Evaluation of rapid diagnostic tests: chlamydia and gonorrhoea

WHO/TDR Sexually Transmitted Diseases Diagnostics Initiative

The cornerstone of sexually transmitted infection (STI) control is early diagnosis and treatment, including the treatment of sexual partners. These measures prevent complications in the treated individuals and interrupt onward disease transmission. Many STIs cause no symptoms, and such asymptomatic infections can only be detected by screening or through partner notification. The WHO estimates that 92 million and 62 million new cases of genital *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection, respectively, occur every year, mostly in areas with limited or no access to laboratory services[1]. Rapid point-of-care diagnostic tests (RDTs) are particularly valuable as they allow immediate diagnosis and treatment. This is especially important in settings where patients find it difficult or impossible to return to a clinic to obtain the results of laboratory tests[2,3]. RDTs are also useful for outreach programmes designed to reach individuals who are at high risk of infection but who are marginalised from the healthcare system.

For symptomatic patients who have no access to laboratory services, the WHO recommends a syndromic approach to case management[4]. The principle of syndromic management is to treat patients for all the probable causes of a particular clinical presentation or syndrome. WHO has published guidelines and flowcharts for the syndromic management of STI syndromes, including urethral discharge, vaginal discharge, lower abdominal pain, genital ulcer disease, scrotal swelling in men, and inguinal adenopathy in either sex. National control programmes can adapt these flowcharts to accommodate local patterns of disease and antimicrobial susceptibilities.

Syndromic management has a number of advantages and disadvantages. Although simple to use and inexpensive, the major disadvantage of syndromic management is that it can lead to unnecessary treatment[5,6]. This is especially important for the common syndrome of vaginal discharge, which is more commonly caused by trichomoniasis, candidiasis or bacterial vaginosis than by cervical infection with *C. trachomatis* or *N. gonorrhoeae*. As syndromic management is used in settings where laboratory services are not available, simple RDTs that can be used in the field will increase the specificity of the syndromic management algorithms used and hence reduce unnecessary treatment.

I. TYPES OF CHLAMYDIA AND GONORRHOEA DIAGNOSTIC TESTS

A range of diagnostic tests has traditionally been used in the laboratory diagnosis of *C. trachomatis* and *N. gonorrhoeae* infection, and to guide treatment (TABLE 1). Microscopy of Gram-stained urethral or cervical smears allows direct visualization of *N. gonorrhoeae* as monomorphic, Gram-negative diplococci within polymorphonuclear leukocytes. In men, microscopy using Gram-stained urethral smears to identify gonococci is 84%–95% sensitive compared to bacterial culture, which, under optimal conditions, is close to 100% sensitive. Microscopy of male urethral smears is more sensitive in symptomatic (90%–95%) than in asymptomatic (50%–75%) patients[7]. In women, microscopy of a cervical smear only detects approximately 50% of infections and is not recommended for routine use[8]. Microscopy is not appropriate for pharyngeal specimens as other diplococci can be present. Cytological staining methods are not useful for the diagnosis of *C. trachomatis* infection but direct immunofluorescence staining has been used in low-throughput situations.

Antigen-detection tests that use monoclonal or polyclonal antibodies to capture chlamydial or gonococcal antigens are commercially available. These tests are available in a laboratory-based immunoassay format or as immunochromatographic strips (ICS) encased in plastic cassettes for a visual readout, which detect the chlamydial or gonococcal antigen using high-affinity antibodies fixed onto nitrocellulose strips. Most do not require any additional equipment and can give a visual result within 30 minutes.

These tests are suitable for use in primary healthcare settings but there are limited data on their performance characteristics and whether they address disease control needs[9–15]. Evaluating the performance of these tests, their utility in disease control programmes and their acceptability to patients and healthcare providers will hopefully improve the diagnosis of STIs in primary healthcare settings in developing countries and reduce unnecessary treatment that results from syndromic management.

II. THE NEED FOR FIELD EVALUATION OF CHLAMYDIA AND GONORRHOEA RDTs

Until recently, laboratory testing for gonococcal and chlamydial infection was carried out in a laboratory with trained personnel, refrigeration for the storage of reagents and electricity to run equipment including a refrigerator, centrifuge and incubators for the growth of *N. gonorrhoeae* on artificial media or *C. trachomatis* in cell culture.

