510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K220407

B Applicant

Visby Medical

C Proprietary and Established Names

Visby Medical Sexual Health 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 demonstrate that the performance of the Visby Medical Sexual Health Test (Visby Test, K220407/CW220001) is equivalent to the performance of the FDA cleared Visby Medical

Sexual Health Click Test (Click Test, K200748/CW200003). The Visby Test is a modified version of the Click Test. The Visby Test was developed to further simplify the user interface and to enable the automated manufacture of the device. The Visby Test has no changes to the PCR primer and probe sequences, reagent formulations, detection method, or result interpretations.

B Measurand:

- *Chlamydia trachomatis* (CT) DNA
- *Neisseria gonorrhoeae* (NG) DNA
- *Trichomonas vaginalis* (TV) DNA

C Type of Test:

Qualitative PCR

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 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 using 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:

Single-use test without special instrument requirement.

IV Device/System Characteristics:

A Device Description:

Similar to the previously FDA cleared Visby Medical Sexual Health Click Test (referred as "Click Test" hereafter, K200748/CW200003), the Visby Medical Sexual Health Test (referred as "Visby Test" hereafter) is a single-use (disposable), fully integrated and compact device containing a PCR-based assay for direct qualitative detection and differentiation of DNA from CT, NG, and TV from self-collected female vaginal swab samples. The Visby Test was developed to further simplify the user interface and to enable the automated manufacture of the device. The Visby Test has no changes to the PCR primer and probe sequences, reagent formulations, detection method, or result interpretations.

The test system includes the Visby Medical Sexual Health device (see figure below), the reusable Visby Medical power adaptor, the Visby Medical Vaginal Specimen Collection kit, and fixed-volume transfer pipette. The Visby Medical Vaginal Collection kit includes a flocked swab and a tube containing the Visby Collection Media. Patients are instructed to self-collect the sample and elute it into the Visby Collection Media.

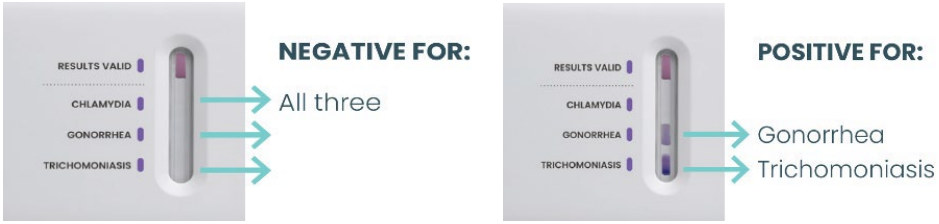
Visby Medical Sexual Health Device (Visby Test)

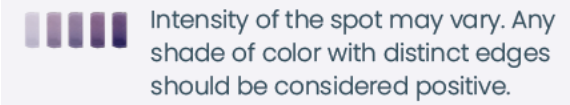
A test operator transfers the collection media (containing patient specimen) into the sample port of the device using the provided fixed-volume pipette and then slides a purple switch on the front of the device to both close the sample port and initiate the fully automated testing process. The device processes self-collected vaginal swab samples by automatically performing all steps required to complete lysis, polymerase chain reaction, and amplicon detection.

There are four LED lights on the lower left corner of the device that are used to communicate the test status, see below. Stable white light in the shape of a power symbol will appear indicating the test is plugged in. In addition, three progress lights to the right of the power light will each blink for ~ 10 minutes in sequence and then provide a stable white light to indicate the progression of the test. At the conclusion of the test, a green check mark next to the white lights signals that the test run completed successfully. A 'Red X' during or at the end of the run indicates a run failure.

When the run has completed, the operator visually interprets the status lights on the front of the device and the colorimetric output in the detection window. As shown in the figure below, a valid test will have both an illuminated green check mark and a purple spot adjacent to "RESULTS VALID" in the detection window as shown below.

For valid tests, a purple spot next to the name of a pathogen indicates a positive result for that target. The following figures illustrate some examples of valid test results, including a negative result for all pathogens (upper left figure) and a positive result for NG and TV (upper right figure). In addition, any shade of purple with distinct edges next to the target is a positive result (figure on the bottom).





In the case of a "Red X" error or lack of a purple "RESULTS VALID" spot (see figure below), the test is invalid, and the operator is instructed to repeat the test. If the subsequent test is also invalid, the operator is instructed to collect a new sample and repeat the test with a new device.

The device has built-in procedural controls. These include an internal process control and built-in electronic control. The internal process control monitors effective sample preparation, PCR amplification, and detection. The electronic control monitors if device is being operated outside of its temperature range or if there are any other device errors. The result of the internal process control is displayed in the detection window while the results of the electronic controls are displayed using the status lights.

