May 23, 2019

Cepheid
Sudhakar Marla
Senior Director, Regulatory Affairs
904 Caribbean Drive
Sunnyvale, California 94089

Re: K190441
Trade/Device Name: Xpert CT/NG, GeneXpert Dx System, GeneXpert Infinity-48s and GeneXpert Infinity-80 Systems, GeneXpert Infinity-48 System, Xpert Vaginal/Endocervical Specimen Collection, Xpert Urine Specimen Collection Kit, Xpert Swab Specimen Collection Kit
Regulation Number: 21 CFR 866.3393
Regulation Name: Device to detect nucleic acids from non-viral microorganism(s) causing sexually transmitted infections and associated resistance marker(s)
Regulatory Class: Class II
Product Code: QEP, MKZ, LSL, OOI, QBD
Dated: February 22, 2019
Received: February 25, 2019

Dear Sudhakar Marla:

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 (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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for

Uwe Scherf, Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

510(k) Summary

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (408) 548-8946 Fax number: (408) 541-4192
Contact:	Sudhakar Marla, Ph.D.
Date Submitted:	May 20, 2019
Proprietary/Trade name:	Xpert® CT/NG
Common name:	Xpert CT/NG
Type of Test:	Automated, multiplex real-time polymerase chain reaction (PCR) assay intended for the *in vitro* qualitative detection and differentiation of DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG).
Regulation Number Classification Name:	21 CFR 866.3393 Device to detect nucleic acids from non-viral microorganism(s) causing sexually transmitted infections and associated resistance marker(s)
Primary Product code:	QEP; Class II
Secondary Product code:	LSL, MKZ, OOI, QBD
Classification Advisory Panel	Microbiology (83)
Prescription Use	Yes
Predicate Device – Assay:	Aptima Mycoplasma genitalium Assay [De Novo #DEN180047]
Predicate Devices – Ancillary Specimen Collection Kits:	Xpert Vaginal/Endocervical Specimen Collection Kit [510(k) #K173840] BD MAX UVE Specimen Collection Kit [510(k) #K043144]

Device Description:

The Xpert CT/NG test is an automated *in vitro* diagnostic test for qualitative detection and differentiation of DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG). The test is performed on the Cepheid GeneXpert Instrument Systems. The Xpert CT/NG test on the GeneXpert Instrument System automates and integrates sample purification, nucleic acid amplification and detection of the target sequences in simple or complex samples using real-time PCR. The system consists of an instrument, personal computer, and preloaded software for running the tests and viewing the results. The system requires the use of single-use disposable cartridges that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination between samples is minimized.

The Xpert CT/NG test includes reagents for the detection and differentiation of CT and NG. A Sample Processing Control (SPC), a Sample Adequacy Control (SAC), and a Probe Check Control (PCC) are also included. The SPC is present to control for adequate processing of the target bacteria and to monitor the presence of inhibitors in the PCR reaction. The SAC reagents detect the presence of a single copy human gene and monitor whether the specimen contains human cells. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The GeneXpert Instrument Systems, comprised of the GeneXpert Dx Systems, the GeneXpert Infinity-48 System, GeneXpert Infinity-48s, and the GeneXpert Infinity-80 System, have 1 to 80 randomly accessible modules, depending upon the instrument, that are each capable of performing separate sample preparation and real-time PCR tests. Each module contains a syringe drive for dispensing fluids (i.e., the syringe drive activates the plunger that works in concert with the rotary valve in the cartridge to move fluids between chambers), an ultrasonic horn for lysing cells or spores, and a proprietary I-CORE® thermocycler for performing real-time PCR and detection.

The ancillary specimen collection kits for use with the Xpert CT/NG test are the Xpert Vaginal/Endocervical Specimen Collection Kit, Xpert Swab Specimen Collection kit and the Xpert Urine Specimen Collection kit.

Device Intended Use:

The Xpert® CT/NG test, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* real-time PCR test for the automated detection and differentiation of genomic DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) to aid in the diagnosis of chlamydial and gonorrheal disease in the urogenital tract and extragenital sites (pharynx and rectum). The assay may be used to test the following specimens from asymptomatic and symptomatic individuals: female and male urine,

patient-collected vaginal swabs (collected in a clinical setting), clinician-collected endocervical swabs, and female and male pharyngeal and rectal swabs.

Ancillary Collection Kits:

Xpert Vaginal/Endocervical Specimen Collection Kit

The Cepheid Xpert® Swab Specimen Collection Kit is designed to collect, preserve, and transport *Chlamydia trachomatis, Neisseria gonorrhoeae,* and *Trichomonas vaginalis* DNA in endocervical swab specimens (collected by a clinician) and patient-collected vaginal swab specimens (collected in a clinical setting) from symptomatic and asymptomatic women prior to analysis with the Xpert CT/NG Assay and the Xpert TV Assay.

