DECISION SUMMARY

I Background Information:

A 510(k) Number

K200748

B Applicant

Visby Medical

C Proprietary and Established Names

Visby Medical Sexual Health Click Test

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QEP	Class II	21 CFR 866.3393 - Device To Detect Nucleic Acids From Non-Viral Microorganism(S) Causing Sexually Transmitted Infections And Associated Resistance Marker(S)	MI - Microbiology
MKZ	Class I, reserved	21 CFR 866.3120 - Chlamydia serological reagents	MI - Microbiology
LSL	Class II	21 CFR 866.3390 - Neisseria spp. direct serological test reagents	MI - Microbiology
OUY	Class II	21 CFR 866.3860 - Trichomonas vaginalis nucleic acid assay	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain market clearance for a new diagnostic device and, concurrently, a CLIA waiver for the test.

B Measurand:

Chlamydia trachomatis DNA,
Neisseria gonorrhoeae DNA, and
Trichomonas vaginalis DNA.

C Type of Test:

Qualitative, PCR detection.

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for 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*.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

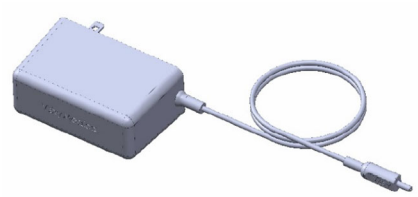
D Special Instrument Requirements:
Self-contained

IV Device/System Characteristics:

A Device Description:

The Visby Medical Sexual Health Click Test is a single-use (disposable), fully integrated, rapid, compact device containing a PCR-based assay for direct qualitative detection and differentiation of DNA from *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), and *Trichomonas vaginalis* (TV). 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 unit is outlet powered with a reusable power adaptor that is packaged separately.



The Visby main test unit contains all the hardware and reagents required to run the test. Single-use, disposable, fixed-volume transfer pipettes (Visby pipettes) are included in the primary kit.

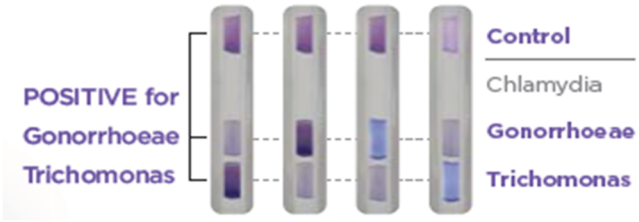
Each vaginal specimen collection kit, packaged separately, contains a tube of collection media and a single use, sterile collection swab.

There are three LED lights (white circle, green check mark, and red x) on the top of the device that are used to communicate the test status.

The following steps describe the workflow:

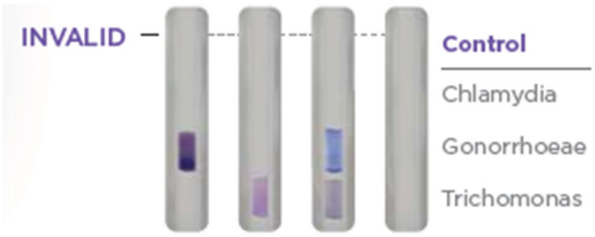
- Upon receipt of the sample, the operator uses the Visby transfer pipette to load a fixed volume of the sample into the sample port located under Button 1.

- Button 1 is slid to the right over the sample port, then pressed down to allow the sample to enter the lysis chamber.
- Next, Button 2 is pressed down to unlock Button 3.
- Button 3 is pressed down, using two thumbs, to pierce the reagent seals and begin the reaction.
- The unit is connected to the power adapter and a stable white light appears on top of the device, indicating the test is running.
- After approximately 27 minutes, a green LED check mark will appear on top of the device to indicate the test is complete.
- The results are interpreted visually by discerning the presence or absence of purple-colored rectangles in the four reaction zones, identified on the side of the Result Window.
- A valid test is indicated by the green LED checkmark and the presence of the purple rectangular spot next to the Control; a red X error light indicates an invalid result and the test must be repeated.
- A positive test for any of the three pathogens is depicted by the presence of a rectangular spot next to the respective pathogen marked on the device.
    - The following image depicts a valid test, positive for gonorrhea and for trichomonas, showing the possible varying intensities of the purple spots.



    - The following image depicts a valid negative result.

    - The following image depicts invalid tests (with and without purple spots next to the pathogens) due to Control failure; the test must be repeated.



