid tests at the physician's office. While laboratory-based tests for chlamydia and gonorrhea have high accuracy, they are far removed from patients and performed on an average sample-to-result-to-patient timeline of 3 to 5 days. Trichomoniasis testing is conducted using wet mount microscopy in the physician's office but has a poor sensitivity of 50-70% [reference 21 in the protocol]. Nucleic acid amplification tests (NAATs) for TV have provided highly sensitive and specific diagnoses but require laboratory infrastructure [references 22-25 in the protocol].

Agencies such as the CDC understand that NAATs are the most sensitive tests and can be performed on easily obtainable specimens such as vaginal swabs (either Health Care Professional [HCP]- or patient-collected) or urine [reference 3 in the protocol]. However, at this time, no simple, rapid NAAT test exists for physicians to test male and female samples for these three pathogens at the same time at the physician's office.

The amount of time until diagnosis, the lack of symptoms in most people, and the subsequent lack of treatment result in preventable disease spread. Thus, there is an urgent need for point-of-care STI diagnostic devices that provide rapid and highly accurate results. The performance of such diagnostics should be similar to the gold standard of NAATs [references 26, 27 in the protocol].

Click Diagnostics (Click) has developed a small, single-use, fully disposable point-of-care (POC) diagnostic device that is capable of being used to rapidly and accurately detect any form of infectious disease. Through dramatic miniaturization, optimization, and cost reductions, Click has reinvented PCR technology. Commercialization of this technology would dramatically expand the reach of molecular diagnostic testing, moving it from centralized test laboratories and large healthcare facilities to small clinics and outreach settings. The device in this clinical study focuses on detecting three of the most common sexually transmitted infections in women that cause significant morbidity.

Current laboratory-based STI tests have an average sample-to-result-to-patient timeline of 3 to 5 days. This is a significant problem as many patients are lost to follow up before the test result is available, and without treatment, patients may continue to spread the infections and risk complications such as pelvic inflammatory disease, infertility, and perinatal complications. Women could benefit from the Click device because they suffer the most serious consequences of STIs, which could be curtailed with single visit POC diagnosis and treatment.

The intended use of the Click device is for the qualitative detection and differentiation of DNA from CT, NG and TV to aid in the diagnosis of chlamydial, gonorrheal, and trichomonas infections, respectively. The assay is to be used with vaginal swabs collected by self-collection from asymptomatic and symptomatic females age 14 or older.

The hypothesis of this clinical study is that the Click Diagnostics Sexual Health Test performs substantially equivalent to the NAAT predicate system. The Patient Infected Status (PIS) provides the reference for this

study. This algorithm incorporates results from three recognized FDA-cleared methods for the CT and NG pathogens and from three recognized FDA-cleared methods for TV:

- BD ProbeTec™ CT/GC Qx Amplified DNA Assays – BD Molecular Diagnostics
- BD ProbeTec™ Trichomonas vaginalis Qx Assay – BD Molecular Diagnostics
- APTIMA COMBO 2 Assay – Hologic, Inc.
- APTIMA Trichomonas Vaginalis Assay – Hologic, Inc.
- BD MAX™ CT/GC/TV – BD Molecular Diagnostics

2.2. Purpose of the Analyses

These analyses will assess the performance of the Click device for detection of CT, NG, and TV in self-collected vaginal specimens as compared to three approved comparator assays using vaginal specimens collected by a qualified HCP in support of obtaining FDA clearance and a Clinical Laboratory Improvement Amendments (CLIA) Waiver and will be included in the final report.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Objective

To assess the performance of the Click device for detection of CT, NG, and TV in self-collected vaginal specimens as compared to PIS determined by three approved comparator assays using vaginal specimens collected by a qualified HCP in support of obtaining FDA clearance and a Clinical Laboratory Improvement Amendments (CLIA) Waiver.

3.1.2. Secondary Objectives

1. To assess the performance of the Click device for detection of CT, NG, and TV in self-collected vaginal specimens among symptomatic subjects as compared to PIS determined by three approved comparator assays using vaginal specimens collected by a qualified HCP.
2. To assess the performance of the Click device for detection of CT, NG, and TV in self-collected vaginal specimens among asymptomatic subjects as compared to PIS determined by three approved comparator assays using vaginal specimens collected by a qualified HCP.

3.1.3. Exploratory Objective

To assess the usability by non-laboratorian operators of the Click device for detection of CT, NG, and TV with subject self-collected vaginal specimens.

3.2. Study Outcome Measures

3.2.1. Primary Outcome Measure

1. The i) percent sensitivity and ii) percent specificity of Click device for detection of CT in self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP.
2. The i) percent sensitivity and ii) percent specificity of Click device for detection of NG in self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP.
3. The i) percent sensitivity and ii) percent specificity of Click device for detection of TV in self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP.

3.2.2. Secondary Outcome Measures

1. The i) percent sensitivity and ii) percent specificity of Click device using self-collected vaginal swabs for detection of CT from self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP among symptomatic subjects.
2. The i) percent sensitivity and ii) percent specificity of Click device for detection of NG in self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP among symptomatic subjects.

3. The i) percent sensitivity and ii) percent specificity of Click device for detection of TV in self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP among symptomatic subjects.
4. The i) percent sensitivity and ii) percent specificity of Click device for detection of CT in self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP among asymptomatic subjects.
5. The i) percent sensitivity and ii) percent specificity of Click device for detection of NG in self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP among asymptomatic subjects.
6. The i) percent sensitivity and ii) percent specificity of Click device for detection of TV in self-collected vaginal specimens as compared to PIS using vaginal specimens collected by a qualified HCP among asymptomatic subjects.

3.2.3. Exploratory Outcome Measures

1. Usability will be measured by 5-point Likert scale responses, yes/no questions, and open-text questions from study operators on questions around three domains of interest: i) instructions, ii) operations, and iii) visual interpretation for the Click device for detection of CT, NG, and TV with patient self-collected vaginal specimens.
2. The percentage of subjects with CT, NG, and TV overall and within the symptomatic and asymptomatic sub-populations.

3.3. Study Definitions and Derived Variables

3.3.1. Patient Infected Status

The Patient Infected Status (PIS) is a ternary variable (Positive/Negative/Indeterminate) calculated via an algorithm incorporating results from the three comparators assays. A PIS designation is derived for each specimen and organism.

For each organism, the specimen will first be tested using the BD Probtec and Hologic Aptima assays.

If the result of both assays is Positive, then the PIS designation will be Positive.

If the result of both assays is Negative, then the PIS designation will be Negative.

If the result of both assays is Equivocal, then the PIS designation will be Indeterminate.

If the result of both assays is Invalid, then the PIS designation will be Indeterminate.

If the results of the assays are discordant, then the BD MAX assay will be used as a tie-breaker. Table 1 below presents the possible combinations of results of the three assays and the corresponding PIS designation for each combination.

Table 1: PIS Designations when Tie-Breaker Assay is used

BD Probtec Result	Hologic Aptima Result	BD Max Result	PIS Designation
Positive	Equivocal	Positive	Positive
		Negative	Indeterminate
		Unresolved or Invalid	Indeterminate
	Negative	Positive	Positive
		Negative	Negative
		Unresolved or Invalid	Indeterminate
	Invalid	Positive	Positive
		Negative	Indeterminate
		Unresolved or Invalid	Indeterminate
Negative	Positive	Positive	Positive
		Negative	Negative
		Unresolved or Invalid	Indeterminate
	Equivocal	Positive	Indeterminate
		Negative	Negative
		Unresolved or Invalid	Indeterminate
	Invalid	Positive	Indeterminate
		Negative	Negative
		Unresolved or Invalid	Indeterminate
Equivocal	Positive	Positive	Positive
		Negative	Indeterminate
		Unresolved or Invalid	Indeterminate
	Negative	Positive	Indeterminate
		Negative	Negative
		Unresolved or Invalid	Indeterminate
	Invalid	Positive	Indeterminate
		Negative	Indeterminate
		Unresolved or Invalid	Indeterminate
Invalid/Missing	Positive	Positive	Positive
		Negative	Indeterminate
		Unresolved or Invalid	Indeterminate
	Equivocal	Positive	Indeterminate
		Negative	Indeterminate
		Unresolved or Invalid	Indeterminate
	Negative	Positive	Indeterminate
		Negative	Negative
		Unresolved or Invalid	Indeterminate

3.3.2. Valid Results and Re-Tested Specimens

3.3.2.1. Comparator Assays

For each of the comparator assays, a valid result is one that is either Positive or Negative. A comparator result for an organism is invalid if the reported result is: Invalid, Equivocal, Indeterminate, Unresolved, or the test ran with errors for any reason. If an invalid result occurs for at least one organism for that specimen, a single retest will be performed. The results of the retest for the organism(s) whose initial result(s) were invalid will be used in the PIS calculation and the initial result(s) from the first test will be excluded (but will be included in subject listings).

