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SIMPLE 2 TEST – PACKAGE INSERT

(FOR *IN VITRO* DIAGNOSTIC USE)

For Detection of chlamydia and gonorrhea with:

Simple 2 Urine Home Collection Kit (Penile) and Simple 2 Swab Home Collection Kit (Vaginal)

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Intended Use:

The Simple 2 Test is intended for in vitro detection and identification of *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC) in home-collected specimens which are shipped to a clinical laboratory for testing using the Aptima Combo 2 Assay on the Panther System. This product is available over-the-counter (OTC) to consumers 18 years of age and older.

The Simple 2 Test contains all the necessary components to collect urine from male patients (Simple 2 Urine Home Collection Kit (Penile)) or vaginal swabs from female patients (Simple 2 Swab Home Collection Kit (Vaginal)) in their home, or in similar environments, without supervision from a healthcare provider.

The Simple 2 Test Collection Kits may also be used to self-collect specimens in a clinic.

The testing is performed, as determined to be appropriate, based on the results of LetsGetChecked's Suitability Questionnaire.

This test system is not a substitute for visits to a healthcare provider. The information provided by this product should not be used to start, stop, or change any course of treatment unless advised by your healthcare provider.

Testing is limited to the manufacturer, PrivaPath laboratories (d.b.a. LetsGetChecked, Inc.).

Simple 2 Urine Home Collection Kit (Penile)

Urine collection cup

Urine sample tube

Biohazard bag

Tube holder

Kit box

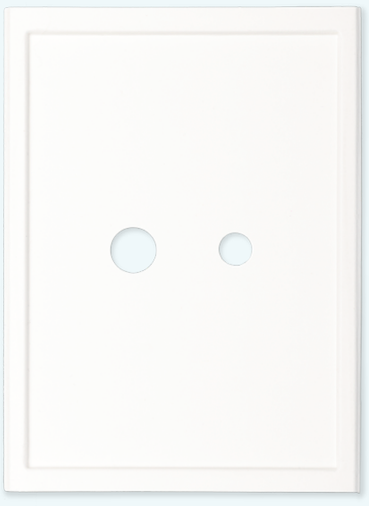
Pipette

Simple 2 Swab Home Collection Kit (Vaginal)

Sample transport tube

Swab

Biohazard bag



Tube holder

Kit box

Summary and Explanation of the Test

Chlamydia trachomatis (CT) and *Neisseria gonorrhoeae* (GC) infections are two of the most common sexually transmitted infections worldwide. In the United States alone, an estimated 1,808,703 (552.8 cases per 100,000 population) cases of CT and 616,392 (188.4 per 100,000 population) cases of GC infections were reported to the Centers for Disease Control and Prevention (CDC) in 2019 (1). CDC STD Treatment Guidelines include testing and screening recommendations for CT and GC and provide guidance on testing methodology and frequency, as well as the appropriate specimen types for specific patient populations.

C. trachomatis are nonmotile, gram-negative, obligate intracellular bacteria. The CT species is comprised of at least fifteen serovars (A, B, Ba, C, D, E, F, G, H, I, J, K, L1, L2, and L3) that can cause disease in humans (2). Serovars D through K are the major cause of genital chlamydial infections in men and women (3). CT can cause nongonococcal urethritis, epididymitis, proctitis, cervicitis, acute salpingitis, and pelvic inflammatory disease (PID) (4, 5, 6, 7). Children born to infected mothers are at significantly higher risk for inclusion conjunctivitis and chlamydial pneumonia (8, 9, 10).

N. gonorrhoeae is the causative agent of gonorrhea. *N. gonorrhoeae* are nonmotile, gram-negative diplococci. The majority of gonococcal infections are uncomplicated lower genital tract infections and may be asymptomatic. However, if left untreated in women, infections can ascend and cause PID, which can manifest as endometritis, salpingitis, pelvic peritonitis, and tubo-ovarian abscesses. A smaller percentage of persons with gonococcal infections may develop disseminated gonococcal infection (DGI) (11, 12). When left untreated in men, urethritis, dysuria, epididymitis, and scrotal pain may persist. CT and GC oropharyngeal infections may present with sore throat although most are asymptomatic. Rectal infections, when symptomatic, may present with discharge, anal itching, soreness, bleeding, and painful bowel movements.

Both chlamydia and gonorrhea infections are often asymptomatic in both males and females which can delay diagnosis and treatment. When left untreated these infections, whether symptomatic or asymptomatic, can have severe and irreversible health consequences including infertility. Both chlamydia and gonorrhea can be successfully treated with antibiotics (13, 14).

The Simple 2 Test is designed for collection of specimens for CT and GC testing in the privacy of the home environment. The Simple 2 Urine Home Collection Kit (Penile) is designed for collection of a urine sample from males, and the Simple 2 Swab Home Collection Kit (Vaginal) is designed for collection of a vaginal swab sample from females. These kits can be purchased online at the LetsGetChecked.com website or through the LetsGetChecked smart phone application.

All materials required for home sample collection, packaging, and shipment are provided in the kit. The instructions, included in each kit, guide the user through each step of the procedure: online kit activation, sample collection, packaging of the sample, and returning the sample to the laboratory. Samples should be shipped on the same day as sample collection.

For individuals with male anatomy, a urine sample is collected. For individuals with female anatomy, a vaginal swab sample is collected. For both urine and vaginal swab samples, the user should carefully follow the detailed sample collection instructions provided with the kit to prevent sample rejection by the laboratory or incorrect test results. The user can contact the LetsGetChecked care team, who will answer any questions about the process of sample collection.

