TARGET PRODUCT PROFILE

for the detection of a case of yaws and the detection of azithromycin resistance

World Health Organization

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Contents

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Yaws is a bacterial infection that is found across the tropics. More than 80 countries/territories are known to have previously reported or currently report cases of yaws.

1. Epidemiology

Yaws is caused by infection with *Treponema pallidum* subsp. *pertenue*. The disease is now predominantly reported in West and Central Africa and the Pacific but has previously been endemic throughout the tropics *(1, 2)*. Most cases of yaws are found in children. Transmission is believed to occur through skin-to-skin contact with infectious lesions of primary yaws. *T.p.* subsp. *pertenue* is closely related to *T.p.* subsp. *Pallidum*, the causative agent of syphilis, but unlike the latter is not transmitted through sexual contact or from mother to the developing fetus during pregnancy.

The clinical course of yaws starts with primary yaws, characterized by a single infectious lesion. If the individual is untreated, the initial lesion will heal but the infection will continue. This asymptomatic state is called latent yaws. The individual may then progress to develop secondary yaws, during which time new infectious lesions occur. The patient may alternate between asymptomatic latent yaws and further episodes of secondary yaws for several years. If the patient remains untreated for a long time (> 5–10 years), tertiary yaws may develop. The lesions of tertiary yaws are destructive and disfiguring but not infectious.

2. Public health response

Yaws has been targeted for eradication since the mid-20th century. Previous efforts focused on the use of mass or targeted treatment with penicillin. Although these efforts reduced the prevalence of yaws by > 90%, they were ultimately not successful at achieving eradication *(1)*. In 2012, WHO launched a new strategy – the Morges strategy – based on mass treatment with azithromycin *(3)*. Central to this strategy is the identification of all endemic communities, followed by community mass treatment. Small-scale pilot projects of this strategy have been implemented in several settings.

Once the number of yaws cases has fallen, ongoing case-finding and treatment is required to identify and treat remaining cases and their close contacts. Once no further cases of yaws are detected, the programme switches to surveillance, including serological surveillance of children aged < 5 years *(4)*.

As the aim of the programme is eradication, detection of single cases is important. This detection occurs in two scenarios: (i) deciding whether to initiate a programme – in this setting, finding a single yaws case is sufficient to declare a community endemic and needing treatment; and (ii) surveillance after mass treatment – in this setting, it is important to exclude that even a single suspected case is truly yaws and therefore that interventions can stop.

A major concern has been the identification of a small number of cases of yaws in whom resistance to azithromycin has developed *(5)*. Two mutations are known to confer resistance to azithromycin. Detection of phenotypic resistance is complicated by the inability to routinely culture *T. pallidum*, and therefore the focus of resistance detection is to identify (a) cases of clinical treatment failure, and (b) known mutations associated with resistance to azithromycin.

The new road map for neglected tropical diseases 2021–2030 has set a target of yaws eradication by 2030 *(6)*.

3. Available diagnostic tools

To date, clinical examination combined with serological tests are the mainstay of yaws diagnosis. Serological tests can be performed either in a laboratory or in the field through lateral flow assays. Molecular diagnostic tests including polymerase chain reaction are commonly used in research and increasingly within programmes.

4. WHO Diagnostic Technical Advisory Group for Neglected Tropical Diseases

WHO's Department of Control of Neglected Tropical Diseases manages a diverse portfolio of 20 diseases and disease groups, each with its own unique epidemiological and diagnostic challenges. At its 12th meeting (Geneva, 29–30 April 2019), the Strategic and Technical Advisory Group (STAG), the principal advisory group to WHO on the control, elimination and eradication of NTDs, decided to establish a single WHO working group to ensure use of a unified approach to identify and prioritize diagnostic needs, and to inform WHO strategies and guidance on the subject *(7)*.

At its inaugural meeting (Geneva, 30–31 October 2019), the Diagnostic Technical Advisory Group for Neglected Tropical Diseases (DTAG) discussed priorities for the year ahead as well as how to manage the complexity of supporting the diagnostics agenda across the entirety of WHO's NTD portfolio. Recommendations were made, based on the understanding that they would be reviewed at the next meeting, as it had been made clear that all NTDs had diagnostic needs that would have to be addressed in due course.

