CLIA Waiver by Application Approval Determination
Decision Summary

I. Document Number

CW250004

II. Parent Document Number

K251501

III. CLIA Waiver Type

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

IV. Applicant

Visby Medical, Inc.

V. Proprietary and Established Names

Visby Medical Men's Sexual Health Test

VI. Measurand (analyte)

Chlamydia trachomatis DNA
Neisseria gonorrhoeae DNA

VII. Sample Type(s)

Male urine

VIII. Type of Test

Qualitative, Polymerase Chain Reaction (PCR)

IX. Test System Description

A Overview

The Visby Medical Men's Sexual Health Test is a single-use (disposable), fully automated, rapid, compact device that contains PCR assays for qualitative detection of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) DNA in male urine samples from

symptomatic or asymptomatic individuals. The device automatically performs all steps required to complete lysis, PCR amplification, and detection.
The Visby Medical Men's Sexual Health Test contains the test cartridge, a fixed volume pipette to transfer the specimen to the dropper tube, and a dropper tube containing sample buffer solution. The test is designed to be simple to use. The patient collects a first catch urine sample in a standard urine collection cup (not provided). The operator starts the test by using a provided fixed-volume disposable transfer pipette to transfer ~ 450 µL of urine from the collection cup into a dropper tube containing ~900 µL of Visby Medical Men's Sexual Health Buffer. The operator transfers the entire volume (~1.35 mL) of the sample (urine in buffer) into the sample port of the device by squeezing the dropper tube to release all of the sample into the device sample port. The operator then slides a purple switch on the front of the device to both close the sample port and initiate the fully automated testing process. At this point, blinking white lights on the front of the device indicate the test is in progress. Test results are available in just under 30 minutes at which time a green "READY" status light will appear at the bottom of the device, and a purple color will appear in the "RESULTS VALID" spot, indicating a valid test. A purple spot adjacent to "CHLAMYDIA" and/or "GONORRHEA" signifies the presence of amplified CT and/or NG DNA in the sample

B Test System Components

The Visby Medical Men's Sexual Health Test contains the following test components:

- Visby Medical Men's Sexual Health Test cassette (10 per kit)
- Disposable Transfer Pipette (10 per kit)
- Dropper Tube containing buffer (10 per kit)
- Quick Reference Guide

Sample collection kits, gloves, power adapter, and external controls are not provided in the test kit. They are available separately.

X. Specific Contents for CLIA Waiver

A Demonstrating "Simple":

- The device is a fully automated, single use test.
- Uses a direct specimen: patient-collected urine that the operator adds into a dropper tube by using a fixed volume disposable transfer pipette. No additional sample processing is required.
- Needs only basic, non-technique-dependent specimen manipulation. An untrained operator can conduct the test by performing three simple steps: 1) transfer the specimen using a fixed volume pipette to the dropper tube containing buffer; 2) add the diluted buffer to the cassette entry port; 3) close the port door which begins the test.
- The device is packaged with a fixed volume pipette which ensures that an appropriate sample volume is loaded onto the device. Sample volume measurement is not needed for the operator.
- There is no reagent handling, all reagents are inside the device components.
- Needs no operator intervention during the analysis as all steps are automated and performed within the device.

- Needs no technical or specialized training with respect to troubleshooting or interpretation of multiple or complex error codes.
- Needs no electronic or mechanical maintenance as the device is for single use and there are no serviceable parts.
- Produces results that require no operator calibration, interpretation, or calculation. The test is purely qualitative (presence or absence of a spot at the test result window).
- The test status is indicated by LED lights on the front of the device to indicate if the test is in progress, is completed, or error occurred.
- Contains a procedural control which, when positive, confirms that the test was properly executed.
- The results are interpreted visually.
- Contains a Quick Reference Guidance (QRG) sheet that is written at a 7th grade reading level.

B Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-Safe Mechanisms

1. Risk Analysis:

   Risk analysis was performed by the firm using the Failure Modes and Effects Analysis (FMEA) Method; the detailed analysis was included in the submission. Potential sources of errors that could adversely affect system performance were identified and mitigated first through system design and then through additional cautions in the labeling. The identified risks which could result in erroneous test results were evaluated in flex studies which stressed the functional limits of the test.

2. Fail-Safe and Failure Alert Mechanisms:

   The Visby test has the following fail-safe and failure alert mechanisms built into the test system to prevent erroneous results:

   ● Internal process control
   The internal process control is a PCR assay to a control organism (*Neisseria subflava*) that is contained in the device. The process control is designed to ensure that all steps in the testing process including lysis, amplification of target sequences, and amplicon detection are working properly. A purple spot adjacent to "RESULTS VALID" in the results window indicates a successful internal process control. If a purple spot is not present in the "RESULTS VALID" window, then the test result is invalid.