Xpert Urine Specimen Collection Kit

The Cepheid Xpert® Urine Specimen Collection Kit is designed to preserve and transport *Chlamydia trachomatis, Neisseria gonorrhoeae,* and *Trichomonas vaginalis* DNA in first-catch female and male urine specimens from symptomatic and asymptomatic individuals prior to analysis with the Xpert CT/NG Assay and the Xpert TV Assay.

Xpert Swab Specimen Collection Kit

The Xpert® Swab Specimen Collection Kit is designed to collect, preserve, and transport endocervical, vaginal, pharyngeal, and rectal swab specimens. This transport system is for use for testing with Xpert tests.

Substantial Equivalence:

The Xpert CT/NG is substantially equivalent to the predicate device, Aptima Mycoplasma genitalium Assay [De Novo #DEN180047: January 23, 2019].

Table 8-1 shows the similarities and differences between Xpert CT/NG and the predicate device.

Table 8-1: Comparison of Similarities and Differences of Xpert CT/NG with the Predicate Device

Similarities		
	Device	**Predicate Device**
Item	**Cepheid Xpert CT/NG**	**Aptima Mycoplasma genitalium Assay**
Nucleic Acid Extraction	Yes	Yes
Assay Results	Same	Qualitative
Indication for Use	Same	Asymptomatic and symptomatic patients

Differences		
Item	**Device**	**Predicate Device**
	Cepheid Xpert CT/NG	**Aptima Mycoplasma genitalium Assay**
Technology/ Detection	Multiplex real-time polymerase chain reaction (PCR)	Transcription-mediated nucleic acid amplification and hybridization
Specimen Type	Female and male urine, endocervical swab, patient-collected vaginal swab (collected in a clinical setting), and female and male pharyngeal and rectal swabs	Clinician-collected and self-collected vaginal swabs (in a clinical setting), clinician-collected endocervical swabs, female and male urine, clinician-collected male urethral swabs, and self-collected penile meatal swabs (in a clinical setting)
Intended Use	The Xpert® CT/NG test, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* real-time PCR test for the automated detection and differentiation of genomic DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae*	The Aptima Mycoplasma genitalium assay is an *in vitro* nucleic acid amplification test (NAAT) for the qualitative detection of ribosomal RNA (rRNA) from *Mycoplasma genitalium* on the fully automated Panther system. It

Differences		
Item	**Device**	**Predicate Device**
	Cepheid Xpert CT/NG	**Aptima Mycoplasma genitalium Assay**
	(NG) to aid in the diagnosis of chlamydial and gonorrheal disease in the urogenital tract and extragenital sites (pharynx and rectum). The assay may be used to test the following specimens from asymptomatic and symptomatic individuals: female and male urine, patient- collected vaginal swabs (collected in a clinical setting), clinician-collected endocervical swabs, and female and male pharyngeal and rectal swabs.	is intended for use as an aid in the diagnosis of *M. genitalium* urogenital infections in male and female patients suspected of *M. genitalium* infection. The assay may be used to test the following specimens: clinician-collected and self-collected vaginal swabs (in a clinical setting), clinician-collected endocervical swabs, female and male urine, clinician-collected male urethral swabs, and self-collected penile meatal swabs (in a clinical setting). For females, a vaginal swab is the preferred specimen type due to higher clinical sensitivity for detecting *M. genitalium* than other specimen types; however, female urine or clinician-collected endocervical swabs may be used as alternative specimens when vaginal swab specimens are not available. If female urine or clinician-collected endocervical swab specimens test negative, testing with a vaginal swab may be indicated, if *M. genitalium* infection is suspected.

Differences		
Item	**Device**	**Predicate Device**
	Cepheid Xpert CT/NG	**Aptima Mycoplasma genitalium Assay**
Assay Targets	DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG)	Ribosomal RNA from *Mycoplasma genitalium*
Instrument System	Cepheid GeneXpert Instrument System	Panther System
Assay Controls	Internal sample processing control (SPC), sample adequacy control (SAC), and probe check control (PCC). External controls available	Internal Control (IC). External calibrators available.

The Xpert Swab Specimen Collection Kit is substantially equivalent to the following predicate devices:

- Cepheid Xpert Vaginal/Endocervical Specimen Collection Kit [510(k) #K173840]
- Becton Dickinson BD MAX UVE Specimen Collection Kit [510(k) #K043144]

Similarities and differences between the Cepheid Xpert Swab Specimen Collection Kit and the predicate collection devices are shown in Table 8-2.