As organisms are tested in tandem (i.e. in a single run) for certain assays, a retest may be triggered due to an invalid result from one organism despite having a valid result for another organism. In this scenario, if an organism's result was valid for the first test, the initial result will be used in the PIS calculation and the result from the retest will be excluded (but will be included in subject listings). To illustrate using an example, if the initial BD MAX results for a specimen are:

- NG: Positive
- CT: Invalid
- TV: Negative

And the retested results are:

- NG: Negative
- CT: Positive
- TV: Negative

Then the BD MAX results to be used in the PIS calculation will be:

- NG: Positive
- CT: Positive
- TV: Negative

3.3.2.2. PIS Designation

For PIS, a valid positive/negative designation for a specimen is defined as a designation that is either Positive or Negative (see Section 3.3.1).

3.3.2.3. Click Device

For the Click device, a valid positive/negative result for a specimen is a result where the following was reported on the Operator Diagnostic Test Result form:

- "Did the device run successfully?" was answered with "Yes"
- "…interpret the results of the test and answer the following questions" was answered with "Positive" or "Negative".

If the Click test is invalid, the same specimen is used for a retest using a second Click device. When retests are performed, the results of the second test for all organisms are used in analyses and the initial results from the first test for all organisms are excluded (but will be included in subject listings).

3.3.3. Symptomatic Status

If a subject reports "Yes" to any of the following symptoms on the Clinical Symptoms Assessment case report form, the subject will be classified as Symptomatic.

- Unusual vaginal discharge
- Vaginal irritation (itching, burning, soreness)
- Lower abdominal/pelvic pain
- Painful urination
- Increased urinary frequency
- Abnormal bleeding/spotting
- Pain or bleeding with sex/intercourse

Otherwise, the subject will be classified as "Asymptomatic".

3.3.4. Sensitivity

The sensitivity of the Click device will be calculated as follows:

TP = the number of specimens where both the Click result and the PIS designation are Positive

FN = the number of specimens where the Click result is Negative and the PIS designation is Positive

Sensitivity = 100 * TP / (TP + FN)

Below is SAS pseudo code for calculating sensitivity and its 95% Wilson confidence interval:

```
proc freq;
    where PISResponse = 1;
    weight Count;
    tables ClickResponse / binomial(level="1" wilson);
run;
```

3.3.5. Specificity

The specificity of the Click device will be calculated as follows:

TN = the number of specimens where both the Click result and the PIS designation are Negative

FP = the number of specimens where the Click result is Positive and the PIS designation is Negative

Specificity = 100 * TN / (TN + FP)

Below is SAS pseudo code for calculating specificity and its 95% Wilson confidence interval:

```
proc freq;
    where PISResponse = 0;
    weight Count;
    tables ClickResponse / binomial(level="0" wilson);
run;
```

3.3.6. Accuracy

The accuracy (total agreement) of the Click device will be calculated as follows:

TP = the number of specimens where both the Click result and the PIS designation are Positive

TN = the number of specimens where both the Click result and the PIS designation are Negative

N = number of subjects in the evaluable population

Accuracy = 100 * (TP + TN) / N

Below is SAS pseudo code for calculating accuracy and its 95% Wilson confidence interval:

```
proc freq;
    weight Count;
    tables Click*PIS / agree;
      ods output CrossTabFreqs=freq;
run;
data freqout;
      set freq(where=(Click = PIS and PIS > .) in=ina)
            freq(where=(Click ^= PIS and PIS > . and Click > .) in=inb);
      if ina then type = 1; else type = 2;
run;
proc means data=freqout2 sum;
      var frequency;
      by type;
      ods output summary=diagcnt;
run;
proc freq data=diagcnt;
      weight frequency_sum;
    tables type / binomial(wilson);
run;
```

3.3.7. Positive Predictive Value

For the primary analysis, the PPV of the Click device will be calculated as follows:

TP = the number of specimens where both the Click result and the PIS designation are Positive

FP = the number of specimens where the Click result is Positive and the PIS designation is Negative

PPV = 100 * TP / (TP + FP)

Below is SAS pseudo code for calculating PPV and its 95% Wilson confidence interval:

```
proc freq;
    where ClickResponse = 1;
    weight Count;
    tables PISResponse / binomial(level="1" wilson);
run;
```

For the supplementary analysis (See Section 8.1.2), PPV will be calculated using the observed sensitivity of the Click device and hypothetical prevalences. For these analyses, PPV will be calculated as follows (assuming all input parameters are scaled to [0,1]):

Sens = sensitivity

Spec = specificity

P = hypothetical prevalence

PPV = 100 * Sens * P / [Sens * P + (1 – Spec) * (1 – P)]

3.3.8. Negative Predictive Value

For the primary analysis, the NPV of the Click device will be calculated as follows:

TN = the number of specimens where both the Click result and the PIS designation are Negative

FN = the number of specimens where the Click result is Negative and the PIS designation is Positive

NPV = 100 * TN / (TN + FN)

Below is SAS pseudo code for calculating NPV and its 95% Wilson confidence interval:

```
proc freq;
    where ClickResponse = 0;
    weight Count;
    tables PISResponse / binomial(level="0" wilson);
run;
```

For the supplementary analysis (See Section 8.1.2), NPV will be calculated using the observed sensitivity of the Click device and hypothetical prevalences. For these analyses, NPV will be calculated as follows (assuming all input parameters are scaled to [0,1]):

Sens = sensitivity

Spec = specificity

P = hypothetical prevalence

NPV = 100 * Spec * (1 – P) / [(1 – Sens) * P + Spec * (1 – P)]

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This study is a multi-center study with a minimum of three CLIA-waived intended operator sites in the United States; approximately one-third of the total number of sites will have a patient population of low NG, CT, or TV prevalence. Low prevalence sites are defined as sites with a prevalence ≤2% for any of the three targets. Sites with a prevalence higher than 2% for all the three targets will be defined as high prevalence sites. The study will enroll approximately 1750 female subjects. The study will continue enrolling subjects until the targets for positive specimens are met (as outlined below). Approximately one-third of the total subjects shall be recruited from low prevalence sites for the infections of interest.

Female subjects seen at the participating sites for any reason will be evaluated for enrollment in this study. All subjects will be managed per standard of care as applicable. Subjects who meet the inclusion/exclusion criteria will be offered enrollment into the study. Subjects who are enrolled in the study will provide clinical and demographic information, perform self-collection with a vaginal swab for the Click device, and allow the HCP to collect three additional vaginal swabs for the comparator methods. Subjects will complete the study in a single visit. The order of the swabs for comparator methods will be randomized per subject to account for the possibility that the yield of the swab is affected by previous swabs at the same anatomic site. The study specimens shall be collected according to institutional procedures as well as the manufacturer's instructions. The self-collected specimen shall be collected according to the Click self-collection instructions.

The study will include typical CLIA-waived collection and testing sites. At least nine different study operators among the study sites will perform the Click device testing, with each study operator testing a minimum of five positive and five negative specimens to support CLIA-waived status for CLIA categorization. Selected study operators should have non-laboratory background education and must not have certification for moderate or high-complexity testing to ensure representation of intended study operators to evaluate the use of the Click device. Study operators of typical CLIA-waived testing sites will receive no additional instructions (e.g., written or verbal training, coaching, or prompting) beyond providing them with the Click Quick Start Instructions. Operators will not know the SOC results of the subject's specimens. Operators will be instructed not to discuss the test with other operators or otherwise coach or observe each other. Study operators will also be instructed not to discuss the test with clinic staff.