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External controls are available from ZeptoMetrics Corporation and the directions state that they must be tested, at the minimum, with each new shipment of kits and for each new operator.

B Principle of Operation:

When the sample is added to the sample port, it rehydrates a lyophilized internal process control. The sample enters a lysis module, where the DNA in 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 successful internal process control. A purple spot adjacent to "Chlamydia," "Gonorrhoeae," and/or "Trichomonas" signifies the presence of amplified CT, NG, and/or TV DNA in the sample. In the rare case of a hardware failure, a red X will appear on the face of the device. If the unit has a red X, or no Control spot is visible, the operator is instructed to run a new test.

Instrument Description Information:

1. Instrument Name:

   Visby Medical Sexual Health Click Test - the instrument is integrated into the reaction cartridge.

2. Specimen Identification:

   Manual.

3. Specimen Sampling and Handling:

   The specimen is self-collected by the patient and placed in the Visby collection media. Thus, a liquid sample is available for transfer onto the device. All further sample processing takes place within the device.

4. Calibration:

   No calibration is required.

5. Quality Control:

Internal process control is extracted and amplified together with the patient DNA in the sample.

External controls are available from ZeptoMetrix Corporation.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Cepheid Xpert CT/NG Assay
Cepheid Xpert TV Assay

B Predicate 510(k) Number(s):

K121710
K151565, K161619

C Comparison with Predicate(s):

Device & Predicate Device(s):	K200748	K121710	K151565, K161619
Device Trade Name	Visby Medical Sexual Health Click Test	Cepheid Xpert CT/NG Assay	Cepheid Xpert TV Assay
General Device Characteristic Similarities			
Intended Use/Indications For 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	The Xpert® CT/NG Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* real-time PCR test for the automated detection and differentiation of genomic DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) to aid in the diagnosis of chlamydial and 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	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

	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*.	patient-collected vaginal swab (collected in a clinical setting).	diagnosis of trichomoniasis in symptomatic or asymptomatic individuals.
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.
Type of Test	Qualitative	Qualitative	Qualitative
Target Patient Population	Asymptomatic and symptomatic female patients.	Asymptomatic and symptomatic male and female patients.	Asymptomatic and symptomatic male and female patients.
Specimen Types	• Patient-collected vaginal swab	• Endocervical swab • Patient-collected vaginal swab • Urine -Male and Female	• Endocervical Swab • Patient-collected vaginal swab • Urine-Female
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
Sample Extraction	Cell lysis	Cell lysis followed by capture and purification of nucleic acids.	Cell lysis followed by capture and purification of nucleic acids.
Collection Kit(s)	Swab collection kit	Urine collection kit Swab collection kit	Urine collection kit Swab collection kit
Time to Results	Approx. 30 minutes	Approx. 90 minutes	Approx. 90 minutes
Assay Controls	• Internal sample processing control • External controls available.	• Internal sample processing control • Sample adequacy control • Probe check control • External controls available.	• Internal sample processing control • Sample adequacy control • Probe check control • External controls available.
General Device Characteristic Differences			

Instrument	Integrated into the Test Device - Visby Medical Sexual Health Click Test	Cepheid GeneXpert Instrument Systems	Cepheid GeneXpert Instrument Systems
Interpretation of Results	Visual	Automated	Automated
Reaction Signal	Colorimetric	Fluorescent reporter dye	Fluorescent reporter dye

VI Standards/Guidance Documents Referenced:

Standards No.	Organization	Title	Version	Date Issued
14-408	ISO	Biological Evaluation Of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals	10993-7	10/15/2008
19-34	IEC	Safety requirements for electrical equipment for measurement, control, and laboratory use - Part l: General requirements	61010-1:2010	6/10/2010
2-174	ISO	Biological Evaluation Of Medical Devices - Part 10: Tests For Irritation And Skin Sensitization	10993-10:2010	8/1/2010
2-245	ISO	Biological Evaluation Of Medical Devices - Part 5: Tests For In Vitro Cytotoxicity	l 0993-5:2009/(R) 2014	6/1/2009
2-220	ISO	Biological Evaluation Of Medical Devices - Part 1: Evaluation And Testing Within A Risk Management Process	l 0993-1:2009/(R) 2013	10/15/2009
14-452	ANSI/AAMI/ISO	Sterilization of Health Care Products - Ethylene Oxide - Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices	11135:2014	10/15/2008

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The reproducibility of the Visby Medical Sexual Health Click Test, when used by untrained operators, was evaluated at three CLIA waived testing sites. The operators performing the testing were non-laboratorians representing healthcare professionals that may be encountered at such sites. The study evaluated four panel members that were prepared by spiking cultured organisms into negative pooled clinical vaginal swab matrix (previously determined to be negative for CT, NG, TV). The study was performed with negative (un-spiked) and moderate positive samples. A total of six study operators (two operators at each site) tested the panel three times each testing day, over six non-consecutive days. Three lots of devices were included in the study. A summary of the results is presented in the table below.