As such facilities are generally not available in remote areas, samples had to be transported to regional or central facilities for testing. The results were therefore available only days or weeks after testing. If those who were tested did not return for their results, they were not treated, resulting in adverse clinical outcomes, continued transmission of infection and a waste of resources[2,3].

III. GENERAL ISSUES IN STUDY DESIGN

1. Reference standards

The reference standard for the laboratory diagnosis of gonococcal infection remains bacterial culture, which is usually performed on selective solid media such as modified Thayer-Martin media, followed by confirmation using biochemical tests such as oxidase and sugar fermentation tests[16–22]. Although bacterial culture has the highest sensitivity and specificity under ideal conditions, its performance is often affected by transport conditions.

For settings where bacterial culture is not possible, or transport conditions might compromise its sensitivity, nucleic acid amplified tests (NAATs) of genital swabs can be used as an alternative reference standard. NAATs generally have good sensitivity compared to culturing and antigen-detection tests but the specificity of some NAATs appears to have been compromised by cross-reactivity with other *Neisseria* species such as *Neisseria subflava* and *Neisseria cinerea*[23,24]. The high sensitivity of NAATs has led to many studies on the use of non-invasive samples such as urine, or minimally invasive specimens such as vaginal swabs, both of which can be self-collected. The use of urine samples for the detection of *N. gonorrhoeae* by NAATs is not acceptable because of their relatively poor sensitivity with these assays (mean = 55.6% (95% confidence intervals 36.3%–74.9%)). The use of NAATs requires a well equipped laboratory and highly trained personnel to perform the tests to avoid false positive results owing to contamination.

The best reference standard against which all chlamydial tests should be compared is a commercial NAAT performed using an endocervical swab. However, cervical swabs might not be available in all circumstances. If the RDT uses vaginal swabs or first-catch urine specimens it is appropriate to compare the performance of the RDT against the performance of NAATs using these specimen types[25,26].

2. Local epidemiology, choice of study population and sampling

The local epidemiology of chlamydial and gonococcal infections is important in selecting the appropriate test. In certain areas, some subgroups of the population might have a disease prevalence that is much higher than the general population. Hence, the study population must be clearly defined.

Where the evaluation is to investigate whether the test can be used to improve the specificity of syndromic management, only women with a primary complaint of vaginal discharge should be included in the study. Where the RDT is to be used to screen patients, all women at risk of infection with *N. gonorrhoeae* or *C. trachomatis* should be included, regardless of symptoms.

Consecutive women presenting to the clinic at the evaluation sites who fit the inclusion criteria should be asked to participate in the study. Patients who give informed consent should undergo an interview and a physical examination according to the routine clinic protocol at the site. Vaginal and cervical samples can be taken. In addition, the subjects should be asked questions relating to their age, sexual behaviour and symptoms, and any signs of infection on examination should be noted (a sample data-collection form is shown in APPENDIX 1). Study participants should be treated for *N. gonorrhoeae* and *C. trachomatis* infection syndromically. Those not treated syndromically but whose reference tests prove positive for *N. gonorrhoeae* or *C. trachomatis* infection should subsequently receive treatment. As part of their routine medical care, subjects should also be treated syndromically for bacterial vaginosis, trichomoniasis, candidiasis and, if necessary, genital ulcers.

IV. FACTORS AFFECTING TEST PERFORMANCE

1. Specimen sampling and preparation

The usual presenting symptoms of gonorrhoea and chlamydial infection are different in men and women. Urethral discharge is the most frequent presenting syndrome in men. In women, both infections are usually localized in the endocervix and are frequently asymptomatic.

Sterile dacron, rayon or cotton swabs (some cotton swabs and calcium alginate swabs have been shown to be toxic for *N. gonorrhoeae*) can be used for specimen collection if the type of swab is not specified in the test kit instructions. The use of antiseptics, analgesics and lubricants when collecting specimens should be avoided, as these substances can be inhibitory for laboratory tests.

Two or three vaginal swabs and two or three cervical swabs should be collected to allow one set to be used with the RDT, the second with NAATs or for bacterial culture, and the optional third set for further testing if necessary. The vaginal swabs should be collected before the cervical swabs to avoid contamination of the vaginal canal with cervical discharge. The three vaginal swabs can be collected simultaneously whereas the cervical swabs should be collected in sequence.

