EVALUATION OF AUTOMATIC CLASS III DESIGNATION FOR
Visby Medical Women's Sexual Health Test
DECISION SUMMARY

I Background Information:

A De Novo Number

DEN240020

B Applicant

Visby Medical, Inc.

C Proprietary and Established Names

Visby Medical Women's Sexual Health Test

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
SEA	Class II	21 CFR 866.3386 - Test for detection of microorganism(s) causing sexually transmitted infections performed by lay users	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

De Novo request for evaluation of automatic class III designation for the Visby Medical Women's Sexual Health Test.

B Measurand:

Chlamydia trachomatis DNA
Neisseria gonorrhoeae DNA
Trichomonas vaginalis DNA

C Type of Test:

Qualitative, automated polymerase chain reaction

III Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Visby Medical Women's Sexual Health Test is a single use (disposable), automated PCR (Polymerase Chain Reaction) in vitro diagnostic self-test for the rapid detection and differentiation of DNA from *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* in self-collected vaginal swab specimens. This test is intended to be sold over-the-counter (OTC) for use by females suspected of sexually transmitted infection with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis*. This test is not a substitute for visits to a healthcare provider. The information provided by this product should not be used to start, stop or change any treatments without a healthcare provider.

C Special Conditions for Use Statement(s):

OTC - Over The Counter

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

The Visby Medical Women's Sexual Health Test is a single-use (disposable), automated, rapid, compact device containing a PCR-based assay for the direct qualitative detection and differentiation of DNA from *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), and *Trichomonas vaginalis* (TV) in self-collected vaginal swab specimens tested at home.

The Visby Medical Women's Sexual Health Test system includes the Visby Medical Women's Sexual Health device; the Visby Medical Women's Sexual Health Vaginal Specimen Collection Kit (flocked swab and media); a sample transfer syringe; tube holder; Visby power adaptor; printed instructions and Frequently Asked Questions (FAQs); and smartphone application (Visby Medical Application).

The user self-collects the vaginal swab specimen using the provided flocked swab ("Visby Medical Women's Sexual Health Collection Swab") and elutes it into the Visby Medical Women's Sexual Health Collection Media. Using the provided sample transfer syringe, the user transfers the collection media (containing their specimen) into the sample port of the device (~650 µL). The user then slides a purple switch on the front of the device to both close the sample port and initiate the fully automated testing process. A blinking white light indicates the test is in progress. Test results are available in less than 30 minutes.

B Principle of Operation

The Visby Medical Women's Sexual Health device houses all the reagents and hardware to perform the testing process. When the patient sample enters the lysis module, it rehydrates a lyophilized internal process control organism contained within the device. 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 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. Successful completion of a test is indicated when a green light appears next to "READY".

The Visby Medical Application runs on a user-provided smartphone. The user downloads the application by scanning a QR code or searching for the application in the iOS App store or the Google Play application store. The user sets up an account and scans an activation code, which launches test-specific step-by-step video and on-screen instructions. At the conclusion of the video instructions, after a 30-minute timer, the user captures an image of the test result using the camera within the Visby Medical Application for automatic test interpretation. If the user performed the test procedure using the printed instructions, the application is used for the test interpretation step. The application also offers the user the option to generate a test report, access educational materials designed to help the user understand the test results, and access to telemedicine.

V Standards/Guidance Documents Referenced:

IEC 60601-1-2 Edition 4.1 2020-09 "Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests"

IEC 61010-1 Edition 3.1 2017-01 "Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements"

ANSI AAMI HE75:2009/(R)2018 "Human factors engineering - Design of medical devices"

ANSI AAMI IEC 62366-1:2015+ADMI:2020 "Medical devices Part 1: Application of usability engineering to medical devices"

ISO 14971 Third Edition 2019-12 "Medical Devices – Application of Risk Management to Medical Devices"

IEC TR 60601-4-2 Edition 1.0 2016-05 "Medical electrical equipment - Part 4-2: Guidance and interpretation - Electromagnetic immunity: performance of medical electrical equipment and medical electrical systems"

IEC 62304 Edition 1.1 2015-06 "Medical device software - Software life cycle processes"

ISO 10993-1:2018 "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"

USP-NF M98900-01-01 "151 Pyrogen Test (USP Rabbit Test)"

AAMI TIR57:2016 "Principles for medical device security - Risk management"

AAMI SW96:2023 "Standard for medical device security - Security risk management for device manufacturers"

AAMI TIR97:2019 "Principles for medical device security - Postmarket risk management for device manufacturers"

VI Performance Characteristics:

A Analytical Performance:

1. Precision:

A single-site precision study was conducted to assess the variability of the Visby Medical Women's Sexual Health Test across lots, operators, and days. This study was conducted using negative, low positive, and moderate positive blind coded specimens. Device lot testing was randomized by day. The percent positive results for the moderate positive samples were 100% across all analytes, lots, and operators. The percent positive results were 100% for low positive NG and TV samples across all lots and operators, and ≥ 96.9% for low positive CT samples across all lots and operators. The percent positive results for the negative samples were 0% across all analytes, lots, and operators. There were no significant differences observed within run (replicates tested by one operator), between days (12 different days), or between operators (two operators). The lot-to-lot precision study qualitative results (percent positive results and counts) are presented in the table below.

