January 26, 2024

Hologic, Inc.
Jon Kukowski
Regulatory Affairs Specialist
10210 Genetic Center Drive
San Diego, California 92121

Re: K231329
Trade/Device Name: Aptima Neisseria gonorrhoeae Assay
Regulation Number: 21 CFR 866.3390
Regulation Name: Neisseria Spp. Direct Serological Test Reagents
Regulatory Class: Class II
Product Code: LSL, QEP
Dated: December 28, 2023
Received: December 28, 2023

Dear Jon Kukowski:

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

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

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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

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

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

Sincerely,

Himani Bisht -S

Himani Bisht, Ph.D.
Assistant Director
Viral Respiratory and HPV Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K231329

Device Name
Aptima Neisseria gonorrhoeae Assay

Indications for Use *(Describe)*
The Aptima Neisseria gonorrhoeae (GC) Assay is an in vitro qualitative nucleic acid amplification (NAAT) test for the detection of ribosomal RNA (rRNA) from Neisseria gonorrhoeae (GC) to aid in the diagnosis of gonococcal urogenital disease using the Panther System. The assay may be used to test male urine specimens from symptomatic and asymptomatic individuals.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary

Contact Details

Applicant Name: Hologic, Inc.

Applicant Address: 10210 Genetic Center Drive San Diego CA 92121 United States

Applicant Contact Telephone: 858-410-8245

Applicant Contact: Jon Kukowski

Applicant Contact Email: jonathan.kukowski@hologic.com

Device Name

Device Trade Name: Aptima Neisseria gonorrhoeae Assay

Common Name: Neisseria spp. direct serological test reagents

Classification Name: DNA-Reagents, Neisseria

Regulation Number: 866.3390

Regulatory Class: Class II

Product Code: LSL

Legally Marketed Predicate Devices

Predicate #: K063664

Predicate Trade Name: Aptima Neisseria gonorrhoeae Assay

Product Code: LSL

Device Description Summary

Clearance of this pre-market application will allow the Aptima Neisseria gonorrhoeae Assay to be performed on the Panther system using male urine specimens.

The Aptima GC assay is a target amplification nucleic acid probe test for in vitro qualitative detection of ribosomal RNA (rRNA) from *Neisseria gonorrhoeae* (GC). The Aptima Neisseria gonorrhoeae Assay combines the technologies of target capture, transcription-mediated amplification (TMA), and hybridization protection assay (HPA).

Specimens are collected and transferred into their respective specimen transport tubes. The transport solution in these tubes releases the rRNA target and protects it from degradation during storage. When the Aptima Neisseria gonorrhoeae Assay is performed in the laboratory, the target rRNA molecule is isolated from the specimens by use of a capture oligomer via target capture

that utilizes magnetic microparticles. The capture oligomer contains a sequence complementary to a specific region of the target molecule as well as a string of deoxyadenosine residues. During the hybridization step, the sequence specific region of the capture oligomer binds to a specific region of the target molecule. The capture oligomer:target complex is then captured out of solution by decreasing the temperature of the reaction to room temperature. This temperature reduction allows hybridization to occur between the deoxyadenosine region on the capture oligomer and the poly-deoxythymidine molecules that are covalently attached to the magnetic particles. The micro particles, including the captured target molecule bound to them, are pulled to the side of the reaction vessel using magnets and the supernatant is aspirated. The particles are washed to remove residual specimen matrix that may contain amplification reaction inhibitors. After the target capture steps are completed, the specimens are ready for amplification.

Target amplification assays are based on the ability of complementary oligonucleotide primers to specifically anneal and allow enzymatic amplification of the target nucleic acid strands. The Hologic TMA reaction replicates a specific region of the 16S rRNA from GC via DNA intermediates. A unique set of primers is used for the target molecule. Detection of the rRNA amplification product sequences (amplicon) is achieved using nucleic acid hybridization. A single-stranded chemiluminescent DNA probe, which is complementary to a region of the target amplicon, is labeled with an acridinium ester molecule. The labeled DNA probe combines with amplicon to form stable RNA:DNA hybrids. The Selection Reagent differentiates hybridized from unhybridized probe, eliminating the generation of signal from unhybridized probe. During the detection step, light emitted from the labeled RNA:DNA hybrids is measured as photon signals in a luminometer, and are reported as Relative Light Units (RLU).

The device reagents are identical to the Aptima Neisseria gonorrhoeae Assay reagents for use on the Tigris DTS system but are intended for use on the Panther system with different specimen type indications. The Panther and Tigris DTS systems use the same principles of operation.

