Point-of-care tests for sexually transmitted infections

Target product profiles

World Health Organization

human reproduction programme hrp
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Point-of-care tests for sexually transmitted infections: target product profiles

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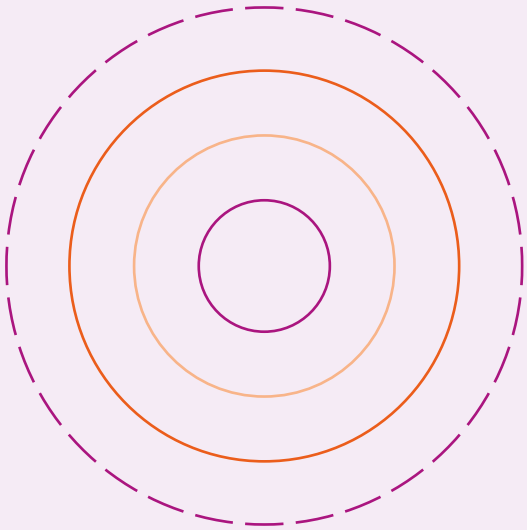
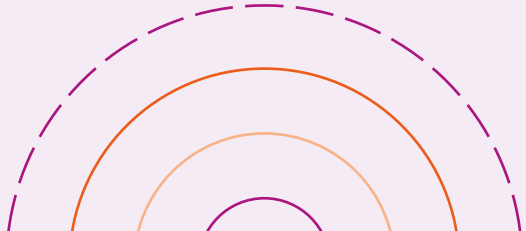
Contents

Abbreviations

FTP	file transfer protocol
GPS	Global Positioning System
GPRS	General Packet Radio Service
GSM	Global System for Mobile communication
HIV	human immunodeficiency virus
HL7	Health Level Seven
ISO	International Organization for Standardization
NAAT	nucleic acid amplification test
RPR	rapid plasma reagin
TPPA	*Treponema pallidum* passive particle *agglutination assay*





Introduction

In 2020, WHO estimated 374 million new cases per year of the four main curable sexually transmitted infections: gonorrhoea *(Neisseria gonorrhoeae)*, chlamydia *(Chlamydia trachomatis)*, trichomoniasis *(Trichomonas vaginalis)* and syphilis *(Treponema pallidum) (1)*.

In addition, *Mycoplasma genitalium* infections are prevalent in many settings, human papillomavirus is associated with 311 000 people dying from cervical cancer each year *(2)* and an estimated 1.5 million people acquired HIV in 2021 *(3)*. Low- and middle-income countries have the highest global burden of non-viral and viral sexually transmitted infections. Sexually transmitted infections may lead to severe reproductive sequelae and neonatal death, are associated with the development of cancer resulting in high mortality and can facilitate the transmission and acquisition of HIV.

Many urogenital and the vast majority of extragenital non-viral sexually transmitted infections are asymptomatic. These cases are most often identified through sexual contact notification and as a result of opportunistic testing and screening. Screening or significantly enhanced testing of people at increased risk of sexually transmitted infections and early and accurate diagnosis of infection are important to provide correct treatment and to control the spread of sexually transmitted infections and their sequelae. The need to advance the development of point-of-care tests for sexually transmitted infections has been recognized, since these will substantially improve the management of sexually transmitted infection cases *(4)*. Point-of-care testing will potentially reduce the overuse and misuse of antibiotics and could thus decrease the selection pressure for the development of antimicrobial resistance among sexually transmitted pathogens and bystander commensal or pathogenic bacterial species *(5)*. Point-of-care tests can lower health-care costs, reduce waiting times, speed up and increase the accuracy of treatment and improve patient follow-up.

Accurate, rapid and affordable point-of-care tests could increase access to testing and identification of sexually transmitted infections in a single health service user visit in both low- and middle-income countries and high-income countries and could be used at all levels of health-care systems while also contributing to improving surveillance for sexually transmitted infections *(6)*.

Diagnostics are often undervalued, but they are just as important to attaining the Sustainable Development Goals as medicines and vaccines. In particular, improved access to diagnostics will be essential to reach Sustainable Development Goal 3.7: ensure universal access to sexual and reproductive health care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes and Sustainable Development Goal 3.8: achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.

In close alignment with the Sustainable Development Goals are WHO's Triple Billion goals, which include improved access to diagnostics for primary health care as a means to enable universal health coverage for 1 billion more individuals. To achieve this goal, moving testing closer to the health service user will be essential. WHO's Global health sector strategies on, respectively, HIV, viral hepatitis, and sexually transmitted infections for the period 2022-2030 recognizes point-of-care testing as an innovation that enables improvement in all steps of the sexually transmitted infection services cascade *(7)*.

In 2006, WHO introduced the ASSURED criteria for point-of-care tests: affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free and deliverable to end users. Although notable progress has been made in developing diagnostic tests for syphilis, chlamydial and gonococcal infections and trichomoniasis, there are still no tests available that comply with all these criteria.

To accelerate advances in point-of-care testing for sexually transmitted infections, WHO facilitated landscape analyses of point-of-care diagnostic technologies for dual HIV and syphilis tests, *Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis* and human papillomavirus, available and in the pipeline. It concurrently organized expert meetings to conceive target product profiles for point-of-care tests for these infections. Moreover, to strengthen the capacity of countries to perform laboratory testing for sexually transmitted infections, WHO has updated the laboratory diagnosis of sexually transmitted infections, including HIV *(8)*. This is being updated to reflect the development in point-of-care tests for sexually transmitted infections.

In 2018, WHO initiated the development of target product profiles for point-of-care tests for *Neisseria gonorrhoeae* to address antimicrobial resistance. A target product profile for improved antimicrobial stewardship for gonococcal infection was conceived in 2019 *(9,10)*.

The target audience for the target product profiles is broad and includes clinicians, researchers working on diagnostics, laboratory experts, including, microbiologists and virologists, public health experts, epidemiologists, developers and representatives for manufacturers, including biotech engineers, policy- and decision-makers as well as representatives from regulatory bodies and agencies, donor agencies and international organizations *(11)*.

Development

The development of the target product profiles was initiated by reviewing the pooled performance data from systematic reviews commissioned by WHO, published predictive models to inform test performance and the lower limits of detection of technologies identified in the landscape analysis and then further developed through a series of face-to-face and online consultations with an international expert group using an adapted Delphi method.

The initial list of 28 parameters for the target product profiles was adapted from the target product profile for dual HIV and syphilis tests commissioned in 2013 by Unitaid. The target product profile parameters were expressed as minimal and optimal characteristics to reflect the range of needs of health-care providers and health service user populations within the intended use of the tests using a public health approach.

