Visby Medical, Inc.
Beth Lingenfelter
Clinical and Regulatory Affairs
3010 N. First Street
San Jose, California 95134

August 26, 2021

Re: K200748
Trade/Device Name: Visby Medical Sexual Health Click Test
Regulation Number: 21 CFR 866.3393
Regulation Name: Nucleic acid detection system for non-viral microorganism(s) causing sexually transmitted infections.
Regulatory Class: Class II
Product Code: QEP, MKZ, LSL, OUY
Dated: June 24, 2021
Received: June 25, 2021

Dear Beth Lingenfelter:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K200748

Device Name
Visby Medical Sexual Health Click Test

Indications for Use *(Describe)*
The Visby Medical Sexual Health Click Test is a single-use (disposable), fully-integrated, automated Polymerase Chain Reaction (PCR) in vitro diagnostic test intended for use in point of-care or clinical laboratory settings for the rapid detection and differentiation of DNA from Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis in self-collected female vaginal swab specimens using the Visby Medical Sexual Health Vaginal Specimen Collection Kit in a health care setting. The test results are to aid in the diagnosis of symptomatic or asymptomatic infections with Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence

A. Submitter

Name:	Visby Medical, Inc.
Address:	3010 N. First Street San Jose, CA 95134
Phone:	(408) 650 - 8878
Contact:	Beth Lingenfelter
Date Prepared:	August 11, 2021

B. Device

Trade Name:	Visby Medical Sexual Health Click Test
Classification Name:	Nucleic acid detection system for non-viral microorganism(s) causing sexually transmitted infections,
Regulatory Number:	866.3393
Regulatory Class:	Class II
Product Code:	QEP
Subsequent Product Codes:	MKZ, LSL, OUY

C. Predicate Devices

The Visby Medical Sexual Health Click Test is substantially equivalent to the Cepheid Xpert® CT/NG Assay and Cepheid Xpert® TV Assay, cleared under K121710 and K151565 on December 27, 2012 and October 16, 2015, respectively.

D. Intended Use

The Visby Medical Sexual Health Click Test is a single-use (disposable), fully-integrated, automated Polymerase Chain Reaction (PCR) *in vitro* diagnostic test intended for use in point of-care or clinical laboratory settings for the rapid detection and differentiation of DNA from *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* in self-collected female vaginal swab specimens using the Visby Medical Sexual Health Vaginal Specimen Collection Kit in a health care setting. The test results are to aid in the diagnosis of symptomatic or asymptomatic infections with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis*.

E. Device Description

The test system includes the Visby Medical Sexual Health Click device, the Visby Medical power supply, the Visby Medical Vaginal Collection kit, and fixed-volume transfer pipettes. The device processes a vaginal swab sample by automatically performing all steps required to complete lysis, polymerase chain reaction, and amplicon detection.

The patient uses the Visby Medical Vaginal Collection Kit to self-collect a vaginal specimen with the provided flocked swab, and then the patient elutes the specimen into the Visby Medical Collection Media. The test operator transfers the collection media containing the patient specimen into the sample port of the device using the provided fixed-volume pipette where it rehydrates a lyophilized internal process control. The sample enters a lysis module, where the DNA of the sample and the internal process control are extracted using a combination of chemical lysis and high temperature. The extracted DNA enters a mixing chamber where it rehydrates lyophilized PCR reagents, followed by thermocycling to amplify target DNA. If present, the amplified pathogen target (CT, NG, and/or TV) and internal process control hybridize to specific probes located on a flow channel. Detection of the target-specific PCR product is accomplished via an enzyme-linked colorimetric assay using streptavidin bound horseradish peroxidase (HRP) and a colorimetric substrate that forms a purple precipitate. Test results can be expected in approximately 30 minutes: a green check mark will appear, and a purple color will appear in the “Control” spot, indicating a valid test. A purple spot adjacent to “Chlamydia,” “Gonorrhoeae,” and/or “Trichomonas” signifies the presence of amplified CT, NG, and/or TV DNA in the sample. Tests with invalid results due to an error (indicated by a red X status light) or failure to develop a purple spot in the “Control” spot, are retested with a new Visby device.