Summary of Results from Reproducibility Study

Panel Member	Site 1	Site 2	Site 3	Overall Agreement 95% CI	
	% Agreement with Expected Results (No. Correct/ Total Tested)				
CT Positive (49.7 EB/mL)	100% (35/35) [a]	100% (36/36) [b]	100% (36/36) [c]	100% (107/107)	96.5%-100%
NG Positive (22.7 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 positive result for CT, 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.

The study demonstrated that the Visby Medical Sexual Health Click Test performed reproducibly when used by untrained users, with no significant effect observed for the components of variation evaluated (sites, days, operators, lots).

An additional study, using low positive (spiked at ~1x LoD) and negative (un-spiked) samples was performed to evaluate the performance of the Visby Test with samples near the assay LoD when tested by untrained users in CLIA waived settings. A total of six operators (two operators at each site) tested the blinded and randomized panel twice a day for five days. The results from the study are shown in the table below.

Summary of Results Testing Samples Near Assay LoD

Panel Member	Site 1	Site 2	Site 3	Overall Agreement 95% CI
	% Agreement with Expected Results (No. Correct/ No. Tested)			

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) [a]	100% (20/20)	100% (20/20)	100% (58/58)	93.8%-100%

[a]Two samples were invalid and were omitted from the analysis.

The study demonstrated that untrained users could perform the test accurately when testing samples with organism concentrations near the assay LoD.

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Cross-reactivity

   The cross-reactivity of the Visby Test was evaluated by testing 144 microorganisms likely to be found in the vaginal area of female anatomy. Quantified stocks of whole microorganisms were spiked into negative clinical matrix and tested at high concentrations ($>10^6$ genomic copies/mL for bacteria and $>10^5$ genomic copies/mL for viruses). All tests returned negative results indicating no cross-reactivity with any of the organisms tested.

   Three organisms could not be obtained for direct testing (Bacterial Vaginosis Associated Bacteria 2 (BVAB-2), *Megasphaera* type 1, and *Dientamoeba fragilis*) and were evaluated *in silico* by bioinformatic analysis of the genetic targets against the Visby Medical Sexual Health Click primer and amplicon sequences; no match was found for any of the three organisms.

   Microbial Interference

   Microbial interference was evaluated by testing the same organisms as above, at high concentrations, in the presence of low concentrations of the target organisms. All tests returned the expected positive results, indicating that there was no microbial interference by the tested organisms.

   The following table lists the microorganisms tested in both studies.

Organisms tested for Cross-reactivity and Microbial Interference with the Visby Test

Achromobacter xerosis (14780)	*Lactobacillus vaginalis (49540)*
Acinetobacter calcoaceticus (23055)	*Lactococcus lactis (19435)*