The international expert group consisted of 32 internationally recognized sexually transmitted infection experts, including clinicians, microbiologists, professionals in the field of laboratory medicine, public health, social science and diagnostic technology and development, from all WHO regions. The international expert group also comprised representatives from WHO, Unitaid and the Foundation for Innovative New Diagnostics. All experts were assessed for potential conflict of interest, and none was found.

At the first meeting in May 2014, the group assessed and endorsed the list of target product profile parameters. Small-group work resulted in the first draft target product profiles for each of the point-of-care tests to detect sexually transmitted infections.

The draft target product profiles were then discussed with all the participants and reconciled according to the feedback, taking into consideration agreements and disagreements between the small groups and the plenary. During both the small-group and plenary sessions, the first sexually transmitted infection diagnostic landscape was used as a reference by participants, enabling them to compare proposed minimal and optimal target product profile characteristics with those of existing sexually transmitted infection tests.

The refined target product profiles were then presented and reviewed at the second technical consultation in July 2015. All comments and points discussed during the second expert group meeting were documented and reflected in the revised target product profiles as a consensus-based agreement among all stakeholders. The international expert group assessed and endorsed the target product profile parameters through several rounds of online consultations. The final target product profiles were agreed on and then published on the WHO website. The target product profiles were revised during the third technical consultation on sexually transmitted infection point-of-care tests in December 2019, followed by online consultations.

The target product profiles were published on the WHO website for public review from June to October 2021. The review included a structured online questionnaire (available upon request) and allowed for any comments and suggestions. The feedback received was carefully reviewed and considered, resulting in the current document. The target product profiles and research questions for human papillomavirus will undergo a separate review process and are thus not included in this document. They will be published separately.

This work was supported by the UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), and the Department of the Global HIV, Hepatitis and Sexually Transmitted Infections Programmes.

Glossary

Intended use and target population(s)

The current target product profiles propose the main use and populations of the specific point-of-care tests, but this should be adapted to the context, guided by local burdens of infection and patterns of disease.

Performance

The analytic performance, based on a sample size sufficient to achieve confidence intervals of ±5% around a point estimate of sensitivity and specificity.

Target price per test

The cost per test, excluding distributor costs and taxes, excluding the cost of a device or reader in case the point-of-care test is device-based and/or requires a reader for obtaining the result.

Stability of valid result

Also called the read window, the time period within which a test result is stable. This requirement only applies to tests that require reading by eye or a reader device.

Specimen preparation

Steps to be undertaken and time needed between the collection of the sample and insertion into the test.

Duration of sample stability

The maximum time period allowed from specimen collection to insertion into the test, following the manufacturer's instruction for use.

Safety precautions

Containment principles, technologies and practices to prevent unintentional exposure to pathogens and toxins or their accidental release.

Data export

For point-of-care tests that are reader or device based.

Internal quality control

Used to check specimen adequacy and detect problems or failure in one or more reagents with a test.

Case management

Sexually transmitted infection case management entails: history-taking and examination, diagnosis and treatment (including referral if needed), counselling and education, contact tracing and data gathering (recording).

Quantification

At present, point-of-care tests usually provide a positive or negative result; other quantitative laboratory-based methods may be used for quantification, hence this parameter is not included in the target product profiles.