The Simple 2 Test qualitatively detects CT and/or GC rRNA in vaginal swab specimens and penile urine specimens. Samples collected at home with the Simple 2 Home Collection Kits (Penile Urine and Vaginal Swab) are tested in a clinical laboratory with the Aptima Combo 2® Assay. The Aptima Combo 2® Assay utilizes a highly sensitive method of nucleic acid amplification and detection.

Important Cautions:

- Anyone with recent sexual contact with a person known to have a sexually transmitted infection, should visit a healthcare provider for treatment and evaluation as soon as possible (www.cdc.gov/std/ept/default.htm)
- This test is not a substitute for visits to a healthcare provider. The information provided by this product should not be used to start, stop, or change any course of treatment unless advised by your healthcare provider.
- You must be over the age of 18 to use this sample collection kit.
- Please discuss any symptoms that you are experiencing with a healthcare provider.

Warnings and precautions

General

- Please check the expiration date before you use the kit.
  Do not use this kit after its expiration date.
- If you have a condition that makes it difficult to use the test (e.g., problems with vision, handling the test components, or understanding test instructions or results), please contact a healthcare provider prior to collecting the sample.
- The kit must be activated on your own personal LetsGetChecked account, and the sample must be your own. If it becomes apparent that a third-party account has been used, test results will not be released.
- The sample sent to the laboratory must be your own in all circumstances.
- The information you provide on the included laboratory label must match that provided during kit activation.

- Accurate results are dependent on adequate product storage and adherence to the specimen collection and testing procedures. If you do not follow the instructions you may get incorrect results and/or your sample may not be processed by the laboratory.
- A negative test result does not preclude the possibility of infection with other bacteria or viruses.
- Some medications and supplements may impact your test results.
- Protective eyewear and gloves are recommended while using this kit.
- Avoid contact with skin and eyes. If the contents of the tube come in contact with the body, rinse with water. If the contents of the tube are splashed in your eyes, immediately flush your eyes with water. If irritation persists, seek medical advice. Do not ingest.
- Do not remove liquid from the sample tube at any point. If the contents of the tube are spilled, you will need a new sample collection kit.
- Use only the components included in this single use kit for collecting your sample. Do not use the kit if any of the components are missing or damaged.
- The sample must be returned in the kit box.
- Dispose of the leftover kit contents, including the collection cup and pipette, in household trash.
- Choking hazard – This kit contains small parts, which may present a choking hazard to small children. Keep out of reach of children.

Simple 2 Urine Home Collection Kit (Penile):

- The test sample must be collected from a penile urine stream.
- In persons with male anatomy, symptoms such as pain in the pelvis or testicles can be a sign of epididymitis (inflammation of the tube that carries and stores sperm). Contact your healthcare provider if you are experiencing these symptoms.
- Please make sure that hands are free of soap by washing, rinsing, and drying your hands thoroughly before sample collection as presence of soap in the sample can cause incorrect test results.
- Do not use hand sanitizer while using this kit as this can cause incorrect results.
- Transfer the urine from the collection cup to the transport tube immediately after collection.

Simple 2 Swab Home Collection Kit (Vaginal):

- This kit is for vaginal use only. Using the swab in any other parts of the body may result in serious injury or infection.
- Don’t collect your sample during your menstrual period or if you are using a tampon.
- Before collecting your sample, inform your healthcare provider if you are pregnant or if you have symptoms suggestive of pelvic inflammatory disease (including but not limited to recent pelvic pain, pain with sexual intercourse, unusual vaginal discharge, or bad odor).
- The vaginal swab collection kit is not a replacement for a pelvic exam with a healthcare provider. Prompt diagnosis and treatment of pelvic inflammatory disease can help prevent infertility and ectopic pregnancy associated with PID.
- Do not insert the swab into the vagina after it has been placed into the sample transport tube and/or after it has been inserted into the liquid inside the sample transport tube.
- If sample collection is difficult or if you experience any pain during the process, please stop and consult your healthcare provider. In the event that the swab or any other component of the kit becomes lodged or broken internally, or if you experience abnormal bleeding, spotting, discomfort, or pain after using this kit, seek medical attention immediately.

Laboratory Related

Test Related

- The Aptima Combo 2 Assay is for in vitro diagnostic use in a clinical laboratory.
- Follow the Aptima Combo 2 Assay (Panther® System) Package Insert for specimen storage conditions once the sample is received in the laboratory.
- For additional specific warnings, precautions, and procedures to control contamination for the Panther System, consult the Panther System Operator's Manual.

Specimen Related

The Simple 2 Test is for use with the following specimens on the Panther® System:

- Male urine specimens collected with the Simple 2 Urine Home Collection Kit (Penile) according to the instructions provided will be processed by the laboratory.
- Vaginal swab specimens collected with the Simple 2 Swab Home Collection Kit (Vaginal) according to the instructions provided will be processed by the laboratory.

General sample rejection criteria:

- Insufficient/Mismatching identification information, e.g., kits not activated, label missing information, or mismatch between kit information provided online and the label information.
- Foil punctured or damaged on the sample transport tube cap.
- Specimens collected more than 120 hours before receipt at the laboratory.
- Sample collected with an expired kit.

Urine sample rejection criteria

- A sample collected in a sample transport tube other than that provided with Simple 2 Urine Home Collection Kit (Penile).
- The liquid level in the collection tube is outside the two black indicator lines on the tube label.

Vaginal swab sample rejection criteria

- A sample collected in a sample transport tube or with a swab type other than that provided with Simple 2 Swab Home Collection Kit (Vaginal).
- No swab present in the sample transport tube.
- The broken end of swab present in the sample transport tube.
- Level of liquid in the sample transport tube has been altered, e.g., specimen leaked in transit.
- Swab tip not submerged in sample transport tube liquid.