Acinetobacter lwoffii (15309)	*Legionella pneumophila (33152, 33153)*
Actinomyces israelii (12102)	*Listeria monocytogenes (19115)*
Aerococcus viridans (700406)	*Megashaera type 1 (N/A) **
Aeromonas hydrophila (35654)	*Micrococcus luteus (4698)*
Alcaligenes faecalis (8750)	*Mobiluncus curtisii (35241)*
Arcanobacterium pyogenes (49698)	*Mobiluncus mulieris (35243)*
Atopobium vaginae (BAA-55)	*Moraxella lacunata (17967)*
Bacteroides fragilis (25285)	*Moraxella osloensis (19976)*
Bacteroides ureolyticus (33387)	*Moraxella (Branhamella) catarrhalis (25240)*
Bergeriella denitrificans (14686)	*Morganella morganii (25830)*
Bifidobacterium adolescentis (15703)	*Mycobacterium smegmatis (14468)*
Bifidobacterium breve (15700)	*Mycoplasma genitalium (49123)*
Bifidobacterium longum (15697)	*Mycoplasma hominis (23114)*
Blastocystis hominis (50629)	*Neisseria elongata (25295, 29315, 49378)*
Brevibacterium linens (21330)	*Neisseria cinerea (14685)*
BV associated bacteria (BVAB-2, N/A) *	*Neisseria subflava (14221)*
Campylobacter jejuni (33291)	*Neisseria flavescens (13116, 13120)*
Candida albicans (801504, Zeptometrix)	*Neisseria perflava (14799)*
Candida glabrata (90030)	*Neisseria lactamica (23970, 23971, 23972, 49142)*
Candida parapsilosis (22019)	*Neisseria meningitidis serogroup a (13077)*
Candida tropicalis (750)	*Neisseria meningitidis serogroup b (13090)*
Chlamydophila pneumoniae (53592)	*Neisseria meningitidis serogroup c (13102, 13105, 13112, 19577)*
Chlamydophila psittaci (MBC013-R, Vircell)	*Neisseria meningitidis serogroup D (13113)*
Chlamydia trachomatis LGVII (VR-902B)	*Neisseria meningitidis serogroup w-135 (35559)*
Chromobacterium violaceum (12472)	*Neisseria meningitidis serogroup y (35561)*
Citrobacter freundii (8090)	*Neisseria polysaccharea (43768)*
Clostridium difficile (9689)	*Neisseria subflava (49275)*
Clostridium perfringens (13124)	*Neisseria mucosa (19695, 25998, 49233)*
Corynebacterium genitalium (33034)	*Pantoea agglomerans (27155)*
Corynebacterium xerosis (373)	*Paracoccus denitrificans (13543)*
Cryptococcus neoformans (66031)	*Neisseria sicca (9913, 29193, 29256)*
Cryptosporidium parvum (PRA-67DQ)	*Pentatrichomonas hominis (30000)*
Cutibacterium acnes (6919)	*Peptostreptococcus anaerobius (27337)*
Deinococcus radiodurans (13939)	*Peptostreptococcus productus (Blautia producta) (35244)*

Derxia gummosa (15994)	*Plesiomonas shigelloides (51903)*
Dientamoeba fragilis (N/A) *	*Prevotella bivia (29303)*
Eikenella corrodens (23834)	*Proteus mirabilis (7002)*
Elizabethkingia meningoseptica (13253)	*Proteus vulgaris (6380)*
Entamoeba histolytica (30458)	*Providencia stuartii (33672)*
Enterococcus faecalis (29212)	*Pseudomonas aeruginosa (801519, Zeptometrix)*
Enterococcus faecium (19434)	*Pseudomonas fluorescens (13525)*
Enterobacter cloacae (13047)	*Pseudomonas putida (12633)*
Enterococcus raffinosus (avium) (49464)	*Rahnella aquatilis (33071)*
Erysipelothrix rhusiopathiae (19414)	*Rhodospirillum rubrum (11170)*
Escherichia coli (700928D-5)	*Saccharomyces cerevisiae (9763)*
Fusobacterium nucleatum (25586)	*Salmonella minnesota (49284)*
Gardnerella vaginalis (801894)	*Salmonella typhimurium (19585)*
Gemella haemolysans (10379)	*Serratia marcescens (13880)*
Giardia intestinalis (50581)	*Staphylococcus aureus (12600)*
Haemophilus ducreyi (33940)	*Staphylococcus epidermidis (14990)*
Haemophilus influenzae (49247)	*Staphylococcus saprophyticus (15305)*
Herpes simplex virus I (VR-539)	*Streptococcus agalactiae (13813)*
Herpes simplex virus II (VR-540)	*Streptococcus bovis (35034)*
HIV-1 (synthetic RNA) (VR-3245SD)	*Streptococcus mitis (49456)*
Human papilloma virus 16 (synthetic DNA) (VR-3240SD)	Streptococcus mutans (25175)
Human papilloma virus 16 E6/E7 (Transformed cells) (CRL-2616)	Streptococcus pneumoniae (6303)
Kingella dentrificans (33394)	*Streptococcus pyogenes (19615)*
Kingella kingae (23330)	*Streptococcus salivarius (13419)*
Klebsiella aerogenes (13048)	*Streptococcus sanguinis (10556)*
Klebsiella oxytoca (49131)	*Streptomyces griseinus (23915)*
Klebsiella pneumoniae (801506, Zeptometrix)	*Ureaplasma urealyticum (27618)*
Lactobacillus acidophilus (4356)	*Trichomonas tenax (30207)*
Lactobacillus brevis (14869)	*Vibrio parahaemolyticus (17802)*
Lactobacillus crispatus (33820)	*Yersinia enterocolitica (23715)*
Lactobacillus jensenii (25258)	

*Tested *in silico*

Competitive Interference

A study was conducted to determine whether any of the target organism, when present at high concentrations (10^6 units/mL) could interfere with the detection of the other two organisms when present at low concentrations (~3x LoD). The test samples were prepared by spiking quantified stocks of CT, NG and TV into negative clinical matrix in different combinations of concentrations (a total of 13 combinations). Each sample was tested in three replicates. The following test panel was prepared.