1. Combined and single point-of-care tests for gonorrhoea

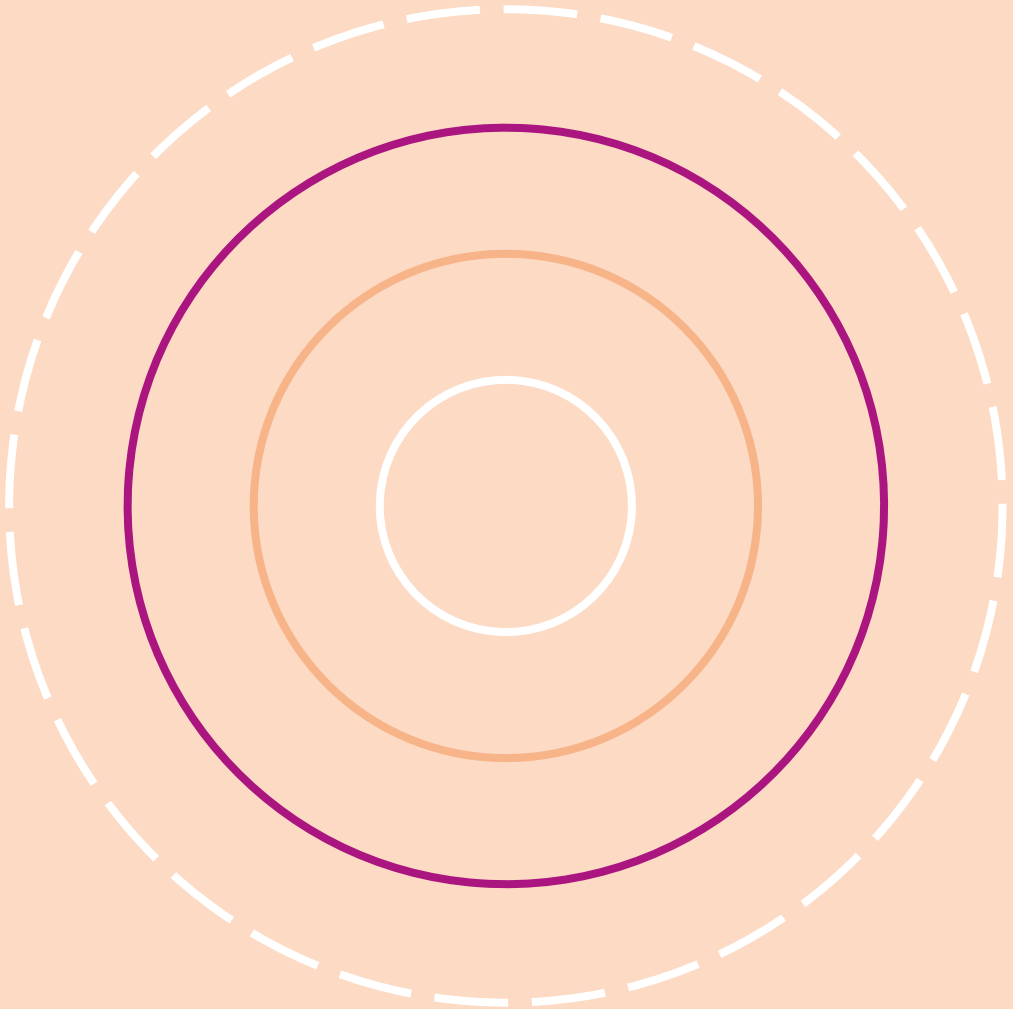


Table 1. Combined and single point-of-care tests for gonorrhoea

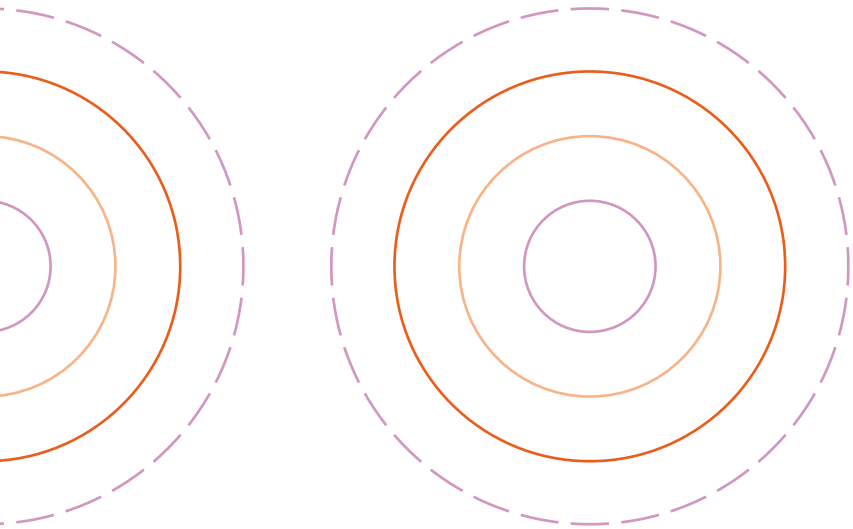
Goal of test	To detect *Neisseria gonorrhoeae*	
Intended use and target population(s)	**Surveillance and case management:** Sexually active population, including key populations (such as gay men and other men who have sex with men, sex workers and transgender people) and attendees of a clinic or service for sexually transmitted infections **Screening and regular testing:** Key populations and other populations at increased risk of sexually transmitted infections	
Target use setting	Health-care settings, especially at primary care level (level 1) or above	
Results	Clear positive, negative or invalid result with minimal instructions for interpretation	
Equipment	Single use, biodegradable or recyclable disposable diagnostic test preferred, reader optional (small, portable, table-top or handheld, no external electricity or power supply required)	
Target use(s)	Testing health service user	
Reference technology	Laboratory-based NAAT	
Performance	**Minimal**	**Optimal**
Clinical sensitivity	90% (genital)	98% (genital)
Clinical specificity	90% (genital)	>98% (genital)
Operational characteristics	**Minimal**	**Optimal**
Specimen	Vaginal swab or urine	Urine, vaginal, anorectal and oropharyngeal swabs
Specimen preparation	Minimal sample processing; no more than one operator step	Integrated
Specimen collection method	By a health-care provider	Self-collected samples or by a health-care provider
Steps to be performed between specimen preparation and result	No more than three operator steps that are not timed or labour intensive	One operator step (none of which has a timed interval), excluding waste disposal
Additional consumables required but not provided within the test kit	None, except for specimen collection	
Cold chain	None required at any point	
Test kit	All materials required for test procedure, including devices, reagents or other consumables (for example, lancets or alcohol swabs) to diagnose one individual, included in packaged, self-contained kit (either packaged individually as one test per test kit or sufficient to perform the number of tests packaged in the test kit box – such as 30, 50 or 100 tests)	
Test kit stability and storage conditions	12 months, stable between 2 °C and 35 °C, 70% humidity, 3000 metres altitude	18 months, stable between 0 °C and 50 °C, 90% humidity, 4500 metres altitude

Table 1 (continued). Combined and single point-of-care tests for gonorrhoea

Environmental tolerance of packaged test kit	• Transport packaging not needed • Transport stress (48 hours with fluctuations up to 50 °C and down to 0 °C) • Tolerate exposures between 2 °C and 45 °C at an altitude up to 3000 metres, up to and including condensing humidity	
Operating conditions	• Between 15 °C and 40 °C at an altitude up to 2000 metres • Extremely low relative humidity	• Between 10 °C and 45 °C at an altitude up to 4500 metres • Both low and high humidity • Result interpretation in low-light settings
Training required	<90 minutes	30 minutes
Clean water	None	
Time to result	≤60 minutes	≤15 minutes
Duration of sample stability	It is inherent to the definition of a point-of-care test that, following specimen collection, there should be minimal delay in testing the specimen	
Stability of valid result	• At least 30 minutes (after which results may be *false* or *invalid*) • Clear language in the instructions for users regarding test reading	• ≥1 hour (after which results give *invalid* rather than *false* results) • Clear language in the instructions for users regarding test reading
Safety precautions	Closed, self-contained system; unprocessed sample transfer only; no open handling of biohazardous material	
Waste and disposal requirements	Safe waste disposal	Small environmental footprint; compostable plastics for test kit materials
Internal quality control – reagents	Procedural (reagent-addition) control internalized in test for each individual test run; positive control for internal quality control available for purchase separately	Procedural (specimen-addition) control internalized in test for each individual test run; positive control for internal quality control provided in each box of test kits
Device control	Indicator of instability or expiration	Indicator of instability, expiration, inadequate sample and incorrect procedure and/or use but not as an additional component
Regulatory requirements	Compliance with appropriate ISO standard	
Identification capability	Yes – simple, self-contained way to indicate a health service user identifier	
Result display and interpretation	The result can be read with the naked eye with minimal instructions for interpretation required by the user or with an integrated reader with an easy pictorial display: reactive, non-reactive, invalid for each test	
Data acquisition and display	If combined with a reader, on-device visual read-out; able to add information (health service user ID, operator ID, date, location etc.); able to store health service user results; able to print results using commoditized paper products (standard paper specifications and sizes); needs to consider privacy and data security laws	
Connectivity	If combined with a reader, reader has integrated GPS module	If combined with a reader, internally integrated GPS/GPRS module and conformity with HL7 messaging standards

Table 1 (continued). Combined and single point-of-care tests for gonorrhoea

Data export	If combined with a reader, full data export over mobile phone network, encrypted data only	• If combined with a reader, full data export over mobile phone network, encrypted data only (data transmission can automatically select between GPRS or more advanced networks and GSM, based on available coverage) • GPRS should be able to use the internet FTP to transmit data: data transfer should be initiated every 6–12 hours automatically by the reader; data can be exported in a format compatible with HL7 standards, where appropriate; instrument tracks and transmits quality assurance data over time (such as identify shifts or trends)
Target price per test	<US$ 5	<US$ 1