   ● Built-in electronic sensors
   The device firmware has built-in electronic controls that monitor the device during the run to ensure that it is operating within specifications. If the run is successful, a green circle LED next to "READY" illuminates when the testing process is complete and ready to read and turns off when the results read window timeframe has expired. If the firmware detects an out-of-specification condition, the firmware will prevent the automated test process from being initiated or stop it from proceeding (depending on when the error is encountered). Conditions that cause an error include:

   - The device is operated outside of the specified operating temperature (13-31°C).

- The power is interrupted during the test run.
- The firmware detects a firmware error.

● External Controls

Ready-to-use external control swabs are available from ZeptoMetrix and are recommended to be used with every new shipment and each new operator. The external controls are tested in the same manner as a patient urine sample and are meant to alert the operator when a new shipment of devices is not operating as intended. They are also used to ensure that new operators are able to follow the test kit instructions and obtain reliable test results.

- Lockout Features

The device is designed such that it is not possible to reuse it once a sample is loaded. This feature also prevents amplicon contamination of the work area by containing the testing materials in the device housing. The device can be plugged in either before or after the switch is closed. The action of closing the switch prevents reuse of the device, as follows:

- Once the sample port slider switch is closed, it is not possible to access the sample port and it cannot be pried open.
- Once the device is plugged in and testing is initiated by closing the sample port slider, the test cannot be used again because the firmware recognizes that the testing process was already initiated, and it will not allow it to be restarted.

3. Flex Studies:

Sixteen experiments were performed to evaluate the conditions that presented a low but potential risk of obtaining an incorrect result due to operator errors performing the procedure or to environmental conditions outside of the intended use specifications of the device. For these flex studies, five replicates of negative and double positive (CT and NG in each sample) samples were prepared in clinical urine matrix and tested using the Visby Medical Men's Sexual Health Test. Positive samples were tested at 3x LOD (each).

Flex Test 1: Delayed starting of the test. Following addition of the diluted sample to the test port, a slider is moved over top of the port which signals the electronics to begin the test. Variables tested in this study included a delay of 30 minutes, 115 minutes, 130 minutes before sliding the port cover closed. Results: all expected results were obtained for the baseline, 30 minutes, and 115 minutes time points. The cassette locked out at 130 minutes and provided an 'invalid' result as intended in the device design fail safe.

Flex Test 2: Test cassette unwrapped and let to sit prior to use. Unwrapped cassettes were allowed to sit for 2 hours, 8 hours, or 24 hours prior to use. All test conditions provided the expected results.

Flex Test 3: Test cover slider is left partially open or completely open during test procedure. For this test, the test slider was left 90% closed (not completely closed), 50% closed, or completely open. Due to built-in fail safe mechanisms, the cassette indicated all invalid results for 0% and 50% closed tests and 4 out of 10 invalid results for the 90% test condition. There were no false results observed for any of the test conditions.

Flex Test 4: Operator reads the test result outside of the allowed time following test completion. Variables tested include 0 hours, 2 hours, 6 hours, 24 hours following test completion. For this test, four different results were tested: negative, CT only positive, NG only positive, CT and NG double positive. Operators in this test were instructed to ignore the green light indicator that instruct when a test result can be read. No false results or invalids were observed in any of the test conditions.

Flex Test 5: Urine sample is too low or too high a volume when added to the buffer. Variables tested were 100 µl, 200 µl, 300 µl, 400 µl, 450 µl (intended volume), 500 µl, or 900 µl. There were no false results observed in the testing, although many aberrant volumes produced invalid results during initial and re-testing.

Flex Test 6: Diluted specimen volume is too low or too high. For this test, 1350 µl of diluted sample is intended to be added to the sample port. This flex study tested the results if 100, 400, 700, 900, 1400 µl of diluted sample is added to the sample port. All test conditions returned expected results.

Flex Test 7: Diluted specimen is improperly mixed, vigorously mixed, or delayed before adding to the sample port. Test conditions were: wait 15 minutes before adding sample to port, invert 5x, invert 25x vigorously (i.e.; excessive shaking). All test conditions returned the expected results.

Flex Test 8: Improper specimen or reagent used. Variables tested included: undiluted urine, vaginal swab in collection media, saline in place of test buffer, water in place of test buffer. All tests using undiluted (un-buffered) urine were invalid. Two out of five NG tests returned a false negative result when water was used in place of dilution buffer. All other test conditions returned expected results. To avoid this risk of false results due to the use of water, the labeling instructs the operator to use the provided dilution buffer.

Flex Test 9: Specimen stored outside of proper storage conditions. Results showed that storage at 30 °C (higher end of room temperature) for 24 hours produced 1 false positive CT and 4 false negative NG. This study reinforces the importance of proper specimen storage conditions. The labeling was edited to include numerous warnings regarding risks of improper specimen storage and an emphasis to test a specimen as soon as possible.