Competitive Interference Panel

Panel Member	CT	NG	TV
1	Low	Low	Low
2	Low	High	High
3	Low	High	Neg
4	Low	Neg	High
5	High	Low	High
6	High	Low	Neg
7	Neg	Low	High
8	High	High	Low
9	Neg	High	Low
10	High	Neg	Low
11	High	Neg	Neg
12	Neg	High	Neg
13	Neg	Neg	High

All samples tested returned expected results, demonstrating that the target organisms, even when present at high concentrations in the patient sample, do not interfere with the detection of the other targets.

Interfering Substances

The performance of the Visby Test was evaluated in the presence of potentially interfering substances that may be found in a vaginal swab sample. The potential interfering substances were diluted in the negative swab matrix and tested in the presence of low concentrations (3x LoD) of CT, NG, and TV organisms. The testing was also performed with negative clinical swab matrix samples. All samples were tested in triplicate. The following substances were tested and found not to interfere with the assay up to the concentrations shown below.

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
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
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
Dove 0% alcohol anti-perspirant spray[a]	0.19% w/v
RepHresh Odor Eliminating pH Balancing Gel[b]	1.25% w/v
Replens Long Lasting Vaginal Moisturizer[c]	2.50% 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)

Three substances, as mentioned above, were observed to interfere when at concentrations higher than shown.

4. Assay Reportable Range:

Not applicable.

This is a qualitative colorimetric test with binary output (positive/negative). The intensity of the color is not proportional to the concentration of the target organisms.

5. Specimen Stability

To demonstrate the specimen stability, test samples were prepared by spiking quantified stocks of CT, NG and TV into negative clinical matrix targeting concentrations of 2x LoD. All samples were tested with the Visby Test after preparation (time 0), and then aliquoted into individual sample collection tubes, and placed for storage at the following temperatures:

(a) Room temperature (incubator set to 30°C)
(b) Refrigerated storage (2-8°C)

(c) Frozen storage (<20°C)

The samples were tested with the Visby Test after preparation (time 0), and then, following storage, at 2 hours, 3 hours, 4 hours and 8 hours. The samples stored frozen were evaluated at 1 month, 3 months and 4 months. All conditions were evaluated with at least 20 replicates of positive samples and with 5 replicates of negative samples. The sample was considered stable if at least 19/20 replicates returned expected results. The summary of results is shown below.

Results Summary from Specimen Stability Study

Condition	Time Point	CT	NG	TV
RT (~30°C)	2 hours	20/20	19/20	20/20
	3 hours	20/20	20/20	20/20
	4 hours	20/20	20/20	20/20
	8 hours	20/20	20/20	20/20
Refrigerator (2-8°C)	2 hours	20/20	19/20	20/20
	3 hours	20/20	19/20	20/20
	4 hours	20/20	20/20	20/20
	8 hours	20/20	20/20	20/20
Freezer (<20°C)	30 days	20/20	20/20	20/20
	90 days	20/20	20/20	20/20
	120 days	20/20	20/20	20/20

All negative samples were negative for all target organisms in all samples tested.

The data demonstrated that samples may be stored at the temperatures and for the duration shown below, prior to testing with the Visby Test.

- Room Temperature (up to 30°C) - up to 4 hours
- Refrigerator (2°-8°C) – up to 4 hours
- Frozen (<20°C) – up to 90 days

6. Detection Limit:

Limit of Detection (LoD)

Two strains (or serovars) were tested to determine the limit of detection (LoD). Each organism was individually spiked into clinical swab matrix, which was pooled and checked for negativity prior to testing. The LoD was first estimated by probit analysis by testing five concentrations of each organisms in 20 replicates. The calculated LoD for each strain was verified by testing 20 replicates at the estimated concentration and demonstrating that at least 19 out of 20 replicates were positive. If the criteria of at least 19 out of 20 positive replicates were not met, the results were added to the data set and re-analyzed to obtain a new estimated LoD value. An additional 20 replicates were tested at the revised estimate and the process was repeated until at least 19 out of 20 replicates gave a positive test result.