One of the recommendations was to prepare target product profiles (TPPs) for diagnostics to support emerging yaws control programmes.

5. Purpose of the TPP

The purpose of this TPP is to lead to development of new diagnostic tools for "detection of a case of yaws" and "detection of an azithromycin-resistant case of yaws".

For detection of a case of yaws, the tool or tools must be able to detect a single case of active yaws infection.

For detection of a case of azithromycin resistant yaws, the tool or tools must be able to detect mutations known to be associated with azithromycin resistance in yaws.

6. Audiences engaged and external consultations to develop the TPP

In order to initiate the development of TPP for Yaws, Dr Noah Fongwen and Dr Michael Marks gathered together a group of seven experts on yaws. The group was divided into a group of clinical experts on yaws and a group of experts on diagnostics. After discussions a draft TPP was developed by Dr Noah Fongwen and Dr Michael Marks. The draft was submitted to the D-TAG group chair, Dr Patrick Lammie, for comments before finalization and publication for the online consultation and adapted based on their comments.

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Use case needs statements

Identify a single case of yaws	Detect azithromycin resistance
Objective: To determine if an area is endemic for yaws.	**Objective**: To detect resistance to azithromycin in a patient with yaws.
Testing target: Need to be able to detect a single case of yaws (*T.p. pertenue*) and confirm active yaws infection.	**Testing target**: Need to detect azithromycin resistance in those with active and/or latent yaws (minimum = active yaws; ideal = active and latent yaws).
Ages tested: Need to be able to conduct testing in all ages and genders (especially in children aged 5–15).	**Ages tested**: Need to be able to test all genders/age groups (especially children aged 5–15).
Testing location: Need to be appropriate for use in the field with the possibility of referral to central facilities.	**Testing location**: Need to be appropriate for use in the field with possibility of referral to central facilities.
Test simplicity: Need to be able to conduct testing by staff in the field with minimal additional training.	**Test simplicity**: Need to be able to conduct testing through field staff with minimum of additional training.
Test price: Need to be able to provide tests at appropriate cost for implementation by the health ministry in low and middle-income countries.	**Test price**: Need to be able to provide tests at appropriate cost for implementation by the health ministry in low and middle-income countries.
Sample type: Need to conduct analyses on dry swabs from a suspected yaws lesion.	**Sample type**: Need to conduct analyses on dry swab from a suspected yaws lesion.
Performance: Need to meet requirements for sensitivity and specificity and be able to not only accurately detect a single case of active yaws.	**Performance**: Need to meet requirements for sensitivity and specificity.
Time to result: Need to generate test results in < 30 min (ideally) and within a day (acceptable).	**Time to result**: Need to generate test results in < 30 min (ideally) and within a day (acceptable).
Equipment: Need to have minimal-to-no additional equipment required for the test.	**Equipment**: Need to have minimal-to-no additional equipment required for the test.
Cold chain: Need to ideally have minimal requirements around cold chain shipping, storage or operation (commonly referred to as no cold chain required).	**Cold chain**: Need to ideally have minimal requirements around cold chain shipping, storage or operation (commonly referred to as no cold chain required).