Flex Test 10: Power interruption before or during test. Unplugging and plugging back in prior to starting a test did not affect the testing or result. Interruption of power during a test resulted in the expected error message.

Flex Test 11: Temperature, humidity, and pressure variations during testing. Many variables were tested. Results of the testing showed no false results, but invalid results were frequent when test temperature was below 13 °C or above 34 °C. The labeling specifies that proper operating temperature are between 13 °C and 31 °C.

Flex Test 12: Operators read test results in various lighting conditions. Many variables were tested. Results of the testing showed no false results.

Flex Test 13: Cassette orientation during running of test. In this test, cassettes were placed at various angles while the test result was running. The test returned frequent invalid results when the test cassette was improperly placed. There was 1 false negative NG result when the cassette was placed at 90 degree to the instructed position. A warning was added to the labeling of the risk of false results if the cassette is not placed flat on the surface during the running of the test.

Flex Test 14: Device agitation during running of the test. For this study, test cassettes were bumped or dropped from various heights to simulate a disturbance of the test cassette during the test procedure. Most conditions returned the expected results. For the test condition of a 1 meter drop, an error message resulted due to power interruption caused by the drop.

Flex Test 15: Test used after having been frozen. For this test, a test kit was frozen and then thawed and brought to operating temperature before performing the test. All samples returned expected results.

Flex Test 16: Device and reagents stored at elevated temperature and humidity. For this test, a complete test kit was stored at 38 °C and 95% relative humidity for 1 hour before performing testing. All samples returned the expected results.

The results of these flex tests indicate the Visby Medical Men's Sexual Health Test is robust to foreseeable user-dependent variations in the assay workflow and that in-built assay controls and fail-safe and/or failure alert mechanisms are effective in preventing the generation of erroneous results due to operator error and/or use of the Visby Medical Men's Sexual Health Test outside the specified operating environmental conditions.

C Demonstrating "Insignificant Risk of an Erroneous Result" - Accuracy

1. Comparison Study

   a. Study Sites and Duration

   Clinical performance for the Visby Men's Sexual Health Test was established through a prospective study enrolling individuals at seven geographically diverse intended use CLIA-waived sites. The study was designed to enroll sexually active users aged 14 and above. Participants were provided a collection cup and instructions to collect a first-catch urine specimen. An operator, untrained in the use of the subject device, immediately collected the specimen cup and performed the Visby Medical Men's Sexual Health Test according to the instructions for use. The remaining specimen was aliquoted and sent to two reference laboratories for comparator testing using three FDA cleared nucleic acid amplification tests (NAATs). The samples were tested first by two NAATs and then with a third NAAT as a tie breaker if the first two NAATs results were discordant. The study consisted of 1289 prospectively participants enrolled from October 2024 through March 2025.

   b. Operators

   A total of 16 operators, representative of intended CLIA waived users across the seven clinical testing sites, participated in this clinical study. The participants consisted of administrative personnel, medical assistants, nurses, research/study coordinators,

administrative managers, and other patient care providers. The test operators who participated in the study were untrained in the use of the subject device and none were trained laboratory technicians. Upon completion of the study, the operators at each site were asked to complete an Operator Questionnaire that asked them to rate the ease of use of the test procedure.

c. Instructions for Use

The operators were given the product instructions and the Quick Reference Guide. No other materials or instructions were provided and the operators received no training in the use of the test.

d. Participants (Patients)

There were a total of 1289 participants enrolled into the study from October 2024 through March 2025.

Inclusion Criteria
1. Willing and able to provide written informed consent (or assent when applicable) as required by the reviewing IRB.
2. Participant had a penis at the time of enrollment.
3. ≥14 years of age at the time of enrollment.
4. Able to read and understand sample collection instructions provided for the study.
5. Willing and able to follow all study procedures

Exclusion Criteria
1. Had a medical condition, serious intercurrent illness, or other circumstance that, in the investigator's judgment, could jeopardize the participant's safety, or could interfere with study procedures.
2. Had consumed oral or intramuscular or intravenous antibiotics, within 48 hours prior to enrollment.
3. The participant had urinated within the last one (1) hour prior to urine sample collection.
4. Had an in-dwelling catheter or practices intermittent catheterization for urinary drainage.
5. Had been previously enrolled in this study.

e. Samples

The study consisted of 1289 participants prospectively enrolled from October 2024 through March 2025. Of the 1289 enrolled participants, 14 were excluded from the performance evaluation due to procedural errors by site study staff or incomplete study procedures (n=8), withdrawal of consent (n=4), and for the subject not meeting inclusion criteria (n=2), leaving 1275 evaluable specimens. Of these, 3 were excluded due to invalid subject test results leaving 1272 Visby Medical Men's Sexual Health Test results with paired valid comparator results. Participants self-collected one urine specimen using the provided instructions. Specimens were immediately tested by study operators; leftover urine specimen was aliquoted and shipped to the reference laboratories for comparator testing.