The LoD concentrations determined in this study for each strain are summarized in the table below.

Organism	LoD Concentration	No. Pos/No. Tested
CT Serovar H (VR-879)	16.0 EB/mL	19/20
CT Serovar D (VR-885)	5.9 EB/mL	19/20
NG (ATCC 19424)	5.7 cfu/mL	20/20
NG (ATCC 49226)	6.2 cfu/mL	19/20
TV (ATCC 30001, metronidazole susceptible)	1.2 troph/mL	19/20
TV (ATCC 30238, metronidazole resistant)	0.24 troph/mL	20/20

Inclusivity

An inclusivity study was conducted to evaluate the detection capability of the assay for additional strains of the target organisms, that were not tested in the LoD study. The study included 14 strains of CT, 30 strains of NG, and 15 strains of TV, each individually seeded into pooled, clinical vaginal sample matrix and initially tested at 2x LoD in three replicates. If the initial concentration tested did not yield 3/3 positive results for a particular strain, then an additional 20 replicates were tested at 4x LoD. If this second round of testing did not yield at least 19/20 positive results, then the concentration was increased and tested with another 20 replicates. This process was repeated until a concentration yielded at least 19/20 positive replicates.

For CT:

- 12 of the 14 strains were detected at 32 EB/mL in 3/3 replicates.
- One strain (CT LGV II VR-902B) was detected at 64 EB/mL in 20/20 replicates.
- One strain (CT Serovar I VR-880) was detected at 128 EB/mL) in 20/20 replicates.

For NG:

- 29 of the 30 strains were detected at 12.4 CFU/mL in 3/3 replicates.
- One strain (NG ATCC BAA-1847) was detected at.8 CFU/mL in 20/20 replicates.

For TV:

- All 15 TV strains tested were detected at 2.4 troph/mL in 3/3 replicates.

7. Assay Cut-Off:

Not applicable. This is a visually interpreted test where any shade of purple indicates a positive reaction.

8. Carry-Over:

Not applicable. This is a single-use test and is not subject to carryover from previously tested specimens.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   See the Clinical Studies section below.

2. Matrix Comparison:

   Not applicable.

C Clinical Studies:

The clinical performance of the Visby Medical Sexual Health Click Test was evaluated in two multi-center studies conducted at 14 clinical sites representative of CLIA waived testing facilities. 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 table below shows the prevalence of each pathogen at each study site as determined by the comparator results.

Pathogen Prevalence by Site and Overall based on Comparator Results)

	% Prevalence (No. Infected Total Tested)		
Site	**CT**	**NG**	**TV**
1	1.6% (3/185)	0.5% (1/184)	0.0% (0/184)
2	3.9% (9/233)	1.3% (3/236)	18.9% (42/222)
3	1.5% (1/66)	1.5% (1/67)	4.6% (3/65)
4	27.2% (72/265)	9.3% (25/269)	9.8% (26/266)
5	6.6% (4/61)	4.9% (3/61)	13.3% (8/60)
6	8.6% (23/268)	0.7% (2/269)	0.7% (2/269)
7	3.7% (12/326)	0.9% (3/330)	11.2% (37/330)
8	0.0% (0/15)	6.7% (1/15)	13.3% (2/15)
9	6.8% (4/59)	1.7% (1/59)	6.8% (4/59)
10	0.0% (0/51)	0.0% (0/51)	5.9% (3/51)
11	6.4% (5/78)	2.6% (2/78)	3.9% (3/77)
12	10.5% (6/57)	1.8% (1/57)	1.8% (1/57)
13	11.1% (7/63)	1.6% (1/63)	4.8% (3/63)
14	14.9% (7/47)	2.1% (1/47)	6.4% (3/47)
Total	8.6% (153/1774)	2.5% (45/1786)	7.8% (137/1765)

Each female self-collected one vaginal swab and placed it in the Visby Collection Media Tube.. The samples were then handed over to the 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.

Three additional vaginal swabs were collected from each female by a licensed clinician and were sent to one central laboratory for comparator testing with three FDA cleared nucleic acid amplification tests (NAATs) detecting CT, NG and TV.