Table 1. Lot-to-Lot Precision

Panel Member		Lot 1			Lot 2			Lot 3		
		Operator 1	Operator 2	Overall	Operator 1	Operator 2	Overall	Operator 1	Operator 2	Overall
Moderate Positive (5x LoD)	CT	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)
	NG	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)
	TV	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)
Low Positive (2x LoD)	CT	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	93.8% (15/16)	96.9% (31/32)	93.8% (15/16)	100.0% (16/16)	96.9% (31/32)
	NG	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)
	TV	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)	100.0% (16/16)	100.0% (16/16)	100.0% (32/32)

Negative	0% (0/16)	0% (0/16)	0% (0/32)	0% (0/16)	0% (0/16)	0% (0/32)	0% (0/16)	0% (0/16)	0% (0/32)

2. Linearity:
   Not applicable.

3. Analytical Specificity/Interference:

Cross-reactivity

Cross-reactivity of the Visby Medical Women's Sexual Health Test was evaluated by testing 143 microorganisms in replicates of three. Quantified stocks of whole microorganisms were used to spike negative vaginal swab matrix for testing at high concentrations (> 10^6 genomic copies/mL for bacteria and > 10^5 genomic copies/mL for viruses) unless indicated in Table 2 below. No cross-reactivity was observed with any of the organisms tested.

Table 2. Microorganisms Evaluated for Cross-Reactivity and Microbial Interference

Microorganism (ATCC #)	**Microorganism (ATCC #)**	**Microorganism (ATCC #)**	**Microorganism (ATCC #)**
Achromobacter xerosis (14780)	*Deinococcus radiodurans* (13939)	*Legionella pneumophila* (33152, 33153)	*Plesiomonas shigelloides* (51903)
Acinetobacter calcoaceticus (23055)	*Derxia gummosa* (15994)	*Listeria monocytogenes* (19115)	*Prevotella bivia* (29303)
Acinetobacter lwoffii (15309)	*Dientamoeba fragilis*[1] (N/A)	Megashaera type 1[1] (N/A)	*Proteus mirabilis* (7002)
Actinomyces israelii (12102)	*Eikenella corrodens* (23834)	*Micrococcus luteus* (4698)	*Proteus vulgaris* (6380)
Aerococcus viridans (700406)	*Elizabethkingia meningoseptica* (13253)	*Mobiluncus curtisii* (35241)	*Providencia stuartii* (33672)
Aeromonas hydrophila (35654)	*Entamoeba histolytica* (30458)	*Mobiluncus mulieris* (35243)	*Pseudomonas aeruginosa* (801519, Zeptometrix)
Alcaligenes faecalis (8750)	*Enterococcus faecalis* (29212)	*Moraxella lacunata* (17967)	*Pseudomonas fluorescens* (13525)
Arcanobacterium pyogenes (49698)	*Enterococcus faecium* (19434)	*Moraxella osloensis* (19976)	*Pseudomonas putida* (12633)
Atopobium vaginae (BAA-55)	*Enterobacter cloacae* (13047)	*Moraxella (Branhamella) catarrhalis* (25240)	*Rahnella aquatilis* (33071)
Bacteroides fragilis (25285)	*Enterococcus raffinosus* (avium) (49464)	*Morganella morganii* (25830)	*Rhodospirillum rubrum* (11170)
Bacteroides ureolyticus (33387)	*Erysipelothrix rhusiopathiae* (19414)	*Mycobacterium smegmatis* (14468)	*Saccharomyces cerevisiae* (9763)
Bergeriella denitrificans (14686)	*Escherichia coli* (700928D-5)	*Mycoplasma genitalium** (49123)	*Salmonella minnesota* (49284)
Bifidobacterium adolescentis (15703)	*Fusobacterium nucleatum* (25586)	*Mycoplasma hominis* (23114)	*Salmonella* Typhimurium (19585)
Bifidobacterium breve (15700)	*Gardnerella vaginalis* (801894, ZeptoMetrix)	*Neisseria elongata* (25295, 29315, 49378)	*Serratia marcescens* (13880)
Bifidobacterium longum (15697)	*Gemella haemolysans* (10379)	*Neisseria cinerea* (14685)	*Staphylococcus aureus* (12600)
Blastocystis hominis (50629)	*Giardia intestinalis* (50581)	*Neisseria subflava* (14221)	*Staphylococcus epidermidis** (14990)
Brevibacterium linens (21330)	*Haemophilus ducreyi* (33940)	*Neisseria flavescens* (13116, 13120)	*Staphylococcus saprophyticus* (15305)
BV associated bacteria[1] (BVAB-2, N/A)	*Haemophilus influenzae* (49247)	*Neisseria perflava* (14799)	*Streptococcus agalactiae* (13813)
Campylobacter jejuni (33291)	Herpes simplex virus I* (VR-539)	*Neisseria lactamica* (23970, 23971, 23972, 49142)	*Streptococcus bovis* (35034)