Table 8-2: Comparison of Similarities and Differences of the Xpert Swab Specimen Collection Kit with the Predicate Device Collection Kits

Item	Device	Predicate Devices	
	Cepheid Xpert Swab Specimen Collection Kit	**Cepheid Xpert Vaginal/Endocervical Specimen Collection Kit**	**BD MAX UVE Specimen Collection Kit**
510(k) Number	K190441	K173840	K151589
Intended Use	The Xpert® Swab Specimen Collection Kit is designed to collect, preserve, and transport endocervical, vaginal, pharyngeal, and rectal swab specimens. This transport system is for use for testing with Xpert tests.	The Cepheid® Xpert® Vaginal/Endocervical Specimen Collection Kit is designed to collect, preserve, and transport *Chlamydia trachomatis, Neisseria gonorrhoeae*, and *Trichomonas vaginalis* DNA in endocervical swab specimens (collected by a clinician) and patient-collected vaginal swab specimens (collected in a clinical setting) from symptomatic and asymptomatic women prior to analysis with the Xpert CT/NG Assay and the Xpert TV Assay.	The BD MAX UVE Specimen Collection Kit is intended to be used in clinical settings according to the instructions provided for collection and transport of vaginal and endocervical swab specimens, in addition to the preservation of urine from males and females. This transport system is for use for testing with the BD MAX products.
Description	Contains an individually packaged sterile large cleaning swab (for endocervical samples) and a package containing an individually packaged sterile collection swab (for vaginal and endocervical sampling) and an Xpert Swab Transport Reagent tube. The collection swab is placed into the Transport Reagent Tube after swab sampling to stabilize the nucleic acid until sample preparation.	Contains an individually packaged sterile large cleaning swab (for endocervical samples) and a package containing an individually packaged sterile collection swab (for vaginal and endocervical sampling) and an Xpert Swab Transport Reagent tube. The collection swab is placed into the Transport Reagent Tube after swab sampling to stabilize the nucleic acid until sample preparation.	Contains a BD MAX Specimen Collection Swab, a graduated transfer pipette and a BD MAX UVE Sample Buffer Tube. The BD MAX Specimen Collection Swab is a sterile polyester swab. The swab is placed into the BD MAX UVE Sample Buffer Tube. For urine specimens, a sample of urine is transferred directly into the BD MAX UVE Sample Buffer Tube using the graduated transfer pipette.

Non-Clinical Studies:

Analytical Sensitivity

Pooled Pharyngeal Swab Matrix

Purified and titered elementary bodies from two CT serovars, ATCC vr885 serovar D and ATCC vr879 serovar H, were each tested in a sample matrix of negative pooled clinical pharyngeal swab matrix. Replicates of 20 were evaluated at five concentrations for CT serovar D and for CT serovar H and LoDs were estimated by probit analysis. The claimed LoDs were confirmed by analyzing at least 20 replicate samples with elementary bodies diluted to the estimated LoD concentrations. For this study, the claimed LoD is defined as the lowest concentration at which 95% of at least 20 replicates are positive.

The claimed LoD for purified CT serovar D elementary bodies (EB) in pharyngeal swab matrix is 161 EB/mL (Table 8-3). The claimed LoD for purified CT serovar H elementary bodies in pharyngeal swab matrix is 225 EB/mL (Table 8-3).

Table 8-3: LoD of Two CT Serovars in Pooled Pharyngeal Swab Matrix

Organism	LoD
CT ATCC vr885 serovar D (EB/mL)	161
CT ATCC vr879 serovar H (EB/mL)	225

Two NG strains (ATCC 19424 and ATCC 49226) were tested. Replicates of 20 were evaluated at five concentrations. The LoD was estimated by probit analysis.

The LoD for NG, estimated by probit analysis, is 6.4 – 7.1 CFU/mL in a pooled pharyngeal swab matrix (Table 8-4).

Table 8-4: LoD of Two NG Strains in Pooled Pharyngeal Swab Matrix

Organism	LoD
NG ATCC 19424 (CFU/mL)	7.1
NG ATCC 49226 (CFU/mL)	6.4

Pooled Rectal Swab Matrix

Purified and titered elementary bodies from two CT serovars, ATCC vr885 serovar D and ATCC vr879 serovar H, were each tested in a sample matrix of negative pooled clinical rectal swab matrix. Replicates of 20 were evaluated at five concentrations for CT serovar D and for CT serovar H and LoDs were estimated by probit analysis. The claimed LoDs were confirmed by analyzing at least 20 replicate samples with elementary bodies diluted to the estimated LoD concentrations. For this study, the claimed LoD is defined as the lowest concentration at which 95% of at least 20 replicates are positive.