2. Combined and single point-of-care tests for chlamydia

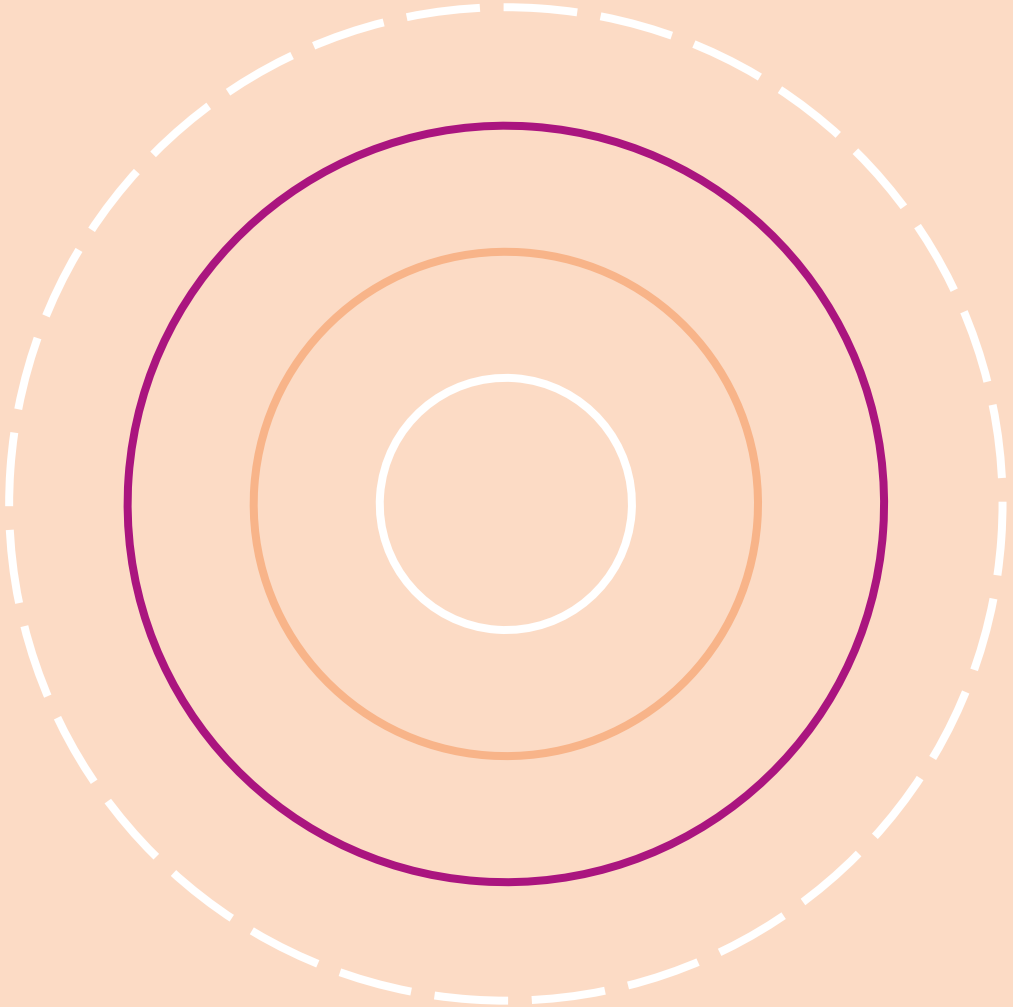


Table 2. Combined and single point-of-care tests for chlamydia

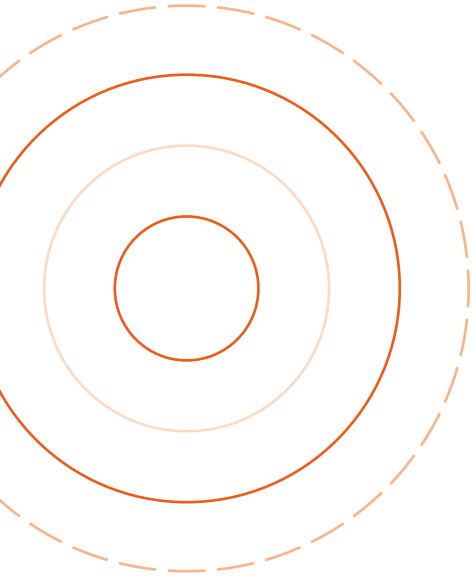
Goal of test	To detect *Chlamydia trachomatis*	
Intended use and target population(s)	**Surveillance and case management:** Sexually active population, including key populations (such as gay men and other men who have sex with men, sex workers and transgender people) and attendees of a clinic or service for sexually transmitted infections **Screening and regular testing:** Key populations and people at increased risk of infection	
Target use setting	Health-care settings, especially at primary care level (level 1) or above	
Results	Clear positive, negative or invalid result with minimal instructions for interpretation	
Equipment	Single use, biodegradable or recyclable disposable diagnostic test preferred, reader optional (small, portable, table-top or handheld, no external electricity or power supply required)	
Target use(s)	Testing health service users	
Reference technology	Laboratory-based NAAT	
Performance	**Minimal**	**Optimal**
Clinical sensitivity	>90% (lower limit > 90%) (genital)	100% (genital)
Clinical specificity	98% (lower limit > 95%) (genital)	100% (genital)
Operational characteristics	**Minimal**	**Optimal**
Specimen	Vaginal swab or urine	Urine, vaginal, anorectal and oropharyngeal swabs
Specimen preparation	By a health-care provider	Self-collected samples or by a health-care provider
Specimen collection method	Minimal sample processing; no more than one operator step	Integrated
Steps to be performed between specimen preparation and result	No more than three operator steps that are not timed nor labour intensive	One operator step (none of which has a timed interval), excluding waste disposal
Additional consumables required but not provided within the test kit	None, except for specimen collection	
Cold chain	None required at any point	
Test kit	All materials required for test procedure, including devices, reagents or other consumables (for example lancets, alcohol swabs) to diagnose one individual, included in packaged, self-contained kit (either packaged individually as one test per test kit or sufficient to perform the number of tests packaged in the test kit box – such as 30, 50 or 100 tests)	
Test kit stability and storage conditions	12 months, stable between 2 °C and 35 °C, 70% humidity, 3000 metres altitude	18 months, stable between 0 °C and 50 °C, 90% humidity, 4500 metres altitude