F. Substantial Equivalence

The Visby Medical Sexual Health Click Test is substantially equivalent to the Cepheid Xpert CT/NG Assay and the Cepheid Xpert TV Assay, cleared under K121710 and K151565 on December 27, 2012 and October 16, 2015, respectively. Table 1 outlines the similarities and differences between the two system

Table 1. Comparison of the Visby Medical Sexual Health Click Test to the Predicate devices

Characteristic	Visby Medical Sexual Health Click Test (K200748)	Predicate: Cepheid Xpert CT/NG Assay (K121710)	Predicate: Cepheid Xpert TV Assay (K151565)
Regulation	21 CFR 866.3393	21 CFR 866.3390	21 CFR 866.3860
Device Class	Class II	Class II	Class II
Technology/ Detection	An automated multiplex polymerase chain reaction with colorimetric detection	An automated multiplex real-time polymerase chain reaction	An automated real-time polymerase chain reaction
Assay Targets	DNA from Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG), and Trichomonas vaginalis (TV)	DNA from Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG)	DNA from Trichomonas vaginalis (TV)
Specimen Types	Patient-collected vaginal swab	Urine (male and female), endocervical swab, and patient-collected vaginal swab	Endocervical Swabs Female Urine Patient-collected vaginal swab
CT Analyte Targets	CT cryptic plasmid DNA	CT genomic DNA	N/A
NG Analyte Targets	NG genomic DNA	NG genomic DNA	N/A
TV Analyte Targets	TV genomic DNA	N/A	T. vaginalis genomic DNA
Assay Results	Qualitative	Qualitative	Qualitative
Collection Kit	Swab collection kit	Urine collection kit Swab collection kit	Urine collection kit Swab collection kit
Sample Extraction	Self-contained and automated after specimen sample elution	Self-contained and automated after specimen sample elution and two single-dose reagent additions.	Self-contained and automated after specimen sample elution and two single-dose reagent additions.
Instrument System	Visby Medical Sexual Health Click Test	Cepheid GeneXpert Instrument Systems	Cepheid GeneXpert Instrument Systems
Turn-around Time	Approximately 30 minutes to results.	Approximately 90 minutes to results.	Approximately 90 minutes to results.

Characteristic	Visby Medical Sexual Health Click Test (K200748)	Predicate: Cepheid Xpert CT/NG Assay (K121710)	Predicate: Cepheid Xpert TV Assay (K151565)
Intended Use	The Visby Medical Sexual Health Click Test is a single-use (disposable), fully-integrated, automated Polymerase Chain Reaction (PCR) in vitro diagnostic test intended for use in point of-care or clinical laboratory settings for the rapid detection and differentiation of DNA from Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis in self-collected female vaginal swab specimens collected in Visby Medical Collection Media in a health care setting. The test results are to aid in the diagnosis of symptomatic or asymptomatic infections with Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis.	An automated, multiplex real-time RT-PCR assay, performed on the GeneXpert Instrument Systems, intended for the in vitro qualitative and differentiation of genomic DNA from Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG) to aid in the diagnosis of chlamydial gonorrheal urogenital disease. The assay may be used to test the following specimens from asymptomatic and symptomatic individuals: female and male urine, endocervical swab, and patient-collected vaginal swab (collected in a clinical setting).	The Cepheid Xpert TV Assay, performed on the GeneXpert Instrument Systems, is a qualitative in vitro diagnostic test for the detection of Trichomonas vaginalis genomic DNA. The test utilizes automated real-time polymerase chain reaction (PCR) to detect Trichomonas vaginalis genomic DNA. The Xpert TV Assay uses female urine specimens, endocervical swab specimens, or patient-collected vaginal swab specimens (collected in a clinical setting). The Xpert TV Assay is intended to aid in the diagnosis of trichomoniasis in symptomatic or asymptomatic individuals.
Indication for Use	Asymptomatic and symptomatic female patients	Asymptomatic and symptomatic patients	Asymptomatic and symptomatic patients
Assay Controls	Internal sample processing control (SPC). External controls available.	Internal sample processing control (SPC), sample adequacy control (SAC), and probe check control (PCC). External controls available.	Internal sample processing control (SPC), sample adequacy control (SAC), and probe check control (PCC). External controls available.