The claimed LoD for purified CT serovar D elementary bodies (EB) in rectal swab matrix is 88 EB/mL (Table 8-5). The claimed LoD for purified CT serovar H elementary bodies in rectal swab matrix is 161 EB/mL (Table 8-5).

Table 8-5: LoD of Two CT Serovars in Pooled Rectal Swab Matrix

Organism	LoD
CT ATCC vr885 serovar D (EB/mL)	88
CT ATCC vr879 serovar H (EB/mL)	161

Two NG strains (ATCC 19424 and ATCC 49226) were tested. Replicates of 20 were evaluated at five concentrations. The LoD was estimated by probit analysis.

The LoD for NG, estimated by probit analysis, is 4.9 – 5.3 CFU/mL in a pooled rectal swab matrix (Table 8-6).

Table 8-6: LoD of Two NG Strains in Pooled Rectal Swab Matrix

Organism	LoD
NG ATCC 19424 (CFU/mL)	4.9
NG ATCC 49226 (CFU/mL)	5.3

Analytical Reactivity (Inclusivity)

Fourteen CT serovars and twenty NG strains were tested in this study. Testing was performed using CT and NG cultures that were diluted in pooled clinical pharyngeal and pooled clinical rectal swab matrices at levels near the analytical LoD. Three replicates were tested for each strain. Results are shown in Table 8-7 and Table 8-8 for CT serovars and NG strains, respectively. All 14 CT serovars and all 20 NG strains were correctly reported using the Xpert CT/NG test.

Table 8-7: Analytical Reactivity Results of the Xpert CT/NG Assay with CT Serovars in Pooled Pharyngeal and Rectal Swab Matrices

C. trachomatis serovar	Concentration Tested in Pharyngeal Swab Matrix	Concentration Tested in Rectal Swab Matrix	Assay Result	
			CT	NG
A	1800 EB/mL	1800 EB/mL	POS	NEG
B	9 EB/mL	8.1 EB/mL	POS	NEG
Ba	0.9 EB/mL	0.81 EB/mL	POS	NEG
C	900 EB/mL	322 EB/mL	POS	NEG
E	450 EB/mL	322 EB/mL	POS	NEG
E/SW2	0.9 IFU/mL[a]	0.81 IFU/mL[a]	POS	NEG
F	450 EB/mL	322 EB/mL	POS	NEG
G	900 EB/mL	644 EB/mL	POS	NEG
I	0.18 EB/mL	0.16 EB/mL	POS	NEG
J	900 EB/mL	644 EB/mL	POS	NEG
K	900 EB/mL	644 EB/mL	POS	NEG
LGV I	450 EB/mL	322 EB/mL	POS	NEG
LGV II	450 EB/mL	322 EB/mL	POS	NEG
LGV III	450 EB/mL	644 EB/mL	POS	NEG

a. IFU/mL = Infectious units per mL.

Table 8-8: Analytical Reactivity Results of the Xpert CT/NG Assay with NG Strains in Pharyngeal and Rectal Swab Matrices

N. gonorrhoeae Strain	Concentration Tested in Pharyngeal Swab Matrix (CFU/mL)	Concentration Tested in Rectal Swab Matrix (CFU/mL)	Assay Result	
			CT	NG
9793	14.2	10.6	NEG	POS
9830	14.2	10.6	NEG	POS
19999	14.2	10.6	NEG	POS
27629	14.2	10.6	NEG	POS
27630	14.2	10.6	NEG	POS
27631	14.2	10.6	NEG	POS
31148	14.2	10.6	NEG	POS
31397	14.2	10.6	NEG	POS
31399	14.2	10.6	NEG	POS

N. gonorrhoeae Strain	Concentration Tested in Pharyngeal Swab Matrix (CFU/mL)	Concentration Tested in Rectal Swab Matrix (CFU/mL)	Assay Result	
			CT	NG
31400	14.2	10.6	NEG	POS
1170	14.2	42.4	NEG	POS
6395	14.2	10.6	NEG	POS
13281	14.2	10.6	NEG	POS
34447	14.2	10.6	NEG	POS
37541	14.2	10.6	NEG	POS
10226	14.2	10.6	NEG	POS
10227	14.2	10.6	NEG	POS
10932	14.2	10.6	NEG	POS
11472	14.2	10.6	NEG	POS
50348	14.2	10.6	NEG	POS

Analytical Specificity (Cross-reactivity and Competitive Interference)