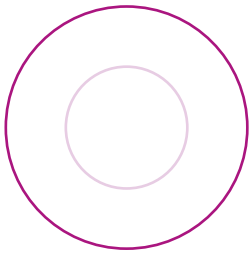
Table 2 (continued). Combined and single point-of-care tests for chlamydia

Environmental tolerance of packaged test kit	• Transport packaging not needed • Transport stress (48 hours with fluctuations up to 50 °C and down to 0 °C) • Tolerates exposure between 2 °C and 45 °C at an altitude up to 3000 metres, up to and including condensing humidity	
Operating conditions	• Between 15 °C and 4 °C at an altitude up to 2000 metres • Extremely low relative humidity	• Between 10 °C and 45 °C at an altitude up to 4500 metres • Both low and high humidity • Result interpretation in low light settings
Training required	<90 minutes	30 minutes
Clean water	None	
Time to result	≤60 minutes	≤15 minutes
Duration of sample stability	It is inherent to the definition of a point-of-care test that, following specimen collection, there should be minimal delay in testing of the specimen	
Stability of valid result	• At least 30 minutes (after which results may be *false* or *invalid*) • Clear language in the instructions for users regarding test reading	• ≥1 hour (after which results give *invalid* rather than *false* results) • Clear language in the instructions for users regarding test reading
Safety precautions	Closed, self-contained system; unprocessed sample transfer only; no open handling of biohazardous material	
Waste and disposal requirements	Safe disposal of all waste materials	Small environmental footprint; compostable plastics for test materials
Internal quality control – reagents	Procedural (reagent-addition) control internalized in test for each individual test run; positive control for internal quality control available for purchase separately	Procedural (specimen-addition) control internalized in test for each individual test run; positive control for internal quality control provided in each box of test kits
Device control	Indicator of instability or expiration	Indicator of instability, expiration, inadequate sample and incorrect procedure and/or use but not as an additional component
Regulatory requirements	Compliance with appropriate ISO standard	
Identification capability	Yes – simple, self-contained way to indicate a health service user identifier	
Result display and interpretation	Naked eyes, minimal instructions, integrated reader	
Data acquisition and display	If combined with a reader, on-device visual read-out; able to add information (health service user ID, operator ID, date, location, etc.); able to store health service user results; able to print out results utilizing commoditized paper products (i.e. standard paper specifications and sizes); needs to consider privacy and data security laws	
Connectivity	If combined with a reader, reader has integrated GPS module	If combined with a reader, internally integrated GPS/GPRS module and conformity with HL7 messaging standards

Table 2 (continued). Combined and single point-of-care tests for chlamydia

Data export	If combined with a reader, full data export over mobile phone network, encrypted data only	• If combined with a reader, full data export over mobile phone network, encrypted data only (data transmission can automatically select between GPRS or more advanced networks and GSM, based on available coverage) • GPRS should be able to utilize the internet FTP to transmit data: data transfer should be initiated every 6–12 hours automatically by the reader; data can be exported in a format compatible with HL7 standards, where appropriate; instrument tracks and transmits quality assurance data over time (such as identify shifts or trends)
Target price per test	<US$ 5	<US$ 1