Intended Use

The Aptima Neisseria gonorrhoeae (GC) Assay is an *in vitro* qualitative nucleic acid amplification (NAAT) test for the detection of ribosomal RNA (rRNA) from *Neisseria gonorrhoeae* (GC) to aid in the diagnosis of gonococcal urogenital disease using the Panther System. The assay may be used to test urine from symptomatic and asymptomatic male individuals.

Indications for Use Comparison

This pre-market application is to clear the Aptima Neisseria gonorrhoeae Assay on an additional platform, the Panther system, for use with male urine specimen type indications. The analytical and clinical study results demonstrate that the Aptima Neisseria gonorrhoeae Assay on the Panther system performs comparably to the predicate device in detecting rRNA of GC from the designated specimen type and support a substantial equivalence decision.

Technological Comparison

The Aptima Neisseria gonorrhoeae Assay incorporates the technologies of target capture, Transcription-Mediated Amplification (TMA), and Hybridization Protection Assay (HPA), which are described in previous 510(k) submissions for the Aptima Neisseria gonorrhoeae Assay including K043144, cleared in March 2005. The Aptima Neisseria gonorrhoeae Assay and system technologies remain unchanged in this submission, including biochemical (e.g., *in vitro* nucleic acid probe test) and physical detection (e.g., chemiluminescence) technologies.

Non-Clinical and/or Clinical Tests Summary & Conclusions

The following studies were conducted to support performance of the Aptima Neisseria gonorrhoeae Assay on the Panther system using male urine specimens.

Analytical Studies

Analytical Sensitivity

Studies were conducted to verify the analytical sensitivity (concentration of analyte giving ≥95% positivity) of the Aptima Neisseria gonorrhoeae Assay on the Panther system by testing panels made by spiking GC organisms into male urine pools, Results showed that the LoD on the Panther was below 125 CFU/mL (250 fg GC rRNA/assay).

Limit of Detection Study

The limit of detection (LoD) was tested and confirmed with sensitivity panels prepared using two strains of GC organisms spiked into pooled negative urine. Testing evaluated one antibiotic susceptible strain; *Neisseria gonorrhoeae* ATCC 49226 (GP1803), and one antibiotic resistant stain; *Neisseria gonorrhoeae* WHO X/NCTC 13820 (GP2730). Sensitivity panels were tested on three Panther instruments with two reagent lots. At least 20 replicates were run for each concentration for each reagent lot for each strain. LoD, defined as the target concentration that can be detected in 95% of the replicates tested for urine specimens is 0.04933 CFU/mL for ATCC 49226 and 0.03986 CFU/mL for stain X/NCTC 13820.

Within-lab Precision Study

Precision was measured using positive panel members consisting of *Neisseria gonorrhea* cells at three different concentrations approximately: 3x LoD (Low Positive), >3x and <5x LoD (Moderate Positive), and >10x LoD (High positive). Cells were spiked into pooled negative urine matrix (Urine mixed 1:1 with Urine Transport Media). The negative panel member consisted of unspiked negative urine matrix. Testing was conducted over the course of at least 20 non-consecutive days using two lots of reagents on three Panther systems by three operators performing at least two daily runs. Agreement to expected results was 100% for all four panel members. The precision of the signal for each panel is shown in table below.

					Between-Lot		Between-Instrument		Between-Operator		Between-Day		Between-Run		Within-Run		Total	
Panel Member	N. gonorrhoeae concentration (CFU/mL)	**N**	**Mean kRLU**	**Agreement to Expected Result**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**
Low positive	0.1431	162	520.1	100%	65.05	12.51	38.39	7.38	0.00	0.00	14.84	2.85	20.11	3.87	62.34	11.99	101.07	19.43
Moderate positive	0.2417	162	809.4	100%	90.32	11.16	52.74	6.52	7.71	0.95	15.00	1.85	24.09	2.98	84.36	10.42	137.55	16.99
High positive	0.5426	162	1529.4	100%	182.18	11.91	78.41	5.13	19.09	1.25	51.45	3.36	0.00	0.00	111.09	7.26	233.86	15.29
Negative	0.000	162	4.2	100%	1.19	28.36	0.87	20.80	0.51	12.28	0.00	0.00	0.00	0.00	3.52	84.17	3.85	92.04

Note: The analysis was performed using SAS PROC MIXED, which applies a lower boundary of 0 to all variance components in the model by default. If a variance component is 0, then SD=0 and CV=0%.