Table 1 | **Performance and operational characteristics of diagnostic tests for chlamydia and gonorrhoea***

			Complexity‡			
Test	**Sensitivity§**	**Specificity§**	**Expertise**	**Equipment**	**Time**	**Relative cost‡**
Bacterial culture	60–70%‖	99–100%	+++	+++	48 hours	++
Microscopy (NG only)	Men: 84–95% Women: 50%	≥95%	++	+	1 hour	+
NAHT	85–90%	95–99%	+++	+++	4 hours	+++
NAAT	90–95%¶	98–100%	++++	++++	4 hours (longer to confirm)	++++
Antigen detection						
EIA	50–70%	95–99%	++	++	4 hours	++
RDT	ND	ND	+	None	30 minutes	ND

EIA, enzyme immunosorbent assay; NAAT, nucleic acid amplification test; NAHT, nucleic acid hybridization test; ND, not determined; NG, *Neisseria gonorrhoeae*; RDT, rapid diagnostic test. *Values taken from REFS 8,9,18–22,26,28–30; ‡ + denotes minimal requirements for training, equipment and cost; ++++ denotes requirement for highly trained personnel, sophisticated equipment/laboratory facilities and high cost; §Test performance compared to a combined reference standard of bacterial culture or two NAATs; ‖Bacterial culture for NG is close to 100% sensitive under optimal conditions; ¶Sensitivity is lower for urine specimens[22].

The instructions for the collection, labelling and transport of vaginal swabs should be clearly described. One of the vaginal swabs (V1) should be used for the RDT, one (V2 or V3) for the reference test and one (V2 or V3) for quality-assurance purposes. Self-taken vulvo-vaginal swabs can be considered as an alternative.

The instructions for the collection, labelling and transport of cervical swabs should be clearly described. The order of swabs collected for the RDT and the reference test should be randomised. The third swab, if collected, can be used for further testing as necessary.

The swabs for the reference test should be transported to the laboratory in accordance with the standard operating procedures (SOPs) at the clinic. Each swab should be labelled with the study number, date and a code that indicates the swab type (for example, V for vaginal swab; C for cervical swab). At the conclusion of the study, all remaining specimens should be disposed of in accordance with routine procedure for disposal of infectious substances at the site.

2. Transport and storage of specimens

If culturing of *N. gonorrhoeae* is available specimens should ideally be inoculated immediately onto the growth medium. The bacterium requires a CO_2-enriched atmosphere for survival. Different methods can be used to enrich the atmosphere in CO_2 (for example, candle jars and CO_2-generating pellets). Immediate incubation at 33–35°C for 18–24 hours will allow initial growth of the bacterium and better survival during transport. Alternatively, non-nutritive swab transport systems can be used and can allow survival of *N. gonorrhoeae* for up to 48 hours. The time between sample collection and plating onto culture medium should be as short as possible as bacterial viability can start to decrease after as little as 6 hours. The transport media should be kept at 20°C ± 5°C.

The specimens to be used for the detection of *C. trachomatis* by NAAT should follow the procedural instructions given in the product's package insert. These can include the use of appropriate or kit-specific swabs or transport media, as other materials might impair the sensitivity and/or specificity of the assay.

All samples should be transported using the appropriate procedure for each test. If the samples are not processed immediately, they should be stored at 4°C. If the samples cannot be processed within 7 days they should be frozen at –20°C or –70°C.

3. Transport and storage of RDTs

Exposure of test kits to high temperatures can be a major contributor to poor test performance, particularly during transport and storage. Transfer from the manufacturer and road transport within a country are particularly vulnerable times. High humidity can rapidly degrade RDTs, especially prolonged exposure to humidity after removal from the envelope or if the envelope is damaged.

Most manufacturers recommend RDT storage at temperatures between 2°C and 30°C. The expiry dates are generally set according to these conditions. If RDT kits are stored at temperatures exceeding the recommended limits, it is likely that their shelf life will be reduced and sensitivity lost before the expiry date. The maintenance of temperatures of less than 30°C for the shipment of RDTs is essential. Transport of RDTs from manufacturers and within countries should be monitored as follows:

3.1. Shipping from the manufacturers. Before shipping, the manufacturer should contact the consignees with details of the air waybill numbers, airline carrier, flight number, numbers of containers and expected arrival time. These details should be sent by e-mail and also by facsimile transmission (fax).