Third-party external positive and negative controls are recommended for use with this test. These controls are not provided with the device and must be purchased separately by the customer directly from the manufacturer. The labeling states that the external controls "must be tested once with each new shipment received and once for each untrained operator."

B Principle of Operation:

The device houses all the reagents to perform the testing process. The patient sample enters the lysis module where it rehydrates a lyophilized internal process control organism. DNA from the sample and the internal process control are released using a combination of chemical lysis and high temperature. The mixture then enters a mixing chamber where it rehydrates lyophilized PCR reagents, followed by 40 cycles of thermocycling to amplify target DNA. If present, the amplified pathogen target (CT, NG, and/or TV) and the amplified internal process control hybridize to specific probes located on a flow cell. 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 and will be visually interpreted by the operator.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Visby Medical Sexual Click Health Test

B Predicate 510(k) Number(s):
K200748

C Comparison with Predicate(s):

Device & Predicate Device(s):	K220407	K200748
Device Trade Name	Visby Medical Sexual Health Test	Visby Medical Sexual Health Click Test
General Device Characteristic Similarities		
Intended Use/Indications For Use	Same, only change is to the name of the device. The **Visby Medical Sexual Health 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	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 using Visby

	collected using 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*.	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.*
Collection/Transport Device	Same	Vaginal Specimen Collection Kit consisting of a flocked swab and a tube containing collection media (3.2 mL).
Specimen	Same	Self-collected female vaginal swab
Assay Results	Same	Qualitative
Organisms Detected	Same	CT, NG and TV
Technology	Same	PCR
Assay Controls	Same	Internal process control
Target Detection	Same	Visual interpretation
General Device Characteristic Differences		
Device Assembly	Automated	Manual

VI Standards/Guidance Documents Referenced:

1. Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA Waiver Applications for Manufacturers of In Vitro Diagnostic Devices, Guidance for Industry and Food and Drug Administration Staff. February 26, 2020

2. Guidance for the Contents of Premarket Submissions for Software Contained in Medical Devices. May 11, 2005

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. <u>Reproducibility:</u>

A reproducibility study was conducted with the Visby Test at three CLIA waived study sites by a total of six untrained operators (two operators at each site). Each operator tested a panel (see table below) three times each testing day over six non-consecutive days. The panel consisted of seven members prepared by spiking cultured organisms in negative pooled clinical vaginal swab matrix. Three reagent lots were used in this study.

Panel Members Tested for Reproducibility Study

Panel Member	Target Concentration
CT Moderate Positive	4xLoD
CT Low Positive	1xLoD
NG Moderate Positive	4xLoD
NG Low Positive	1xLoD
TV ModeratePositive	4xLoD
TV Low Positive	1xLoD
Negative	No target

A summary of percent agreement with expected results for each panel member by site and overall is presented in the following table. The results of this study are comparable to the results observed for the Click Test (refer to K200748). This study demonstrates that untrained users could perform the Visby Test accurately including testing samples with organism concentrations near the assay LoD.

Panel Member	Site 1	Site 2	Site 3	Overall Agreement	
	% Agreement with Expected Results (No. Correct/ Total Tested)			% Agreement	95% CI
CT Moderate Positive	100.0 % (36/36)	100.0% (36/36)	100.0% (36/36)	100.0% (108/108)	96.6%-100.0%
CT Low Positive	97.2% (35/36)	100.0% (36/36) [a]	100.0% (36/36)	99.1% (107/108)	94.9%-99.8%
NG Moderate Positive	100.0 % (36/36)	100.0% (36/36)	97.2% (35/36)	99.1% (107/108)	94.9%-99.8%
NG Low Positive	100.0 % (36/36)	100.0% (36/36)	100.0% (36/36)	100.0% (108/108)	96.6%-100.0%
TV Moderate Positive	100.0 % (36/36)	100.0% (36/36)	100.0% (36/36)	100.0% (108/108)	96.6%-100.0%
TV Low Positive	97.2% (35/36)	97.2% (35/36) [b]	94.4% (34/36)	96.3% (104/108)	90.9%-98.6%
Negative	97.2% (35/36) [c]	100.0% (36/36)	97.2% (35/36) [c]	98.1% (106/108)	93.5%-99.5%

[a] One CT Low Positive sample was unexpectedly positive for TV
[b] One TV Low Positive sample was unexpected positive for CT
[c] One Negative sample was unexpectedly positive for TV

2. Linearity:

Not applicable.