3. Combined and single point-of-care tests for trichomoniasis

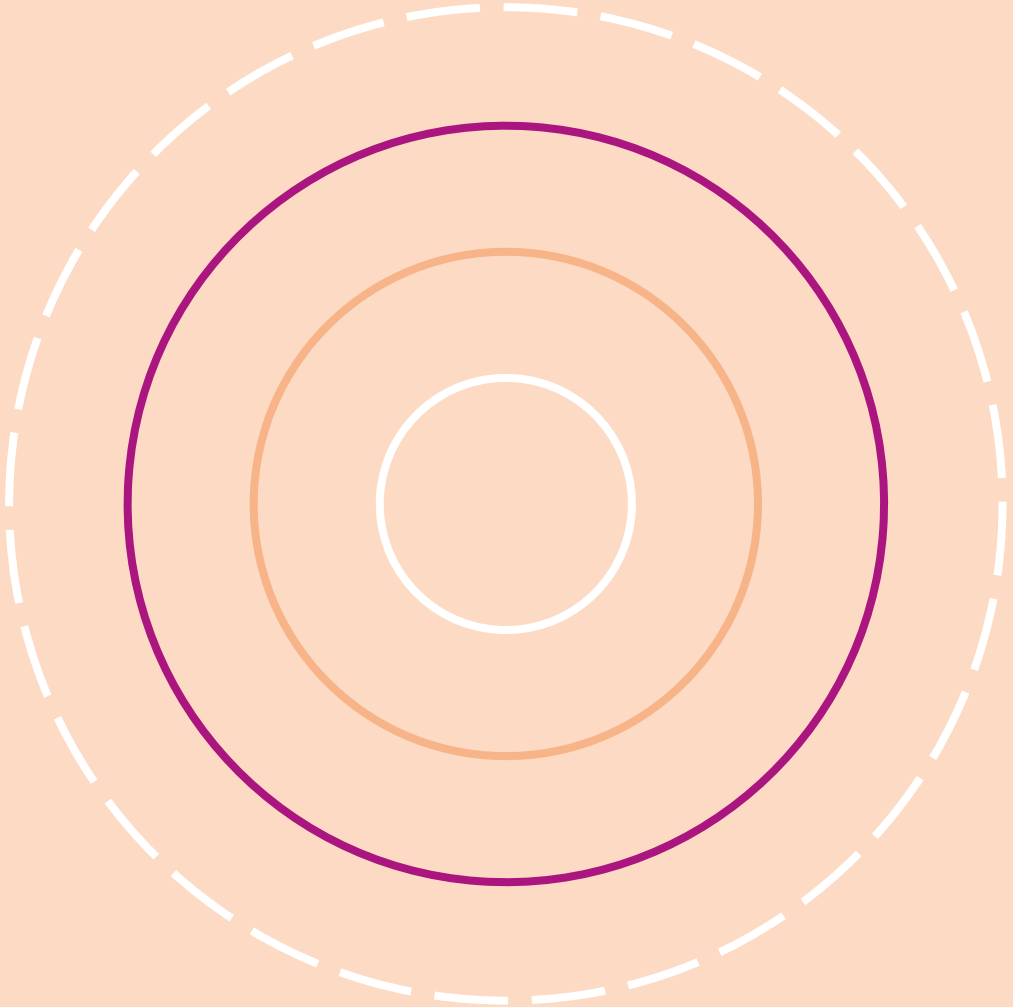


Table 3. Combined and single point-of-care tests for trichomoniasis

Goal of test	To detect *Trichomonas vaginalis*	
Intended use and target population(s)	**Surveillance and case management:** Sexually active population, including key populations and populations at increased risk of sexually transmitted infections	
Target use setting	Health-care settings, especially at primary care level (level 1) or above	
Results	Clear positive, negative or invalid result with minimal instructions for interpretation	
Equipment	Single use, biodegradable or recyclable disposable diagnostic test preferred, reader optional (small, portable, table-top or handheld, no external electricity or power supply required)	
Target use(s)	Testing health service user	
Reference technology	Laboratory-based NAAT	
Performance	**Minimal**	**Optimal**
Clinical sensitivity	85%	98%
Clinical specificity	99%	100%
Operational characteristics	**Minimal**	**Optimal**
Specimen	Vaginal swab	Urine
Specimen preparation	By a health-care provider	Self-collected samples or by a health-care provider
Specimen collection method	Minimal sample processing; no more than one operator step	Integrated
Steps to be performed between specimen preparation and result	No more than three operator steps that are not timed nor labour intensive	Maximum one operator step (none of which has timed interval), excluding waste disposal
Additional consumables required but not provided within the test kit	None, other than for specimen collection	
Cold chain	Not required at any point	
Test kit	All materials required for test procedure, including devices, reagents or other consumables (for example lancets, alcohol swabs) to diagnose one individual, included in packaged, self-contained kit (either packaged individually as one test per test kit or sufficient to perform the number of tests packaged in the test kit box – such as 30, 50 or 100 tests)	
Test kit stability and storage conditions	12 months, stable between 2 °C and 35 °C, 70% humidity, 3000 metres altitude	18 months, stable between 0 °C and 50 °C, 90% humidity, 4500 metres altitude
Environmental tolerance of packaged test kit	• Transport packaging not needed • Transport stress (48 hours with fluctuations up to 50 °C and down to 0 °C) • Tolerate exposures between 2 °C and 45 °C at an altitude up to 3000 metres, up to and including condensing humidity	
Operating conditions	• Between 15 °C and 40 °C at an altitude up to 2000 metres • Extremely low relative humidity	• Between 10 °C and 45 °C at an altitude up to 4500 metres • Both low and high humidity • Result interpretation in low light settings

Table 3 (continued). Combined and single point-of-care tests for trichomoniasis

Training required	<90 minutes	30 minutes
Clean water	None	
Time to result	≤60 minutes	≤30 minutes
Duration of sample stability	It is inherent to the definition of a point-of-care test that following specimen collection there should be minimal delay in testing of the specimen	
Stability of valid result	• At least 30 minutes (after which results may be *false* or *invalid*) • Clear language in the instructions for users regarding test reading	• ≥1 hour (after which results give *invalid* rather than *false* results) • Clear language in the instructions for users regarding test reading
Safety precautions	Closed, self-contained system; unprocessed sample transfer only; no open handling of biohazardous material	
Waste and disposal requirements	Safe disposal of all waste material	Small environmental footprint; compostable plastics for test materials
Internal quality control – reagents	Procedural (reagent-addition) control internalized in test for each individual test run; positive control for internal quality control available for purchase separately	Procedural (specimen-addition) control internalized in test for each individual test run; positive control for internal quality control provided in each box of test kits
Device control	Indicator of instability or expiration	Indicator of instability, expiration, inadequate sample and incorrect procedure and/or use but not as an additional component
Regulatory requirements	Compliance with appropriate ISO standards	
Identification capability	Yes – simple, self-contained way to indicate a health service user identifier	
Result display and interpretation	Result can be read with the naked eye with minimal instructions for interpretation required by user, or with an integrated reader with an easy pictorial display: reactive, non-reactive, invalid for each test	
Data acquisition and display	If combined with a reader, on-device visual read-out; able to add information (health service user ID, operator ID, date, location, etc.); able to store health service user results; able to print out results utilizing commoditized paper products (i.e. standard paper specifications and sizes); needs to consider privacy and data security laws	
Connectivity	Not applicable	Universal reader integrated (such as to GPS module) with local surveillance/ sexually transmitted infection programme initiatives
Data export	If combined with a reader, full data export over mobile phone network, encrypted data only	• If combined with a reader, full data export over mobile phone network, encrypted data only (data transmission can automatically select between GPRS or more advanced networks and GSM, based on available coverage) • GPRS should be able to utilize the internet FTP to transmit data: data transfer should be initiated every 6–12 hours automatically by the reader; data can be exported in a format compatible with HL7 standards, where appropriate; instrument tracks and transmits quality assurance data over time (such as identify shifts or trends)
Target price per test	<US$ 5	<US$ 1