The air carrier should be notified of the temperature storage requirements by the manufacturer in writing and by clear markings on all cartons and related documents (stowage of the shipment close to the skin of some aircraft might result in freezing).

The manufacturer should initiate the shipment only when the consignee confirms that the shipping notification has been received.

The consignees then arrange to have customs agents or other personnel on site to receive the materials. The shipment should then be moved immediately to moderate temperature storage (<30°C if possible). Leaving materials on airport tarmacs, in customs sheds or in vehicles should be avoided as much as possible.

3.2. Ground transportation. Ground transportation during any stage of delivery to the test sites should be carried out without delay and with attention to the ambient temperature while the vehicle is moving and if parked. Avoid leaving RDT kits in vehicles parked in the sun.

3.3 Storage. Storage at the central and final field facilities should be within the manufacturer's specifications (usually below 30°C).

Maximize the time that RDTs are stored in centralized, controlled conditions and minimize uncontrolled storage in remote areas. Smaller box sizes can help achieve this.

Select a cool peripheral storage location; thatch roofing can be cooler than iron. Available shade should be maximised and the use of evaporative cooling cabinets should be considered.

Transport and storage at temperatures above 30°C is sometimes unavoidable in many remote locations where RDTs are most useful. In such circumstances, it is essential that the the sensitivity of the tests is monitored at appropriate intervals. WHO is currently developing recommendations for quality-assurance procedures to address these issues.

4. Training of staff

Adequate training and supervision of the end-users of RDTs should be integrated as far as possible into existing health worker training and quality-assurance schemes. Staff should be proficient at performing the reference test and the RDTs under evaluation. The laboratory should subscribe to an external quality-assurance scheme and participate in Proficiency Panel testing at least twice a year.

Concise, clear SOPs should be prepared in local languages for the health workers who are trained to perform the test. The instructions for sample processing and the interpretation of results should be clear.

5. Recent treatment

Recent antibiotic use can affect test results. Although it is not necessary to exclude individuals who have used antibiotics in the past 2–3 weeks, this should be noted.

6. Laboratory facilities and testing sites

The reference laboratory should have clear SOPs for the RDT. The study should be conducted in accordance with Good Clinical Practice (GCP) and Good Laboratory Practice (GLP) or Good Clinical Laboratory Practice (GCLP) guidelines. GLP guidelines have been largely developed for drug studies to provide data on drug toxicology and efficacy for the purposes of regulatory approval. Some of these materials are inappropriate and often too complex for trials of diagnostics or vaccines. As a result of the EU Clinical Trials Directive, GCLP guidelines have been developed specifically to provide

Box 1 | **General biosafety guidelines**

- Treat all specimens as potentially infectious
- Wear protective gloves and laboratory gown while handling specimens
- Do not eat, drink or smoke in the laboratory
- Do not wear open toe footwear in the laboratory
- Dispose of sharp objects such as lancets and needles in appropriate sharps containers
- Clean up spills with appropriate disinfectants e.g. 1% bleach
- Decontaminate all waste materials with an appropriate disinfectant
- Dispose of all waste, including test kits, in a biohazard container and autoclave, if available

guidance for laboratories involved in clinical trials. GCLP guidelines have been published by the British Association of Research Quality Assurance (BARQA)[27].

7. Co-morbidities

Genital chlamydial and gonococcal infections have been associated with an increased risk of HIV infection and transmission. A positive test for *C. trachomatis* or *N. gonhorrhoeae* therefore presents an excellent opportunity for counselling and to offer testing for HIV and other STIs.

V. CONDUCTING THE EVALUATION

1. Obtaining informed consent

See the discussion of informed consent in the generic guidelines *Evaluation of diagnostic tests for infectious diseases: general principles* in this supplement and the sample informed consent form in APPENDIX 2.

2. Biosafety guidelines

The general biosafety guidelines for clinic and laboratory staff outlined in BOX 1 should be adopted and implemented.

3. Use of test kits

The general guidelines on the use of test kits outlined in BOX 2 should be followed.

4. Testing

All tests should be performed according to the manufacturer's recommendations. Any deviations from the recommended procedure should be recorded.

