K063664

5.0 510(k) SUMMARY

JAN 25 2007

GEN-PROBE® APTIMA® Assay for *Neisseria gonorrhoeae*

General Information

Submitted By:	Company Contact:
Gen-Probe Incorporated 10210 Genetic Center Drive San Diego, California 92121 phone: (858) 410-8000 fax: (858) 410-8622	E. Joseph McMullen Associate Director, Regulatory Affairs **phone: (858) 410-8649** fax: (858) 410-8622 e-mail: josephm@gen-probe.com

Trade Name: GEN-PROBE® APTIMA® Assay for *Neisseria gonorrhoeae*

Common or Usual Name: Ribosomal RNA (rRNA) target-amplified nucleic acid probe test for the *in vitro* diagnostic detection of *Neisseria gonorrhoeae*

Classification Name: DNA Reagents, *Neisseria*

Classification Code:

Medical Specialty: Microbiology

Product Code: LSL

Registration Number: CFR 866.3390

Device Class: 2

Description: Reagents used to identify Neisseria spp. directly from clinical specimens or cultured isolates derived from clinical specimens. The identification aids in the diagnosis of disease caused by bacteria belonging to the genus Neisseria, such as epidemic cerebrospinal meningitis, meningococcal disease, and gonorrhea, and also provides epidemiological information on diseases caused by these microorganisms.

Substantially Equivalent Devices

GEN-PROBE® APTIMA® Assay for *Neisseria gonorrhoeae*

Device Description

Clearance of this premarket notification extends the clinical performance claims of the commercially available GEN-PROBE®APTIMA® Assay for *Neisseria gonorrhoeae* with the testing of gynecological specimens collected in the PreservCyt® Solution and processed with the Cytyc ThinPrep® 2000 System, for use on the TIGRIS® DTS® System. The ancillary kit for this application is commercially available as the GEN-PROBE APTIMA Specimen Transfer Kit. The components of the APTIMA Specimen Transfer Kit include: (1) a transport tube containing transport media with a penetrable cap and (2) specific instructions for use regarding decontamination and specimen processing procedures. The APTIMA Transfer Kit may only be used in conjunction with the APTIMA Assays. Labeling for the transfer kit is provided in Section 13.0.

Intended Use

APTIMA® Assay for Neisseria gonorrhoeae Package Insert:

The APTIMA® Assay for Neisseria gonorrhoeae is a target amplification nucleic acid probe test that utilizes target capture for the in vitro qualitative detection of ribosomal RNA (rRNA) from Neisseria gonorrhoeae (GC) to aid in the diagnosis of gonococcal urogenital disease using the TIGRIS® DTS® Automated Analyzer or semi-automated instrumentation as specified. The assay may be used to test the following specimens from symptomatic individuals: clinician-collected endocervical, vaginal and male urethral swab specimens; and female and male urine specimens. The assay may be used to test the following specimens from asymptomatic individuals: clinician-collected endocervical and vaginal swab specimens; patient-collected[1] vaginal swab specimens; and female and male urine specimens. The assay is also intended for use with the testing of gynecological specimens, from both symptomatic and asymptomatic patients collected in the PreservCyt® Solution and processed with the Cytyc ThinPrep® 2000 System.

[1] Patient-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated. The vaginal swab specimen collection kit is not for home use.

Ancillary Kit Package Insert

The GEN-PROBE APTIMA Specimen Transfer Kit is only for use with GEN-PROBE APTIMA Assays for the detection of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae*. The GEN-PROBE APTIMA Specimen Transfer Kit allows for APTIMA Assay testing of gynecological specimens collected and processed with the Cytyc ThinPrep® 2000 System according to the instructions provided. No changes have been made to the Specimen Transfer Kit package insert as provided in K062440, GEN-PROBE APTIMA Assay for *Neisseria gonorrhoeae* with use of Cytyc ThinPrep (liquid pap transport) cleared on November 7, 2006. The Specimen Transfer Kit package insert is being provided with this application for reference. There have been no changes.

Summary of Non-Clinical (Analytical Laboratory) Performance Data

Limit of Detection (Analytical Sensitivity)

To assess analytical sensitivity of *N. gonorrhoeae* on the TIGRIS DTS System, *N. gonorrhoeae* rRNA was spiked into a post-processed PreservCyt liquid Pap specimen pool at the analytical sensitivity claim, or the equivalent of fifty CFU per assay (250 fg of total GC rRNA). A summary of the percent positivity of *N. gonorrhoeae* in post-processed PreservCyt liquid Pap specimen is shown in Table 5.0-01.