A total of 1899 subjects were initially enrolled, of which 1881 met the study inclusion criteria. Of those, 1789 females (929 symptomatic and 860 asymptomatic) were included in the performance evaluation. Study samples were excluded from the data analysis due to lack of a valid Visby test result (n=28) or for protocol deviations (n=64), e.g., failure to follow the study protocol or improper execution of the Visby test. Samples were also excluded from the data analysis due to lack of a valid comparator test result (CT=15, NG=3 and TV=24). Among the 1817 tests performed on the Visby Test, 119 had an invalid result on the first test, for an overall invalid rate of 6.55% (119/1817), with 95% CI (5.5%-7.8%).

The Visby Sexual Health Click Test results for CT and NG were compared to a composite comparator result (CCR) comprised of results of three FDA-cleared NAATs testing clinician collected vaginal swabs. A positive (infected) comparator result for CT and NG was determined when at least two of the three comparator assays were positive.

The performance estimates for the Visby Test for the detection of CT and NG were calculated as positive percent agreement (PPA) and negative percent agreement (NPA) with the composite comparator result.

The following two tables summarize the clinical performance of the Visby Medical Sexual Health Click Test for CT and NG, as when compared to the CCR algorithm.

Clinical Performance of the Visby Test for CT vs. CCR, by Symptom Status

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

Clinical Performance of the Visby Test for NG vs. CCR, by Symptom Status

Symptom Status	N	TP	FP	TN	FN	Prevalence %	PPA (95% CI)	NPA (95% CI)
Symptomatic	929	25	8	896	0	2.7%	100 % (86.7%-100%)	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 CCR; NPA=Negative Percent Agreement with CCR;
TP=true positive; FP=false positive; TN=true negative; FN=false negative

The clinical performance of the Visby Test for detection of TV was compared to a patient infected status (PIS) algorithm determined by testing clinician collected vaginal swabs with three FDA cleared NAATs for TV. The patient was considered infected if at least two of the three comparator assays were positive for TV. The performance estimates for the Visby Test for the detection of TV were calculated as percent sensitivity and percent specificity when compared with the PIS algorithm.

The following table summarizes the clinical performance of the Visby Medical Sexual Health Click Test for TV when compared to the PIS algorithm.

Clinical Performance of the Visby Test for TV vs. PIS, by Symptom Status

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

The following table shows the results profile of enrolled subjects for CT, presented by infection status as determined by CCR.

Results Profile from Testing for CT

Infection Status	NAAT 1	NAAT 2	NAAT 3	Visby	Symptom Status	
					Symptomatic	Asymptomatic
Infected	+	+	+	+	49	23
Infected	+	+	+	-	1	0
Infected	+	+	-	+	1	1
Infected	+	+	-	-	0	1
Infected	+	+	NA[a]	+	40	29
Infected	+	+	NA[a]	-	0	1
Infected	+	-	+	+	3	0
Infected	+	-	+	-	1	0
Infected	-	+	+	+	2	1
Non-infected	+	-	-	+	1	0
Non-infected	NA[b]	-	-	-	2	1
Non-infected	-	+	-	-	4	5
Non-infected	-	NA[b]	-	-	1	0
Non-infected	-	-	+	-	0	3
Non-infected	-	-	NA[b]	+	1	0
Non-infected	-	-	-	+	14	7
Non-infected	-	-	-	-	317	366
Non-infected	-	-	NA[a]	+	10	3
Non-infected	-	-	NA[a]	-	471	415
Total					**918**	**856**

[a] Test not done

[b] Invalid test result

The following table shows the results profile of enrolled subjects for NG, presented by infection status as determined by CCR.

Results Profile from Testing for NG

Infection Status	NAAT 1	NAAT 2	NAAT 3	Visby	Symptom Status	
					Symptomatic	Asymptomatic
Infected	+	+	+	+	15	5
Infected	+	+	NA[a]	+	8	12
Infected	+	+	NA[a]	-	0	1
Infected	+	-	+	+	1	1
Infected	-	+	+	+	1	1
Non-infected	NA[b]	-	-	-	2	1
Non-infected	+	-	-	+	1	0
Non-infected	+	-	-	-	0	1
Non-infected	-	NA[b]	-	-	1	2
Non-infected	-	NA[b]	-	-	1	0
Non-infected	-	+	-	+	0	1

Non-infected	-	+	-	-	6	4
Non-infected	-	-	NA[b]	-	1	0
Non-infected	-	-	NA[b]	-	1	0
Non-infected	-	-	-	+	6	4
Non-infected	-	-	-	-	372	391
Non-infected	-	-	NA[a]	+	1	3
Non-infected	-	-	NA[a]	-	512	430
Total					**929**	**857**

[a] Test not done

[b] Invalid test result

The following table shows the results profile of enrolled subjects for TV, presented by infection status as determined by the PIS algorithm.