Forty-one microorganisms potentially present in pharyngeal flora (Table 8-9) and forty-three microorganisms potentially present in rectal flora (see Table 8-10) were tested using Xpert CT/NG. The microorganisms were tested in the presence (competitive interference) and absence (cross-reactivity) of 2X LoD CT (Serovar D) and NG (ATCC 49226) organisms and were diluted into pooled clinical negative pharyngeal swab matrix or pooled clinical negative rectal swab matrix for testing. Bacterial strains were tested in triplicate at a concentration of at least 10^6 CFU/mL except for *Treponema denticola,* which was tested at 1.92 x 10^6 genome equivalents/mL. Parasites were tested at 1 x 10^6 cells/mL except for *Entamoeba histolytica,* which was tested at 1 x 10^5 CFU/mL and viruses were tested at 1 x 10^5 $TCID_{50}$/ml or 1 x 10^5 IFU/mL. Positive and negative controls were included in the study. All CT and NG positive samples remained positive and all CT and NG negative samples remained negative, indicating that there was no interference or cross-reactivity with the results of the Xpert CT/NG test for these microorganisms.

Table 8-9: Potential Cross-reacting/Competitive Interfering Microorganisms in Pooled Pharyngeal Swab Matrix

Actinobacillus actinomycetemcomitans	*Klebsiella pneumoniae*	*Staphylococcus aureus*
Adenovirus	*Lactobacillus acidophilus*	*Staphylococcus epidermidis*
Arcanobacterium haemolyticum	*Lactobacillus lactis*	*Streptococcus anginosus*
Bordetella pertussis	*Moraxella catarrhalis*	*Streptococcus dysgalactiae*
Campylobacter rectus	*Mycoplasma pneumoniae*	*Streptococcus mitis*
Candida albicans	*Neisseria flavescens*	*Streptococcus mutans*
Coronavirus	*Peptostreptococcus micros*	*Streptococcus pneumoniae*
Corynebacterium diphtheriae	*Porphyromonas gingivalis*	*Streptococcus pyogenes*
Fusobacterium necrophorum	*Prevotella bivia*	*Streptococcus salivarius*
Haemophilus influenzae	*Prevotella oralis*[a]	*Streptococcus sanguinis*
Herpes virus	*Pseudomonas aeruginosa*	*Tannerella forsythia*[b]
Human influenza virus A	*Respiratory syncytial virus*	*Treponema denticola*[c]
Human influenza virus B	Rhinovirus	*Veillonella parvula*
Human metapneumovirus	*Saccharomyces cerevisiae*	

a. *Bacteroides oralis* is *Prevotella oralis*.
b. *Bacteriodes forsythus* is *Tannerella forsythia*.
c. Genomic DNA tested.

Table 8-10: Potential Cross-reacting/Competitive Interfering Microorganisms in Pooled Rectal Swab Matrix

Acinetobacter baumannii	*Fusobacterium necrophorum*	*Providencia stuartii*
Anaerococcus tetradius	*Fusobacterium nucleatum*	*Pseudomonas aeruginosa*
Anaerococcus hydrogenalis	*Giardia lamblia*	*Salmonella enterica sb enterica sv minnesota*
Bacteroides fragilis	*Helicobacter pylori*	*Salmonella enterica sb enterica sv typhimurium*
Bifidobacterium adolescent	*Klebsiella oxytoca*	*Shigella flexneri*
Campylobacter jejuni	*Lactobacillus acidophilus*	*Shigella sonnei*
Candida albicans	*Lactobacillus delbreueckii*	*Staphylococcus aureus*
Citrobacter freundii	*Listeria monocytogenes*	*Staphylococcus epidermidis*
Clostridium difficile	*Morganella morganii*	*Streptococcus agalactiae*
Entamoeba histolytica	Norovirus	*Streptococcus dysgalactiae*
Enterobacter cloacae	*Peptostreptococcus anaerobius*	*Vibrio cholerae*
Enterococcus faecalis	*Plesiomonas shigelloides*	*Vibrio parahaemolyticus*
Enterococcus faecium	*Prevotella bivia*	*Yersinia enterocolitica*
Enterovirus	*Prevotella oralis*	
Escherichia coli	*Proteus mirabilis*	

Interfering Substances

Potentially interfering exogenous substances were diluted in pooled clinical pharyngeal swab and pooled clinical rectal swab matrices containing two different mixtures of CT and NG cells. The first mixture contained 3x LoD CT serovar D and NG strain ATCC 49226. The second mixture contained 3x LoD CT serovar H and NG strain ATCC 19424.

There was no assay interference in the presence of the substances at the concentrations tested for pharyngeal swab matrix (Table 8-11) and rectal swab matrix (Table 8-12).