Table 5.0-01 Summary of GC Analytical Sensitivity at 50 CFU (250fg)/assay

Specimen Type	N	Positive Results	Percent Positive (95% C.I.)
Post-processed PreservCyt liquid Pap	60	60	100% (95.1 – 100)

Analytical Specificity

Twenty-four (24) culture isolates were selected from the panel of one hundred fifty four (154) organisms originally tested for the APTIMA GC assay (K043144). These included the 17 organisms that are most closely related phylogenetically to *N. gonorrhoeae*. Testing was performed on three different TIGRIS DTS Systems. The culture isolates were tested in PreservCyt liquid Pap media and Swab Transport Media (STM) prepared in a one-part PreservCyt liquid Pap media and three-part STM ratio. This mimics the PreservCyt liquid Pap specimens. The majority of organisms were tested at a concentration of 1 x 10^6 cells/mL. A list of all organisms tested and their concentrations is provided below in Table 5.0-02.

Table 5.0-02 Analytical Specificity – List of Culture Isolates

ORGANISM	ATCC Number	Organism Preparation	Concentration cells/Ml
Derxia gummosa	15994	Lysate	1 x 10^6
Enterococcus faecalis	19433	Lysate	1 x 10^6
Kingella kingae	23332	Lysate	1 x 10^6
Moraxella osloensis	19976	Lysate	1 x 10^6
*Neisseria cinerea**	14685	Lysate	1 x 10^6
Neisseria elongate	49379	Lysate	1 x 10^6
Neisseria flava	14221	Lysate	1 x 10^6
Neisseria flavescens	13120	Lysate	1 x 10^6
Neisseria lGCamica	23970	Lysate	1 x 10^6
N. meningitidis, Serogroup A	13077	Lysate	1 x 10^6
N. meningitidis, Serogroup B	Clinical isolate #399	Lysate	1 x 10^6
N. meningitidis, Serogroup C	13109	Lysate	1 x 10^6
N. meningitidis, Serogroup C	13110	Lysate	1 x 10^6
N. meningitidis, Serogroup C	13112	Lysate	1 x 10^6
N. meningitidis, Serogroup D	13113	Lysate	1 x 10^6
N. meningitidis, Serogroup W135	43744	Lysate	1 x 10^6
N. meningitidis, Serogroup Y	35561	Lysate	1 x 10^6
Neisseria mucosa	19696	Lysate	1 x 10^6
Neisseria polysaccharea	43768	Lysate	1 x 10^6
Neisseria sicca	29193	Lysate	1 x 10^6

Table 5.0-02 Analytical Specificity – List of Culture Isolates (continued)

ORGANISM	ATCC Number	Organism Preparation	Concentration cells/Ml
*Neisseria subflava**	Clinical isolate #4854	Lysate	1×10^6
Chlamydia pneumoniae	VR1360	Lysate	10,000 TCID50/mL
Chlamydia psittaci	VR601	Lysate	64,000 TCID50/mL
Chlamydia psittaci	VR1369	Lysate	1×10^6 TCID50/mL

* Species shown to cross-react in some amplification assays (Amplicor package insert, 1999; ProbeTec Package Insert, 2001; Farrell, D. J. 1999. J. Clin. Microbiol. 37(2):386-390).

Specimen-Caused Inhibition

The frequency of specimen inhibition observed in the APTIMA GC Assay on the TIGRIS DTS System was determined by evaluating the inhibitory status of 240 negative clinical post-processed PreservCyt liquid Pap specimens. Negative specimens were tested for inhibition by the addition of GC rRNA at the limits of detection (250 fg GC rRNA/assay). Spiked negative specimens yielding GC positive results were considered non-inhibitory, whereas specimens yielding repeatable GC equivocal or negative results were considered inhibitory. The frequencies of inhibition for the specimens tested were calculated by dividing the number of inhibitory specimens by the total number tested for inhibition.

For post-processed PreservCyt liquid Pap specimen, no inhibition was detected. The data is shown in Table 5.0-03.