Recruitment goals for the 510(k) phase of the study are at least 100 specimens positive for CT, 100 specimens positive for TV, and 45 specimens positive for NG as determined by PIS. Recruitment goals for the CLIA waiver phase of the study are 120 positive specimens for CT and TV (prospective), and 45 positive specimens for NG. In order to achieve the required precision for sensitivity of NG detection, additional specimens may be required. Banked NG positive specimens may also be used and will be provided to the testing sites for Click device testing. Thus, the maximum target for the number of PIS-positive NG samples is 85. At specified enrollment targets, the sensitivity of the Click device with respect to NG will be estimated. If the NG estimate meets the requirements for the 510(k) and CLIA waiver phases at any of the interim points and the enrollment targets for CT and TV have been met, collection of samples will stop. Otherwise, collection of samples will continue. See Section 6.6 and Section 6.7 for details on the interim reviews. All comparator tests will be performed by a reference laboratory.

4.2. Selection of Study Population

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

1. Willing and able to give voluntary written informed consent (or the parent/legal guardian will provide parental permission) before any study-related procedure is performed.
2. Female at birth. (Pregnant and breastfeeding women are eligible.)
3. Age ≥14 years at the time of enrollment.
4. Able to read and understand the procedural information provided for the study.
5. Able and willing to follow all study procedures, including performing self-collection of one vaginal swab and permitting a licensed HCP to collect three additional vaginal swabs.

Subjects meeting any of the following criteria at enrollment will be excluded from this study:

1. Have a medical condition, serious intercurrent illness, or other circumstance that, in the Investigator's judgment, could jeopardize the subject's safety, or could interfere with study procedures.
2. Enrollment in this study previously.
3. Use of antiperspirants and deodorants or the following vaginal products: douches, washes, lubricants, vaginal wipes, vaginal moisturizers, or feminine hygiene spray in the genital area, within 48 hours prior to enrollment.

Frozen NG banked specimens may be used and will be provided to the testing sites for Click testing as per the criteria in Section 4.0 of the protocol. Positive NG-known subjects providing banked vaginal specimens should meet the following inclusion and exclusion criteria:

Inclusion Criteria:

1. Vaginal specimen is from a female age ≥14 years at the time of specimen collection.
2. A minimum of 2.0 mL of frozen sample taken from well-characterized specimens collected from known NG subjects not being treated since testing positive within the past 4 months.
3. NG comparator results available.
4. Vaginal specimen is obtained from a collection wherein the subject consented/assented to future unspecified research use of her specimen.

Exclusion Criteria:

1. Previously enrolled in this study.

Subjects arriving at the study sites for any reason who may meet the study inclusion/exclusion criteria will be evaluated for enrollment in this study. It is each site's responsibility to enroll only subjects who satisfy the inclusion/exclusion criteria and to obtain parental/legal guardian permission when required. Sites must adhere to local policies and regulations that govern enrollment of either minors or pregnant women.

Sites may use any system for recruitment and enrollment that meets the study objectives and is IRB-approved. Recruitment can be by word-of-mouth, flyers, advertisement online, or any other means, subject to approval by the associated IRB. Each participating institution must provide for the review and approval of this protocol and the associated informed consent documents and recruitment materials by the IRB.

Subjects are considered enrolled in this study once they meet all inclusion/exclusion criteria and sign an informed consent and assent form as applicable. It is recommended that every subject remain in the study until completion of all study procedures; however, a subject's participation in the study may be discontinued. Should this occur, the reason for discontinuation must be documented in the source documentation. Reasons for discontinuation may include, but are not limited to, the following:

- Subject withdrawal: Subject participation in this clinical study is voluntary and the subject may discontinue participation at any time without loss of benefit or penalty.
- Investigator termination: Investigator may terminate the subject's participation without the subject's consent if the Investigator believes it is medically in the subject's best interest.
- Adverse events (AEs): Investigator may terminate the subject's participation for reasons of adverse events associated with study procedures.
- Termination of study: Although the study Sponsor has every intention of completing the study, the Sponsor reserves the right to terminate the study at any time for clinical or administrative reasons. Reasons for termination include, but are not limited to, study closure at the discretion of DMID.
- Other: Subject may be terminated without the subject's consent for various other reasons including, for example, sponsor's decision.

5. SAMPLE SIZE CONSIDERATIONS

Recruitment goals for the 510(k) phase of the study are at least 100 specimens positive for each of CT and TV, and at least 45 specimens positive for NG as determined by PIS. Recruitment goals for the CLIA waiver phase of the study are 120 positive specimens for each of CT, TV, and 45 NG. Approximately 585 subjects will be recruited from low-prevalence sites (one third of the 1,750) and approximately 1165 subjects will be recruited from high prevalence sites. The average expected proportion of samples positive via PIS for CT, TV, and NG among subjects enrolled at the high prevalence sites are, respectively, 12.4%, 19.5%, and 8.1%. The corresponding estimates for the low prevalence sites are 1.7%, 1.0%, and 1.4%. Based on these prevalence estimates, it is expected that the enrollment targets will be met for the three organisms. Thus, the study as designed is expected to meet the 510(k) and CLIA waiver recruitment goals for all three organisms. If NG prevalence is lower than expected, banked NG+ samples may need to be leveraged to meet the recruitment goals for NG. As indeterminate PIS designations or invalid or failed Click device results are expected for a small number of cases, enrollment may extend beyond 1750 to replace these results. The duration of enrollment may be extended if the actual prevalence of any of the organisms is lower than predicted.

For the estimation of the sensitivity and specificity of the Click device, we assume both the sensitivity and specificity is at least 95%. For 510(k) clearance, the study aims to demonstrate that sensitivity to each of CT and NG is at least 95% with a lower bound of the two-sided 95% Wilson Score confidence intervals at least 90%, and to demonstrate that sensitivity to TV is at least 95% with a lower bound of the two-sided 95% Wilson Score confidence intervals at least 85%. Regarding specificity, the study aims to demonstrate specificity to each of CT, TV, and NG is at least 95% with a lower bound of the two-sided 95% Wilson Score confidence intervals at least 90%. For the CLIA waiver, the study aims to demonstrate that both the sensitivity and specificity to each of CT, TV, and NG is at least 95% with a lower bound of the two-sided 95% Wilson Score confidence intervals at least 89%.

To demonstrate this for CT and TV, 95% Wilson Score confidence intervals were calculated for a range of sample sizes, number of PIS-positive samples, and sensitivity/specificity estimates. Given the uncertainty in the exact number of subjects enrolled or PIS-positive samples, the following parameter ranges were explored: total sample sizes of 1500 to 2000, 100 to 200 PIS-positive samples, and sensitivity/specificity estimates of 95% to 99%. Wilson Score confidence intervals were calculated for each combination of sample size, number of PIS-positive samples, and sensitivity/specificity. As an example, Table 2 below displays the lower confidence bound using a sample size of 1750 and a select subset of the number of PIS-positive samples.

Table 2: Lower 95% Wilson Score Confidence Bounds (%) for Various Number of PIS-Positive Samples and Sensitivity and Specificity Values

Number of PIS-Positive Samples	Sensitivity (%)					Specificity (%)				
	95	96	97	98	99	95	96	97	98	99
100	88.8	90.2	91.5	93.0	94.6	93.9	94.9	96.1	97.2	98.4
101	88.9	90.3	91.6	93.1	94.6	93.9	95.0	96.1	97.3	98.4
102	89.0	90.3	91.7	93.1	94.7	93.9	95.0	96.1	97.3	98.4
103	89.1	90.4	91.8	93.2	94.7	93.9	95.0	96.1	97.3	98.4
104	89.2	90.5	91.9	93.3	94.8	93.9	95.0	96.1	97.3	98.4
105	89.3	90.6	91.9	93.3	94.8	93.9	95.0	96.1	97.3	98.4
106	89.4	90.7	92.0	93.4	94.8	93.9	95.0	96.1	97.3	98.4
120	89.5	91.7	92.9	94.1	95.4	93.9	94.9	96.1	97.2	98.4
121	89.6	91.8	93.0	94.2	95.5	93.9	94.9	96.1	97.2	98.4
122	89.7	91.9	93.0	94.2	95.5	93.9	94.9	96.1	97.2	98.4
123	89.8	91.9	93.1	94.3	95.5	93.9	94.9	96.1	97.2	98.4
124	89.8	92.0	93.1	94.3	95.6	93.9	94.9	96.1	97.2	98.4
125	89.9	91.0	93.2	94.4	95.6	93.8	94.9	96.1	97.2	98.4
126	90.0	91.0	93.2	94.4	95.6	93.8	95.0	96.1	97.2	98.4