Storage Instructions for the Collection Kits

When the collection kit is received by the customer, it should be stored at room temperature, **not exceeding 86° F (30°C)**

Simple 2 Urine Home Collection Kit (Penile) and
Simple 2 Swab Home Collection Kit (Vaginal):
Storage temperature: 59°F – 86°F (15°C – 30°C)

Sample Collection Materials Provided:

Simple 2 Urine Home Collection Kit (Penile)
(Catalog #: UO01S)
- Urine collection cup
- Urine Sample Transport Tube
- Pipette
- Biohazard bag
- Kit Box
- Home Collection Instructions
- FAQs

Simple 2 Swab Home Collection Kit (Vaginal)
(Catalog #: VS01S)
- Sterile Vaginal Swab
- Sample Transport Tube
- Biohazard bag
- Kit Box
- Home Collection Instructions
- FAQs

Test Result Interpretation for the User:

Chlamydia trachomatis
Positive (Urine Sample or Vaginal Swab):
Your chlamydia test result was positive. This means that the bacteria that causes chlamydia was found in your sample and you will require treatment for the infection. Please contact a healthcare provider.

Negative (Urine Sample):
Your chlamydia test result was negative, which means that the bacteria that causes chlamydia was not found in your sample. There is usually a 2-week window period from the time of exposure for chlamydia to become detectable. If you think you tested too early you will need to repeat the test. A urine test will not identify if you have chlamydia outside of the genital area, for example, oral or rectal chlamydia. If you think you are at risk of chlamydia in other areas, please contact your healthcare provider. If you are experiencing any symptoms, please ensure that you discuss this with your healthcare provider.

Negative (Vaginal Swab):
Your chlamydia test result was negative, which means that the bacteria that causes chlamydia was not found in your sample. There is usually a 2-week window period from the time of exposure for chlamydia to become detectable. If you think you tested too early or you are concerned you may have been exposed to the infection, you will need to repeat the test. A vaginal swab test will not identify if you have chlamydia outside of the genital area, for example, oral or rectal chlamydia. If you think you are at risk of chlamydia in other areas, please contact your healthcare provider. If you are pregnant or experiencing any symptoms, please ensure that you discuss this with your healthcare provider.

Inconclusive (Urine sample or Vaginal Swab)
You have received an inconclusive test result. An inconclusive result means that it is not possible to determine whether your test was positive or negative. There are many reasons why this might happen. Repeat testing may be required. Please ensure that you discuss this with your healthcare provider.

Neisseria gonorrhoeae
Positive (Urine sample or Vaginal Swab):
Your gonorrhea test result was positive. This means that the bacteria that causes gonorrhea was found in your sample and you will require treatment for the infection. Please contact a healthcare provider.

Negative (Urine Sample):
Your gonorrhea test result was negative. This means that the bacteria that causes gonorrhea was not found in your sample. There is usually a 2-week window period from the time of exposure for gonorrhea to become detectable. If you think you tested too early or you are concerned you may have been exposed to the infection, you will need to repeat the test. A urine test will not identify if you have gonorrhea outside of the genital area, for example, oral or rectal gonorrhea. If you think you are at risk of oral or rectal gonorrhea, please contact your healthcare provider. If you are experiencing any symptoms, please ensure that you discuss this with your healthcare provider.

Negative (Vaginal Swab):
Your gonorrhea test result was negative. This means that the bacteria that causes gonorrhea was not found in your sample. There is usually a 2-week window period from the time of exposure for gonorrhea to become detectable. If you think you tested too early or you are concerned you may have been exposed to the infection, you will need to repeat the test. A vaginal swab test will not identify if you have gonorrhea outside of the genital area, for example, oral or rectal gonorrhea. If you think you are at risk of oral or rectal gonorrhea, please contact your healthcare provider. If you are pregnant or experiencing any symptoms, please ensure that you discuss this with your healthcare provider.

Inconclusive (Urine sample or Vaginal Swab)
You have received an inconclusive test result. An inconclusive result means that it is not possible to determine whether your test was positive or negative. There are many reasons why this might happen. Repeat testing may be required. Please ensure that you discuss this with your healthcare provider.

Sample Rejection Interpretation

For any questions on how to interpret the reason for your sample being rejected please contact our care team or call +1 (929) 376-0056.

Sample Rejection Reason	Description
Cancelled	Your order was cancelled. We cannot provide a result as your sample was not analyzed.
Rejected	It was not possible to provide a result as the laboratory has rejected your sample.
Insufficient Specimen	It was not possible to provide a result for your test as there was not an appropriate sample to perform testing on. The most common cause for this is that the sample provided was too small to perform testing on. Less commonly, this can occur if too much sample was provided. It is not possible to provide you with a test result.
Incorrect Tube	It was not possible to provide a result for your test. The laboratory has rejected your sample because it was returned in the incorrect tube for this kit. This can happen if you had multiple test types and mixed up the tubes and boxes or returned the sample in a tube not provided by us.
Incorrect Volume	It was not possible to provide a result for your test. An incorrect volume result means that the sample tube was filled below or above the marked lines.
No Sample Received	It was not possible to provide a result for your test.
Invalid Order	It was not possible to provide a result for your test.
Invalid	It was not possible to provide a result for your test.
Collection Error	It was not possible to provide a result for your test. Some common reasons for this include if the instructions were not followed correctly and caused an issue which prevented the laboratory from testing your sample. Reasons for rejection can include (but are not limited to): a crucial kit component such as the sample return bag, a preservative element for sample stability was missing, the swab was not in the tube, extra swabs were added to the tube, or the swab was broken at the wrong point.
Sample ID Issue	We were unable to process your sample. We could not match the information between the sample and the kit order.
Uncontactable	Unfortunately, we were unable to provide you with a test result. Critical information required to analyze your sample was missing. We reached out multiple times but were unable to successfully contact you.
Aged Sample	It was not possible to provide a result for your test as the laboratory has rejected your sample. The time between the collection of your sample (when you activated your kit) and when it was received in the laboratory exceeded the maximum time that your sample would remain stable. Samples must be activated, collected, and returned on the same day.
Processing Error	An issue occurred while processing your sample.