*Candida albicans** (801504, Zeptometrix)	Herpes simplex virus II* (VR-540)	*Neisseria meningitidis* serogroup a (13077)	*Streptococcus mitis* (49456)
Candida glabrata (90030)	HIV-1 (NATHIV1-LIN, ZeptoMetrix)	*Neisseria meningitidis* serogroup b (13090)	*Streptococcus mutans* (25175)
Candida parapsilosis (22019)	Human papilloma virus 16 (synthetic DNA) (VR-3240SD)	*Neisseria meningitidis* serogroup c (13102, 13105, 13112, 19577)	*Streptococcus pneumoniae* (6303)
Candida tropicalis (750)	Human papilloma virus 16 E6/E7 (Transformed cells) (CRL-2616)	*Neisseria meningitidis* serogroup D (13113)	*Streptococcus pyogenes* (19615)
*Chlamydophila pneumoniae** (53592)	*Kingella dentrificans* (33394)	*Neisseria meningitidis* serogroup w-135 (35559)	*Streptococcus salivarius* (13419)
*Chlamydophila psittaci** (MBC013-R, Vircell)	*Kingella kingae* (23330)	*Neisseria meningitidis* serogroup y (35561)	*Streptococcus sanguinis* (10556)
Chromobacterium violaceum (12472)	*Klebsiella aerogenes* (13048)	*Neisseria polysaccharea* (43768)	*Streptomyces griseinus* (23915)
Citrobacter freundii (8090)	*Klebsiella oxytoca* (49131)	*Neisseria subflava* (49275)	*Ureaplasma urealyticum* (27618)
*Clostridium difficile** (9689)	*Klebsiella pneumoniae* (801506, Zeptometrix)	*Neisseria mucosa* (19695*, 25998, 49233)	*Trichomonas tenax** (30207)
Clostridium perfringens (13124)	*Lactobacillus acidophilus* (4356)	*Neisseria sicca* (9913, 29193, 29256)	*Vibrio parahaemolyticus* (17802)
Corynebacterium genitalium (33034)	*Lactobacillus brevis* (14869)	*Pantoea agglomerans* (27155)	*Yersinia enterocolitica* (23715)
Corynebacterium xerosis (373)	*Lactobacillus crispatus* (33820)	*Paracoccus denitrificans* (13543)	
Cryptococcus neoformans (66031)	*Lactobacillus jensenii* (25258)	*Pentatrichomonas hominis* (30000)	
Cryptosporidium parvum (PRA-67DQ)	*Lactobacillus vaginalis* (49540)	*Peptostreptococcus anaerobius* (27337)	
Cutibacterium acnes (6919)	*Lactococcus lactis* (19435)	*Peptostreptococcus productus* (*Blautia producta*) (35244)	

[1] Organism was not available for direct testing and was evaluated using *in-silico* analysis.
* Organism was also tested for microbial interference

Microbial Interference

Microbial interference with the Visby Medical Women's Sexual Health Test was evaluated using a subset of 10 microorganisms from Table 2 (denoted with a *), chosen based on either their likelihood to be present in a vaginal specimen or their genetic similarity to the assay's target organisms. Interference was tested in the presence of low concentrations, i.e., 3x LoD, of the target organisms. No microbial interference was observed with any of the organisms tested.

Competitive Interference

Performance of the Visby Medical Women's Sexual Health Test was evaluated for cases of mixed CT, NG, and/or TV infection. Each of the target organisms was spiked into negative clinical vaginal matrix at varying low (3x LoD) and high ($1x10^6$ units/mL) concentration levels and tested in triplicate. No competitive interference was observed when high concentrations of one or two target analytes were present with low concentrations of at least one other target analyte.

Table 3. Competitive Interference for each Target Organism

Organism and Concentration			CT (# positive / # tested)	NG (# positive / # tested)	TV (# positive / # tested)
CT	NG	TV			

Low	Low	Low	3/3	3/3	3/3
Low	High	High	3/3	3/3	3/3
Low	High	Neg	3/3	3/3	0/3
Low	Neg	High	3/3	0/3	3/3
High	Low	High	3/3	3/3	3/3
High	Low	Neg	3/3	3/3	0/3
Neg	Low	High	0/3	3/3	3/3
High	High	Low	3/3	3/3	3/3
Neg	High	Low	0/3	3/3	3/3
High	Neg	Low	3/3	0/3	3/3
High	Neg	Neg	3/3	0/3	0/3
Neg	High	Neg	0/3	3/3	0/3
Neg	Neg	High	0/3	0/3	3/3

Interfering Substances

The performance of the Visby Medical Women's Sexual Health Test was evaluated in the presence of potentially interfering substances that may be found in a vaginal swab specimen. The substances were diluted in negative swab matrix and tested in the presence of low positive (3x LoD of CT, NG, and TV) and negative panel members in a negative clinical swab matrix background. Assay interference was observed in the presence of the following substances: RepHresh Odor Eliminating pH Balancing Gel at a concentration greater than 2.5% w/v; Replens Long Lasting Vaginal Moisturizer at a concentration greater than 1.25% w/v; Dove 0% alcohol antiperspirant spray at concentration greater than 0.2% w/v; menstrual blood at a concentration greater than 1.25% v/v; bleach-based cleaner at a concentration greater than 2.5% v/v; and biotin at concentration greater than 1.75 µg/mL. A summary of all tested substances, and the concentration up to which they were found to not interfere with the assay, are listed in Table 4 below.