Over the entire ranges of parameter values explored, the lower bound of the specificity confidence interval never fell below 93.6%. The lower bound of the sensitivity confidence intervals never fell below 88.8% and was greater than or equal to 89% for all combinations of parameter values except for the following scenario:

- Sample Size = Any, Number of PIS-positive samples = 100 or 101, Sensitivity = 95%

The lower bound of the sensitivity confidence intervals was greater than or equal to 90% for all combinations of parameter values except for the following scenarios:

- Sample Size = Any, Number of PIS-positive samples = 100 to 112, Sensitivity = 95%
- Sample Size = Any, Number of PIS-positive samples = 120 to 126, Sensitivity = 95%

Thus, apart from a few scenarios, assuming the sensitivity/specificity of the Click device is at least 95%, the study as planned should be able to meet the confidence interval estimate requirements for 510(k) clearance and CLIA waiver for CT and TV.

For NG, the minimum number of PIS-positive samples required for the 510(k) and CLIA Waiver reports is 45. The planned maximum sample size for NG-positive samples is 85. Due to the small 510(k) and CLIA Waiver enrollment targets for NG and the difficulty in recruiting NG-positive subjects, reviews of the sensitivity of the Click device with regard to NG detection will occur during the course of the study; see Section 6.5.

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 (CIs) for binomial proportions and differences in binomial proportions will be computed for product performance variables (e.g. sensitivity and specificity). A 5% two-sided significance level will be used; i.e. two-sided 95% confidence intervals will be generated.

All summary tables will include the total population size relevant to that table/column. If applicable and/or appropriate, 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 additionally, dates will not be included.

6.2. Analysis Populations

6.2.1. Enrolled Population

The Enrolled population will include all participants enrolled.

6.2.2. Evaluable Population

The Evaluable analysis population will include all subjects enrolled with a valid Click result and a valid PIS designation. There will be a separate Evaluable population for each organism. A subject will be excluded from the organism-specific evaluable population if any of the following criteria are met:

- Either the Click result is invalid or the PIS designation is indeterminate
- The specimen for either the Click or comparator assays is missing or untested
- The specimen for the Click device was tested more than 2 hours after collection
- The specimen for the comparator assay was tested outside the stability window
- Subject did not meet eligibility criteria
- Any protocol deviation that, in the opinion of the investigators, is deemed to impact validity of assay results
- Any other reason that, in the opinion of the investigators, is deemed to impact validity of assay results (e.g. receipt of a concomitant medication that could interfere with assay results)

See Section 3.3.2 for definitions of valid result and designation.

6.3. Covariates, Center Effects, and Subgroups

Though the study is not designed to adequately assess product performance within subgroups, certain summaries will be presented by operator, clinical site, lot, and symptomatic status (see Section 8.2).

Safety and product performance data will be both broken up and pooled across clinical sites and operators within clinical site. Though Click devices are manufactured and shipped centrally from Click Diagnostics, the sites are using standardized procedures for assessment of unsolicited adverse events, the study utilizes a

central laboratory for comparator testing, and the study is not designed to detect subgroup effects, operator and center effects are possible. See Section 8 and Section 9 for more details.

As necessary, the study Sponsor, their designated Statistics and Data Coordinating Center, and/or authorized Principal Investigators may perform additional analyses depending on the nature of the data acquired, new regulatory directives, or to respond to unforeseen contingencies during the course of the study. Such analyses and their results, including a rationale for performing said analyses, will be described in detail in the study report and/or study publication.

6.4. Multiple Comparisons/Multiplicity

No adjustments for multiplicity are planned.

6.5. Timing of Analysis, Interim Analyses and Data Monitoring

The final analysis will be performed after database lock when all subjects have their data entered and monitored.

In addition, the primary analysis of agreement between the Click device results and PIS will be performed on an ongoing basis during the course of the study. These analyses will track performance of the investigative device and thereby serve to inform the Sponsor team and Click Diagnostics as to the likelihood of successful completion of the study with performance conforming to acceptance criteria, or conversely, to eventual futility of the study for failure to achieve acceptable performance. In no case shall the results of these ongoing analyses initiate an early termination of the study for benefit, i.e. based upon early achievement of acceptable performance.

In accord with DMID Policy, analysis results shall be distributed only to the Sponsor team and to Click Diagnostics and the receiving personnel shall not further distribute the results. No results shall be supplied to study site personnel or to study monitors, and neither the raw data nor the analysis of these ongoing analyses shall be submitted to FDA. The results of these ongoing analyses shall not translate into study design changes, protocol amendments, or investigative device design changes. The ongoing performance tracking is outside the scope of this SAP.

7. STUDY SUBJECTS AND CLICK DEVICES

7.1. Disposition of Subjects and Devices

The disposition of subjects in the study will be tabulated overall and by clinical site. Table 3 will present the number of subjects who are screen failures and the number of subjects that met each inclusion/exclusion criterion. The number of subjects enrolled, who provided valid Click results/PIS designations, included in the Evaluable analysis populations, and who terminated early from the study will be tabulated overall and by clinical site (Table 4). Table 5 will present the reasons for exclusion from the Evaluable analysis populations. A listing of subjects who completed the study, terminated early from study, and the reason for early termination is included in Listing 1. A subject listing of Evaluable population eligibility for all enrolled subjects and the reason(s) for exclusion will be provided (Listing 2).

The disposition of Click devices used in the study will be tabulated overall and by clinical site. Table 6 and Table 7 will present the number of devices which provided valid/invalid results and the reasons for the invalid result. A device listing including all valid and invalid results will be provided (Listing 3). Results of the Click Device operator control testing will be summarized (Table 8) and a separate listing of the results of the control tests will be provided (Listing 4).

7.2. Demographic and Other Baseline Characteristics

Demographic and other baseline characteristics will be summarized for all enrolled subjects and the Evaluable populations. Ethnicity, race, symptomatic status, and age category will be summarized overall and by site (Table 9 and Table 10). 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 categorized as: 14 – 17, 18 – 25, 26 – 30, 31 – 35, 36 – 40, 41 – 45, 46 – 50, 51 – 55, and > 55. Continuous age will also be summarized overall and by site (Table 11 and Table 12). The number and percentage of evaluable subjects who were tested positive by the Click device will be summarized by organism and age category (Table 13).

Subject-reported symptoms occurring within 7 days prior to enrollment will be summarized overall and by organism for all evaluable subjects with positive results from the Click device (Table 14).

Targeted sexual history, including history of CT, NG, and TV, will be summarized for all enrolled subjects and the Evaluable populations (Table 15 and Table 16).

Summaries of medications that were started prior to enrollment and continuing at the time of enrollment will be presented by WHO Drug Anatomical codes (ATC) Level 1 and Level 2 for all enrolled subjects and the Evaluable populations (Table 17 and Table 18). Summaries of genital products used within 7 days prior to enrollment will be presented by category (e.g. gel, foam, wash, etc.) and indication (e.g. contraceptive, lubricant, cleansing, etc.) for all enrolled subjects and the Evaluable populations (Table 19 and Table 20).

Individual subject listings will be presented for all demographics, clinical symptoms, targeted sexual history, concomitant medications, and genital products (Listing 5, Listing 6, Listing 7, Listing 8, and Listing 9).

7.3. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the deviation category, and the type of deviation for all enrolled subjects (Table 21). All subject-specific protocol deviations and non-subject-specific protocol deviations will be included as data listings (Listing 10 and Listing 11, respectively).

8. PRODUCT PERFORMANCE EVALUATION

8.1. Analysis of the Primary Outcome.

8.1.1. Primary Analysis

For the primary analysis, the 2x2 contingency table comparing the results of the Click Device and PIS will be presented by organism (Table 22). Contained in the table for each organism are the number of true positives (top left), false positives (top right), false negatives (bottom left), and true negatives (bottom right) of the Click device as well as the total number of valid positive and negative results for the Click device and PIS (Total rows and columns). For each organism, the sensitivity, specificity, accuracy, PPV, and NPV of the Click device will be presented along with their 95% Wilson confidence intervals.