Limitations:

Specimen Collection Limitations

A Vaginal swab specimen sampling is not designed to replace cervical exams and endocervical specimens for diagnosis of female urogenital infections. Patients may have cervicitis, urethritis, urinary tract infections, or vaginal infections due to other causes or concurrent infections with other agents.

B Reliable results are dependent on adequate specimen collection. Because the transport system used for this assay does not permit microscopic assessment of specimen adequacy, proper specimen collection technique is necessary.

C A negative test result does not preclude a possible infection because results are dependent on adequate specimen collection. Test results may be affected by improper specimen collection, technical error, or target levels below the assay limit of detection.

D This test has not been evaluated on home collected samples from individuals under the age of 18 years old.

E This test cannot be used to determine the presence of infections other than CT and GC. Neither a positive or negative test result can exclude the possibility that other infections may be present.

F Penile urine and vaginal swab specimens can only detect urogenital infections and cannot detect the presence of extragenital infections, including throat or rectal.

G The information provided by this product should not be used to start, stop, or change any course of treatment unless advised by your healthcare provider.

H The sample must reach the lab within 5 days of home collection. This test cannot be performed on home collected samples that have been collected more than 120 hours (5 days) prior to reaching the lab.

Assay Related Limitations

Please refer to the Aptima Combo 2 Assay (Panther® System) Package Insert for assay limitations.

Performance Characteristics:

Clinical Study – Male Urine Performance

A prospective, multi-center clinical study was conducted to establish the performance characteristics (sensitivity and specificity) of the Aptima Combo 2 Assay on the Panther® System in male urine specimens. First catch urine was self-collected from each participant at the clinic. Table 1 and Table 2 shows the sensitivity and specificity of the Aptima Combo 2 assay for CT and GC detection, respectively, in male urine specimens. For further details refer to the Aptima Combo 2 Assay (Panther® System) Package insert.

Clinical Study – Vaginal Swab Performance

A prospective, multi-center clinical study was conducted to establish the performance characteristics of the Aptima Combo 2 Assay on the Panther® System in self-collected vaginal swab specimens. Table 1 and Table 2 show the sensitivity and specificity of the Aptima Combo 2 Assay for CT and GC detection, respectively, with vaginal swabs. For further details refer to the Aptima Combo 2 Assay (Panther® System) Package insert.

Table 1: Performance Characteristics of the Aptima Combo 2 Assay for CT Detection in Female Swab and Male Urine Specimens

Specimen	n	TP	FP	TN	FN	Prev %	Sensitivity	Specificity
Type[1]	—	—	—	—	—	—	(95% CI)[2]	(95% CI)[2]
Vaginal Swab	1274	104	18	1149	3	8.4	97.2% (92.1% – 99.0%)	98.5% (97.6% – 99.0%)
Male Urine	1799	197	3	1589	10	11.5	95.2% (91.3% – 97.4%)	99.8% (99.4% – 99.9%)

CI = Confidence interval.
2 Score CI.
TP = True Positive.
FP = False Negative.
TN = True Negative.
FN = False Negative.
Prev = Prevalence.

Table 2: Performance Characteristics of the Aptima Combo 2 Assay for GC Detection in Female and Male Specimens

Specimen	n	TP	FP	TN	FN	Prev %	Sensitivity	Specificity
Type[1]	—	—	—	—	—	—	(95% CI)[2]	(95% CI)[2]
Vaginal Swab	1258	42	5	1210	1	3.4	97.7% (87.9% – 99.6%)	99.6% (99.0% – 99.8%)
Male Urine	1797	75	5	1716	1	4.2	98.7% (92.9% – 99.8%)	99.7% (99.3% – 99.9%)

CI = Confidence interval.
2 Score CI.
TP = True Positive.
FP = False Negative.
TN = True Negative.
FN = False Negative.
Prev = Prevalence.

Interfering Substances:

Urogenital Specimens Aptima Combo 2 Assay

Aptima Combo 2 Assay performance in the presence of potentially interfering substances was tested, including the following interfering substances individually spiked into swab specimens: 10% blood, contraceptive jelly, spermicide, moisturizer, hemorrhoidal anesthetic, body oil, powder, anti-fungal cream, vaginal lubricants, feminine spray, and leukocytes (1.0×10^6 cells/mL). All were tested for potential assay interference in the absence and presence of CT and GC at the estimated rRNA equivalent of 1.0 CT IFU/assay (5 fg/ assay) and 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 Combo 2 Assay. Refer to the Aptima Combo 2 Assay Package Insert for further details.

Hand Contaminants

Potential interfering substances listed in Table 3 that may be present when the Simple 2 Urine Home Collection Kit (Penile) and the Simple 2 Swab Home Collection Kit (Vaginal) are used by the lay user were evaluated in a separate study. The substances were tested for potential assay interference in the absence and presence of CT and GC (positive samples at 3x empiric LoD). To prepare positive urine samples, negative urine was spiked to obtain the desired GC or CT concentration then added to a urine Aptima Transport Tube along with the potential interfering substance (1% of total sample volume). To prepare positive vaginal swab samples, negative clinical sample transport media (STM) was spiked to obtain the desired GC or CT concentration and placed into a Transport Tube with a swab along with the potential interfering substance (1% of total sample volume). Each potential hand contaminant was tested with 6 replicates for urine samples and five replicates for vaginal swab samples.

For urine samples, no false results were observed for negative or CT positive samples. No false results were also observed for GC positive samples in the presence of water, lotion, and sunscreen at the concentration tested. The presence of some brands of hand soap (Cintas and Soft Soap) and hand sanitizer (GermX) caused false negative results (Table 3).