The Visby Medical Vaginal Specimen Collection Kit is substantially equivalent to the following predicate assays:

- Cepheid Xpert Vaginal/Endocervical Specimen Collection Kits

Table 2. Comparison of the Visby Medical Vaginal Specimen Collection Kit to the Predicate

Characteristic	Visby Medical Vaginal Specimen Collection Kit	Cepheid Xpert Vaginal/Endocervical Specimen Collection Kits
Description	A single use package containing an individually packaged sterile collection swab (for vaginal sampling) and a Visby Medical Collection Media tube. The collection swab is eluted into the Collection Media tube after swab sampling.	Contains one individually packaged sterile large cleaning swab (for endocervical samples) and a package containing an individually packaged sterile collection swab (for vaginal and endocervical sampling) and an Xpert CT/NG Swab Transport Reagent tube. The collection swab is placed into the Transport Reagent Tube after swab sampling to stabilize the nucleic acid until sample preparation.

G. Non-clinical Data

1. Limit of Detection

Limit of Detection (LoD) of the Visby Medical Sexual Health Click Test was determined for CT in elementary bodies per mL (EB/mL), NG in colony forming units per mL (CFU/mL), and TV in trophozoites per mL (troph/mL), from two distinct strains or serovars, seeded into negative clinical vaginal sample matrix (previously determined to be negative for CT, NG, TV). LoD is defined as the lowest concentration of organism that is reliably detected (≥ 95% of tested samples).

The LoD values for each strain were estimated by probit analysis of the results from range-finding studies. The calculated LoDs were verified by testing 20 replicates at the estimated LoD concentration and demonstrating that at least 19 out of 20 replicates were positive. The LoD for each strain is shown in Table 3.

Table 3. LoD of CT Serovars, NG strains, and TV strains

Organism	LoD
CT Serovar H (VR-879)	16.0 EB/mL
CT Serovar D (VR-885)	5.9 EB/mL
NG (ATCC 19424)	5.7 CFU/mL
NG (ATCC 49226)	6.2 CFU/mL
TV (ATCC 30001, metronidazole susceptible)	1.2 troph/mL
TV (ATCC 30238, metronidazole resistant)	0.24 troph/mL

2. Inclusivity

The ability of the Visby Medical Sexual Health Click Test to detect a wide range of target organisms was evaluated by testing 14 serovars of CT, 30 strains of NG, and 15 strains of TV at by spiking them into negative vaginal swab matrix near the assay LoD. For CT, Serovars A, Ba, C, E, F, G, J, K, LGV1 and LGV3 were detected at 32 EB/mL, serovar LGV2 was detected 64 EB/mL and serovar I was detected at 128 EB/mL. For NG, 29 strains were detected at 12.4 cfu/mL and 1 was detected at 24.8 cfu/mL. For TV, all isolates were detected at 2.4 trophs/mL.

3. Cross Reactivity and Microbial Interference

The cross reactivity of the Visby Medical Sexual Health Click Test was evaluated by testing 144 microorganisms seeded into negative vaginal swab matrix at high concentrations (>10^6 genomic copies/mL for bacteria and >10^5 genomic copies/mL for viruses). No cross reactivity was observed with the Visby Sexual Health Click Test when testing the organisms listed in Table 4.

In addition, microbial Interference of the same 144 microorganisms on the Visby Medical Sexual Health Click Test was evaluated by testing the same microorganisms spiked into a low positive (3x LoD) sample containing CT, NG and TV. No microbial interference of these microorganisms was observed when testing high concentrations of the organisms listed in the table in a low positive sample.

Additionally, three organisms could not be obtained for direct testing (Bacterial Vaginosis Associated Bacteria 2 (BVAB-2), *Megasphaera type 1*, and *Dientamoeba fragilis*). The sequences of these organisms were analyzed against the Visby Medical Sexual Health Click primer and amplicon sequences using basic local alignment search tool (BLAST). This in-silico analysis did not predict any cross reactivity or microbial interference.