Listing 12 will present individual product performance data for all subjects including Click result, PIS designation, and the individual comparator assay results. The listing will include subjects excluded from the Evaluable population.

8.1.2. Supplementary Analyses

A series of summaries which provide additional insight into the primary analysis will be generated.

Summaries of comparator assay results for samples where the Click device and comparator assays/PIS were discordant will be presented by organism (Table 23), by symptomatic status (Table 24), by age category (Table 25), and by Click device lot number (Table 26).

Summaries of all observed combinations of valid results among the comparator assays for all samples tested on each assay will be presented by organism (Table 27), by symptomatic status, and age category (Table 28).

The primary analysis summaries contain estimates of PPV and NPV given data observed in this study. As an exploration, hypothetical PPV and NPV estimates will be calculated for each organism using the observed sensitivity and specificity of the Click device and a range of hypothetical prevalence rates (see Section 3.3.6 and Section 3.3.7 for the calculation of PPV and NPV). The hypothetical prevalences (in percentages) that will be explored for each organism are: 1, 2, 5, 10, 20, 25, 30, 50. Table 29 will present the resulting PPV and NPV estimates over the range of prevalences.

The number of positive, negative, and invalid Click device results will be presented by operator (Table 30). For these summaries, a device will be considered to have “Positive” result for a specimen if the test was valid and positive for any of the three organisms. A device will be considered to have a “Negative” result for a specimen if the test was valid and negative for any of the three organisms.

8.2. Analysis of the Secondary Outcome

For each organism, contingency tables and estimates of sensitivity, specificity, accuracy, PPV, and NPV of the Click device will be presented by clinical site (Table 31), symptomatic status (Table 32), age category (Table 33), and Click device lot number (Table 34). Table 35 will present a simplified summary of the symptomatic status analyses.

8.3. Analysis of the Exploratory Outcomes

Table 36 and Table 37 will present summaries of responses to individual items on the Operator ease of use questionnaire. For each item on the questionnaire, the proportion of study operators who select each level of

the response will be provided as well as the distribution of each item's responses (e.g., mean, standard deviation, median, range). Listing 13 will provide a listing of individual operator responses.

For the exploratory outcome measure of prevalence of each organism (as determined by PIS or the Click device), the overall, by site, and by symptomatic status estimates will be contained in the primary and secondary analysis contingency tables described above.

9. SAFETY EVALUATION

9.1. Adverse Events

Adverse reactions are not anticipated in this study, and the study procedures present no anticipated risks beyond the low risks of vaginal swab collection. Thus only a subject listing will be provided for safety data. Listing 14 will include information such as Subject ID, Adverse Event Description, Severity, Relationship to Study Device, Alternate Etiology if Not Related Outcome, Duration of Event in days, and whether the event was an Unanticipated Adverse Device Effect (UADE) or Serious Adverse Event (SAE).

10. REPORTING CONVENTIONS

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", and similar for values > 0.99. Percentages will be reported to the nearest whole number; values < 1% will be presented as "<1", and similar for values > 99%. Sensitivity, specificity, accuracy, PPV, and NPV and their associated confidence intervals will be reported to one decimal place. Values > 99.9% will be presented as ">99.9%".

11. TECHNICAL DETAILS

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

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

The analyses described in this SAP coincide with the analysis descriptions provided in the study protocol.

13. REFERENCES

1. International Conference on Harmonisation (ICH) E9. http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf
2. 21 CFR Section 807.92. https://www.gpo.gov/fdsys/granule/CFR-2012-title21-vol8/CFR-2012-title21-vol8-sec807-92/content-detail.html
3. FDA statistical guidance on Reporting Results from Studies Evaluating Diagnostic Tests https://www.fda.gov/regulatory-information/search-fda-guidance-documents/statistical-guidance-reporting-results-studies-evaluating-diagnostic-tests-guidance-industry-and-fda
4. FDA guidance on Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices https://www.fda.gov/RegulatoryInformation/Guidances/ucm079632.htm

14. LISTING OF TABLES AND LISTINGS

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

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

Table 3: 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

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

Table 4: Subject Disposition by Site

Subject Disposition	Site 1 (N=X)		Site 2 (N=X)		…	All Subjects (N=X)	
	n	%	n	%	…	n	%
Screened	x	--	x	--	…	x	--
Enrolled	x	100	x	100	…	x	100
Terminated early from the study[a]	x	x	x	x	…	x	x
Provided valid Click result	x	x	x	x	…	x	x
Provided valid CT PIS designation	x	x	x	x	…	x	x
Provided valid TV PIS designation	x	x	x	x	…	x	x
Provided valid NG PIS designation	x	x	x	x	…	x	x
Evaluable for CT[b]	x	x	x	x	…	x	x
Evaluable for TV[b]	x	x	x	x	…	x	x
Evaluable for NG[b]	x	x	x	x	…	x	x
PIS CT+	x	x	x	x	…	x	x
PIS TV+	x	x	x	x	…	x	x
PIS NG+	x	x	x	x	…	x	x

Notes: N=Number of enrolled subjects.
[a]Refer to Listing 1 for reasons subjects terminated early.
[b]Refer to Listing 2 for Evaluable Population eligibilities and Table 6 for a summary of reasons subjects were excluded from Evaluable Populations.

Table 5: Summary of Evaluable Populations Exclusions - All Enrolled Subjects

	CT		NG		TV	
	n	%	n	%	n	%
All Enrolled Subjects	x	-	x	-	x	-
Evaluable Subjects	x	x	x	x	x	x
Non-Evaluable Subjects	x	x	x	x	x	x
Reason(s) for Exclusion[a]:						
Subject did not meet eligibility criteria	x	x	x	x	x	x
Invalid Click result	x	x	x	x	x	x
Indeterminate PIS determination	x	x	x	x	x	x
Specimens missing/untested for Click or PIS	x	x	x	x	x	x
Click specimens were not tested within 2 hours of collection	x	x	x	x	x	x
Comparator specimens tested outside the stability window	x	x	x	x	x	x
Any protocol deviation that, in the opinion of the investigators, is deemed to impact validity of assay results	x	x	x	x	x	x
Any other reason that, in the opinion of the investigators, is deemed to impact validity of assay results	x	x	x	x	x	x

Notes: Denominators for percentages is the number of enrolled subjects
[a.] Subjects may be counted under more than one reason for exclusion

Implementation Notes:

Depending on the observed counts of the "Any protocol deviation…" and "Any other reason…" reasons, these rows may be combined into a single row "Any protocol deviation or other reason that, in the opinion of the investigators, is deemed to impact validity of assay results".

Table 6: Click Device Disposition for Clinical Specimens by Site

Test	Device Disposition	Reason for Invalid	Site 1 (N=X)		Site 2 (N=X)		…	All Subjects (N=X)	
			n	%	n	%	…	n	%
Initial Test	Valid Result		x	x	x	x	…	x	x
	Invalid Result	Any Reason	x	x	x	x	…	x	x
		Device Error	x	x	x	x	…	x	x
		Other	x	x	x	x	…	x	x
All Tests (initial and re-test)	Valid Result		x	x	x	x	…	x	x
	Invalid Result	Any Reason	x	x	x	x	…	x	x
		Device Error	x	x	x	x	…	x	x
		Other	x	x	x	x	…	x	x

Notes: N=Number of subjects with an initial test performed, and is used for denominator for all percentages.
For All Tests (initial and re-test) a subject is counted as having a valid result either the initial or re-test result is valid, and counted as an invalid, if result if both initial and re-test results are invalid.

Table with similar format:

Table 7: Click Device Disposition by Lot Number

Implementation Note: The columns will be the Lot Numbers and "All Lots".