Identify a single case of yaws

1. Product use summary	Minimum	Ideal	Background, annotation re requirement risk, etc.
1.1 Intended use	An in vitro laboratory-based test that detects *T. pallidum*-specific analyte(s) for the purpose of identifying a single case of yaws and confirming active infection to know if an area is endemic for yaws.	An in vitro point-of-care test that detects *T. pallidum pertenue*-specific analyte(s) for the purpose of identifying a single case of yaws and confirming active infection to know if an area is endemic for yaws.	
1.2 Targeted population	All ages and gender of individuals (especially children) resident in the population living in the defined geographical area.	All ages and gender of individuals (especially children) resident in the population living in the defined geographical area.	
1.3 Lowest infrastructure level	For a laboratory-based test, tests can be performed in a peripheral health facility/referral centre, regional or national diagnostic testing laboratory.	The test will be performed under "zero-infrastructure" conditions in the field (including but not limited to schools, community health centres, households and outdoor conditions).	
1.4 Lowest level user	For a laboratory-based test, the test will be performed by trained laboratory technicians.	For a point-of-care test, the test will be performed by health personnel, community health workers and community volunteers.	Minimally invasive (fingerprick, skin microbiopsy) or non-invasive (saliva, urine, tears…) Possible techniques without specimen collection
1.5 Training requirements	For a laboratory-based test, < 1 week for trained laboratory technicians; testing job aid/instructions for use should be made available via the Internet for download (i.e. are publicly available).	For a point-of-care test, ≤ 1 day for health personnel, community volunteers and lay persons; testing job aid/instructions for use should be made available via the Internet for download (i.e. are publicly available). A competency panel should be included.	NOTE: it is not a *requirement* to have Internet access to obtain job aids/instructions for use since these must be included with the test itself (per Requirement 4.5); rather, job aids/instructions for use should always be available via the Internet.
2. Design	Minimum	Ideal	Annotation
2.1 Portability	For a laboratory-based test, specific portability and transport requirements should not be beyond those associated with standard laboratory equipment.	For a point-of-care test, highly portable with no specialized transport needs.	"Portability" implies those characteristics described in 2.2-2.4 as well as an absence of locational limitations as to where the test can be performed.
2.2 Instrument/ power requirement	For a laboratory-based test, access to mains power is acceptable.	For a point-of-care test, self-contained kit operates independent of any mains power.	
2.3 Water requirement	For a laboratory-based test, access to laboratory-grade water is acceptable.	For a point-of-care test, self-contained kit operates independent of any water supply.	
2.4 Maintenance and calibration	For a laboratory-based test, periodic maintenance and calibration of any instrumentation must be available in the countries, and should not be needed more frequently than once a year.	For a point-of-care test, no maintenance required (i.e. disposable) and no calibration required. Either single use test or routine cleaning for the portable device.	
2.5 Sample type/ collection	Dry swab of suspected yaws lesion	Finger-prick sample	

2.6 Sample preparation/ transfer device	· Sample preparation for dry swabs from lesion should not exceed transfer of the swab to a sample processing tube holding no more than 500 µL of processing buffer, an aliquot of which is transferred to the testing device after a defined period of time. · Transfer of the sample volume to the testing device shall occur by use of a predefined and provided single-use transfer device (e.g. inverted cup, disposable fixed-volume transfer pipet).	Direct. No need for sample preparation.	
2.7 Sample volume	1–100 uL	1–10 uL	"Sample volume" represents that volume which is introduced to the test device itself.
2.8 Target analyte	**Biomarker(s) specific for current active or latent infection from *T. pallidum*.**	**Biomarker(s) specific for active infection with *T. pallidum pertenue*.**	NOTE: Serological biomarkers do not correlate with active or latent infection. Nucleic acid-based markers have been investigated but have not been shown to be successful in those with latent infection. Other biomarkers have been investigated but their qualification and validation will require significant time and effort going forward. For this reason, this is a **high-risk** requirement.
2.9 Type of analysis	Qualitative	Qualitative	
2.10 Detection	For laboratory-based tests, may include instrument-based detection of a signal that provides unambiguous determination of a qualitative measure.	For point-of-care tests, results shall be a high contrast, clear result for naked eye; indoor and outdoor reading of a signal that provides a definitive result without the need for colour discrimination.	Same as above.
2.11 Quality control	· Internal process control indicator.	· Internal process control indicator · Colorimetric or other indicator to identify excessive heat/humidity exposure. Competency panel included.	For further consideration (i.e. beyond TPP scope): definition of how endogenous positive controls should/ would be used if they are to be included with a test, e.g. will there be a community-wide quality panel, centralized reporting of results?
2.12 Supplies needed	All reagents and supplies included in test kit, including those needed for sample collection and processing, with minimal import restrictions (e.g. animal-free).	All reagents and supplies included in test kit, including those needed for sample collection and processing, with minimal import restrictions (e.g. animal-free).	
2.13 Safety	Normal use of the test does not create any additional hazards to the operator when observing Universal Blood Safety/Body Fluid precautions.	Normal use of the test does not create any additional hazards to the operator when observing Universal Blood Safety/Body Fluid precautions.	