Table 4. Microorganisms Evaluated for Cross-Reactivity and Microbial Interference

Achromobacter xerosis	*Cutibacterium acnes*	*Lactobacillus vaginalis*	*Pentatrichomonas hominis*
Acinetobacter calcoaceticus	*Deinococcus radiodurans*	*Lactococcus lactis*	*Peptostreptococcus anaerobius*
Acinetobacter lwoffii	*Derxia gummosa*	*Legionella pneumophila*	*Peptostreptococcus productus* (*Blautia producta*)
Actinomyces israelii	*Dientamoeba fragilis**	*Listeria monocytogenes*	*Plesiomonas shigelloides*
Aerococcus viridans	*Eikenella corrodens*	*Megashaera type 1**	*Prevotella bivia*
Aeromonas hydrophila	*Elizabethkingia meningoseptica*	*Micrococcus luteus*	*Proteus mirabilis*
Alcaligenes faecalis	*Entamoeba histolytica*	*Mobiluncus curtisii*	*Proteus vulgaris*
Arcanobacterium pyogenes	*Enterococcus faecalis*	*Mobiluncus mulieris*	*Providencia stuartii*
Atopobium vaginae	*Enterococcus faecium*	*Moraxella lacunata*	*Pseudomonas aeruginosa*
Bacteroides fragilis	*Enterobacter cloacae*	*Moraxella osloensis*	*Pseudomonas fluorescens*
Bacteroides ureolyticus	*Enterococcus raffinosus (avium)*	*Moraxella (Branhamella) catarrhalis*	*Pseudomonas putida*
Bergeriella denitrificans	*Erysipelothrix rhusiopathiae*	*Morganella morganii*	*Rahnella aquatilis*
Bifidobacterium adolescentis	*Escherichia coli*	*Mycobacterium smegmatis*	*Rhodospirillum rubrum*
Bifidobacterium breve	*Fusobacterium nucleatum*	*Mycoplasma genitalium*	*Saccharomyces cerevisiae*
Bifidobacterium longum	*Gardnerella vaginalis*	*Mycoplasma hominis*	*Salmonella minnesota*
Blastocystis hominis	*Gemella haemolysans*	*Neisseria elongata* (3)	*Salmonella typhimurium*
Brevibacterium linens	*Giardia intestinalis*	*Neisseria cinerea*	*Serratia marcescens*
BV associated bacteria (BVAB-2) *	*Haemophilus ducreyi*	*Neisseria subflava*	*Staphylococcus aureus*
Campylobacter jejuni	*Haemophilus influenzae*	*Neisseria flavescens* (2)	*Staphylococcus epidermidis*
Candida albicans	Herpes simplex virus I	*Neisseria perflava*	*Staphylococcus saprophyticus*
Candida glabrata	Herpes simplex virus II	*Neisseria lactamica* (4)	*Streptococcus agalactiae*
Candida parapsilosis	HIV-1 (synthetic RNA)	*Neisseria meningitidis serogroup A*	*Streptococcus bovis*
Candida tropicalis	Human papilloma virus 16 (synthetic DNA)	*Neisseria meningitidis serogroup B*	*Streptomyces griseinus*
Chlamydophila pneumoniae	Human papilloma virus 16 E6/E7 (Transformed cells)	*Neisseria meningitidis serogroup C (4)*	*Streptococcus mitis*
Chlamydophila psittaci	*Kingella dentrificans*	*Neisseria meningitidis serogroup D*	*Streptococcus mutans*
*Chlamydia trachomatis LGVII***	*Kingella kingae*	*Neisseria meningitidis serogroup W-135*	*Streptococcus pneumoniae*
Chromobacterium violaceum	*Klebsiella aerogenes*	*Neisseria meningitidis serogroup Y*	*Streptococcus pyogenes*
Citrobacter freundii	*Klebsiella oxytoca*	*Neisseria polysaccharea*	*Streptococcus salivarius*
Clostridium difficile	*Klebsiella pneumoniae*	*Neisseria subflava*	*Streptococcus sanguinis*
Clostridium perfringens	*Lactobacillus acidophilus*	*Neisseria mucosa* (3)	*Trichomonas tenax*
Corynebacterium genitalium	*Lactobacillus brevis*	*Neisseria sicca* (3)	*Ureaplasma urealyticum*
Corynebacterium xerosis	*Lactobacillus crispatus*	*Pantoea agglomerans*	*Vibrio parahaemolyticus*
Cryptococcus neoformans	*Lactobacillus jensenii*	*Paracoccus denitrificans*	*Yersinia enterocolitica*
Cryptosporidium parvum			