Table 4. Potentially Interfering Substances

Interfering Substance	Concentration	Interfering Substance	Concentration
Abreva Cold Sore Cream	0.25% w/v	Progesterone	0.07 mg/mL
Beta Estradiol	0.07 mg/mL	RepHresh Odor Eliminating pH Balancing Gel	2.50% w/v
Biotin	1.75 ug/mL	Replens Long Lasting Vaginal Moisturizer	1.25% w/v
Bleach-based Cleaner	2.50% v/v	Seminal Fluid	5.00% v/v
Dove 0% Alcohol Anti-perspirant Spray	0.20% w/v	Seventh Generation Disinfectant	5.00% v/v
Hand Lotion	5.00% w/v	Hand Soap	0.05% w/v
Hand Sanitizer (Purell)	5.00% w/v	Summer's Eve Cleansing Wash	0.40% w/v
K-Y Jelly Personal Lubricant	0.25% w/v	Summer's Eve Povidone-Iodine Medicated Douche	0.25% w/v
Leukocytes	10^6 cells/mL	Taro 7-day Vaginal Cream	0.25% w/v
Menstrual Blood	1.25% v/v	Vaginal Anti-Fungal	0.25% w/v
Method All-Purpose Cleaner	5.00% v/v	Vagisil Moisturizer	0.25% w/v
Monistat 1	0.25% w/v	Vagisil Regular Strength Anti-Itch Cream	0.25% w/v

Mucin (Bovine)	0.80% w/v	VCF Vaginal Contraceptive Gel	0.25% w/v
Preparation H Hemorrhoidal Ointment	0.25% w/v		

4. Assay Reportable Range:

Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Shelf-life Stability
A multi-lot kit stability study was conducted to determine the shelf-life of the Visby Medical Women's Sexual Health Test kit. All test kits were preconditioned at 45-50°C for either two or four hours to mimic temperature excursions during shipping. Preconditioned kits were evaluated following storage at room temperature (18-22°C), an elevated room temperature (30°C), and at an elevated room temperature with elevated relative humidity (30°C and 75% RH) up to eight months. At two-month intervals, devices from each storage condition were tested with a negative and a low positive sample up to eight months. A false negative CT result was observed at the 4-month time point. The acceptance criteria at subsequent time points (6- and 8-months) were met. The data demonstrate that the finished kit is stable up to 6 months when stored at 18-30°C.

Shipping Stability
A shipping stability study was conducted for a period of 80 hours to evaluate the stability of the Visby Medical Women's Sexual Health Test under conditions representing extreme cold and hot temperatures for durations anticipated during a 72-hour shipping period. Samples for testing included an analyte negative pooled clinical vaginal swab sample and a 3x LoD triple analyte positive sample in pooled clinical vaginal swab matrix. Ten devices per sample type (low positive or negative) were tested at baseline, and following the cold temperature profile, and the hot temperature profile. All devices returned the expected negative or triple positive result.

6. Detection Limit:

The Limit of Detection (LoD) of the Visby Medical Women's Sexual Health Test was determined using two strains of each target organism. Panel members were produced by individually spiking negative clinical vaginal swab matrix. Each sample was tested in a range-finding study consisting of five concentrations in replicates of 20 per concentration. LoD values were estimated by probit analysis using the results of the range-finding study. The estimated LoD was confirmed by testing of 20 replicates, with at least 19 out of 20 replicates testing positive for each strain.

Table 5. Limit of Detection of CT Serovars, NG, and TV Strains in Clinical Negative Vaginal Matrix

Organism	LoD
CT Serovar H (VR-879)	3.0 EB/mL

CT Serovar D (VR-885)	5.5 EB/mL
NG (ATCC 19424)	0.5 cfu/mL
NG (ATCC 49226)	0.8 cfu/mL
TV (ATCC 30001) metronidazole susceptible	0.8 troph/mL
TV (ATCC 30238) metronidazole resistant	0.3 troph/mL

7. Inclusivity:

The ability of the Visby Medical Women's Sexual Health Test to detect 14 CT serovars, 30 NG strains, and 15 TV strains at or near the LoD was evaluated. Each organism was individually spiked into negative clinical vaginal swab matrix at ≤ 2x LoD and tested in three replicates. Strains that were detected at less than 100% were tested at a lower dilution (two-fold) until all three replicates were detected. All 14 CT serovars, 30 NG strains, and 15 TV strains were successfully detected at the following concentrations presented in the tables below.

Table 6. CT Organisms Tested in Inclusivity Study

Serovar	CT concentration tested
F	5.5 EB/mL
Ba	5.5 EB/mL
E	5.5 EB/mL
A	5.5 EB/mL
B	5.5 EB/mL
G	5.5 EB/mL
I	5.5 EB/mL
J	5.5 EB/mL
K	5.5 EB/mL
LGV I	5.5 EB/mL
LGV II	11 EB/mL
LGV III	5.5 EB/mL
C	5.5 EB/mL
E (nvCT, Swedish variant)	5.5 EB/mL

Table 7. NG Organisms Testing in Inclusivity Study

ATCC Number	NG Concentration Tested	ATCC Number	NG Concentration Tested
BAA-1833	1.6 cfu/mL	27632	1.6 cfu/mL
BAA-1839	1.6 cfu/mL	27633	1.6 cfu/mL
BAA-1847	1.6 cfu/mL	31148	1.6 cfu/mL
9826	1.6 cfu/mL	31149	1.6 cfu/mL
9827	1.6 cfu/mL	31151	1.6 cfu/mL
9830	1.6 cfu/mL	31356	1.6 cfu/mL
10874	1.6 cfu/mL	31397	3.2 cfu/mL
11688	1.6 cfu/mL	31398	1.6 cfu/mL
11689	1.6 cfu/mL	31401	1.6 cfu/mL
19088	1.6 cfu/mL	31402	1.6 cfu/mL

23050	1.6 cfu/mL	31403	1.6 cfu/mL
23051	1.6 cfu/mL	31406	1.6 cfu/mL
27628	1.6 cfu/mL	35541	1.6 cfu/mL
27629	1.6 cfu/mL	43069	1.6 cfu/mL
27631	1.6 cfu/mL	49981	1.6 cfu/mL

Table 8. TV Organisms Tested in Inclusivity Study

ATCC Number	TV Concentration Tested
PRA-95	1.6 troph/mL
PRA-98	1.6 troph/mL
30184	1.6 troph/mL
30187	1.6 troph/mL
30188	1.6 troph/mL
30236	1.6 troph/mL
30240	1.6 troph/mL
30245	1.6 troph/mL
50138	3.2 troph/mL
30139	1.6 troph/mL
50141	1.6 troph/mL
50143	1.6 troph/mL
50147	1.6 troph/mL
50167	3.2 troph/mL
50183	1.6 troph/mL

8. Assay Cut-off:

Not applicable.