3. Analytical Specificity/Interference:

a. Cross-reactivity

Please refer to K200748. The cross-reactivity study was performed on the Click Test as demonstrated in K200748, and the data is applicable to the Visby Test.

b. Microbial Interference

Please refer to K200748. The Microbial Interference study was performed on the Click Test as demonstrated in K200748, and the data is applicable to the Visby Test.

c. Competitive Interference

Please refer to K200748. The Competitive Interference study was performed on the Click Test as demonstrated in K200748, and the data is applicable to the Visby Test.

d. Interfering Substances

Please refer to K200748. The Interfering Substances study was performed on the Click Test as demonstrated in K200748, and the data is applicable to the Visby Test.

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:

Please refer to K200748. The Specimen Stability study was performed on the Click Test as demonstrated in K200748, and the data is applicable to the Visby Test.

6. Detection Limit:

To demonstrate that the LoD of the Visby Test is comparable to that of the Click Test, pooled negative clinical vaginal swab matrix spiked at the LoD established with the Click Test were prepared and tested with 20 Visby Tests and 20 Click Tests by trained operators in house. If at least 19/20 devices returned a positive test result, the organism was diluted three-fold and the testing was repeated until the detection rate was <19/20 for both devices. The LoD values were determined to be equivalent if the lowest concentrations of organism with at least 19/20 detection

rate from the two devices were within three-fold of each other. The results presented in the following table confirm that the LoD of the Visby Test is comparable to that of the Click Test.

LoD Comparison between Visby Test and Click Test

Organism	LoD Multiple	Target Concentration	Detection Rate (Positive Valid Devices / Total Valid Devices Tested)	
			Click Test	Visby Test
CT Serovar H (VR-879)	1x	16.00 EB/mL	20/20	20/20
	1/3x	5.33 EB/mL	13/20	18/20
CT Serovar D (VR-885)	1x	5.90 EB/mL	20/20	20/20
	1/3x	1.97 EB/mL	11/20	19/20
	1/9x	0.66 EB/mL	7/20	10/20
NG (ATCC 49226)	1x	6.20 cfu/mL	19/20	20/20
	1/3x	2.06 cfu/mL	10/20	19/20
	1/9x	0.68 cfu/mL	5/20	9/20
NG (ATCC 19424)	3x	17.1 cfu/mL	20/20	20/20
	1x	5.7 cfu/mL	17/20	20/20
	1/3x	1.9 cfu/mL	17/20	19/20
	1/9x	0.63 cfu/mL	8/20	9/20
TV (ATCC 30001)[a]	1x	1.2 troph/ mL	19/20	20/20
	1/3x	0.4 troph/mL	20/20	19/20
	1/9x	0.13 troph/mL	16/20	16/20
TV (ATCC 30238)[b]	1x	0.24 troph/mL	20/20	20/20
	1/3x	0.08 troph/mL	17/20	17/20

a. Metronidazole susceptible
b. Metronidazole resistant

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 between the Visby Test and the Click Test:

   To demonstrate that the performance of the Visby Test is comparable to that of the Click Test, the following three studies were conducted:

- Testing performed at external CLIA waived sites. A total of 102 remnant vaginal swab specimens, a subset from the previous clinical study for Click Test, were tested with the Visby Test at external CLIA waived sites by untrained operators.
- In-house testing with trained operators. A second clinical comparison study was performed to supplement the number of positive specimens tested, with a focus on testing a sample set representing a natural distribution of the pathogen loads in the intended use population, including those with low target levels. Therefore, for this study, all remnant specimens, with sufficient volume and patient consent, from the previous clinical study of the Click Test were included in this study. The above specimens were further supplemented with archived and banked frozen self-collected samples from two other previous studies conducted by Visby Medical. These specimens were tested in house by trained operators.
- In-house study with contrived samples at near LoD target concentrations. Each individual sample was prepared in an individual negative clinical matrix, with the intention to mimic the patient specimen as much as possible.

1) Testing at external CLIA waived sites

Archived frozen vaginal swab patient samples that had been previously characterized in the clinical study for the Click Test were tested. The frozen samples were de-identified, randomized, and blinded to the study staff and test operators. The panel included 30 CT positive, 20 NG positive, 30 TV positive and 33 specimens that were negative for all three pathogens. The testing was performed with Visby Tests at three external study sites in the United States representing CLIA waived settings by a total of six untrained operators (two operators at each site). Operators thawed the samples and tested them on-site by following the instructions in the QRG. The performance of the Visby Test was evaluated by comparing the Visby Test results to the results from Click Test recorded during the previous clinical study. Of the 102 specimens (seven of these samples are double positive and two are triple positive) included in the study, two (2.4%) had an initial invalid test result. One sample was excluded from the performance evaluation because it was invalid upon retesting. There were no additional exclusions. Please refer to the following table for performance evaluation.