Blinding is necessary to ensure independence of the test results in the evaluation. Laboratory staff should be blinded to the RDT results at the clinic, and vice versa.

As the interpretation of RDT results is subjective, it is recommended that at least two individuals read the test results independently.

As staff at busy clinics might not be able to read the RDT results at exactly the time recommended, it would be of interest to assess whether the results are stable 1 hour after the recommended time for reading.

VI. QUALITY ASSURANCE

As the temperatures that RDTs are subjected to during transport can affect their sensitivity, the sensitivity of RDTs should be checked at a central laboratory with a well-characterized quality-control panel on receipt from the manufacturer, and periodically throughout the recommended shelf life of the test. Peripheral health centres should be alerted to any depreciation of test quality during transport

All positive reference standard testss and 10% of the specimens that test negative (these should be selected sequentially, for example, select every tenth negative sample) should be sent to an external laboratory for validation.

Box 2 | **General guidelines for the use of test kits**

- Note lot number and expiry date: a kit should not be used beyond the expiry date
- Ensure correct storage conditions: if a desiccant is included in the package, do not use the kit if the desiccant has changed colour
- If test kits are stored in the refrigerator, they should be brought to room temperature (about 30 minutes) before use. The use of cold test kits can lead to false negative results.
- Damaged kits should be discarded
- Use test kits immediately after opening
- Reagents from one kit should not be used with those of another kit
- Test should be performed exactly as described in the product insert

VII. RECORDING AND ANALYSIS OF RESULTS, AND ARCHIVING OF SPECIMENS

The results of the two readings of the RDT results should be recorded in separate notebooks to ensure independent interpretation of the test results. The results of the RDT and reference test for each specimen should be recorded in a spreadsheet. The results of both the reference tests and the RDTs performed by laboratory personnel should be used to assess the performance of the RDTs in the clinic.

Data from the patient (APPENDIX 1), the results from the tests at the clinic, the results of the RDTs from the reference laboratory and the results of the reference standard test should be entered into a standardized spreadsheet for analysis. Double entry reduces the chance of error. Some form of data backup such as transfer to a disc should be performed at the end of each day.

The collected information should be kept until the study has ended, the data have been analysed and final publication achieved. Unused samples should be destroyed at the end of the study unless informed consent has been obtained to retain the samples for future studies.

VIII. ANALYSIS OF RESULTS

The sensitivity, specificity, positive and negative predictive values and 95% confidence intervals for each RDT compared to the results obtained with the reference test should be calculated.

BOX 3 contains a checklist of all the points that should be considered in the design and conduct of all evaluations of comparative field trials of chlamydia and gonorrhoeae RDTs.

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Box 3 | **Minimum standards for field component of sensitivity/specificity trials of chlamydia and gonorrhoea RDTs**

All trials should follow the general criteria for diagnostics trials outlined in *Evaluation of diagnostic tests for infectious diseases: general principles* in this supplement. The points listed below should be considered in the design and conduct of all evaluations of all comparative field trials of chlamydia and gonorrhoeae RDTs, and should be documented. This information should also be recorded in published trials.

Checklist for study design and analysis of results

Rationale for the evaluation and for what indication, for example:
- ❑ Need rapid tests to increase the specificity of syndromic management or for screening high-risk population
- ❑ Need to evaluate performance and ease of use in field setting

Record details of RDTs used:
- ❑ Manufacturer (company name, site of manufacture)
- ❑ Batch number
- ❑ Packaging type (sealed individually, multiple strips in same canister, and so on)
- ❑ Inclusion of desiccant with strips
- ❑ Inclusion of swabs etc needed to perform the test (or otherwise note the items used)
- ❑ Is product under evaluation for regulatory approval or is it commercially available?