Table 8: Success Rates of Click Device Operator Control Testing

	Initial Test			Re-Test		
Control Type	n	N	%	n	N	%
Negative	x	x	x	x	x	x
Positive	x	x	x	x	x	x
All	x	x	x	x	x	x

Table 9: Summary of Categorical Demographic and Baseline Characteristics by Site – All Enrolled Subjects

Variable	Characteristic	Site 1 (N=X)		Site 2 (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
Age	14-17	x	x	x	x	…	x	x
	18-25	x	x	x	x	…	x	x
	26-30	x	x	x	x	…	x	x
	…	x	x	x	x	…	x	x
	51-55	x	x	x	x	…	x	x
	>55	x	x	x	x	…	x	x

Note: N = Number of enrolled subjects

Tables with similar format:

Table 10: Summary of Categorical Demographic and Baseline Characteristics by Site – Evaluable Populations

Implementation Note: Table will include a column added to the left of "Variable titled "Organism" with values "CT", "TV", and "NG".

Table 11: Summary of Continuous Demographic and Baseline Characteristics by Site – All Enrolled Subjects

Variable	Statistic	Site 1 (N=X)	Site 2 (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 enrolled subjects

Tables with similar format:

Table 12: Summary of Continuous Demographic and Baseline Characteristics by Site – Evaluable Populations

Implementation Note: Table will include a column added to the left of "Variable titled "Organism" with values "CT", "TV", and "NG".

Table 13: Click Positive Specimens by Organism and Age - Evaluable Populations

				CT		NG		TV	
Age	N Enrolled	n Evaluable	% Evaluable	n Positives	Positivity Rate	n Positives	Positivity Rate	n Positives	Positivity Rate
14-17	x	x	x	x	x.x	x	x.x	x	x.x
18-25	x	x	x	x	x.x	x	x.x	x	x.x
26-30	x	x	x	x	x.x	x	x.x	x	x.x
…	…	…	…	…	…	…	…	…	..
51-55	x	x	x	x	x.x	x	x.x	x	x.x
>55	x	x	x	x	x.x	x	x.x	x	x.x
Total	x	x	x	x	x.x	x	x.x	x	x.x

Positives are specimens that were tested positive by the Click Device
Positivity rate uses the number of evaluable subjects in the specified age category as the denominator.

Table 14: Summary of Clinical Symptoms Within 7 Days Prior to Enrollment by Click-Positive Organism – Evaluable Populations

Number of Subjects Exhibiting:	CT+ **(N=X)**		NG+ **(N=X)**		**TV+ (N=X)**	
	n	**%**	**n**	**%**	**n**	**%**
At least one clinical symptom	x	x	x	x	x	x
Change in vaginal discharge	x	x	x	x	x	x
Vaginal irritation (itching, burning, soreness)	x	x	x	x	x	x
Lower abdominal/pelvic pain	x	x	x	x	x	x
Painful urination	x	x	x	x	x	x
Increased urinary frequency	x	x	x	x	x	x
Abnormal bleeding/spotting	x	x	x	x	x	x
Pain or bleeding with sex/intercourse	x	x	x	x	x	x

Note: For each column, N = number of evaluable subjects with positive result from the Click device for the specified organism.

Table 15: Summary of Targeted STI History by Site – All Enrolled Subjects

Interview Question	Site 1 (N=X)		Site 2 (N=X)		…	All Subjects (N=X)	
	n	%	n	%	…	n	%
Has been diagnosed with Chlamydia in their lifetime	x	x	x	x	…	x	x
Has been diagnosed with Chlamydia within past 7 days	x	x	x	x	…	x	x
Has been diagnosed with Trichomoniasis in their lifetime	x	x	x	x	…	x	x
Has been diagnosed with Trichomoniasis within past 7 days	x	x	x	x	…	x	x
Has been diagnosed with Gonorrhea in their lifetime	x	x	x	x	…	x	x
Has been diagnosed with Gonorrhea within past 7 days	x	x	x	x	…	x	x
Has been diagnosed with Bacterial Vaginosis in their lifetime	x	x	x	x	…	x	x
Has been diagnosed with Bacterial Vaginosis within past 7 days	x	x	x	x	…	x	x
Has been diagnosed with Candidiasis in their lifetime	x	x	x	x	…	x	x
Has been diagnosed with Candidiasis within past 7 days	x	x	x	x	…	x	x
Currently pregnant	x	x	x	x	…	x	x
Menstruating at time of enrollment	x	x	x	x	…	x	x

Note: N = number of enrolled subjects

Tables with similar format:

Table 16: Summary of Targeted STI History by Site – Evaluable Populations

Implementation Note: Table will include a column added to the left of "Variable titled "Organism" with values "CT", "TV", and "NG".

Table 17: Summary of Prior and Concurrent Medications by WHO Drug Classification and Site - All Enrolled Subjects

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Site 1 (N=X)		Site 2 (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 enrolled subjects
n = Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

Tables with similar format:

Table 18: Summary of Prior and Concurrent Medications by WHO Drug Classification and Site – Evaluable Population

Table 19: Summary of Genital Products by Category, Indication, and Site – All Enrolled Subjects

Implementation Notes: The first two columns will be Category and Indication, respectively. Only reported combinations of category and indication will be presented.

Table 20: Summary of Genital Products by Category, Indication, and Site – Evaluable Populations

Implementation Notes: The first two columns will be Category and Indication, respectively. Only reported combinations of category and indication will be presented. Table will include a column added to the left of "Variable titled "Organism" with values "CT", "TV", and "NG".

Table 21: Distribution of Protocol Deviations by Category, Type, and Site – All Enrolled Subjects

Category	Deviation Type	Site 1 (N=X)			Site 2 (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
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
	Missed swab testing	x	x	x	x	x	x	…	x	x	x
	Delayed swab testing	x	x	x	x	x	x	…	x	x	x
	Swab(s) not collected	x	x	x	x	x	x	…	x	x	x
	Operator Form photo not available	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
	Swabs collected in the incorrect order	x	x	x	x	x	x	…	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x	…	x	x	x
	Other	x	x	x	x	x	x	…	x	x	x
Device accountability	Any type	x	x	x	x	x	x	…	x	x	x
	Quarantined/defective device used	x	x	x	x	x	x	…	x	x	x
	Other	x	x	x	x	x	x	…	x	x	x

Note: N = Number of enrolled subjects

Table 22: Comparison of Click Device Results and PIS Designations by Organism

Organism	Click Device Result	PIS Designation			Sensitivity (95% CI[a])	Specificity (95% CI[a])	Accuracy (95% CI[a])	PPV (95% CI[a])	NPV (95% CI[a])
		Positive	Negative	Total					
		n Row % Column %	n Row % Column %	n Row % Column %					
CT (N = X)	Positive	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)
	Negative	x x x	x x x	x x x					
	Total	x x x	x x x	x x x					
TV (N = X)	Positive	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)
	Negative	x x x	x x x	x x x					
	Total	x x x	x x x	x x x					
NG (N = X)	Positive	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)
	Negative	x x x	x x x	x x x					
	Total	x x x	x x x	x x x					

Notes: The denominator for estimates is based on the number of subjects in the Evaluable population for the specified organism (N).
[a] 95% CI = 95% Wilson confidence interval

Table 23: Summaries of Discordant Click Device and Comparator Assay Results by Organism

Organism	Discordance Type	BD Probtec		Hologic Aptima		BD Max		PIS Designation	
		n	%	n	%	n	%	n	%
CT	Click Positive, Comparator Negative	x	x	x	x	x	x	x	x
	Click Negative, Comparator Positive	x	x	x	x	x	x	x	x
	Total Discordances	x	-	x	-	x	-	x	-
TV	Click Positive, Comparator Negative	x	x	x	x	x	x	x	x
	Click Negative, Comparator Positive	x	x	x	x	x	x	x	x
	Total Discordances	x	-	x	-	x	-	x	-
NG	Click Positive, Comparator Negative	x	x	x	x	x	x	x	x
	Click Negative, Comparator Positive	x	x	x	x	x	x	x	x
	Total Discordances	x	-	x	-	x	-	x	-

Note: Denominator for percentages is the total number of discordant results between Click and comparator assay/PIS for the specified organism.