Table 8-11: Potentially Interfering Substances Tested in Pooled Pharyngeal Swab Matrix

Potentially Interfering Substances to be Evaluated	Concentration Tested
Mucin (pig gastric mucin)	25 mg/mL
Whole human blood	5% v/v
Mouthwash (Cool Mint Listerine, antiseptic)	5% v/v
Cough Medicine Guaifenesin (Guaiacol glyceryl)	5 mg/mL
Cough Medicine Dextromethorphan HBr	100 µg/mL
Antibiotic (Penicillin G)	1.2 mg/mL
Antibiotic (Erythromycin)	15 µg/mL
Sugar-containing cold and flu remedies (Acetaminophen)	5% v/v
Chloraseptic	5% v/v
Salt-modifying remedy (sodium chloride)	50% v/v
Foods/drinks that increase salivary viscosity (milk)	5% v/v
pH Modifying Remedy (orange juice)	5% v/v
Cold Sore medication Abreva	5% v/v

Table 8-12: Potentially Interfering Substances Tested in Pooled Rectal Swab Matrix

Potentially Interfering Substances to be Evaluated	Concentration Tested
Barium sulfate	0.25% w/v
Ciprofloxacin	0.25% w/v
Condom	1 condom (#)
Cortizone	0.25% w/v
ExLax	0.25% w/v
Fecal fat (Stearic acid/Palmitic acid/Cholesterol)	0.25% w/v
Imodium	0.25% w/v
K-Y Jelly	0.25% w/v
Milk of Magnesia	0.25% w/v
Mineral Oil	0.25% w/v
Neosporin (Polymixin B/ Neomycin/Bacitracin)	0.25% w/v
Nystatin	0.25% w/v
Pepcid	0.25% w/v
Pepto-Bismol	0.25% w/v
Preparation H	0.25% w/v
Prilosec	0.25% w/v
Saline	0.25% w/v
Tagamet	0.25% w/v
Vagisil	0.25% w/v

Carry-Over Contamination Study

Please refer to the previously FDA-cleared 510(k) #K121710 for additional information.

Linearity

Please refer to the previously FDA-cleared 510(k) #K121710 for additional information.

Clinical Performance Characteristics:

Reproducibility and Precision

Please refer to the previously FDA-cleared 510(k) #K121710 for additional information.

Clinical Performance Study

Performance characteristics of Xpert CT/NG were determined in a multi-site prospective investigational study at 9 US institutions by comparing Xpert CT/NG to the anatomic site infected status (ASIS) algorithm based on combined results from two NAAT tests, with a tiebreaker NAAT test if applicable.

The anatomic site was considered to be infected if both of the reference test results were positive. The anatomic site is considered to be not infected when both reference test results were negative. If there was discordance between the reference tests, an additional NAAT was tested as a tiebreaker. In this case, agreement of 2/3 of the reference NAATs determined the ASIS result. If two tests were equivocal or one equivocal and one not run, the third test result stood as the ASIS if positive or negative. If two tests were not run, the ASIS was considered invalid and excluded from the analysis. The tiebreaker test was run by the lab if any NAAT was not concordant with the others and interpreted only in the case of discordant results between the two planned reference tests for each assay. As the tiebreaker test was not a combination test, the tiebreaker was only run for the organism with disagreement (e.g., if NG disagrees and CT agrees, the tiebreaker was only run for NG).

Study participants included consenting adults seeking sexually transmitted disease (STD) testing at the participating clinics, which included clinics focused on sexually transmitted diseases, women's health, student health and family planning , as well as clinics specializing in lesbian, gay, bisexual, and transgender (LGBT) health. Potential subjects were identified, assessed for eligibility and approached for informed consent. Both symptomatic and asymptomatic individuals were included in the study population. The study specimens consisted of prospectively collected rectal and pharyngeal swabs. Performance of Xpert CT/NG was calculated relative to the ASIS for each of the two sample types.

A total of 2767 study participants were enrolled in the study, of which 2577 pharyngeal swab and 2538 rectal swab specimens were eligible for inclusion in the data analyses. One hundred and ninety (190) pharyngeal specimens were excluded from the data analyses due to the following reasons: 167 for temperature excursions during shipment, 4 participants withdrew consent, 2 specimens shipment errors, 2 post-swab collection

errors, 1 specimen not collected, 1 participant receiving antibiotics, and 13 specimens with Xpert results not available or non-determinate. Two hundred and twenty-nine (229) rectal specimens were excluded from the data analyses due to the following reasons: 167 for temperature excursions during shipment, 6 participants withdrew consent, 5 specimens shipment errors, 2 post-swab collection errors, 1 specimen not collected, 1 participant receiving antibiotics, and 46 specimens with Xpert results not available or non-determinate.