3. Performance	Minimum	Ideal	Annotation
3.1 Species differentiation/ detection	*T. pallidum*	*T. pallidum pertenue*	There should be no interference/non-specific signals as a result of other infections such as: *T. pallidum pallidum* (syphilis), *T. pallidum endemicum* (bejel); *T. pallidum carateum* (pinta). *Haemophilus ducreyi*
3.2 Diagnostic/clinical sensitivity	> 95%	> 95%	**In situations where the number of suspected cases being tested is low (< 5), further testing could be considered such as repeated testing, or testing for a second target could be considered to compensate for imperfect sensitivity.**
3.3 Diagnostic/clinical specificity	> 99.9%	> 99.9%	**In situations where the number of positives is low (< 5), further testing could be considered such as testing for a second target or sequencing to improve specificity.**
3.4 Time to results	For a laboratory-based test, within 1 day	< 0.5 h to developed test result	
3.5 Result stability	Developed test result remains stable for 0.5 h	Developed test result remains stable for 24 h	Ability to interpret final test results in a manner not constrained by timed steps helps greatly in resource-constrained settings.
3.6 Throughput	For laboratory-based tests, ≥ 100 tests/day per tester	For point-of-care tests, ≥ 10 individual tested/hour per tester	"Throughput" represents how many tests can be run in parallel within an hour and is separate from the time to results.
3.7 Target shelf-life/ stability	≥ 18 months, 2–40 °C, 75% relative humidity (no cold chain required); temperature excursion/prolonged deviation of 50 °C for 2 weeks acceptable.	≥ 24 months, 2–40 °C, 75% relative humidity (no cold chain required); temperature excursion/prolonged deviation of 50 °C for 2 weeks acceptable.	
3.8 Ease of use	For laboratory-based tests, ≤ 5 timed steps; ≤ 15 user steps. Instructions for use should include diagram of method and interpretation of results.	For laboratory-based tests, ≤ 1 timed step; ≤ 5 user steps. Instructions for use should include diagram of method and interpretation of results. For point-of-care tests, must be able to use in an unprotected external environment.	This is in relation to the test operation *only*.
3.9 Ease of results interpretation	For laboratory-based tests, a definitive "Yes/No" result can be interpreted by a suitable instrument that meets requirements defined in 2.10 "Minimum".	For point-of-care tests, a definitive "Yes/No" result can be interpreted by eye that meets requirements defined in 2.10 "Minimum".	
3.10 Operating temperature	15–40 °C, 75% relative humidity	15–40 °C, 75% relative humidity	

4. Product Configuration	Minimum	Ideal	Annotation
4.1 Shipping conditions	For laboratory-based tests, conformance to applicable requirements of ASTM D4169-05 and ISO 11607-1:2006 (or equivalent); cold-chain shipping (e.g. 0–4 °C) is acceptable for any test components/ consumables used in the laboratory.	For point-of-care tests, conformance to applicable requirements of ASTM D4169-05 and ISO 11607-1:2006 (or equivalent); no cold-chain shipping required.	
4.2 Storage conditions	For laboratory-based tests, cold storage is acceptable for any laboratory-based testing components/ consumables.	For point-of-care tests, ambient storage conditions, 2–40 °C; no cold storage required.	
4.3 Service and support	For laboratory-based tests, support must be available from manufacturer for any laboratory-based equipment and/or procedures.	For point-of-care tests, minimal support needed.	
4.4 Waste disposal	Does not include material that cannot be disposed of in normal laboratory biohazard waste streams.	Does not include material that cannot be disposed of in normal laboratory biohazard waste streams.	
4.5 Labelling and instructions for use (IFUs)	Compliance required per in vitro diagnostic regulation (IVDR) requirements and WHO prequalification (PQ) guidance (see *WHO TGS-5: Designing instructions for use for in vitro diagnostic medical devices*); product insert shall be available in relevant local language(s) and shall include IFUs for the test. Must provide accurate material safety data sheet information on components that are potentially toxic.	Compliance required per in vitro diagnostic regulation (IVDR) requirements and WHO prequalification (PQ) guidance (see *WHO TGS-5: Designing instructions for use for in vitro diagnostic medical devices*); product insert shall be available in relevant local language(s) and shall include IFUs for the test. Must provide accurate material safety data sheet information on components that are potentially toxic.	WHO PQ label/IFU guidance should be applied, regardless of whether the test is prequalified by WHO or not.