Table 5.0-03 Results of post-processed PreservCyt liquid Pap Specimen Inhibition Testing

Specimen Type	Inhibitory Specimens		Non-Inhibitory Specimens		Inhibition Frequency
	Number	RLU Range	Number	RLU Range (x1000)	
PreservCyt liquid Pap	0	NA	240	3,402 – 5,148	0% (0/240)

Interference by Whole Blood

Fresh blood was added to clinical post-processed PreservCyt liquid Pap specimen pools, then tested for potential assay interference in the absence and presence of *N. gonorrhoeae* at the estimated rRNA equivalent of fifty GC CFU/assay (250 fg/assay). Specimens were tested on two TIGRIS instruments.

To evaluate blood interference, blood was added to three negative PreservCyt liquid Pap specimen pools to result in a final concentration of 10% (v/v). Subsequently, the PreservCyt liquid Pap specimen pools containing blood was processed with Swab Transport Media at a one-part PreservCyt liquid Pap specimen and three-part STM ratio. One aliquot of each post-processed PreservCyt liquid Pap specimen pool to which no blood was added served as a control.

The post-processed PreservCyt liquid Pap specimen aliquots were tested for the absence and presence of GC rRNA. The data demonstrate that for PreservCyt liquid Pap specimens up to 10% (v/v) blood yielded background signals below the assay cut-off.

For spiked PreservCyt liquid Pap specimens, the data demonstrate that the presence of up to 10% (v/v) blood in the specimen, did not interfere with the recovery of a positive signal.

Summary of Clinical Performance Data

A prospective, multi-center clinical study was conducted to ascertain equivalent performance between the previously validated DTS Systems and the TIGRIS DTS System (TIGRIS System) when performing the APTIMA GC (AGC) Assay (Gen-Probe Incorporated, San Diego, CA) in PreservCyt liquid Pap specimens. Symptomatic and asymptomatic female subjects attending family planning, OB/GYN, public health, and STD clinics were enrolled in the clinical study and PreservCyt liquid Pap specimens were collected. The PreservCyt liquid Pap specimens were processed for cytology and then transferred for testing in accordance with the ThinPrep 2000 Processor Operator's Manual and the APTIMA Specimen Transfer Kit package insert, respectively. These specimens were first screened using FDA-cleared applications of the APTIMA COMBO 2 (AC2) Assay. Based on the screening results, these specimens were then assigned for use in the Clinical Specimen and/or Clinical Panel study. Specimens with final invalid or equivocal screening results were not selected for testing in the APTIMA GC Clinical Specimen study.

In a Clinical Specimen study, 51 PreservCyt specimens were tested with the AGC Assay on the DTS Systems and on the TIGRIS DTS System. Results from the DTS Systems and TIGRIS DTS System were compared by calculating percent agreement. Table 5.0-04 shows a summary of the DTS Systems and TIGRIS System results, the overall, positive, and negative agreements (with 95% CI) by symptom status. For 34 symptomatic and 17 asymptomatic female subjects with PreservCyt specimens, agreements were 100% (51/51). Therefore, performance of the GC Assay on the TIGRIS System was equivalent to performance on the DTS Systems in PreservCyt specimens.

A Clinical Panel study performed demonstrated equivalent performance between the DTS Systems and the TIGRIS System when using the AGC Assay in Gen-Probe-prepared clinical panels. Residual volume from PreservCyt specimens from female subjects with negative GC results (as determined by screening with the AC2 Assay) were pooled and confirmed to be negative by testing with the AGC Assay on the DTS Systems.

The negative PreservCyt specimens were then pooled and spiked or not spiked with GC ribosomal RNA (rRNA) to create five panel members of varying GC concentration. Thirty (30) aliquots of each GC-positive panel member and 12 aliquots of the GC-negative panel member resulted in a panel consisting of 132 replicates. The panel was tested with the AGC Assay on the DTS Systems and on the TIGRIS System at one testing site. All samples had final valid results on both systems. Results from testing on the DTS Systems and the TIGRIS System were compared by calculating percent agreements. The percent agreement for each level of rRNA in PreservCyt liquid Pap specimens with the expected GC results for the TIGRIS System and for the DTS Systems was 100% for all panel members (Table 5.0-05).