B Comparison Studies:

1. Method Comparison:

Not applicable.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

Clinical performance for the Visby Medical Women's Sexual Health Test was established through a prospective study enrolling females with various demographics and pregnancy status at 13 geographically diverse testing sites. The study enrolled sexually active lay users between the ages of 15 and 76 years of age, the average age being 34 years old. Participants were provided with the Visby Medical Women's Sexual Health Test Kit, labeling, and a mobile device and completed testing, including set-up and sample collection, in a simulated home environment. Site

staff were present but did not influence or interact with the subjects unless intervention was required for safety reasons. One self-collected vaginal swab specimen in Visby Medical Collection Media and four HCP-collected vaginal swab specimens were collected in respective comparator test media from each subject. For CT and NG, the positive comparator result was determined by at least two positive results from FDA-cleared NAATs. For TV, the patient infection status was determined by at least two positive comparator results. The study consisted of 2293 prospectively enrolled lay users from March 2023 to April 2024. Of the 2293 enrolled subjects, 298 subjects were not included because they did not obtain a test result using the Visby smart phone application. Another 50 subjects were excluded due to procedural error or not meeting inclusion criteria, leaving 1945 evaluable subjects. For CT, two additional specimens were excluded that did not have comparator result, leaving 1943 evaluable subjects. There were 75 initial invalid results with the Visby Medical Women's Sexual Health Test (3.8%, 75/1950), including specimens that did not have an initial test result, but a retest result was available. Clinical performance for the Visby Medical Women's Sexual Health Test is summarized in Tables 9, 10, and 11 below.

Table 9. Clinical Performance of the Visby Women's Sexual Health Test for CT vs. Composite Comparator Results, by Symptom Status

Symptom Status	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Symptomatic	835	42	5[a]	787	1	97.7% (87.9-99.6)	99.4% (98.5-99.7)
Asymptomatic	1108	61	17[b]	1028	2	96.8% (89.1-99.1)	98.4% (97.4-99.0)
Overall	1943[c]	103	22	1815	3	97.2% (92.0-99.0)	98.8% (98.2-99.2)

[a] CT nucleic acid was detected in 3 out of 5 specimens when tested by an alternate molecular assay.
[b] CT nucleic acid was detected in 2 out of 17 FP samples by an alternate molecular assay.
[c] For two specimens, the composite comparator result could not be determined.

Table 10. Clinical Performance of the Visby Women's Sexual Health Test for NG vs. Composite Comparator Results, by Symptom Status

Symptom Status	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Symptomatic	836	22	2[a]	812	0	100.0% (85.1-100.0)	99.8% (99.1-99.9)
Asymptomatic	1109	21	15[b]	1073	0	100.0% (84.5-100.0)	98.6% (97.7-99.2)
Overall	1945	43	17	1885	0	100.0% (91.8-100.0)	99.1% (98.6-99.4)

[a] One out of 2 FP results was due to an apparent specimen mix-up.
[b] NG nucleic acid was detected in 3 out of 15 FP specimens by an alternate molecular assay.

Table 11. Clinical Performance of the Visby Women's Sexual Health Test for TV vs. PIS, by Symptom Status

Symptom Status	N	TP	FP	TN	FN	Sensitivity % (95% CI)	Specificity % (95% CI)
Symptomatic	836	77	12[a]	743	4[b]	95.1% (88.0-98.1)	98.4% (97.2-99.1)
Asymptomatic	1109	97	15[c]	997	0	100.0% (96.2-100.0)	98.5% (97.6-99.1)
Overall	1945	174	27	1740	4	97.8% (94.4-99.1)	98.5% (97.8-98.9)

[a] TV nucleic acid was detected in 10 out of 12 FP specimens when tested by an alternate molecular assay.
[b] One out of 4 FP results was caused by an apparent specimen mix-up.
[c] TV nucleic acid was detected in 9 out of 15 specimens when tested by an alternate molecular assay, of which 3 were positive by one of the comparator assays.

Summary of baseline demographic information:

Self-reported demographic data were collected from subjects at the time of enrollment in the clinical study. Most subjects were between the ages of 18-50. The average age among study participants was 34 years, with a range of 15 to 76 years of age. Of the enrolled participants, 43.0% presented with symptoms and 57.0% of participants had no symptoms of sexually transmitted infection.