For vaginal swab samples, no false positive or negative results were observed at the concentrations tested for any of the tested substances (Table 3).

Table 3: Hand Contaminants Interference Data

Product	Brand	Agreement with Expected Results					
		CT/GC Negative		CT Positive		GC Positive	
		Urine	Swab	Urine	Swab	Urine	Swab
Hand Soap	Soft Soap	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(0/6) 0%*	(5/5) 100%
	Summit	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
	Cintas	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(4/6) 67%*	(5/5) 100%
Hand Sanitizer	U-Line	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
	Level 1 Health	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(3/6) 50%*	(5/5) 100%
	GermX	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
Lotion	Aveeno	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
	Flocon de Neige	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
	Power Protect	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
Sunscreen	MD Solar Sciences	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
	Banana Boat	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
	Equate	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%
Tap Water	N/A	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%	(6/6) 100%	(5/5) 100%

* Where 100% agreement with expected results was not observed, applicable warnings and limitations have been added to the instructions for use.

Usability and Comprehension Studies:

Simple 2 Urine Home Collection Kit (Penile)

A usability study was performed to evaluate the lay user's ability to follow the home collection instructions, overall ease of use of the Simple 2 Urine Home Collection Kit (Penile), and comprehension of the test results. Eighty nine (89) adult males (Table 4) followed the hard copy of the home collection Instructions for Use (IFU) provided with the kit to collect, package, and ship a sample to the laboratory, and a randomized group also watched the instructional video. The study was performed from the participants' home, and the process was observed over video conference (excluding urination into the collection cup). Participants answered questions to assess their understanding of the IFU and test results then shipped their sample to the laboratory. Laboratory staff assessed the acceptability of each sample for testing including the sample volume and time from sample collection. Participants' responses to assessment questions indicated good understanding of test results and when and how to collect a urine sample. No significant difference in comprehension of the IFU and performance of sample collection was noted between the two randomized groups (those who viewed the instructional video and those who did not view the instructional video).

In a follow up study, 32 adult males (Table 4) followed the hard copy home collection IFU provided with the kit to prepare, package, and ship a simulated urine sample to the laboratory. Similar to customers, participants were prompted with an option to watch the instructional video following the completion of kit activation or could access the instructional video using a link provided in the IFU. 15/32 (47%) participants used only the paper instructions provided with the kit and 17/32 (53%) also watched the instructional video. The participants followed the collection kit instructions from their home and were observed over video conference by study staff. After sample packaging was complete, participants answered questions to assess their understanding of the home collection instructions, the Frequently Asked Questions (FAQs), and test results. Participants then shipped their sample to the laboratory, and laboratory staff evaluated the acceptability of each sample for testing. All of the participants (32/32, 100%) transferred an acceptable amount of simulated urine from the collection cup to the sample tube using the provided pipette. One sample (1/32, 3%) was received beyond 120 hours from sample collection. No other critical errors that would cause sample rejection were noted. Participant performance and responses to assessment questions demonstrated overall comprehension of the instructions, safety/warning information, possible test results, and general information from the FAQs about gonorrhea and chlamydia infections. No significant difference in comprehension of the IFU and performance of sample collection was noted between the those who viewed the instructional video and those who did not view the instructional video. Participant comprehension of the critical information included in the IFU exceeded the acceptance criteria (≥ 95% success rate) as demonstrated through direct observation and sample rejection recorded at accessioning.

Table 4: Demographic Characteristics of Participants of Simple 2 Urine Home Collection Kit (Penile) Usability Study

	Usability Study 1		Usability Study 2	
Sex	**N**	%	**N**	%
Male	89	100	32	100
Age Group				
18-25	7	8%	5	16%
26-35	25	28%	10	31%
36-45	17	19%	6	19%
46-55	20	22%	3	9%
56-65	14	16%	5	16%
> 65	6	7%	3	9%
Education				
< High school	0	0%	1	3%
High school diploma	10	11%	4	13%
Some college/Associates Degree/Vocational Degree	32	35%	11	34%
Bachelor's degree	23	26%	12	38%
Graduate degree	24	27%	4	13%
Literacy (SAHL)[a]				
Low (<14)	N/A	N/A	0	0%
Average (15-16)	N/A	N/A	2	6%
High (17-18)	N/A	N/A	30	94%
Race/Ethnicity				
Caucasian	55	62%	15	47%
Asian	7	8%	2	6%
Hispanic/Latin American	9	10%	8	25%
Black/African American	11	12%	3	9%
Mixed/Unknown/Other	7	8%	3	9%

[a]The short assessment of health literacy (SAHL) was modified into a questionnaire format to assess the literacy of participants.

Simple 2 Swab Home Collection Kit (Vaginal)

A usability study was performed to evaluate lay user's ability to follow the home collection instructions, the overall ease of use of the Simple 2 Swab Home Collection Kit (Vaginal), and comprehension of the test results. Eighty five (85) adult females (Table 5) followed the hard copy of the home collection IFU provided with the kit to prepare, package, and ship a swab sample to the laboratory, and a randomized group also watched the instructional video. The participants followed the kit instructions from their home. Participants answered questions to assess their understanding of the IFU and test results over video conference then shipped their sample to the laboratory. Laboratory staff assessed the acceptability of each sample for testing such as sample volume, time from sample collection etc. 99% of samples received at the laboratory were acceptable for processing. Participant response to questions indicated overall good understanding of when and how to collect a vaginal swab sample. No significant difference in comprehension of the IFU and sample preparation was noted between the two randomized groups (those who viewed the instructional video and those who did not view the instructional video).