Analytical Specificity

A total of 155 culture isolates were evaluated using the Aptima Neisseria gonorrhoeae Assay on the DTS system or Panther system. These isolates included 87 organisms that may be isolated from the urogenital tract and 68 additional organisms that represent a phylogenetic cross-section of organisms. The tested organisms included bacteria, fungi, yeast, parasites and viruses. All organisms except *C. psittaci, C. pneumoniae, U. urealyticum, C. trachomatis* and the viruses were tested at 1.0 x 10^6 cells/ assay. *C. psittaci* VR601 was tested at 8.0 x 10^4 cells/assay and *C. psittaci* VR125 was tested at 1.0 x 10^5 cells/assay. *C. pneumoniae* was tested at 4 x 10^3 cells/assay and *U. urealyticum* was tested at 6.7 x 10^6 cells/assay. C. trachomatis was tested at 1.0 x 10^4 IFU/mL. The viruses were tested as follows: (a) herpes simplex virus I: 2.5 x 10^4 $TCID_{50}$/assay, (b) herpes simplex virus II: 6.0 x 10^4 $TCID_{50}$/assay, (c) human papillomavirus 16: 2.9 x 10^6 DNA copies/assay and (d) cytomegalovirus: 4.8 x 10^5 cells/assay.

Interfering Substances

For a nucleic acid amplification assay, analytical specificity with respect to potentially interfering substances is largely determined by the chemistry of the assay (e.g. oligonucleotide sequences) rather than by the platform. Because the reagents for the Aptima Neisseria gonorrhoeae Assay are identical between DTS and Panther systems, data generated on the DTS system supports the performance of the assay on Panther system.

The following interfering substances were individually spiked into urine specimens: 10% blood, contraceptive jelly, spermicide, moisturizer, hemorrhoidal anesthetic, body oil, powder, anti-fungal cream, vaginal lubricants, feminine spray and leukocytes (1.0 x 10^6 cells/mL). The following interfering substances were individually spiked into urine specimens: 30% blood, urine analytes, protein, glucose, ketones, bilirubin, nitrate, urobilinogen, pH 4 (acidic), pH 9 (alkaline), leukocytes (1.0 x 10^6 cells/mL), cellular debris, vitamins, minerals, acetaminophen, aspirin and ibuprofen. All were tested for potential assay interference in the absence and presence of GC at the estimated rRNA equivalent of 50 GC cells/assay (250 fg/assay). The rRNA equivalents were calculated based on the genome size and estimated DNA:RNA ratio/cell of each organism. No interference was observed with any of the tested substances. No inhibitors of amplification were observed in the Aptima Neisseria gonorrhoeae Assay.

Mucin and seminal fluid were tested on the Panther system by spiking into pooled negative urine negative in the presence or absence of *Neisseria gonorrhoeae* ATCC 49226. Mucin at (0.1% Vol/vol) and seminal fluid (at 1% vol/vol) did not interfere with the assay.

Carryover Study

A multi-run analytical study was conducted using spiked panels on three Panther Systems. Carryover was assessed using approximately 20% high titer GC samples (>2 x 10^5 cells/mL, or rRNA equivalent) dispersed between negative samples. Testing was carried out using 5 runs on each of three Panther Systems with a total of 2941 negative samples. The overall carryover rate was 0.07% with a 95% confidence interval of 0.02–0.25%.

Run-Size Validity

This study was to confirm that there are no front-to-back positional effects within a run for the Aptima Neisseria gonorrhoeae Assay on the Panther system. Panels and controls with known concentrations were tested and results were examined for front-to-back effects when compared to expected results. Negative and Positive panel member results produced 100% agreement with the expected results, with no difference in performance between the front and back of the runs.

Control Validity

This study was to demonstrate that Aptima Neisseria gonorrhoeae Assay run controls meet performance criteria and properly control for run validity over the timeframe allowed by the Panther software. The acceptance criteria for this study were met. Results at time-point 0 hour and time-point 30 hour (24 hours + 25%) yielded the expected results for the study and the control RLUs were within the expected range. Run controls met performance criteria and properly control for run validity over the 24-hours control validity timeframe allowed by the Panther software.

Control Effectiveness

This study was to demonstrate that the Aptima Neisseria gonorrhoeae Assay run controls are properly invalidated under fault conditions that are not detected by instrument process controls and that may exist during assay processing. The performance of the GC Controls correctly

predicted the sample results in 8 out of 8 of the conditions tested for the assay when run on the Panther system. Results met the acceptance criteria of the study and demonstrated that performance of the Aptima Neisseria gonorrhoeae Assay controls properly determine run and test validity under fault conditions that are not detected by Panther system process controls.

Environmental Conditions

This study was to demonstrate that the Aptima Neisseria gonorrhoeae Assay on the Panther system meets performance requirements at the limits of Panther system environmental conditions for external ambient temperature (15-30ºC) and relative humidity (20-85%) specifications. Target panels at or below the sensitivity claims for the assays were tested. Negative and Positive panel member results produced 100% agreement with the expected results. The Aptima Neisseria gonorrhoeae Assay on the Panther system meets performance requirements at the limits of Panther system environmental conditions for external ambient temperature (15-30ºC) and relative humidity (20-85%) specifications.