Table 12. Clinical Performance Study Summary of Age and Symptom Status

Age (years)	Symptomatic		Asymptomatic		Total	
	N	%	N	%	N	%
<18	1	16.7%	5	83.3%	6	0.3%
18-30	387	41.3%	549	58.7%	936	48.1%
31-50	348	44.3%	438	55.7%	786	40.4%
>50	100	46.1%	117	53.9%	217	11.2%
Total	836	43.0%	1109	57.0%	1945	100.0%

Table 13. Clinical Performance Study Summary Distribution of Subjects Enrolled by Ethnicity

Self-reported subject ethnicity	N	%
Hispanic/Latino	327	16.8%
Not Hispanic/Latino	1600	82.2%
Declined to state	9	0.5%
Unknown	9	0.5%
Total	1945	100%

Table 14. Clinical Performance Study Summary Distribution of Subjects Enrolled by Race

Self-reported subject race	N	%
Black or African American	1166	60.0%
White	611	31.4%
Other	63	3.2%
Multiracial	37	1.9%
Asian	31	1.6%
Declined to state	19	1.0%
Unknown	7	0.4%
American Indian or Alaska Native	9	0.5%
Native Hawaiian or Pacific Islander	2	0.1%
Total	1945	100%

D Clinical Cut-Off:

Not Applicable.

E Expected Values/Reference Range:

In the Visby Medical Women's Sexual Health Test clinical study, 1945 evaluable specimens were tested between March 23, 2023 and April 1, 2024. The positivity rate for CT, NG, and TV for subjects enrolled at each site, when tested with the Visby Medical Women's Sexual Health Test, is presented in Table 15 below.

Table 15. Positivity Rate of the Visby Medical Women's Sexual Health Test for Detection of CT, NG, and/or TV during the Clinical Study

Site	% Positive (# positive / # tested)						
	CT only positive	NG only positive	TV only positive	CT & NG positive	CT & TV positive	NG & TV positive	CT, NG & TV positive
1	5.8% (13/226)	2.2% (5/226)	16.4% (37/226)	0.0% (0/226)	0.9% (2/226)	0.4% (1/226)	0.0% (0/226)
2	1.7% (6/358)	1.1% (4/358)	13.7% (49/358)	0.0% (0/358)	0.3% (1/358)	0.6% (2/358)	0.0% (0/358)
3	9.8% (8/82)	0.0% (0/82)	3.7% (3/82)	0.0% (0/82)	0.0% (0/82)	0.0% (0/82)	1.2% (1/82)
4	5.2% (10/193)	2.1% (4/193)	4.1% (8/193)	0.0% (0/193)	0.5% (1/193)	0.0% (0/82)	0.0% (0/82)
5	5.1% (8/156)	3.2% (5/156)	5.1% (8/156)	1.3% (2/156)	1.9% (3/156)	0.6% (1/156)	1.3% (2/156)
6	2.1% (3/144)	0.7% (1/144)	13.2% (19/144)	0.0% (0/144)	2.8% (4/144)	1.4% (2/144)	0.0% (0/144)
7	2.1% (1/48)	2.1% (1/48)	6.3% (3/48)	2.1% (1/48)	0.0% (0/48)	0.0% (0/48)	0.0% (0/48)
8	7.2% (8/111)	0.9% (1/111)	7.2% (8/111)	0.0% (0/111)	1.8% (2/111)	0.9% (1/111)	0.0% (0/111)
9	5.8% (13/224)	2.7% (6/224)	1.3% (3/224)	2.7% (6/224)	1.3% (3/224)	0.5% (1/224)	0.0% (0/224)
10	5.8% (12/208)	1.4% (3/208)	6.3% (13/208)	2.4% (5/208)	0.5% (1/208)	0.5% (1/208)	0.5% (1/208)
11	25.0% (1/4)	25.0% (1/4)	0.0% (0/4)	0.0% (0/4)	0.0% (0/4)	0.0% (0/4)	0.0% (0/4)
12	3.5% (3/85)	1.2% (1/85)	4.7% (4/85)	0.0% (0/85)	1.2% (1/85)	0.0% (0/85)	0.0% (0/85)
13	1.9% (2/106)	0.0% (0/106)	11.3% (12/106)	0.0% (0/106)	1.9% (2/106)	0.0% (0/106)	0.9% (1/106)
All	4.5% (88/1945)	1.7% (32/1945)	8.4% (164/1945)	0.7% (14/1945)	1.0% (20/1945)	0.5% (9/1945)	0.3% (5/1945)

F Other Supportive Performance Characteristics Data:

Usability and User Comprehension

Device usability/comprehension was assessed in female participants ages 14 to > 61 years old of different backgrounds, across a range of education levels. The first study with 140 lay users evaluated the testing process, from set-up to obtaining test results and lay users' understanding to determine the appropriate next step based on the test result. The results of the usability study demonstrated that the Visby Medical Women's Sexual Health Test is easy to use by lay users.

A second separate study with 31 participants further assessed user comprehension of additional possible results combinations. Testing was conducted in a simulated home environment. Participants were provided with the User Instructions, the FAQ, an iPhone12 with the Visby app

pre-downloaded, and five mock Visby Medical Women's Sexual Health Test devices with results representing different possible scenarios. An observer recorded successful scenario completion, use errors, close calls, and any observed difficulties. The results of the user label comprehension study demonstrated that the Visby Medical Women's Sexual Health Test is easy to understand by lay users.

FMEA, Residual Risks, and Mitigations

A comprehensive hazard analysis of the Visby Medical Women's Sexual Health Test was conducted in accordance with ISO 14971:2019. Risks associated with human factors, sample and device handling, storage, and environmental factors were evaluated. The hazard analyses included identification of the potential hazard, probability of occurrence, probability of a hazardous situation leading to harm, severity of potential harm, hazard control measure(s), and assignment of pre- and post-control risk levels.