A follow up usability study was performed to evaluate the lay users' ability to use the Simple 2 Swab Home Collection Kit (Vaginal) and asses comprehension of the results report and educational materials provided with the kit. 34 adult females (Table 5) followed the hard copy of the home collection IFU provided with the kit to handle, package, and ship a sample to the laboratory. Similar to customers, participants were prompted with an option to watch the instructional video following the completion of kit activation or could access the instructional video using a link provided in the IFU. 22/34 (65%) participants used only the paper instructions provided with the kit and 12/34 (35%) also watched the instructional video. Participants followed the collection kit instructions from their home. Participants were not required to collect a vaginal swab specimen, but performed all other steps of the instructions under observation over video conference. After sample packaging was complete, participants answered questions to assess their understanding of the home collection instructions, the FAQs, and test results. Participants then shipped their sample to the laboratory, and laboratory staff evaluated the acceptability of each sample for testing upon receipt. Over 95% of participants placed the swab inside the sample transport tube correctly in the correct orientation, and the sample transport tube was then placed into the biohazard bag and properly sealed. Three samples (3/34, 9%) were received beyond 120 hours from sample collection. Participant performance and response to assessment questions demonstrated overall comprehension of the instructions, safety/warning information, possible test results, and general information from the FAQs about gonorrhea and chlamydia infections. No significant difference in comprehension of the IFU and performance of sample collection was noted between those who viewed the instructional video and those who did not view the instructional video. Participant comprehension of the critical information included in the IFU exceeded the acceptance criteria (≥ 95% success rate) as demonstrated through direct observation and errors recorded at sample accessioning.

Table 5: Demographic Characteristics of Participants of Simple 2 Swab Home Collection Kit (Vaginal) Usability Study

	Usability Study 1		Usability Study 2	
Gender	**N**	**%**	**N**	**%**
Female	85	100%	33	97%
Transgender Male*	0	0%	1	3%
Age Group				
18-25	17	20%	5	15%
26-35	34	40%	8	24%
36-45	14	16%	8	24%
46-55	15	18%	9	26%
56-65	4	5%	3	9%
> 65	1	1%	1	3%
Education				
< High school	2	2%	1	3%
High school diploma	19	22%	6	18%
Some college/Associates Degree/Vocational Degree	30	35%	15	44%
Bachelor's degree	23	27%	10	29%
Graduate degree	11	13%	2	6%
Literacy (SAHL)[α]				
Low (<14)	N/A	N/A	2	6%
Average (15-16)	N/A	N/A	6	18%
High (17-18)	N/A	N/A	26	77%
Race/Ethnicity				
Caucasian	44	52%	15	44%
Asian	7	8%	3	9%
Hispanic/Latin American	14	16%	5	15%
Black/African American	14	16%	9	26%
Mixed/Unknown/Other	6	7%	2	6%

*participant self-reported having female anatomy

[α]The short assessment of health literacy (SAHL) was modified into a questionnaire format to assess the literacy of participants.

Specimen Shipping Stability Studies:

Simple 2 Urine Home Collection Kit (Penile)

Experiments to evaluate sample shipping stability were performed using simulated summer and winter shipping profiles designed to mimic extreme temperature conditions. CT/GC negative urine samples (n=10) and positive urine samples spiked with live microorganisms at 2x empiric LoD (n=30) and 10x empiric LoD (n=10) were prepared and evaluated against summer and winter shipping profiles. 100% agreement with expected results was obtained for all samples except CT samples spiked at 2x empiric LoD tested under the winter shipping profile (Table 6 and 7).

Table 6: Summer Shipping Stability Results for Simple 2 Urine Home Collection Kit (Penile)

Concentration	CT Detection			GC Detection		
	Positive	Negative	Agreement	Positive	Negative	Agreement
2x empiric LoD	30	0	(30/30) 100%	30	0	(30/30) 100%
10x empiric LoD	10	0	(10/10) 100%	10	0	(10/10) 100%
Negative	0	10	(10/10) 100%	0	10	(10/10) 100%

Table 7: Winter Shipping Stability Results for Simple 2 Urine Home Collection Kit (Penile)

Concentration	CT Detection			GC Detection		
	Positive	Negative	Agreement	Positive	Negative	Agreement
2x empiric LoD	29	1	(29/30) 97%	30	0	(30/30) 100%
10x empiric LoD	10	0	(10/10) 100%	10	0	(10/10) 100%
Negative	0	10	(10/10) 100%	0	10	(10/10) 100%

Simple 2 Swab Home Collection Kit (Vaginal)

Experiments to evaluate sample shipping stability were performed using simulated summer and winter shipping profiles designed to mimic extreme temperature conditions that may be experienced during shipment. CT/GC negative vaginal swab samples (n=10) and positive vaginal swab samples spiked with live microorganisms at 2x empiric LoD (n=30) and 10x empiric LoD (n=10) were prepared containing a swab and evaluated against summer and winter shipping profiles. All positive and negative samples generated expected results (100% agreement) for both CT and GC under both summer (Table 8) and winter (Table 9) shipping profiles.

Table 8: Summer Shipping Stability Results for Simple 2 Swab Home Collection Kit (Vaginal)

Concentration	CT Detection			GC Detection		
	Positive	Negative	Agreement	Positive	Negative	Agreement
2x empiric LoD	30	0	(30/30) 100%	30	0	(30/30) 100%
10x empiric LoD	10	0	(10/10) 100%	10	0	(10/10) 100%
Negative	0	10	(10/10) 100%	0	10	(10/10) 100%

Table 9: Winter Shipping Stability Results for Simple 2 Swab Home Collection Kit (Vaginal)

Concentration	CT Detection			GC Detection		
	Positive	Negative	Agreement	Positive	Negative	Agreement
2x empiric LoD	30	0	(30/30) 100%	30	0	(30/30) 100%
10x empiric LoD	10	0	(10/10) 100%	10	0	(10/10) 100%
Negative	0	10	(10/10) 100%	0	10	(10/10) 100%

Flex Studies:

The Simple 2 Urine Home Collection Kit (Penile) and Simple 2 Swab Home Collection Kit (Vaginal) were evaluated for robustness against several sample preparation variables. Appropriate labelling precautions were introduced to mitigate potential errors that could occur when collection of penile urine and vaginal swab specimens is performed in a home setting with the Simple 2 Home Collection Kits without healthcare provider supervision.