5. Product cost and channels	Minimum	Ideal	Annotation
5.1 Target pricing per test	< US$ 30	< US$ 5	Actual price details will depend on other factors separate from the test itself, which include shipping, storage, quantities purchased and other factors commonly encountered in national procurement for NTD programmes. Tests should be at appropriate cost for implementation by the health ministry in low and middle-income countries.
5.2 Capital cost	For laboratory-based tests, capital costs may vary but should not exceed US$ 5000.	For point-of-care tests, none required.	
5.3 Product lead times	< 8 weeks	< 6 weeks	"Lead time" includes fulfillment and delivery of ordered tests to procurer. **NOTE**: May be adjusted to longer lead times provided shelf-life is of sufficient duration, e.g. 2 years. Purpose for information is to address design decisions that can impact line/process design for production, and hence impact lead times.
5.4 Targeted countries	WHO prioritized countries	WHO prioritized countries	
5.5 Product registration (i.e., substantiation to regulatory body of product claims)	· CE Mark/IVDR (or other SRA) as relevant · Any registration required for export from country of origin (e.g. KMFDS from Korea) · WHO PQ, if required/applicable · Country-level registration (if required/applicable for target countries)	· CE Mark/IVDR (or other SRA) as relevant · Any registration required for export from country of origin (e.g. KMFDS from Korea) · WHO PQ, if required/applicable · Country-level registration (if required/applicable for target countries)	Need to confirm that WHO PQ will process dossiers for NTD diagnostics.

Azithromycin resistance

1. Product use summary	Minimum	Ideal	Background, annotation re requirement risk, etc.
1.1 Intended use	An in vitro laboratory-based test that detects *T. pallidum*-specific analyte(s) for the purpose of detecting azithromycin resistance in yaws patients with active or latent infection.	An in vitro point-of-care test that detects *T. pallidum pertenue*-specific analyte(s) for the purpose of detecting azithromycin resistance in yaws patients with active infection.	
1.2 Targeted population	All ages and gender of individuals (especially children) resident in the population living in the defined geographical area.	All ages and gender of individuals (especially children) resident in the population living in the defined geographical area.	
1.3 Lowest infrastructure level	For a laboratory-based test, tests can be performed in a peripheral health facility/referral centre, regional or national diagnostic testing laboratory.	The test will be performed under "zero-infrastructure" conditions in the field (including but not limited to schools, community health centres, households and outdoor conditions).	
1.4 Lowest level user	For a laboratory-based test, the test will be performed by trained laboratory technicians.	For a point-of-care test, the test will be performed by health personnel, community health workers and community volunteers.	
1.5 Training requirements	For a laboratory-based test, < 1 week for trained laboratory technicians; testing job aid/instructions for use should be made available via the Internet for download (i.e. are publicly available).	For a point-of-care test, ≤ 1 day for health personnel, community volunteers and lay persons; testing job aid/instructions for use should be made available via the Internet for download (i.e. are publicly available). A competency panel should be included.	NOTE: It is not a *requirement* to have Internet access to obtain job aids/instructions for use since these must be included with the test itself (per Requirement 4.5); rather, job aids/instructions for use should always be available via the Internet.
2. Design	Minimum	Ideal	Annotation
2.1 Portability	For a laboratory-based test, specific portability and transport requirements should not be beyond those associated with standard laboratory equipment.	For a point-of-care test, highly portable with no specialized transport needs.	"Portability" implies those characteristics described in 2.2–2.4 as well as an absence of locational limitations as to where the test can be performed.
2.2 Instrument/ power requirement	For a laboratory-based test, access to mains power is acceptable.	For a point-of-care test, self-contained kit operates independent of any mains power.	
2.3 Water requirement	For a laboratory-based test, access to laboratory-grade water is acceptable.	For a point-of-care test, self-contained kit operates independent of any water supply.	
2.4 Maintenance and calibration	For a laboratory-based test, periodic maintenance and calibration of any instrumentation must be available in the countries, and should not be needed more frequently than once a year.	For a point-of-care test, no maintenance required (i.e. disposable) and no calibration required.	
2.5 Sample type/ collection	Dry swab of suspected yaws lesion	Finger-prick sample	