f. Comparative Method (CM)

The comparator consisted of three FDA-cleared molecular assays run comparator algorithm. Results were determined by at least two out of three concurrent results.

g. Results

Clinical Performance for CT and NG in urine specimens in Symptomatic and Asymptomatic participants is shown below:

Clinical Performance for CT:

Symptom Status	N	TP	FP	TN	FN	Sensitivity (95% CI)	Specificity (95% CI)
Symptomatic	310	57	2	249	2	96.6% (88.5-99.1%)	99.2% (97.1-99.8%)
Asymptomatic	962	88	6	863	5	94.6% (88.0-97.7%)	99.3% (98.5-99.7%)
Overall	1272	145	8	1112	7	95.4% (90.8-97.8%)	99.3% (98.6-99.6%)

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

Clinical Performance for NG:

Symptom Status	N	TP	FP	TN	FN	Sensitivity (95% CI)	Specificity (95% CI)
Symptomatic	310	48	1	261	0	100.0% (92.6-100.0%)	99.6% (97.9-99.9%)
Asymptomatic	962	7	7	948	0	100.0% (64.6-100.0%)	99.3% (98.5-99.6%)
Overall	1272	55	8	1209	0	100.0% (93.5-100.0%)	99.3% (98.7-99.7%)

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

2. Device Performance with Analyte Concentrations Near the Cutoff

A reproducibility study of the Visby Medical Men's Sexual Health Test was conducted by untrained operators from three external sites representative of CLIA waived settings. Six untrained operators (two untrained operators per site) performed the study using panels of blind coded specimens containing low (1X LOD) or moderate (4X LOD) positive CT or NG, or negative samples. Samples were prepared in pooled negative clinical matrix (male urine). Operators tested multiple samples of each panel member over six days. The percent positive results for the CT moderate and CT low positive samples were 100% (108/108) and 98.1% (106/108), respectively. The percent positive results for the NG moderate and NG low positive samples were 100% (108/108) and 100% (108/108), respectively. The Reproducibility Study site-to-site qualitative results (percent positive results) are presented in the table below.

Panel Member	Site 1	Site 2	Site 3	Overall Agreement	
	% Agreement[1] (count)	% Agreement (count)	% Agreement (count)	% Agreement (count)	95% Confidence Interval
Moderate Positive CT	100% (36/36)	100% (36/36)	100% (36/36)	100% (108/108)	96.6-100%
Low Positive	97.2% (35/36)	97.2% (35/36)	100% (36/36)	98.1% (106/108)	93.5-99.5%
Moderate Positive NG	100% (36/36)	100% (36/36)	100% (36/36)	100% (108/108)	96.6-100%
Low Positive	100% (36/36)[2]	100% (36/36)	100% (36/36)	100% (108/108)	96.6-100%
Negative	100% (36/36)	100% (36/36)	100% (36/36)	100% (108/108)	96.6-100%

[1] Agreement = agreement with expected results

[2] One test was unexpectedly positive for CT

The study results demonstrated that users untrained in the test procedure of the Visby Medical Men's Sexual Health Test were able to perform the test correctly and the test provided the expected result for samples near the limit of detection.

3. Operator Questionnaire

All study operators that tested samples during the clinical study were asked to complete the "Ease of Use Questionnaire" after enrollment was completed. Of the 16 operators that tested subject samples in the study, responses were gathered from 15. One operator resigned prior to study completion and could not be reached to complete questionnaire. Questions 1 through 11 and 13 through 15 were rated on a scale from 1 (strongly disagree) to 5 (strongly agree) or (yes/no) for question 12. The average score assigned by the 15 operators for each of the questions was between 4.7 to 4.9 with a median score of 5.0. Overall, based on the Visby test study operator responses, the device was easy to set up and use by following the instructions provided in the quick reference guide.

D Labeling for Waived Devices

The labeling consists of:
1. Instructions for Use/Package Insert
2. Quick Reference Guide (QRG)

The following elements are appropriately present:
- The QRG is written in simple language and contains graphics which visually aid the user in processing samples.
- The labeling identifies the system as CLIA Waived.
- A statement informing the user that the test procedure must be followed as written to maintain the CLIA waived status is present.
- The QRG includes instructions for performing Quality Control testing.
- Technical support telephone number is prominently displayed.
- All appropriate cautions regarding sample handling and processing are present.

- The labeling includes the statement that a Certificate of Waiver is required to perform the test in a waived setting.
- The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

XI. Conclusion

The submitted information in this CLIA waiver application supports a CLIA waiver approval decision.