4. Combined and single point-of-care tests for syphilis

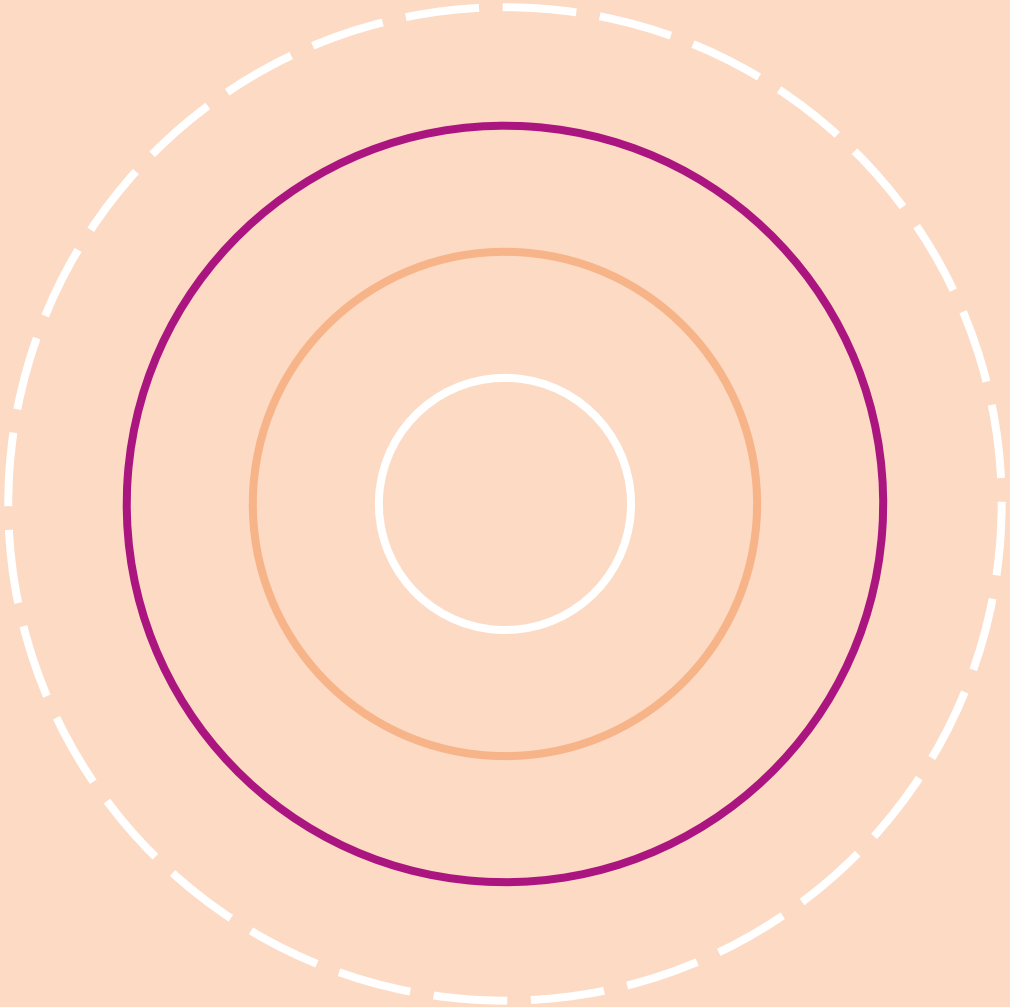


Table 4. Combined and single point-of-care tests for syphilis

Goal of test	To detect *Treponema pallidum* specific antibodies and non-*Treponema pallidum* specific antibodies			
Intended use and target population(s)	**Surveillance and case management:** Sexually active population, including key populations (such as gay men and other men who have sex with men, sex workers and transgender people) and attendees of a clinic or service for sexually transmitted infections **Screening and regular testing:** Pregnant women, key populations, populations at increased risk of sexually transmitted infections			
Target use setting	Clinical and non-clinical, including community-based, settings			
Results	Clear reactive, non-reactive or invalid result with minimal instructions for interpretation			
Equipment	Single use diagnostic test preferred, reader optional (small, portable, table-top or handheld, no external electricity or power supply required)			
Target use(s)	*Treponema pallidum* component		Non-*Treponema pallidum* component	
Reference technology	TPPA		RPR	
Performance	**Minimal**	**Optimal**	**Minimal**	**Optimal**
Clinical sensitivity	>80%[1]	>90%	>95% of high titre (>1 in 8) specimens	>99% of high titre (>1 in 8) specimens
Clinical specificity	>90%	>95%	>90% of high titre (>1 in 8) specimens[2]	>95% of high titre (>1 in 8) specimens[2]
Operational characteristics	**Minimal**		**Optimal**	
Specimen	Finger prick capillary blood (maximum 50 µL)		Finger prick capillary blood (maximum 20 µL) and oral fluids	
Specimen preparation	Minimal sample processing; no more than one operator step		Integrated	
Specimen collection method	By a health-care provider		Self-collected samples or by a health-care provider	
Steps to be performed between specimen preparation and result	No more than three operator steps that are not timed nor labour intensive		Maximum one operator step (none of which has a timed interval), excluding waste disposal	
Additional consumables required but not provided within the test kit	None, other than for specimen collection			
Cold chain	None required at any point			
Test kit	All materials required for test procedure, including devices, reagents or other consumables (for example lancets, alcohol swabs) to diagnose one individual, included in packaged, self-contained kit (either packaged individually as one test per test kit or sufficient to perform the number of tests packaged in the test kit box – such as 30, 50 or 100 tests)			
Test kit stability and storage conditions	12 months, stable between 2-35 °C, 70% humidity, 3000 metres altitude		18 months, stable between 0-50 °C, 90% humidity, 4500 metres altitude	

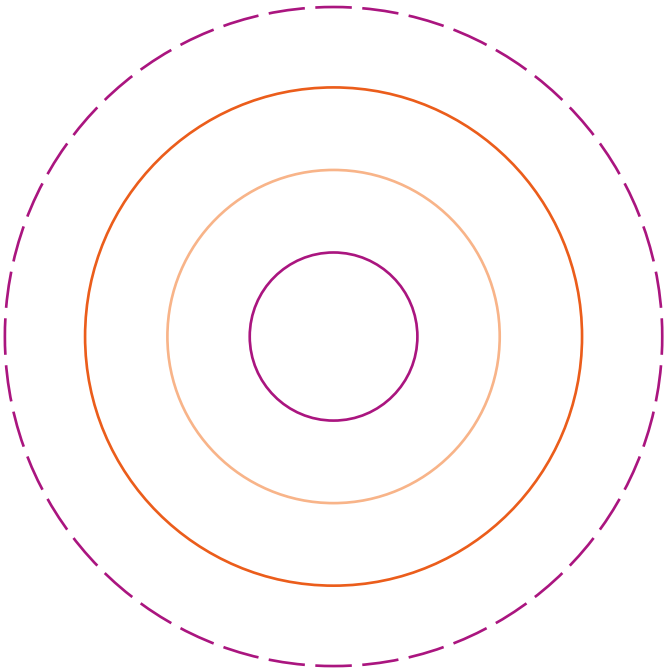
1 For the treponemal component, while minimal clinical sensitivity is stated as >80%, optimal performance of >90% should be prioritized
2 The current cardiolipin-based, gold standard non-treponemal tests (RPR) are not specific for syphilis but may be falsely reactive, at low titres (< 1 in 8), in the presence of various acute and chronic diseases. It is important that any new non-treponemal point-of-care test is as specific (90 -95%) as the lab-based test, at higher titres (≥1 in 8), recognizing that it may also lack some specificity for syphilis.