* These organisms were not available for direct testing and were evaluated using in-silico analysis

** This organism was correctly positive with the CT assay and negative for NG and TV

(n) number of strains tested

4. Competitive Interference

The Visby Medical Sexual Health Click test was evaluated for performance in the case of a mixed infection (the presence of multiple target organisms). Each of the target organisms (CT, NG, and TV) were seeded into clinical negative vaginal sample matrix at varying concentrations and then tested in triplicate. Low concentrations were prepared at 3x LoD for the respective organism and high concentrations were prepared at 1 x 10^6 units/mL. Three (3) replicates were tested for each condition. No competitive interference was observed at the levels tested for all three target organisms.

5. Interfering Substances

The performance of the Visby Medical Sexual Health Click Test in the presence of potentially interfering substances that may be found in a vaginal swab sample was evaluated. Substances were tested in positive (3x LoD) samples for CT, NG, and TV as well as samples negative for CT, NG, and TV. The following substances were tested and found not to interfere with the assay up to the concentrations shown below.

Table 5. Potentially Interfering Substances

Substances	Concentration
Abreva Cold Sore Cream	0.25% w/v
Biotin	3.5 µg/mL
Menstrual Blood	10.0% v/v
Beta Estradiol	0.07 mg/mL
Dove 0% alcohol anti-perspirant spray[a]	0.19% w/v
Mucin (bovine)	0.80% w/v
KY Jelly personal lubricant	0.25% w/v
Leukocytes	1x10^6 cells/mL
Monistat 1	0.25% w/v
Preparation H Hemorrhoidal Ointment	0.25% w/v
Progesterone	0.07 mg/mL
RepHresh Odor Eliminating pH Balancing Gel[b]	1.25% w/v
Replens Long Lasting Vaginal Moisturizer[c]	2.50% w/v
Seminal fluid	5.00% v/v
Summer's Eve Povidone-Iodine Medicated Douche	0.25% w/v
Summer's Eve, Cleansing Wash	0.40% w/v
Vaginal anti-fungal	0.25% w/v
7-day Vaginal cream	0.25% w/v
Vagisil Moisturizer	0.25% w/v
Vagisil Regular Strength Anti-Itch Creme	0.25% w/v
VCF Vaginal Contraceptive Gel	0.25% w/v
Yeast Gard Douche Advanced	0.25% w/v

[a]Dove 0% alcohol anti-perspirant spray may cause false positive results for CT, NG, and/or TV when present at a concentration greater than 0.19% (w/v)
[b]RepHresh Odor Eliminating pH Balancing Gel may cause false negative results for CT and/or NG when present at a concentration greater than 1.25% (w/v)
[c]Replens Long Lasting Vaginal Moisturizer may cause invalid results when present at a concentration greater than 2.50% (w/v)

6. Reproducibility

A reproducibility study was performed to evaluate the reproducibility of the Visby Medical Sexual Health Click Test when used by untrained users in CLIA waived settings. The operators performing the testing were non-laboratorians representing healthcare professionals that may be encountered at such sites. The study evaluated four (4) panel members that were prepared using cultured organisms in negative clinical vaginal swab matrix. The study was performed with negative (unspiked) and positive samples. A total of six (6) study operators (2 operators at each site) tested the panel three (3) times each testing day, over six (6) non-consecutive days. Three reagent lot were used in the study. A summary of the results (count correct / total count) and % agreement for each analysis is presented in the table below. The Visby Medical Sexual Health Click test demonstrated robust reproducibility with no significant effect observed for the components of variation evaluated (sites, days, operators, lots).