Analytical Studies for Aptima Combo 2 Assay

Analytical Sensitivity

Chlamydia trachomatis analytical sensitivity (limit of detection) was determined by testing dilutions of CT organisms in the Aptima Combo 2 Assay. The analytical sensitivity claim for the assay is 1 IFU/assay (7.25 IFU/swab and 5.0 IFU/mL urine). However, dilutions of less than 1 IFU/assay tested positive in the Aptima Combo 2 Assay for the following 12 serovars: D, E, F, G, H, I, J, K, L1, L2, L2a, and L3 in samples containing CT concentrations of 1.89 IFU/mL.

Neisseria gonorrhoeae analytical sensitivity (limit of detection) was determined by testing dilutions of GC organisms in the Aptima Combo 2 Assay. The analytical sensitivity claim for the assay is 50 cells/assay (362 cells/swab and 250 cells/mL urine). However, dilutions of less than 50 cells/assay tested positive in the Aptima Combo 2 Assay for 30 different strains of GC in samples containing GC concentrations of 0.36 cells/mL. Please refer to the Aptima Combo 2 Assay Package Insert (Panther System) for further details.

Analytical Specificity

A total of 154 cultured isolates were evaluated using the Aptima Combo 2 Assay. These isolates included 86 organisms that may be isolated from the urogenital tract and 68 additional organisms that represent a phylogenetic cross-section of organisms. The tested organisms (Table 10) included bacteria, fungi (including yeast), parasites, and viruses. All organisms except *C. psittaci*, *C. pneumoniae*, and the viruses were tested at 1.0×10^6 cells/assay in STM. The Chlamydia and Neisseria organisms were tested in PreservCyt solution medium. *C. psittaci* and *C. pneumoniae* were tested at 1.0×10^5 IFU/assay. The viruses were tested as follows: (a) herpes simplex viruses I and II: 2.5×10^4 $TCID_{50}$/assay, (b) human papilloma virus 16: 2.9×10^6 DNA copies/assay, and (c) cytomegalovirus: 4.8×10^5 infected cell culture cells/assay. Only CT and GC samples produced positive results in the Aptima Combo 2 Assay. Please refer to the Aptima Combo 2 Assay Package Insert (Panther® System) for further details.

Table 10: Organisms tested for analytical specificity

Organism		
Achromobacter xerosis	*Flavobacterium meningosepticum*	*Proteus vulgaris*
Acinetobacter calcoaceticus	*Fusobacterium nucleatum*	*Providencia stuartii*
Acinetobacter lwoffi	*Gardnerella vaginalis*	*Pseudomonas aeruginosa*
Actinomyces israelii	*Gemella haemolvsans*	*Pseudomonas fluorescens*
Actinomyces pyogenes	*Haemophilus ducreyi*	*Pseudomonas putida*
Aerococcus viridans	*Haemophilus influenzae*	*Rahnella aquatilis*
Aeromonas hydrophila	Herpes simplex virus I	*Rhodospirillum rubrum*
Agrobacterium radiobacter	Herpes simplex virus II	*Saccharomyces cerevisiae*
Alcaligenes faecalis	Human papilloma virus 16	*Salmonella minnesota*
Bacillus subtilis	*Kingella dentnificans*	*Salmonella typhimurium*
Bacteriodes fragilis	*Kingella kingae*	*Serratia marcescens*
Bacteriodes ureolyticus	*Klebsiella oxvtoca*	*Staphylococcus saprophyticus*
Bifidobacterium adolescentis	*Klebsiella pneumoniae*	*Staphylococcus aureus*
Bifidobacterium brevi	*Lactobacillus acidophilus*	*Staphylococcus epidermidis*
Branhamella catarrhalis	*Lactobacillus brevis*	*Streptococcus agalactiae*
Brevibacterium linens	*Lactobacillus jensonii*	*Streptococcus bovis*
Campylobacter jejuni	*Lactobacillus lactis*	*Streptococcus mitis*
Candida albicans	*Legionella pneumophila (2)*	*Streptococcus mutans*
Candida glabrata	*Leuconostoc paramensenteroides*	*Streptococcus pneumonia*
Candida parapsilosis	*Listeria monocytogenes*	*Streptococcus pyogenes*
Candida tropicalis	*Micrococcus lutes*	*N. meningitidis Serogroup D*
Chlamydia pneumonia	*Moraxella lacunata*	*N. meningitidis Serogroup Y*
Chlamvdia psittaci (2)	*Moraxella osloensis*	*N. meningitidis Serogroup W135*
Chromobacterium violaceum	*Morganella morganii*	*Neisseria cinerea (4)*
Citrobacter freundi	*Mycobacterium smegmatis*	*Neisseria dentrificans*
Clostridium perfringens	*Mycoplasma genitalium*	*Streptococcus salivarius*
Corynebacterium genitalium	*Mycoplasma hominis*	*Streptococcus sanguis*
Corvnebacterium erosis	*N. meningitidis Serogroup A*	*Streptomyces griseinus*
Cryptococcus neoformans	*N. meningitidis Serogroup B*	*Trichomonas vaginalis*
Cytomegalovirus	*N. meningitidis Serogroup C (4)*	*Ureaplasma urealyticum*
Deinococcus radiodurans	*Neisseria mucosa (3)*	*Neisseria elongata (3)*
Derxia gummosa	*Neisseria sicca (3)*	*Vibrio parahaemolyticus*
Eikenella corrodens	*Neisseria subflava (14)*	*Neisseria flava*
Enterobacter aerogenes	*Neisseria perfiava*	*Yersinia enterocolitica*
Enterobacter cloacae	*Neisseria polysaccharea*	*Neisseria flavescens (2)*
Entercoccus avium	*Paracoccus denitrificans*	*Neisseria lactamica (9)*
Entercoccus faecalis	*Peptostreptococcus anaerobius*	
Entercoccus faecium	*Peptostreptococcus productus*	
Envinia herbicola	*Plesiomonas shigelloides*	
Erysipelothrix musiopathiae	*Propionibacterium acnes*	
Escherichia coli	*Proteus mirabilis*	