Table 4 (continued). Combined and single point-of-care tests for syphilis

Environmental tolerance of packaged test kit	• Transport packaging not needed • Transport stress (48 hours with fluctuations up to 50 °C and down to 0 °C) • Tolerate exposures between 2 °C and 45 °C at an altitude up to 3000 metres, up to and including condensing humidity	
Operating conditions	• Between 15 °C and 40 °C at an altitude up to 2000 metres • Extremely low relative humidity	• Between 10 °C and 45 °C at an altitude up to 4500 metres • Both low and high humidity • Result interpretation in low light settings
Training required	< 90 minutes	30 minutes
Clean water	None	
Time to result	≤30 minutes	≤15 minutes
Duration of sample stability	It is inherent to the definition of a point-of-care test that following specimen collection there should be minimal delay in testing of the specimen	
Stability of valid result	• At least 15 minutes (after which results may be *false* or *invalid*) • Clear language in the instructions for users regarding test reading	• ≥1 hour (after which results give *invalid* rather than *false* results) • Clear language in the instructions for users regarding test reading
Safety precautions	Closed, self-contained system; unprocessed sample transfer only; no open handling of biohazardous material	
Waste and disposal requirements	Safe disposal of all waste materials	Small environmental footprint; compostable plastics for test materials
Internal quality control – reagents	Procedural (reagent-addition) control internalized in test for each individual test run; positive control for internal quality control available for purchase separately	Procedural and specimen adequacy control internalized in test for each individual test run; positive control for internal quality control provided in each box of test kits
Device control	Indicator of instability or expiration	Compliance with appropriate ISO standard
Regulatory requirements	Compliance with appropriate ISO standard	
Identification capability	Yes; simple, self-contained way to indicate a health service user identifier	
Result display and interpretation	Result can be read with the naked eye with minimal instructions for interpretation required by user, or with an integrated reader with an easy§ pictorial display: reactive, non-reactive, invalid for each test	
Data acquisition and display	If combined with a reader, on-device visual read-out; able to add information (health service user ID, operator ID, date, location, etc.); able to store health service user results; able to print out results utilizing commoditized paper products (i.e. standard paper specifications and sizes); needs to consider privacy and data security laws	
Connectivity	If combined with a reader, reader has integrated GPS module	If combined with a reader, internally integrated GPS/GPRS module and conformity with HL7 messaging standards

Table 4 (continued). Combined and single point-of-care tests for syphilis

Data export	If combined with a reader, full data export over mobile phone network, encrypted data only	• If combined with a reader, full data export over mobile phone network, encrypted data only (data transmission can automatically select between GPRS or more advanced networks and GSM, based on available coverage) • GPRS should be able to utilize the internet FTP to transmit data: data transfer should be initiated every 6–12 hours automatically by the reader; data can be exported in a format compatible with HL7 standards, where appropriate; instrument tracks and transmits quality assurance data over time (such as identify shifts or trends)
Target price per test	<US$ 3	<US$ 1



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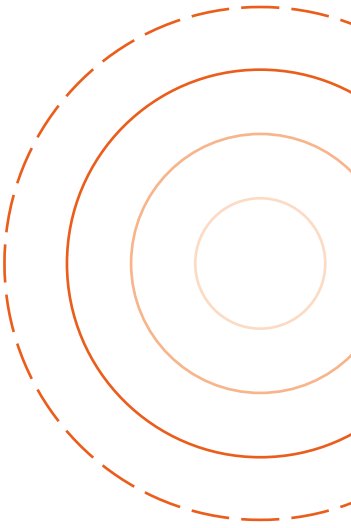

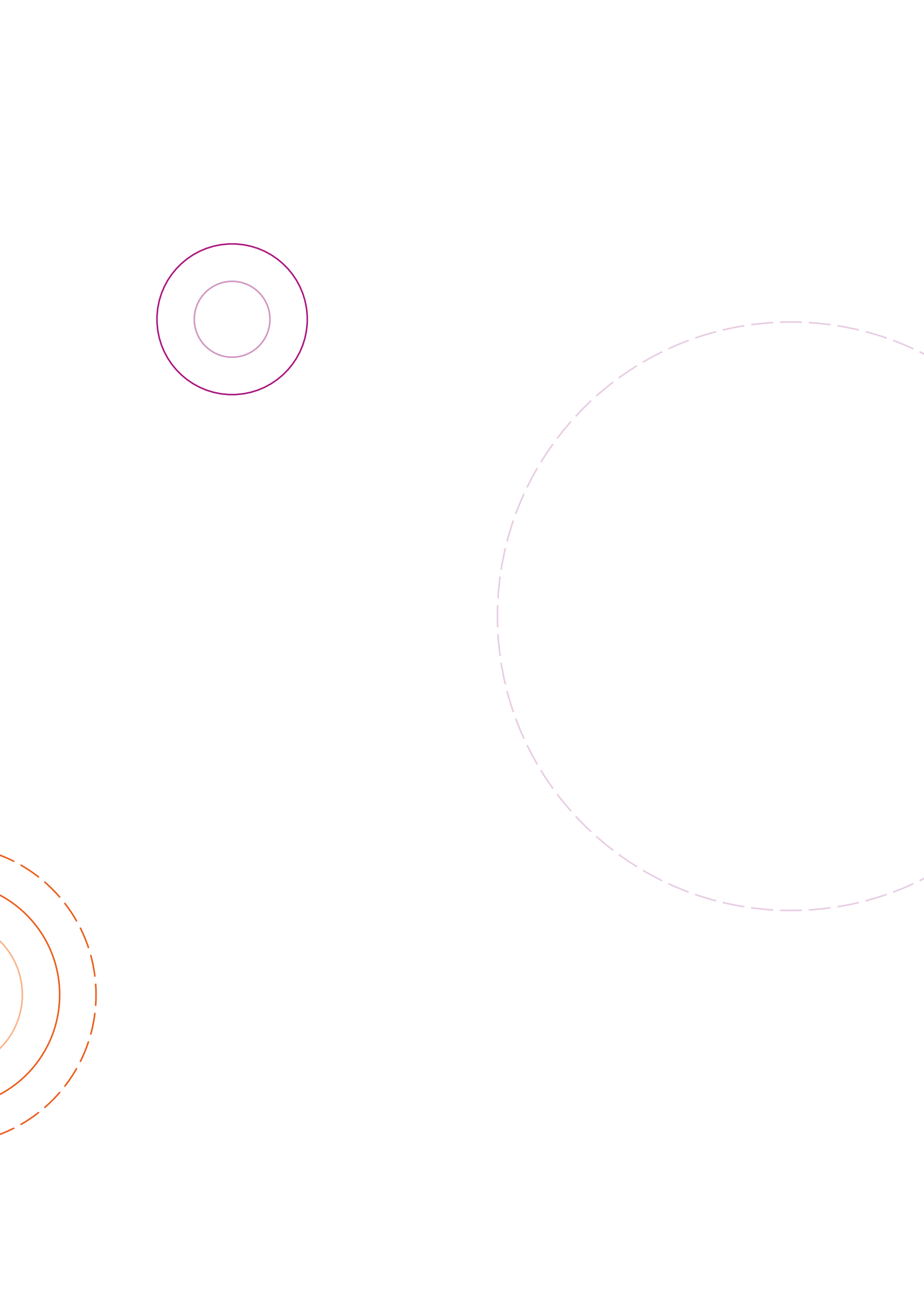

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