Table 24: Summaries of Discordant Click Device and Comparator Assay Results by Organism and Symptomatic Status

Symptomatic Status	Organism	Discordance Type	BD Probtec		Hologic Aptima		PIS Designation	
			n	%	n	%	n	%
Symptomatic	CT	Click Positive, Comparator Negative	x	x	x	x	x	x
		Click Negative, Comparator Positive	x	x	x	x	x	x
		Total Discordances	x	-	x	-	x	-
	TV	Click Positive, Comparator Negative	x	x	x	x	x	x
		Click Negative, Comparator Positive	x	x	x	x	x	x
		Total Discordance	x	-	x	-	x	-
	NG	Click Positive, Comparator Negative	x	x	x	x	x	x
		Click Negative, Comparator Positive	x	x	x	x	x	x
		Total Discordances	x	-	x	-	x	-
Asymptomatic	…	…	…	…	…	…	…	…

Note: Denominator for percentages is the total number of discordant results between Click and compartor assay/PIS for the specified symptomatic status and organism.

Tables with similar format:

Table 25: Summaries of Discordant Click Device and Comparator Assay Results by Organism and Age

Implementation Note: The first column will be Age category where the age categories will be those displayed in Table 7.

Table 26: Summaries of Discordant Click Device and Comparator Assay Results by Organism and Click Device Lot

Implementation Note: The first column will be Device Lot number.

Table 27: Observed Combinations of Click and Comparator Assay Results by Organism

Organism	Combination of Results					Observed Frequency	
	Click	BD Probetec	Hologic Aptima	BD Max	PIS Designation	n	%
CT (N = X)	Positive	Positive	Positive	NA	Positive	x	x
	Positive	Positive	Negative	Positive	Positive	x	x
	…Continue for all observed combinations…						
TV (N = X)	Positive	Positive	Positive	NA	Positive	x	x
	Positive	Positive	Negative	Positive	Positive	x	x
	…Continue for all observed combinations…						
NG (N = X)	Positive	Positive	Positive	NA	Positive	x	x
	Positive	Positive	Negative	Positive	Positive	x	x
	…Continue for all observed combinations…						

Note: Denominator of percentages is the number of subjects in the Evaluable population for the specified organism (N).

Table 28: Observed Combinations of Click and Comparator Assay Results by Organism and Baseline Characteristics

Characteristic	Organism	Combination of Results					Observed Frequency	
		Click	BD Probetec	Hologic Aptima	BD Max	PIS Designation	n	%
Characteristic #1	CT (N = X)	Positive	Positive	Positive	NA	Positive	x	x
		Positive	Positive	Negative	Positive	Positive	x	x
		…Continue for all observed combinations…						
	TV (N = X)	Positive	Positive	Positive	NA	Positive	x	x
		Positive	Positive	Negative	Positive	Positive	x	x
		…Continue for all observed combinations…						
	NG (N = X)	Positive	Positive	Positive	NA	Positive	x	x
		Positive	Positive	Negative	Positive	Positive	x	x
		…Continue for all observed combinations…						
Characteristic #2	…	…	…	…	…	…	…	…

Note: Denominator of percentages is the number of subjects in the Evaluable population for the specified characteristic and organism (N).

Implementation Notes: The Characteristics that will be included in the table are:

- Symptomatic status (Symptomatic, Asymptomatic)
- Age Category (Age categories displayed in Table 7)

Table 29: PPV and NPV Estimates across Range of Hypothetical Prevalances by Organism

Hypothetical Prevalence (%)	CT		TV		NG	
	PPV	NPV	PPV	NPV	PPV	NPV
1	x.x	x.x	x.x	x.x	x.x	x.x
2	x.x	x.x	x.x	x.x	x.x	x.x
5	x.x	x.x	x.x	x.x	x.x	x.x
10	x.x	x.x	x.x	x.x	x.x	x.x
20	x.x	x.x	x.x	x.x	x.x	x.x
25	x.x	x.x	x.x	x.x	x.x	x.x
30	x.x	x.x	x.x	x.x	x.x	x.x
50	x.x	x.x	x.x	x.x	x.x	x.x

Table 30: Click Device Results by Operator

Click Device Result	Operator 1	Operator 2	…	Operator K
Positive	x	x	…	x
Negative	x	x	…	x
Invalid	x	x	…	x
Total	x	x	…	x

Table 31: Comparison of Click Device Results and PIS Designations by Organism and Site

Site	Organism	Click Device Result		PIS Designation			Sensitivity (95% CI[a])	Specificity (95% CI[a])	Accuracy (95% CI[a])	PPV (95% CI[a])	NPV (95% CI[a])
				Positive	Negative	Total					
				n Row % Column %	n Row % Column %	n Row % Column %					
Site 1	CT (N = X)	Positive	n Row % Column %	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)
		Negative	n Row % Column %	x x x	x x x	x x x					
		Total	n Row % Column %	x x x	x x x	x x x					
	TV (N = X)	Positive	n Row % Column %	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)
		Negative	n Row % Column %	x x x	x x x	x x x					
		Total	n Row % Column %	x x x	x x x	x x x					
	NG (N = X)	Positive	n Row % Column %	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)
		Negative	n Row % Column %	x x x	x x x	x x x					
		Total	n Row % Column %	x x x	x x x	x x x					
…	…	…	…	…	…	…	…	…		…	…

Notes: The denominator for estimates is based on the number of subjects in the Evaluable population for the specified organism and site (N).
[a] 95% CI = 95% Wilson confidence interval

Tables with similar format:

Table 32: Comparison of Click Device Results and PIS Designations by Organism and Symptomatic Status

Implementation Notes: The first column will be "Symptomatic Status" instead of "Site". "Symptomatic" rows will be displayed above "Asymptomatic" rows.

Table 33: Comparison of Click Device Results and PIS Designations by Organism and Age

Implementation Notes: The first column will be "Age Category" instead of "Site". The age categories will be those displayed in Table 7.

Table 34: Comparison of Click Device Results and PIS Designations by Organism and Click Device Lot

Implementation Notes: The first column will be "Device Lot Number" instead of "Site".

Table 35: Click Device Sensitivity and Specificity Estimates by Organism and Symptomatic Status

Organism	Symptomatic Status	Sensitivity			Specificity			Prevalence (%)
		Estimate (n / N)	Estimate (%)	95% CI (%)	Estimate (n / N)	Estimate (%)	95% CI (%)	
CT	Symptomatic	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%
	Asymptomatic	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%
	All	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%
TV	Symptomatic	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%
	Asymptomatic	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%
	All	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%
NG	Symptomatic	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%
	Asymptomatic	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%
	All	x / x	xx.x	xx.x, xx.x	x / x	xx.x	xx.x, xx.x	x.x%

Table 36: Responses to Operator Ease of Use Questionnaire by Site

Questionnaire Item	Response	Site 1			…	All Sites		
		Number of Operators with Response n	Number of Operators Queried N	Percentage of Operators with Response	…	Number of Operators with Response n	Number of Operators Queried N	Percentage of Operators with Response
It was easy to set up the device	Strongly Agree	x	x	x	…	x	x	x
	Agree	x	x	x	…	x	x	x
	Neutral	x	x	x	…	x	x	x
	Disagree	x	x	x	…	x	x	x
	Strongly Disagree	x	x	x	…	x	x	x
The instructions for the device were easy to follow	Strongly Agree	x	x	x	…	x	x	x
	Agree	x	x	x	…	x	x	x
	Neutral	x	x	x	…	x	x	x
	Disagree	x	x	x	…	x	x	x
	Strongly Disagree	x	x	x	…	x	x	x
It was easy to understand the Click Quick Start Instructions for performing external control testing	Strongly Agree	x	x	x	…	x	x	x
	Agree	x	x	x	…	x	x	x
	Neutral	x	x	x	…	x	x	x
	Disagree	x	x	x	…	x	x	x
	Strongly Disagree	x	x	x	…	x	x	x
…	…	…	…	…	…	…	…	…

Table 37: Response Statistics to Operator Ease of Use Questionnaire by Site

Questionnaire Item	Site 1			…	All Sites		
	Mean (STD)	Median	Range	…	Mean (STD)	Median	Range
Item #1	x.x (x.x)	x.x	x, x	…	x.x (x.x)	x.x	x, x
Item #2	x.x (x.x)	x.x	x, x	…	x.x (x.x)	x.x	x, x
Item #3	x.x (x.x)	x.x	x, x	…	x.x (x.x)	x.x	x, x
…	…	…	…	…	…	…	…

Implementation Note: Yes/No items will be excluded from this table.