*(n) represents the number of strains tested.
All organisms tested produced a negative result in the Aptima Combo 2 Assay (AC2) based on kinetic profile type and RLU.

Within Laboratory Precision Study

Aptima Combo 2 Assay precision was evaluated using the Panther® System. Testing was performed over 24 days using three Panther® Systems and three lots of assay reagents. Reproducibility panel members were created using negative STM. The positive panel members were created by spiking CT and/or GC organisms to the targeted concentrations. Table 11 presents the percent agreement with expected results for each panel member. Please refer to the Aptima Combo 2 Assay Package Insert (Panther® System) for further details.

Table 11: Within Laboratory Precision Study Summary Data

Matrix	Target Concentration		Agreed /N	Agreement (%)
	CT (IFU/mL)	GC (CFU/mL)		
STM	0	0	96/96	100
	0.25	0	95/95	100
	2.5	0	96/96	100
	25	0	95/95	100
	0	12.5	96/96	100
	0	125	96/96	100
	0	1250	96/96	100
	2.5	125	96/96	100
	12.51	2500	96/96	100
	1000	2500	96/96	100
	1000	125	96/96	100

CFU=colony forming units, IFU=inclusion forming unit, N=number of samples, STM=sample transport medium

Carryover Studies for the Panther System

Two studies were conducted to evaluate carryover on the Panther System. In the first study, carryover was assessed in multiple runs on three Panther Systems with approximately 20% high titer GC samples dispersed between negative samples. The runs included clusters of high positive samples with clusters of negative samples as well as single high positives dispersed within the run. High titer samples were made using GC rRNA spiked into STM to give a final concentration equivalent to 2.5×10^5 CFU/mL. Five runs were performed on each of three Panther Systems. Carryover was calculated from a total of 2938 valid negative results. The overall carryover rate from this study was 0% with a 95% confidence interval of 0–0.1%.

The second carryover study was conducted on one Panther System with high titer GC positive samples (GC rRNA spiked into STM at the equivalent of 2.5×10^5 CFU/mL) alternately processed with negative samples in a checkerboard format. Five checkerboard runs were performed. The overall carryover rate from this study was 0.74% (1/135 negative samples). Please refer to the Aptima Combo 2 Assay Package Insert (Panther® System) for further details.

Reproducibility Studies

Reproducibility of the Aptima Combo 2 Assay on the Panther System was evaluated in two different studies using panel members created with STM in Reproducibility Study 1 and using panel members created with clinical urine specimens in Reproducibility Study 2.

Aptima Combo 2 Assay reproducibility was evaluated using the Panther® System with panel members created using STM at three external US laboratories for Reproducibility study 1 (Table 12) and with panel members created using clinical urine specimens at 2 external US laboratories and in-house for Reproducibility study 2 (Table 13). For both studies, testing was performed using one lot of assay reagents and a total of six operators (two at each site). Testing was performed over at least 10 days at each site. In study 1, the negative panel member consisted of STM and positive panel members were created by spiking STM with lysate from CT and/or GC organisms to result in panel members with expected targeted concentrations. In study 2, the negative panel member consisted of negative urine and the positive panel members were created by spiking negative urine with lysate from CT and/or GC organisms to result in panel members with expected targeted concentrations. Reproducibility studies demonstrated acceptable variability for both GC and CT microorganisms at all concentrations tested when results were compared between sites, between operators, between days, between runs, within runs, and overall. Please refer to the Aptima Combo 2 Assay Package Insert (Panther® System) for further details.

Table 12: Reproducibility Study 1

Target Concentration		Agreed/N	Agreement (%)
CT (IFU/mL)	GC (CFU/mL)		
0	0	180/180	100
0.25	0	180/180	100
2.5	0	180/180	100
25	0	180/180	100
1000	0	180/180	100
0	0.25	180/180	100
0	12.5	179/179	100
0	125	180/180	100
0	1250	180/180	100
0	2500	179/179	100
2.5	125	178/178	100
2.5	2500	180/180	100
1000	125	179/179	100
1000	2500	180/180	100

Agmt=agreement, CFU=colony forming units, IFU=inclusion forming unit, N=number of samples, STM=sample transport medium

Table 13: Reproducibility Study 2

Target Concentration		Agreed/N	Agreement (%)
CT (IFU/mL)	GC (CFU/mL)		
0	0	178/180	98.9
0.25	0	180/180	100
2.5	0	178/178	100
25	0	180/180	100
1000	0	180/180	100
0	0.25	177/179	98.9
0	12.5	179/180	99.4
0	125	180/180	100
0	1250	180/180	100
0	2500	180/180	100
2.5	125	180/180	100
2.5	2500	180/180	100
1000	125	179/179	100
1000	2500	180/180	100

Agmt=agreement, CFU=colony forming units, IFU=inclusion forming unit, N=number of samples, STM=sample transport medium

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