Table 6. Summary of Reproducibility Study Results

	Site 1	Site 2	Site 3	Overall Agreement	
Panel Member	**% Agreement (count)**	**% Agreement (count)**	**% Agreement (count)**	**% Agreement (count)**	**95% CI**
CT Positive (49.72 EB/mL)	100% (35/35) [a]	100% (36/36) [b]	100% (36/36) [c]	100% (107/107)	96.5%-100.0%
NG Positive (22.68 cfu/mL)	97.1% (34/35) [a]	94.3% (33/35) [a]	100% (36/36)	97.2% (103/106)	92.0%-99.0%
TV Positive (21.6 troph/mL)	100% (36/36)	100% (35/35) [a]	100% (35/35) [a]	100% (106/106)	96.5%-100%
Negative	97.2% (35/36) [d]	100% (36/36)	97.2% (35/36) [e]	98.1% (106/108)	93.5%-99.5%

a One sample had invalid results and was omitted from the analysis.
b One sample was CT positive, but unexpectedly positive for NG and TV
c Two samples were CT positive, but unexpected positive for TV
d One sample was unexpectedly positive for TV
e One sample was unexpectedly positive for NG

An additional study using low positive (spiked at ~1x LoD) and negative (unspiked) samples was performed to evaluate the repeatability of test results near the assay limit of detection when tested by untrained users in a CLIA waived setting. A total of six (6) operators (2 operators at each site) tested the panel twice a day for 5 days. The composition of the panel members along with summary of results (count correct / total count) and percent agreement with the expected result for each panel member is presented in the table below. The study demonstrated that untrained users can perform the test and interpret the results accurately when testing samples with organism concentrations near the LoD.

Table 7. Summary of Study with Sample Near Assay LoD

	Site 1	Site 2	Site 3	Overall Agreement	
Panel Member	**% Agreement (count)**	**% Agreement (count)**	**% Agreement (count)**	**% Agreement (count)**	**95% CI**
CT Low Positive (16.0 EB/mL)	100% (20/20)	100% (20/20)	100% (20/20)	100% (60/60)	94.0%-100%
NG Low Positive (6.2 cfu/mL)	95.0% (19/20)	95.0% (19/20)	100% (20/20)	96.7% (58/60)	88.6%-99.1%
TV Low Positive (1.2 troph/mL)	100% (20/20)	95.0% (19/20)	95.0% (19/20)	96.7% (58/60)	88.6%-99.1%
Negative	100% (18/18)*	100% (20/20)	100% (20/20)	100% (58/58)	93.8%-100%

*Two samples had invalid results and were omitted from the analysis.

7. External Control Lot-to-Lot Reproducibility

Lot-to-lot reproducibility of the external controls manufactured by ZeptoMetrix Corporation (Buffalo, NY) was evaluated. Three (3) unique lots of the single-use positive control and three (3) unique lots of the single-use negative control were evaluated on five Visby Medical Sexual Health Click tests each for a total of 30 tests. 100% concordance with expected results across all lots was observed.

During the analytic studies positive and negative controls were tested on each day that testing was performed. During the clinical study and reproducibility studies, a positive and negative control was tested for each new operator, for each new lot or shipment of reagents and every 30 days. A total of 490 external controls were tested during the analytic and clinical testing. Of these 459 (93.7%, 459/490) had an initial valid result. Of the 31 external controls that required a test, 29 had the correct valid result first retest and 2 required a 2nd retest to obtain a valid result.

8. Specimen Stability

Vaginal specimen stability was evaluated for specimens collected using the Visby Medical Sexual Health collection kit. Storage was evaluated at room temperature (15-30°C), refrigerated (2-8°C), and frozen (<-15°C) conditions. All three target organisms (CT, NG, and TV) were seeded into negative vaginal sample matrix at low (2x LoD), moderate (10x LoD), and high (1000x LoD) concentrations. For a time-point to be considered acceptable, 95% concordance with expected results for low concentration samples and 100% concordance for moderate and high concentration samples were required.

Based on the results of this study the claimed stability for vaginal specimens in the Visby Medical Sexual Health collection kit is 4 hours for room-temperature specimens, 4 hours for refrigerated specimens, and 90 days for frozen specimens.