2.6 Sample preparation/ transfer device	· Sample preparation for dry swabs from lesion should not exceed transfer of the swab to a sample processing tube holding no more than 500 µL of processing buffer, an aliquot of which is transferred to the testing device after a defined period of time. · Transfer of the sample volume to the testing device shall occur by use of a predefined and provided single-use transfer device (e.g. inverted cup, disposable fixed-volume transfer pipet)	Direct	
2.7 Sample volume	1–100 uL	1–10 uL	"Sample volume" represents that volume which is introduced to the test device itself.
2.8 Target analyte	**Biomarker(s) specific for the DNA of azithromycin-resistant *T. pallidum* pertenue (azithromycin-resistant genes) in those with active or latent yaws infection.**	**Biomarker(s) specific for the DNA of azithromycin-resistant *T. pallidum pertenue* (azithromycin-resistant genes) in those with active yaws infection.**	NOTE: Most of the nucleic acid assays are still in the stage of development. The assays detect genotypic resistance to known genes and not unknown genes. The assays have also not been shown to be successful in those with latent infection. Other markers are under investigation but their qualification and validation will require significant time and effort going forward. For this reason, this is a **high-risk** requirement.
2.9 Type of analysis	Qualitative	Qualitative	
2.10 Detection	For laboratory-based tests, may include instrument-based detection of a signal that provides unambiguous determination of a qualitative measure.	For point-of-care tests, results shall be a high contrast, clear result for naked eye; indoor and outdoor reading of a signal that provides a definitive result without the need for colour discrimination.	Same as above.
2.11 Quality control	· Internal process control indicator.	· Internal process control indicator · Colorimetric or other indicator to identify excessive heat/humidity exposure. A competency panel should be included.	For further consideration (i.e. beyond TPP scope): definition of how endogenous positive controls should/ would be used if they are to be included with a test, e.g. will there be a community-wide quality panel, centralized reporting of results?
2.12 Supplies needed	All reagents and supplies included in test kit, including those needed for sample collection and processing, with minimal import restrictions (e.g. animal-free).	All reagents and supplies included in test kit, including those needed for sample collection and processing, with minimal import restrictions (e.g. animal-free).	
2.13 Safety	Normal use of the test does not create any additional hazards to the operator when observing Universal Blood Safety/Body Fluid precautions.	Normal use of the test does not create any additional hazards to the operator when observing Universal Blood Safety/Body Fluid precautions.	

3. Performance	Minimum	Ideal	Annotation
3.1 Species differentiation/ detection	*T. pallidum*	*T. pallidum pertenue*	There should be no interference/non-specific signals as a result of other infections such as: *T. pallidum pallidum* (syphilis), *T. pallidum endemicum* (bejel); *T. pallidum carateum* (pinta). *Haemophilus ducreyi*
3.2 Diagnostic/ clinical sensitivity	**> 95% sensitivity**	**> 99% sensitivity**	**In the absence of perfect sensitivity, programmes will need to presumptively treat cases that fail first-line treatment as cases of resistant yaws.**
3.3 Diagnostic/ clinical specificity	**> 95 specificity**	**> 99% specificity**	**Recognition that in the absence of perfect specificity some patients will receive benzathine penicillin, but this has previously been the standard of care and is considered acceptable.**
3.4 Time to results	For a laboratory-based test, within a day	< 0.5 h to developed test result	
3.5 Result stability	Developed test result remains stable for 0.5 h	Developed test result remains stable for 24 h	Ability to interpret final test results in a manner not constrained by timed steps helps greatly in resource-constrained settings.
3.6 Throughput	For laboratory-based tests, ≥ 100 tests/day per tester	For point-of-care tests, ≥ 10 individual tested/hour per tester	"Throughput" represents how many tests can be run in parallel within an hour and is separate from the time to results.
3.7 Target shelf-life/ stability	≥ 18 months, 2–40 °C, 75% relative humidity (no cold chain required); temperature excursion/prolonged deviation of 50 °C for 2 weeks acceptable.	≥ 24 months, 2–40 °C, 75% relative humidity (no cold chain required); temperature excursion/prolonged deviation of 50 °C for 2 weeks acceptable.	
3.8 Ease of use	For laboratory-based tests, ≤ 5 timed steps; ≤ 15 user steps. Instructions for use should include diagram of method and interpretation of results.	For laboratory-based tests, ≤ 1 timed step; ≤ 5 user steps. Instructions for use should include diagram of method and interpretation of results. For point-of-care tests, must be able to use in an unprotected external environment.	This is in relation to the test operation *only.*
3.9 Ease of results interpretation	For laboratory-based tests, a definitive "Yes/No" result can be interpreted by a suitable instrument that meets requirements defined in 2.10 "Minimum".	For point-of-care tests, a definitive "Yes/No" result can be interpreted by eye that meets requirements defined in 2.10 "Minimum".	
3.10 Operating temperature	15–40 °C, 75% relative humidity	15–40 °C, 75% relative humidity	