Table 5.0-04: Clinical Specimen Agreement Study: Positive, Negative, and Overall Agreements by Symptom Status in PreservCyt Liquid Pap Specimens

Symptom	N	DTS+ TIGRIS+	DTS+ TIGRIS-	DTS- TIGRIS+	DTS- TIGRIS-	Positive % Agreement (95% CI)	Negative % Agreement (95% CI)	Overall % Agreement (95% CI)
Sympt.	34	28	0	0	6	100 (87.7-100)	100 (54.1-100)	100 (89.7-100)
Asympt.	17	12	0	0	5	100 (73.5-100)	100 (47.8-100)	100 (80.5-100)
All	51	40	0	0	11	100 (91.2-100)	100 (71.5-100)	100 (93.0-100)

"+" denotes a positive result, "-" a negative result, CI = confidence interval

Table 5.0-05 GC rRNA Spiked Clinical Panel Agreement Study in PreservCyt Liquid Pap Specimens

Panel Member	Concentration (fg rRNA/Assay)	Replicates	TIGRIS % Agreement	DTS % Agreement	Overall % Agreement between TIGRIS and DTS (95% CI)
No Target	0	12	100	100	100 (97.2-100)
Very Low	25	30	100	100	
Low	250	30	100	100	
Medium	2,500	30	100	100	
High	25,000	30	100	100	

The findings of the Clinical Specimen Study demonstrate equivalent performance between AGC Assay on the DTS Systems and the TIGRIS System when using Cytyc® PreservCyt (ThinPrep) processed liquid Pap specimens, and support the proposed intended use of the AGC Assay on the TIGRIS System.

Conclusions from Non-Clinical and Clinical Data

The non-clinical and clinical study results support the use of the cleared AGC Assay using PreservCyt Solution for specimen collection and processed with the Cytyc ThinPrep® 2000 System, on the TIGRIS® DTS® Automated Analyzer.

The data demonstrate reasonable evidence that when the AGC Assay with the APTIMA Specimen Transfer Kit on the TIGRIS® DTS® System are labeled as proposed, the AGC Assay continues to be safe and effective for its stated intended use.

Contraindications and Cautions

There are no contraindications or cautions

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Mr. E. Joseph McMullen
Associate Director, Regulatory Affairs
Gen-Probe Incorporated
10210 Genetic Center Drive
San Diego, CA 92121

JAN 25 2007

Re: k063664
Trade/Device Name: GEN-PROBE APTIMA Assay® for *Neisseria gonorrhoeae* on the TIGRIS® DTS® System
Regulation Number: 21 CFR 866.3390
Regulation Name: *Neisseria* spp. direct serological test reagents
Regulatory Class: Class I
Product Code: LSL
Dated: December 7, 2006
Received: December 8, 2006

Dear Mr. McMullen:

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. 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.

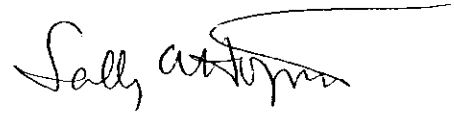
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish 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 Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240)276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

4.0 INDICATIONS FOR USE STATEMENT

510(k) Number: K063664

(if known)

Device Name: GEN-PROBE APTIMA® Assay for *Neisseria gonorrhoeae* on the TIGRIS® DTS® System

Indications for Use:

The GEN-PROBE APTIMA® Assay for *Neisseria gonorrhoeae* is a target amplification nucleic acid probe test that utilizes target capture for the *in vitro* qualitative detection of ribosomal RNA (rRNA) from *Neisseria gonorrhoeae* (GC) to aid in the diagnosis of gonococcal urogenital disease using the TIGRIS® DTS® Automated Analyzer or semi-automated instrumentation as specified. The assay may be used to test the following specimens from symptomatic individuals: clinician-collected endocervical, vaginal and male urethral swab specimens; and female and male urine specimens. The assay may be used to test the following specimens from asymptomatic individuals: clinician-collected endocervical, vaginal swab specimens; patient-collected [1]vaginal swab specimens; and female and male urine. The assay is also intended for use with the testing of gynecological specimens, from both symptomatic and asymptomatic patients collected in the PreservCyt® Solution and processed with the Cytyc ThinPrep® 2000 System.

[1] Patient-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated. The vaginal swab specimen collection kit is not for home use.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) OR Over-the-Counter Use_____ (Part 21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED

Concurrence of CDRH, Office of Device Evaluation (ODE)

K063664

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k)