H. Clinical Data

Performance characteristics of the Visby Sexual Health Click Test were established in two multi-center CLIA Waived studies conducted at 14 clinical sites. The sites were geographically distributed across the United States and included an OB/GYN physician's office, Sexual Health clinics, Primary Care clinics, a Public Health clinic, a university Student Health clinic, an HIV/AIDS clinic, and STD clinics. A total of 32 untrained operators, representative of CLIA waived users, participated in the study. The study subjects were prospectively enrolled females, 14 years of age and older, who self-collected vaginal swab specimens using the Visby Vaginal Collection Kit. The average age among study participants was 34 years, with a range between 14 to 80 years of age.

The collected samples were provided to participating study operators who tested them on-site using the Visby Medical Sexual Health Click Test. The participating operators conducted the test by following the instructions in the Quick Reference Guide (QRG). The study operators had no formal training or experience with CLIA high or moderate complexity testing and did not receive any training on the use of the Visby test.

The Visby Sexual Health Click Test results were compared to a composite comparator result (CCR) for CT and NG and a patient infected status algorithm (PIS) for TV. The CCR and PIS was comprised of three FDA-cleared NAAT assays. A study participant was considered infected for CT, NG, or TV if a positive result was reported from two NAAT tests. If the test results of the first two NAAT were discordant, the CCR/PIS was determined by the third NAAT.

1899 subjects were initially enrolled, of which 1881 were eligible for inclusion. Of those, 1789 were included in the data analysis. The tables below summarize the clinical performance of the Visby Sexual Health Test.

Table 8. Clinical Performance of the Visby Test for CT vs. Composite Comparator Results

Symptom Status	N	TP	FP	TN	FN	Prevalence%	PPA (95% CI)	NPA (95% CI)
Symptomatic	918	95	26	795	2	10.6%	97.9% (92.8-99.4%)	96.8% (95.4-97.8%)
Asymptomatic	856	54	10	790	2	6.5%	96.4% (87.9-99.0%)	98.8% (97.7-99.3%)
Overall	1774	149	36	1585	4	8.6%	97.4% (93.5-99.0%)	97.8% (96.9-98.4%)

PPA=Positive Percent agreement with CCR; NPA=Negative Percent Agreement with CCR;
TP=true positive; FP=false positive; TN=true negative; FN=false negative

Table 9. Clinical Performance of the Visby Test for NG vs. Composite Comparator Results

Symptom Status	N	TP	FP	TN	FN	Prevalence %	PPA (95% CI)	NPA (95% CI)
Symptomatic	929	25	8	896	0	2.7%	100.0% (86.7-100.0%)	99.1% (98.3-99.6%)
Asymptomatic	857	19	8	829	1	2.3%	95.0% (76.4-99.1%)	99.0% (98.1-99.5%)
Overall	1786	44	16	1725	1	2.5%	97.8% (88.4-99.6%)	99.1% (98.5-99.4%)

PPA=Positive Percent agreement with CRA; NPA=Negative Percent Agreement with CRA;
TP=true positive; FP=false positive; TN=true negative; FN=false negative

Table 10. Clinical Performance of the Visby Test for TV vs. PIS

Symptom Status	N	TP	FP	TN	FN	Prevalence %	Sensitivity % (95% CI)	Specificity % (95% CI)
Symptomatic	916	83	35	797	1	9.2%	98.8% (93.6%-99.8%)	95.8% (94.2%-97.0%)
Asymptomatic	849	53	18	778	0	6.2%	100% (93.2%-100.0%)	97.7% (96.5%-98.6%)
Overall	1765	136	53	1575	1	7.8%	99.3% (96.0%-99.9%)	96.7% (95.8%-97.5%)

TP=true positive; FP=false positive; TN=true negative; FN=false negative

I. CLIA Waiver Considerations

A CLIA waiver application was also submitted for the Visby Medical Sexual Health Click test. Comprehensive flex testing was performed to evaluate the robustness of the test when subjected to a variety of environmental stresses and operational error. The results of these studies have demonstrated that the test gave the expect result or invalid results when subjected to operational errors (e.g., incorrect order of operation, reading results after the 2-hour read window, adding the incorrect sample type or sample volume, testing samples outside of the established specimen stability limits, incorrect device positioning) or exposure environmental conditions that are outside of the operating specifications (e.g., temperature, humidity, vibration, lighting, device positioning and agitation. There were no instances of erroneous test results in these studies.