Among the study participants included in the data analyses for pharyngeal swab performance 20.8% were female at birth and 79.2% were male at birth. The average age was 33.8 years (range = 18 to 76 years).

Among the study participants included in the data analyses for rectal swab performance 20.9% were female at birth and 79.1% were male at birth. The average age was 33.7 years (range = 18 to 76 years).

Of the 2572 study participants eligible for inclusion in the pharyngeal and rectal swab analyses for CT detection, 0.9% (22/2572) were positive for CT by pharyngeal swab and rectal swab by ASIS. Of the 2573 study participants eligible for inclusion in the pharyngeal and rectal swab analyses for NG detection, 3.7% (95/2573) were positive for NG by pharyngeal swab and rectal swab.

Among the 5163 tests performed, 198 (3.8%) had to be retested due to ERROR, INVALID or NO RESULT outcomes. Of those, 151 specimens yielded valid results upon repeat assay (2 specimens were not retested). The overall valid reporting rate of the assay was 99.1% (5116/5163).

***Chlamydia trachomatis* Performance Results – Pharyngeal and Rectal Swabs**
Results from Xpert CT/NG were compared to the ASIS algorithm for determination of sensitivity and specificity. Results for CT by symptomatic status are shown in Table 8-13.

Table 8-13: Xpert CT/NG vs. ASIS for CT Detection by Symptomatic Status – Pharyngeal Swabs and Rectal Swabs

Specimen	Status	n	TP	FP	TN	FN	Prev %	Sensitivity % (95 CI)	Specificity % (95 CI)
PS	Sym	306	9	0	297	0	2.9	100.0% (70.1-100.0)	100.0% (98.7%-100.0)
	Asym	2269	38	8	2221	2	1.8	95.0% (83.5-98.6)	99.6% (99.3-99.8)
	All	2575	47	8	2518	2	1.9	95.9% (86.3-98.9)	99.7% (99.4-99.8)
RS	Sym	188	22	1	160	5	14.4	81.5% (63.3-91.8)	99.4% (96.6-99.9)
	Asym	2347	175	14	2131	27	8.6	86.6% (81.3-90.7)	99.4% (98.9-99.6)
	All	2535	197	15	2291	32	9.0	86.0% (80.9-89.9)	99.4% (98.9-99.6)

TP=true positive**, FP**=false positive, **TN**=true negative, **FN**=false negative, **PS**=pharyngeal swab, **RS**=rectal swab

***Neisseria gonorrhoeae* Performance Results – Pharyngeal and Rectal Swabs**

Results from Xpert CT/NG were compared to the ASIS algorithm for determination of sensitivity and specificity. Results for NG by symptomatic status are shown in Table 8-14.

Table 8-14: Xpert CT/NG vs. ASIS for NG Detection by Symptomatic Status – Pharyngeal Swabs and Rectal Swabs

Specimen	Status	n	TP	FP	TN	FN	Prev %	Sensitivity % (95 CI)	Specificity % (95 CI)
PS	Sym	306	39	3	261	3	13.7	92.9% (81.0-97.5)	98.9% (96.7-99.6)
	Asym	2269	156	26	2079	8	7.2	95.1% (90.7-97.5)	98.8% (98.2-99.2)
	All	2575	195	29	2340	11	8.0	94.7% (90.7-97.0)	98.8% (98.3-99.2)
RS	Sym	188	38	0	149	1	20.7	97.4% (86.8-99.6)	100.0% (97.5-100.0)
	Asym	2348	149	9	2173	17	7.1	89.8% (84.2-93.5)	99.6% (99.2-99.8)
	All	2536	187	9	2322	18	8.1	91.2% (86.6-94.4)	99.6% (99.3-99.8)

TP=true positive**, FP**=false positive, **TN**=true negative, **FN**=false negative, **PS**=pharyngeal swab, **RS**=rectal swab

Table 8-15 and Table 8-16 show the number of results designated as infected or not infected with CT based on the ASIS algorithm for pharyngeal and rectal specimens, respectively.

Table 8-15: Anatomic Site Infected Status – Pharyngeal CT

ASIS[a]	NAAT1	NAAT2	Tiebreaker NAAT	Xpert	Total
NI	-	-	NA[b]	-	2504
NI	NR[c]	-	-	-	6
NI	-	-	NA	+	4
NI	-	+	-	-	5
NI	+	-	-	-	2
NI	-	+	-	+	1
NI	+	-	-	+	1
NI	EQ[d]	-	-	-	1
IND[e]	+	-	EQ	+	1
IND	NR	-	+	+	1
Total Not Infected					2526
I	+	+	NA	+	40
I	-	+	+	+	5
I	+	-	+	+	2
I	+	+	NA	-	1
I	-	+	+	-	1
Total Infected					49

a. ASIS = Anatomic Site Infected Status: NI=Not Infected; I=Infected; IND=indeterminate, considered not infected.
b. NA=Not applicable; both reference NAAT tests agreed.
c. NR = Not run
d. EQ=Equivocal
e. IND=Indeterminate. Considered infected if Xpert Negative and not infected if Xpert positive to evaluate under worst-case scenario.