A risk value between 1 and 25 was assigned based on the likelihood of occurrence and the severity of harm, with the lower values indicating a lower risk. Risk values of less than 10 were deemed acceptable. A risk mitigation plan was developed for all identified risks. Mitigations were implemented via the following:

- System design to eliminate the error.
- Fail-safes and failure alert mechanisms.
- Labeling to alert users to potential errors.

Frequently Asked Questions

To improve user label comprehension, the labeling includes a Frequently Asked Questions (FAQ) section. The FAQ section was created to provide users information to adequately understand the purpose, limitations, and meaning of the test results as well as where users can access additional information regarding chlamydia, gonorrhea, and trichomoniasis pathology and epidemiology. The concepts covered in the FAQ section include:

- The purpose of the test and description of the test and the analyte.
- Who should and who should not use the test (self-selection).
- Significance of the test results.
- When to re-test (e.g., following an invalid result).
- Follow-up for appropriate health management.

Flex Studies

The operational limits of the device were evaluated in a series of studies simulating conditions of use outside of the intended use environment or in instances of user errors. Studies were run by trained operators using a testing panel of contrived samples, unless otherwise noted. Each study also contained a control condition in which tests were run within the specifications indicated by the instructions for use. For most of the test conditions, five replicates were tested per condition.

The results demonstrate that the test is robust to stresses of environmental conditions and potential user errors.

Table 16. Flex Studies

Study Title	Objective	Outcome
Delayed Testing	To assess device performance when there is a delay in specimen testing	The testing panel included a negative and a triple analyte low positive.

	after collection. Test initiation was delayed up to 115 minutes.	No false results were observed. The system generated invalid results when testing was delayed by 130 minutes. A labeling mitigation includes instructions that users should add sample and close the slider without any delay.
Slider Actuation	To assess device performance when the slider is not fully closed.	The testing panel included a negative and a triple analyte low positive. No false results were observed. Leaving the actuator open caused all invalid results. Leaving the actuator half open caused 80% invalid results. Leaving the actuator slightly open caused 30% invalid results. A labeling mitigation includes instructions that users should add sample and close the slider without any delay. The slider both closes the sample port and initiates the test.
Time to Reading of Results	To assess the effect of reading the test result outside of the stated timeframe. The following times were tested: 0 hours, 2 hours, 6 hours, and 24 hours.	The testing panel included a negative and a triple analyte low positive. No false results were observed. All results were as expected up to and including 24 hr delay. The labeling directs the user to read the result within two hours.
Sample Input Volume	To assess device performance with sample loading volumes outside of 650 µL. The following sample loading volumes were tested: no sample, 200 µL, 300 µL, 400 µL, 500 µL, 600 µL, 700 µL, 1300 µL, and overflow to simulate filling to the brim.	The testing panel included a negative and a triple analyte low positive. One false negative result was observed at 300 µL. As a mitigation, a fixed-volume syringe is included in the kit. Users fill the syringe with the collected specimen to the fill line.
Sample Dilution Volume	To assess device performance when the user inadvertently spills the collection media and adds water to the tube. A total of three different buffer to water dilutions were tested: 1:1 (1.6 mL buffer: 1.6 mL water); 1:2 (1.6 mL buffer: 3.2 mL water); 1:3 (1.6 mL buffer: 4.8 mL buffer)	The testing panel included a negative and a triple analyte low positive. The frequency of false negative results increased with increasing dilution of the sample buffer. Mitigations include adding language in the User Instructions that use of another tube or liquid can lead to incorrect results and to contact customer support if the user spills the liquid in the tube.
Sample Mixing Conditions	To assess device performance when there is variation in sample mixing. The following conditions were tested: no inversion, invert 5x and wait 10 minutes, invert 5x and wait 30 minutes, invert 5x and wait 2 hours, and invert vigorously 25x.	The testing panel included a negative and a triple analyte low positive. All conditions generated expected results.
Swab Elution Condition	To assess device performance when there is variation in how the swab is	The testing panel included a negative and a triple analyte low positive.

	eluted. The following conditions were tested: tap for 15 seconds (control), tap for 5 seconds, dip swab in and take out (no tapping), place swab in buffer for 5 seconds (no tapping), place swab in buffer for 15 seconds (no tapping), foam swab (tap for 15 seconds), cotton swab (tap for 15 seconds).	All conditions generated expected results. Users should use only the swab provided in the kit.
Incorrect Specimen – Male urine and Saline	To assess device performance when the wrong specimen type is used for testing. The following sample types were evaluated: saline, male urine, and water.	The testing panel included a negative and a triple analyte low positive. False results were observed with saline and water. Invalid results were observed with male urine. A labeling mitigation has been included that instructs users that the test is for self-collected vaginal swab specimens only.
Specimen Stability (Delay in Testing)	To assess device performance when testing of the collected specimen is delayed and stored for an extended period before testing. The following conditions were tested: < -15°C for at least 1 week, 4°C for 24-30 hours, 4°C for 72-78 hours, 4°C for 7-10 days, 30°C for 24-30 hours, 30°C for 72-78 hours, 30°C for 7-10 days. A supplemental study was conducted with samples stored at 38˚C and high humidity for 1 hour and then tested.	The testing panel included a negative and a triple analyte low positive. No false or invalid results were observed. All test results were as expected. The device is robust to samples that are not tested immediately.
Power Interruption	To assess device performance when there is a power fluctuation during testing.	The testing panel included a negative and a triple analyte low positive. All results were invalid when the device was unplugged during operation then plugged back in. Valid results were observed when the power fluctuation occurred before testing. No false results were observed.
Temperature, Humidity, and Barometric Pressure	To assess device performance while running the test outside of the recommended conditions. The following humidity conditions were tested, held at 23°C (% relative humidity): 5%, 20%, 80%, and 95%. The following temperature conditions were tested at both 5% and 95% RH: 9°C, 11°C, 13°C, 15°C, 17°C, 31°C, 33°C, 35°C, 37°C, and 39°C. The following altitude conditions were tested: -60 m at 23°C, -30 m at 23°C, 2184 m at 22.6°C, and 2970 m at 23.5°C.	The testing panel included a negative and a triple analyte low positive. Invalid results were observed at temperatures higher than room temperature (>30°C). One sample gave an invalid result at 11°C but was valid with retest. No false results were observed. Labeling instructs users of the proper testing conditions.
Visibility of Indicator Signals (Lighting Conditions)	To assess device performance when there is variation in the LED light signal of the progress lights. The following lighting conditions were tested for the power icon, progress 1,	The testing panel included a negative, a CT low positive, a CT and NG low positive, a CT and TV low positive, an NG low positive, an NG and TV low positive, a TV low positive, and a CT, NG, and TV low positive sample.