Results Profile from Testing for TV

Patient Infected Status	NAAT 1	NAAT 2	NAAT 3	Visby	Symptom Status	
					Symptomatic	Asymptomatic
Infected	+	+	+	+	26	19
Infected	+	+	NA[a]	+	53	31
Infected	NA[b]	+	+	+	0	1
Infected	+	+	NA[a]	-	1	0
Infected	+	-	+	+	4	2
Non-infected	NA[b]	-	-	+	0	1
Non-infected	NA[b]	-	-	-	1	1
Non-infected	+	-	-	+	0	3
Non-infected	+	-	-	-	14	13
Non-infected	-	+	-	+	1	0
Non-infected	-	+	-	-	2	2
Non-infected	-	-	NA[b]	-	1	0
Non-infected	-	-	NA[b]	-	1	0
Non-infected	-	-	-	+	15	7
Non- infected	-	-	-	-	330	356
Non-infected	-	-	NA[a]	+	19	7
Non-infected	-	-	NA[a]	-	448	406
Total					**916**	**849**

[a] Test not done

[b] Invalid test result

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

The table below lists the positivity rates observed with the Visby Test for the detection of CT, NG, and TV infections during the clinical study, including the rates of co-infection, at each of the clinical site and overall.

Positivity Rate of the Visby Test for CT, NG, and/or TV observed during the Clinical Study

Site	CT only positive	NG only positive	TV only positive	CT and NG positive	CT and TV positive	NG and TV positive	CT, NG and TV positive
1	2.7% (5/185)	0.5% (1/185)	1.1% (2/185)	0.0% (0/185)	0.0% (0/185)	0.0% (0/185)	0.0% (0/185)
2	2.1% (5/236)	1.3% (3/236)	18.6% (44/236)	0.0% (0/236)	2.5% (6/236)	0.0% (0/236)	0.0% (0/236)
3	1.5% (1/67)	1.5% (1/67)	9.0% (6/67)	0.0% (0/67)	0.0% (0/67)	0.0% (0/67)	0.0% (0/67)
4	21.2% (57/269)	4.1% (11/269)	8.2% (22/269)	3.3% (9/269)	3.7% (10/269)	1.1% (3/269)	2.2% (6/269)
5	1.6% (1/61)	1.6% (1/61)	14.8% (9/61)	0.0% (0/61)	1.6% (1/61)	1.6% (1/61)	3.3% (2/61)
6	8.6% (23/269)	0.7% (2/269)	0.4% (1/269)	0.4% (1/269)	0.4% (1/269)	0.0% (0/269)	0.0% (0/269)
7	3.0% (10/332)	0.6% (2/332)	12.3% (41/332)	0.3% (1/332)	1.2% (4/332)	0.0% (0/332)	0.3% (1/332)
8	0.0% (0/15)	6.7% (1/15)	13.3% (2/15)	0.0% (0/15)	0.0% (0/15)	0.0% (0/15)	0.0% (0/15)
9	5.1% (3/59)	0.0% (0/59)	10.2% (6/59)	1.7% (1/59)	1.7% (1/59)	0.0% (0/59)	0.0% (0/59)
10	3.9% (2/51)	0.0% (0/51)	7.8% (4/51)	0.0% (0/51)	2.0% (1/51)	0.0% (0/51)	2.0% (1/51)
11	6.4% (5/78)	1.3% (1/78)	5.1% (4/78)	1.3% (1/78)	0.0% (0/78)	0.0% (0/78)	0.0% (0/78)
12	10.5% (6/57)	0.0% (0/57)	5.3% (3/57)	5.3% (3/57)	0.0% (0/57)	1.8% (1/57)	0.0% (0/57)
13	12.7% (8/63)	1.6% (1/63)	3.2% (2/63)	1.6% (1/63)	3.2% (2/63)	1.6% (1/63)	3.2% (2/63)
14	10.6% (5/47)	2.1% (1/47)	6.4% (3/47)	0.0% (0/47)	2.1% (1/47)	0.0% (0/47)	0.0% (0/47)
Overall	7.3% (131/1789)	1.4% (25/1789)	8.3% (149/1789)	1.0% (17/1789)	1.5% (27/1789)	0.3% (6/1789)	0.7% (12/1789)

F Other Supportive Instrument Performance Characteristics Data:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.