Describe storage /transport conditions since receipt at evaluation site
- ❑ Date of manufacture, if available
- ❑ Date of expiry
- ❑ Duration of storage on site
- ❑ State and type of packaging, and whether canisters of test strips or reagent bottles have been opened before the start of the study (tests in damaged packaging should not be used)
- ❑ General temperature and humidity at storage (monitoring of temperature and humidity if possible). Tests should be stored away from direct sunlight.
- ❑ Time to complete use from opening of canister or bottled reagents (when dipsticks with this type of packaging are used)

Describe the trial site:
- ❑ Climatic conditions (mean local temperature and humidity)
- ❑ Workplace conditions (type of facility, lighting used for reading RDTs)
- ❑ Local STI epidemiology, if known

Describe the study population:
- ❑ Inclusion criteria (symptoms and signs, if any)
- ❑ Exclusion criteria (menstruating women)
- ❑ Demographics (age, sex)
- ❑ Recent treatment or antibiotic use

Describe the recruitment process:
- ❑ Who will be responsible for recruitment?
- ❑ Describe the process of obtaining informed consent*

Describe the evaluation procedure:
- ❑ Time of strip or device package opening to time of use
- ❑ Specimen collection (instructions for collecting vaginal swabs or urine specimens)
- ❑ Specimen processing and transfer to test device or strip (device provided by manufacturer or pipette, for example)
- ❑ Time from specimen collection to placing sample on RDT, how specimens are stored in this interval
- ❑ Time taken to obtain reading (per manufacturer's instructions, or if delayed, for how long and reason for delay)
- ❑ Record each line on the strip separately, starting with the control line. A record of intensity is not necessary as the test is not quantitative

Record organization and training of test readers/technicians:
- ❑ One or multiple readers
- ❑ Same technician/reader per test type, or alternating
- ❑ Blinding to reference standard test results, results of other RDT readers, and to clinical presentation (the latter might not be possible in some circumstances)
- ❑ Identity of technicians/readers for later analysis (can be coded)
- ❑ Training/experience in use of test (including date of training and validation of quality of training), and comparison with intended end-users

Record significant difficulties encountered with testing:
- ❑ Significant or recurrent problems encountered in kit preparation or specimen collection (including opening of packaging, etc.)
- ❑ Any deviations from manufacturer's instructions
- ❑ Record what is done with indeterminate results, how many tests had to be repeated
- ❑ Consider a formal independent qualitative appraisal of 'ease of use' of product by each technician

Ensure reference standard test is performed correctly:
- ❑ Kit or reagents used
- ❑ Proficiency and training of technicians (subscription to external quality-assurance programmes)
- ❑ Mechanism for blinding from RDT results

Describe methods of data analysis:
- ❑ Consider collecting extra swabs or saving urine specimens to allow for additional testing as necessary. The criteria for settling discordant results should be formulated beforehand and clearly stated.
- ❑ Describe what test results will be used to guide treatment of patients

*Issues concerning ethics and patient consent are detailed in *Evaluation of diagnostic tests for selected infectious diseases: general principles* in this supplement. See APPENDICES 1 and 2 for sample data-collection and informed consent forms.

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APPENDIX 1 | SAMPLE CLINIC DATA-COLLECTION FORM FOR THE EVALUATION OF CHLAMYDIA AND GONORRHOEA RDTs

Study number: _____

Date of clinic visit: _____ (day/month/year)
(study site will be incorporated in study number, see above)

Date of birth: _____ (day/month/year)
Age _____ years

	Yes	No
Woman has received care at this clinic before based on national guidelines	❑	❑

Risk factors for high-risk women:

	Yes	No
Age < 25 years	❑	❑
At least 10 partners in the last week	❑	❑
Vaginal pH > 4.5 (or absence of lactobacilli)	❑	❑
Any sign of cervicitis or motion tenderness	❑	❑

Symptoms:
If Yes, tick all that are applicable below:

	Yes	No
Vaginal discharge	❑	❑
Dysuria	❑	❑
Pain on intercourse	❑	❑
Irregular periods	❑	❑
Lower abdominal pain	❑	❑

Other: specify_____

Physical examination:

	Yes	No
Vaginal discharge:	❑	❑

If Yes:
Colour_____ profuse___/scanty___

	Yes	No
Discharge from the cervical os:	❑	❑

If Yes:
Colour _____ profuse___/scanty___

	Yes	No
Visible bleeding after swab collection:	❑	❑

For women with lower abdominal pain:

	Yes	No
Cervical motion tenderness	❑	❑
Pelvic mass	❑	❑

	Yes	No
Is patient pregnant?	❑	❑

Treated syndromically for:

	Yes	No
GC and CT	❑	❑
BV/TV	❑	❑
Candida	❑	❑
Genital ulcers	❑	❑

	Yes	No
If a rapid test is available at this clinic, are you willing to wait for the results?	❑	❑

If Y, will you wait 30 min. ___, 1 hour ____, 2 hours ____?