Table 8-16: Anatomic Site Infected Status – Rectal CT

ASIS[a]	NAAT1	NAAT2	Tiebreaker NAAT	Xpert	Total
NI	-	-	NA[b]	-	2221
NI	NR[c]	-	-	-	47
NI	-	-	NA	+	12
NI	+	-	-	-	11
NI	-	+	-	-	10
NI	-	+	-	+	2
NI	-	EQ[d]	-	-	2
IND[e]	+	EQ	-	+	1
Total Not Infected					2306
I	+	+	NA	+	172
I	-	+	+	+	14
I	-	+	+	-	11
I	+	+	NA	-	9
I	+	-	+	+	6
I	+	-	+	-	5
I	+	EQ	+	+	3
I	-	EQ	+	-	2
I	NR	+	+	+	2
I	+	EQ	+	-	1
I	+	EQ	NR	-	1
I	NR	E	+	-	1
IND	-	NR	+	-	1
IND	+	-	NR	-	1
Total Infected					**229**

a. ASIS = Anatomic Site Infected Status: NI=Not Infected; I=Infected; IND=indeterminate, considered not infected.
b. NA=Not applicable; both reference NAAT tests agreed.
c. NR = Not run
d. EQ=Equivocal
e. IND=Indeterminate. Considered infected if Xpert negative and not infected if Xpert positive to evaluate under worst-case scenario.

Table 8-17 and Table 8-18 show the number of results designated as infected or not infected with NG based on the ASIS algorithm for pharyngeal and rectal specimens, respectively.

Table 8-17: Anatomic Site Infected Status – Pharyngeal NG

ASIS[a]	NAAT1	NAAT2	Tiebreaker NAAT	Xpert	Total
NI	-	-	NA[b]	-	2317
NI	-	-	NA	+	19
NI	-	+	-	-	14
NI	-	+	-	+	4
NI	+	-	-	-	4
NI	+	-	-	+	4
NI	NR[c]	-	-	-	5
NI	-	EQ[d]	-	+	1
IND[e]	-	+	EQ	+	1
Total Not Infected					**2369**
I	+	+	NA	+	175
I	+	+	NA	-	4
I	-	+	+	+	16
I	-	+	+	-	5
I	+	-	+	+	2
I	NR	+	+	+	2
IND	+	EQ	-	-	1
IND	-	EQ	+	-	1
Total Infected					**206**

a. ASIS = Anatomic Site Infected Status: NI=Not Infected; I=Infected; IND=indeterminate, considered not infected.
b. NA=Not applicable; both reference NAAT tests agreed.
c. NR = Not run
d. EQ=Equivocal
e. IND=Indeterminate. Considered infected if Xpert negative and not infected if Xpert positive to evaluate under worst-case scenario.

Table 8-18: Anatomic Site Infected Status – Rectal NG

ASIS[a]	NAAT1	NAAT2	Tiebreaker NAAT	Xpert	Total
NI	-	-	NA[b]	-	2261
NI	NR[c]	-	-	-	49
NI	-	-	NA	+	6
NI	+	-	-	-	5
NI	-	+	-	-	4
NI	+	-	-	+	2
NI	-	EQ[d]	-	-	2
NI	-	NR	-	-	1
IND[e]	+	EQ	-	+	1
Total Not Infected					**2331**
I	+	+	NA	+	172
I	-	+	+	+	13
I	+	+	NA	-	8
I	-	+	+	-	8
I	+	-	+	+	1
I	+	EQ	+	+	1
I	NR	+	+	-	1
IND	-	EQ	+	-	1
Total Infected					**205**

a. ASIS = Anatomic Site Infected Status: NI=Not Infected; I=Infected; IND=indeterminate, considered not infected.
b. NA=Not applicable; both reference NAAT tests agreed.
c. NR = Not run
d. EQ=Equivocal
e. IND=Indeterminate. Considered infected if Xpert negative and not infected if Xpert positive to evaluate under worst-case scenario.

Conclusions

The results of the nonclinical analytical and clinical performance studies summarized above demonstrate that the Xpert CT/NG test performance is equivalent to the predicate.