Reproducibility Study

Aptima Neisseria gonorrhoeae Assay reproducibility was evaluated on the Panther system at two external US laboratories and at Hologic. Testing was performed using two lots of assay reagents and a total of six operators (two at each site). At each site, testing was performed over at least six days.

Reproducibility panel members were created using clinical urine specimens in urine transport medium (UTM). The GC positive panel members were created by diluting GC positive clinical urine specimens with volume from pooled GC negative clinical urine specimens to achieve the appropriate targeted RLU results (low RLU positive or positive). The negative panel member was created using pooled GC negative clinical urine specimens.

The agreement with expected results was 100% for all panel members.

The table below shows the signal variability of assay RLU results for each panel member between sites, between operators, between lots, between runs, within runs, and overall (Total). Only samples with valid results were included in the analyses.

Panel Member	Target RLU (x1000)	N	Mean RLU (x1000)	Between Sites		Between Operators		Between Lots		Between Runs		Within Runs		Total	
				SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)
Negative	<50	108	2.1	0.0	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.2	11.9	0.2	12.0
Low Positive	100 to <2000	105[1]	926.1	81.2	8.8	0.0	0.0	98.4	10.6	86.2	9.3	361.5	39.0	392.9	42.4
Positive	2000 to <12000	107[1]	6196.9	247.5	4.0	23.7	0.4	315.1	5.1	136.5	2.2	187.4	3.0	463.5	7.5

CV = coefficient of variation, RLU = relative light unit, SD = standard deviation.

Notes: The RLU value reported by the software is the total measured RLU divided by 1000 with the digits after the decimal point truncated.

Variability from some factors may be numerically negative. In these cases, SD and CV are shown as 0.0.

[1]Invalid results were excluded from the analyses for low positive (n=3) and positive (n=1) panel members.

Clinical Study

A prospective, multi-center clinical study was conducted to establish the clinical performance characteristics of the Aptima Neisseria gonorrhoeae Assay on the Panther system. Specimens were collected from 2085 symptomatic and asymptomatic men enrolled at 11 geographically and ethnically diverse US clinical sites, including obstetrics and gynecology, family planning, and STI clinics. Subjects were classified as symptomatic if symptoms were reported by the subject. Subjects were classified as asymptomatic if the subject did not report symptoms.

One hundred twenty six (126) enrolled subjects were not evaluable (12 were withdrawn and 114 did not have at least one specimen with a valid non-excluded Aptima Neisseria gonorrhoeae Assay result and a conclusive infected status). The average age among evaluable study subjects was 35.6 years (range = 14 to 84 years).

Symptoms were reported in 42.1% (825/1959) of the evaluable subjects.

One first-catch urine specimen was collected from each male subject. All specimens were collected by the subject at the clinical sites.

Specimens were tested with the Aptima Neisseria gonorrhoeae Assay on the Panther system. Specimens with initial equivocal or invalid Aptima GC assay results or instrument processing errors were retested, volume permitting; valid retest results were included in the performance analyses. Male urine specimens were tested with up to 3 FDA-cleared NAATs to establish the patient infected status (PIS).

Performance of the Aptima Neisseria gonorrhoeae Assay was estimated relative to the PIS.

Of the specimens collected, 2042 were processed in valid Aptima Neisseria gonorrhoeae Assay runs, including 85 (4.2%) that had to be retested due to invalid results. Overall, 2030 (99.4%) had final valid results, and 12 (0.6%) had final invalid results and were excluded from the analyses. A total of 1958 male urine specimens from evaluable subjects were included in the analyses comparing Aptima Neisseria gonorrhoeae Assay results to the PIS: one specimen with final GC equivocal result was excluded from the performance analyses. Overall, the calculated sensitivity is 98.4% (95% CI: 94.4%-99.6%) for male urine. Overall specificity estimate is 99.9% (95% CI: 99.7%-100%) for male urine.

The study data demonstrate that performance of the Aptima Neisseria gonorrhoeae Assay on the Panther system is substantially equivalent to that of currently FDA-cleared assays for male urine specimens.

Conclusion

Analytical and clinical studies performed to evaluate male urine specimen type for use with the Aptima Neisseria gonorrhoeae Assay on the Panther system demonstrated that the device performs as intended and performs as safe and as effective compared to the predicate device. All study results demonstrated that the performance of male urine specimens for use with the Aptima Neisseria gonorrhoeae Assay on the Panther system is consistent with current expectations for GC testing, , and that the assay is safe and effective for its intended use.