APPENDIX 2 | SAMPLE INFORMED CONSENT FORM FOR THE EVALUATION OF CHLAMYDIA RDTs

(A separate patient information sheet containing this information should also be provided)

A | PURPOSE OF THE STUDY

Chlamydial infection is caused by bacteria that are transmitted by sexual intercourse. In women, this infection can cause pelvic pain and, in the long term, increase the risk of infertility. Furthermore, during unprotected sexual intercourse with a man infected with the AIDS virus, a woman infected with chlamydia will have a higher risk of acquiring the AIDS virus than a woman not infected with this bacterium.

To find out whether you have this infection, we need to do some laboratory tests. These tests are expensive and the results are not available the same day. Rapid tests to diagnose chlamydia within 30 minutes are now available but we do not know if they are accurate or reliable. The main purpose of this study is to evaluate a rapid test for the diagnosis of chlamydial infection. We would like to compare the result of this rapid test with a laboratory-based test to see if it is as accurate as laboratory tests.

B | STUDY PROCEDURES

If you agree to participate in the study, you will be assigned a study number. The doctor or nurse will give you a physical examination and ask you some questions according to standard clinic procedure. He/she will take 2 or 3 samples from your vagina and 2 samples from your cervix. Your name will not appear on any samples or on the questionnaire. All the samples will be destroyed at the end of the study. If you are diagnosed with chlamydial infection using the standard laboratory tests, you will be treated with antibiotics on your follow-up visit according to normal clinic procedure. You will not be treated according to the rapid test results as we are not yet sure if it is accurate.

C | VOLUNTARY PARTICIPATION

Your decision not to participate in this study will not affect the care you will receive at the clinic in any way. Even if you do agree to become a study participant, you can withdraw from the study at any time (verbally) without affecting the care that you will receive. During the interview, you can choose not to answer any particular question.

D | DISCOMFORT AND RISKS

You might feel a small amount of discomfort or have a small amount of bleeding from the vagina after the pelvic examination and specimen collection.

E | BENEFITS

There will be no immediate benefits from your participation in the study. When the study results are known and if the rapid tests are acceptable in terms of accuracy, everyone who comes to the clinic could benefit from having this test available to diagnose chlamydia and receive the right treatment the same day.

F | COMPENSATION

There will be no monetary compensation for this study, but routine medical consultation and appropriate referral services are available.

G | CONFIDENTIALITY STATEMENT

The records concerning your participation are to be used only for the purpose of this research project. Your name will not be used on any study forms or labels on laboratory specimens or in any report resulting from this study. At the beginning of the study, we will give you a study identification number and this number will be used on the forms and on the laboratory specimens. Any information obtained in connection with this study will be kept strictly confidential. Only members of the study team will have access to information linking your name with your study number.

H | QUESTIONS AND FREEDOM TO WITHDRAW FROM THE STUDY

You can withdraw from the study at any time without affecting your present or future medical care at the clinic. You can contact any of the study personnel if you have questions about the research. (Please give the contact name, address and telephone number of the contact person for each site).

I | RESULTS PUBLICATION

When the researchers have analysed the data, the results and the explanation of its implications will be posted at the clinic for everyone's information.

J | PARTICIPANT STATEMENT

I have been informed verbally and in writing about this study and understand what is involved. I also know whom to contact if I need more information. I understand that confidentiality will be preserved. I understand that I am free to withdraw from the study at any time without affecting the care I normally receive at the clinic. I agree to participate in this study as a volunteer subject and will be given a copy of this information sheet to keep.

_____ _____

Date Name of participant

_____

Signature (or thumb print or cross) of participant

_____ _____

Date Name of witness

_____

Signature of witness

K | INVESTIGATOR'S STATEMENT

I, the undersigned, have defined and explained to the volunteer in a language she understands, the procedures of this study, its aims and the risks and benefits associated with her participation. I have informed the volunteer that confidentiality will be preserved, that she is free to withdraw from the trial at any time without affecting the care she will receive at the clinic. Following my definitions and explanations the volunteer agrees to participate in this study.

_____ _____

Date Name of investigator who gave the information about the study

Signature: _____