Visby Test vs. Click Test Performance Comparison (External CLIA Waived Sites, Testing Archived Specimens)

Target	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
CT	101	30	0	71	0	100.0% (88.6%-100.0%)	100% (94.9%-100.0%)
NG	101	20	0	81	0	100.0% (83.9%-100.0%)	100.0% (95.5%-100.0%)
TV	101	30	3	68	0	100.0% (88.6%-100.0%)	95.8% (88.3%-98.6%)

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

2) In-house testing with trained operators

All specimens meeting the inclusion criteria (see below) from the previous clinical study of Click Test were included in this study. To obtain a sufficient number of positive specimens (by the comparator assays) for each analyte, these specimens were further supplemented with archived and banked frozen self-collected samples meeting the same inclusion criteria from two other previous studies conducted by Visby Medical. Target negative patient specimens were also included in this study, and all positive and negative specimens were de-identified, randomized and blinded to the operators.

The inclusion criteria for this study:

- Self-collected vaginal swab in Visby Medical Collection Media from a female subject ≥14 years of age at the time of specimen collection.
- Age and symptomatic status of the subject at the time of specimen collection is available.
- Swab specimen was obtained from a collection wherein the subject consented/assented to future unspecified research use.
- Minimum sample volume of 1.0 mL.

A total of 359 de-identified archived frozen self-collected vaginal swab specimens were provided to the operators for testing. One specimen had less than 1 mL of volume and thus could not be tested. Of the remaining 358 specimens, seven were excluded from performance evaluation due to the following listed reasons.

- One specimen had invalid result for both the initial and retest on the Visby Test and thus was excluded.
- Five specimens yielded invalid results on the Visby Test and there was insufficient volume to run a retest, thus these specimens were excluded.
- One specimen had invalid result for both the initial and retest on the Click Test and thus was excluded.

Therefore, a total of 351 specimens were included in the performance evaluation.

Testing with Visby devices was conducted by seven trained operators internally at Visby Medical over seven days under variable lighting conditions throughout the day. When sufficient sample volume was present, specimens were tested on both the Click Test and the Visby Test to allow for performance comparison. Specimens without sufficient volume (27/351) to run on both devices were tested only on the Visby Test, and the original Click Test results from the previous Click Test clinical studies were used for the comparison. Please refer to the following table for performance estimates calculations.

Visby Test vs. Click Test Performance Comparison (Internal Testing of Archived Specimens)

Visby Test vs. Click Test							
Target	**N**	**TP**	**FP**	**TN**	**FN**	**PPA**	**NPA**
CT	351	116	3	232	0	100.0% (95% CI: 96.8% - 100.0%)	98.7% (95% CI: 96.3% - 99.6%)
NG	351	34	0	317	0	100.0% (95% CI: 89.9% - 100.0%)	100.0% (95% CI: 98.8% - 100.0%)
TV	351	100	4	240	7[a]	93.5% (95% CI: 87.1% - 96.8%)	98.4% (95% CI: 95.9% - 99.4%)

a. TV PIS (based on the data from the clinical study for Click Test) for all seven specimens were negative.

Note that 4 CT, 3 NG, and 6 TV positive specimens tested at the external sites in the first study had sufficient volume and were also tested in the internal study. Therefore, a total of 142 CT, 51 NG and 124 TV positive patient specimens (by the comparator assays) were tested in the above two Clinical Comparison studies.

The initial invalid rate for Visby Test is 3.1% (11/358) and the final invalid rate is 0.3% (1/353, five out the 11 initial invalids did not have sufficient volume for retest).

3) In-house testing with contrived samples

20 contrived samples with target concentrations at 1.5x LoD (N=6), 2x LoD (N=10) and 3x LoD (N=4) for each analyte were prepared in individual negative clinical matrices. An additional 20 negatives, prepared with pooled negative clinical matrix collected from consented subjects under IRB-approved protocols, were included in the study. All samples were randomized, blinded and tested on both the Click Test as well as the Visby Test in-house. All 80 contrived samples yielded valid results (no initial invalids) and were included in the final data analysis. The results of this study are presented in the table below.

Visby Test vs. Click Test Performance Comparison (Internal Testing of Contrived Samples)

Target	**Concentration**	**Correct Results/Total Tested**	
		Click Test	**Visby Test**
CT Serovar H (VR-879)	1.5x LoD	6/6	5/6
	2x LoD	10/10	9/10
	3x LoD	4/4	4/4
NG (ATCC 49226)	1.5x LoD	5/6	5/6
	2x LoD	9/10	10/10

	3x	4/4	4/4
TV (ATCC 30001)	1.5x	6/6	6/6
	2x	10/10	10/10
	3x	4/4	4/4
Negative	N/A	20/20	19/20[a]

a. One device was unexpectedly positive for TV.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

For the complete clinical data set in support of the Click Test, refer to K200748.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Please refer to K200748 for Expected Values for the Click Test.

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.