APPENDIX 2. LISTINGS MOCK-UPS

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

LIST OF TABLES

Listing 1: Early Terminations – All Enrolled Subjects

Subject ID	Category	Reason for Early Termination
xxxxxxx	Early Termination/Treatment Discontinuation/Completion	xxxxxxxxxxxxxxxxx
xxxxxxx	Early Termination/Treatment Discontinuation/Completion	xxxxxxxxxxxxxxxxx

Implementation Notes:

- Sort order will be by Category (Completion first, then Early Termination), Subject ID
- Category will be "Early Termination" or "Completion".
- In the “Reason” column, concatenate any “specify” fields, including AE number and DV number.

Listing 2: Evaluable Analysis Population Eligibilities

Subject ID	Organism	Eligible for Evaluable Analysis Population?	Reason(s) Subject Excluded
xxxxxx	CT	Yes/No	xxxxx
	TV	Yes/No	xxxxx
	NG	Yes/No	xxxxx
xxxxxx	CT	Yes/No	xxxxx
	TV	Yes/No	xxxxx
	NG	Yes/No	xxxxx

Implementation Note: Sort order will be Eligible for Evaluable Analysis Population (First Yes, then No), Subject ID

Listing 3: Click Device Results

Lot Number	Click Device Number	Subject ID	Test Type	Valid/Invalid Result?	Invalid Result	Photo Taken?
LN#######	##XXX###	XXXX	Initial Test/Retest	Valid/Invalid	Device error/Control fail/Other	Yes/No
LN#######	##XXX###	XXXX	Initial Test/Retest	Valid/Invalid	Device error/Control fail/Other	Yes/No

Implementation Note: Sort order is Lot Number, Click Device Number.

Listing 4: Click Device Control Test Results

Site	Operator ID	Test Type	Control Test Performed	Test Outcome	Control Tests Category(ies)
Site 1	XYnn	First Test/Retest	Positive/Negative	Incorrect Results/Valid/Invalid	New Lot/New Shipment/Monthly Testing/New Operator/Other
Site 2	XYnn	First Test/Retest	Positive/Negative	Incorrect Results/Valid/Invalid	New Lot/New Shipment/Monthly Testing/New Operator/Other

Implementation Notes:

- Sort order will be by Site, Operator ID, Control Test Performed (Performed, then Negative), Test Type (First Test, then Retest)
- For Control Test Category, if New Lot, display Lot number (e.g. "New Lot: LN########)

Listing 5: Demographic Data – All Enrolled Subjects

Subject ID	Age at Enrollment (years)	Ethnicity	Race
xxxxxx	xx	xxxxxx	xxxxxx
xxxxxx	xx	xxxxxx	xxxxxx
xxxxxx	xx	xxxxxx	xxxxxx

Implementation Notes:

- Sort order will be by Subject ID
- For the Race column, if a subject is Multi-Racial, all races will be listed, separated by a comma

Listing 6: Clinical Symptoms – All Enrolled Subjects

Change in vaginal discharge	Vaginal irritation (itching, burning, soreness)	Lower abdominal/pelvic pain	Painful urination	Increased urinary frequency	Abnormal bleeding spotting	Pain or bleeding with sex/intercourse
Subject ID:						
Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No/NA

Listing 7: Targeted Sexual History – All Enrolled Subjects

	Chlamydia	Trichomoniasis	Gonorrhea	Bacterial Vaginosis	Candidiasis	Is the subject currently pregnant?	Is the subject menstruating at the time of visit?
Subject ID:							
Lifetime	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
Within Past 7 days	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No		

Implementation Notes: Sort order will be by Subject ID

Listing 8: Concomitant Medications – All Enrolled Subjects

Subject ID	Concomitant Medication Number	Medication	Route of Administration	Medication Start Day	Medication End Day	Indication	ATC Level 1 (ATC Level 2)
xxxx	xx	xxxxxx	xxxxxx	xx	xx	xxxxxx	xxxx (xxxx)
xxxx	xx	xxxxxx	xxxxxx	xx	xx	xxxxxx	xxxx (xxxx)

Implementation Notes:

- Sort order is actual Subject ID, concomitant medication number.
- Medication Start Day' and 'Medication End Day' are relative to enrollment (which is Day 1, day before enrollment is Day -1).
- 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.

Listing 9: Genital Products – All Enrolled Subjects

Subject ID	Genital Product Number	Product Name	Study Day of Last Use	Category	Indication
xxxx	xx	xxxxxx	xx	xxxxx	xxxxxx
xxxx	xx	xxxxxx	xx	xxxxx	xxxxxx

Implementation Note: Sort order is actual Subject ID, genital product number.

Listing 10: Subject-Specific Protocol Deviations – All Enrolled Subjects

Deviation Number	Study Day	Deviation Description	Deviation Category	Reason for Deviation	Deviation Affected Device Stability?	Deviation Resulted in AE?	Deviation Resulted in Subject Termination?	Deviation Resolution	Comments
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	--

Implementation Notes:

- Sort order will be by Subject ID, Deviation Number
- In the Deviation Category column concatenate any specify fields
- In the Reason for Deviation column concatenate any specify fields.

Listing 11: Non-Subject-Specific Protocol Deviations

Site	Deviation	Start Date	End Date	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Affected Device Stability?	Deviation Category	Deviation Resolution	Comments
xxxx	xxxx	DDMMMYYYY	DDMMMYYYY	xxxx	Yes/No	Yes/No/NA	xxxx	xxxx	xxxx
xxxx	xxxx	DDMMMYYYY	DDMMMYYYY	xxxx	Yes/No	Yes/No/NA	xxxx	xxxx	xxxx

Implementation Notes:

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

Listing 12: Individual Product Performance Data

Eligible for Evaluable Population	Organism	Click Result	BD Probetec Result	Hologic Aptima Result	BD Max Result	PIS Designation
Subject ID:						
Yes/No	CT	Positive/Negative/Invalid	Positive/ Negative/ Invalid	Positive/ Negative/ Equivocal/ Invalid	Positive/ Negative/ Unresolved or Invalid/ NA	Positive/ Negative/ Indeterminate
Yes/No	TV	Positive/Negative/Invalid	Positive/ Negative/ Invalid	Positive/ Negative/ Equivocal/ Invalid	Positive/ Negative/ Unresolved or Invalid/ NA	Positive/ Negative/ Indeterminate
Yes/No	NG	Positive/Negative/Invalid	Positive/ Negative/ Invalid	Positive/ Negative/ Equivocal/ Invalid	Positive/ Negative/ Unresolved or Invalid/ NA	Positive/ Negative/ Indeterminate

Implementation Notes:

- Sort order is Eligible for Evaluable Population (First Yes, then No), Subject ID.
- Each subject will have a separate row for each organism.

Listing 13: Individual Operator Ease of Use Questionnaire Responses

Operator ID	Questionnaire Item	Item Response
XYnn	1 – It was easy to set up the device	5 – Strongly Agree/ 4 – Agree/ 3 – Neutral/ 2 – Disagree/ 1 – Strongly Disagree
	2 – The instructions for the device were easy to follow	5 – Strongly Agree/ 4 – Agree/ 3 – Neutral/ 2 – Disagree/ 1 – Strongly Disagree
	3 – It was easy to understand the Click Quick Start Instructions for performing external control testing	5 – Strongly Agree/ 4 – Agree/ 3 – Neutral/ 2 – Disagree/ 1 – Strongly Disagree
…	…	…

Implementation Note: Sort order is actual Subject ID, Questionnaire Item.

Listing 14: Adverse Events

Adverse Event	Study Day	Severity	Relationship to Device	In Not Related, Alternative Etiology	Subject Discontinued Due to AE	Outcome	Is the Event a UADE?	Is the Event a SAE?	Study Day Event Became Serious	Reason(s) Event Became Serious
Subject ID: , AE Number:										
xxxxxxx	xx	Mild/ Moderate/ Severe	Related/ Not Related	xxxxx	Yes/No	xxxxx	Yes/No	Yes/No	xx	xxxxx
Comments: xxxxxxxxxxxxx										

Implementation Note: Sort order is Subject ID, AE Number.