	progress 2, progress 3, and green lights: 20-30 fc, 95-125 fc, and ≥ 130 fc.	All results were as expected under variable LED lighting conditions, including very high lighting conditions.
Device Positioning During Run	To Assess device performance when run at non-level positioning. The following conditions were tested: 2° tilt and 10° tilt with the lights down, 2° tilt and 10° tilt with the lights up, 90° rotation on the horizontal edge with lights down, 90° rotation on the horizontal edge with lights up, 90° rotation on the vertical edge with plug up, and upside down.	The testing panel included a negative and a triple analyte low positive. The results show the device is robust to operating when tilted to 2° and 10° in either direction. Invalid results were observed when device was rotated 90°, as this positioning resulted in a control failure. Labeling mitigation includes instructions to choose a flat work area.
Device Agitation and Movement During Analysis	To assess device performance when it is agitated or moved during testing. The following conditions were tested: inversion during lysis (4 min after testing started), inversion during PCR (12 min after testing started), inversion during detection (24 min after testing started), vibration during run, dropped from 1 m before run, and dropped from 1 m during run.	The testing panel included a negative and a triple analyte low positive. All results were as expected. Invalid results were observed when the device was inverted during PCR and detection and when dropped during run. Labeling mitigation includes a warning not to unplug or move the device until the green ready light turns on.
Functionality After Freezing	To assess device performance after freezing.	The testing panel included a negative and a low positive. No false or invalid results were observed.
Bubbles/air in Syringe	To assess device performance when bubbles are in the syringe when the sample is added to the device.	The testing panel included a negative and a triple analyte low positive. All test results were as expected. The presence of bubbles in the syringe does not appear to impact detection of target analytes.
Image capture and lighting conditions	To assess device performance when the results are imaged under suboptimal lighting conditions. Then the result image was captured under low, optimal, and high lighting conditions.	The testing panel included a negative and a triple analyte low positive. All test results were as expected. The device is robust to imaging results under a range of lighting conditions.

VII Proposed Labeling:

The labeling supports the decision to grant the De Novo request for this device.

VIII Identified Risks and Mitigations:

Identified Risks to Health	Mitigation Measures
Risk of false results	Certain labeling information including limiting statements and performance information.

Identified Risks to Health	Mitigation Measures
	Certain design verification and validation including certain analytical and clinical studies, and risk analysis strategies.
Failure of lay users to correctly interpret results	Certain labeling information including limiting statements and performance information. Certain design verification and validation including certain analytical and clinical studies, and risk analysis strategies.
Failure of lay users to correctly operate the device	Certain labeling information including limiting statements and performance information. Certain design verification and validation including certain analytical and clinical studies, and risk analysis strategies.

IX Benefit/Risk Assessment:

A Summary of the Assessment of Benefit:

As an OTC device, the probable clinical benefit of this test will be to reach individuals who otherwise would not engage with the healthcare system and therefore increase access to CT/NG/TV diagnostic testing.

B Summary of the Assessment of Risk:

The risks associated with this device, when used as intended, are those related to the risk of false test results, failure of lay users to correctly interpret the test results, and failure of lay users to correctly operate the device. False-negative results can cause delays in effective treatment and delay entry into medical care, resulting in ongoing chlamydia, gonorrhea, and/or trichomoniasis transmission by individuals unaware of their true infection status. False positive results may lead to incorrect diagnosis and unnecessary treatment for STI infection, and delayed diagnosis and treatment of other infections. There is also a risk that a lay user may not understand the clinical significance of a positive or negative test result.

C Summary of the Assessment of Benefit-Risk:

The risks associated with the device are mitigated by the special controls that address verification and validation requirements and risk analysis strategies, which help to lower the risk of false test results. In addition, labeling that includes step-by-step instructions, limiting statements and an explanation of the meaning of positive and negative results and the appropriate next steps that

will help to lower the risks of failure to correctly interpret the test results or operate the test correctly.

In conclusion, while general controls are not sufficient to ensure safety and effectiveness, in light of the special controls, the clinical benefits outweigh the probable risks for the Visby Medical Women's Sexual Health Test.

X Conclusion:

The De Novo request is granted and the device is classified under the following and subject to the special controls identified in the letter granting the De Novo request:

Product Code(s): SEA
Device Type: Test for detection of microorganism(s) causing sexually transmitted infections performed by lay users.
Class: II
Regulation: 21 CFR 866.3386