4. Product Configuration	Minimum	Ideal	Annotation
4.1 Shipping conditions	For laboratory-based tests, conformance to applicable requirements of ASTM D4169-05 and ISO 11607-1:2006 (or equivalent); cold-chain shipping (e.g. 0–4 °C) is acceptable for any test components/consumables used in the laboratory.	For point-of-care tests, conformance to applicable requirements of ASTM D4169-05 and ISO 11607-1:2006 (or equivalent); no cold-chain shipping required.	
4.2 Storage conditions	For laboratory-based tests, cold storage is acceptable for any laboratory-based testing components/consumables.	For point-of-care tests, ambient storage conditions, 2–40 °C; no cold storage required.	
4.3 Service and support	For laboratory-based tests, support must be available from manufacturer for any laboratory-based equipment and/or procedures.	For point-of-care tests, very minimal support required.	
4.4 Waste disposal	Does not include material that cannot be disposed of in normal laboratory biohazard waste streams.	Does not include material that cannot be disposed of in normal laboratory biohazard waste streams.	
4.5 Labelling and instructions for use (IFUs)	Compliance required per in vitro diagnostic regulation (IVDR) requirements and WHO prequalification (PQ) guidance (see *WHO TGS-5: Designing instructions for use for in vitro diagnostic medical devices*); product insert shall be available in relevant local language(s) and shall include IFUs for the test. Must provide accurate material safety data sheet information on components that are potentially toxic.	Compliance required per in vitro diagnostic regulation (IVDR) requirements and WHO prequalification (PQ) guidance (see *WHO TGS-5: Designing instructions for use for in vitro diagnostic medical devices*); product insert shall be available in relevant local language(s) and shall include IFUs for the test. Must provide accurate material safety data sheet information on components that are potentially toxic.	WHO PQ label/IFU guidance should be applied, regardless of whether the test is prequalified by WHO or not.

5. Product cost and channels	Minimum	Ideal	Annotation
5.1 Target pricing per test	Not more than US$ 30	US$ 5	Actual price details will depend on other factors separate from the test itself, which include shipping, storage, quantities purchased and other factors commonly encountered in national procurement for NTD programmes. Tests should be at appropriate cost for implementation by the health ministry in low and middle-income countries.
5.2 Capital cost	For laboratory-based tests, capital costs may vary but should not exceed US$ 5000.	For point-of-care tests, none required.	
5.3 Product lead times	< 8 weeks	<6 weeks	"Lead time" includes fulfillment and delivery of ordered tests to procurer. **NOTE**: May be adjusted to longer lead times provided shelf-life is of sufficient duration, e.g. 2 years. Purpose for information is to address design decisions that can impact line/process design for production, and hence impact lead times.
5.4 Targeted countries	WHO prioritized countries	WHO prioritized countries	
5.5 Product registration (i.e., substantiation to regulatory body of product claims)	· CE Mark/IVDR (or other SRA) as relevant · Any registration required for export from country of origin (e.g. KMFDS from Korea) · WHO PQ, if required/applicable · Country-level registration (if required/applicable for target countries)	· CE Mark/IVDR (or other SRA) as relevant · Any registration required for export from country of origin (e.g. KMFDS from Korea) · WHO PQ, if required/applicable · Country-level registration (if required/applicable for target countries)	Need to confirm that WHO PQ will process dossiers for NTD diagnostics.

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