Specifications for a Rapid Diagnostic Test for meningitis
African meningitis belt

Background

In 2014, WHO set up a Guideline Development Group to review the evidence and recommendations for meningitis epidemic control in the African meningitis belt. Regarding the use of currently available rapid diagnostic tests (RDTs) in outbreak management, the Group recommended:

(i) the use of RDTs (latex agglutination or immunochromatography dipsticks) in the investigation of meningitis outbreaks and,

(ii) If RDTs are positive for a vaccine preventable serogroup, verification of serogroup by polymerase chain reaction (PCR) or culture is recommended before a decision is taken to initiate a vaccine response.

Hence, on one hand RDTs were recognized as a useful field tool in the surveillance African context, but on the other hand, their limited performance necessitated other testing methods for a definite confirmation of the disease (WER 2014, **89**:580-6).

In addition, the Group also recommended that WHO and partners should strongly promote the production of *heat-stable* RDTs and that the development of RDTs which detect a range of microorganisms (*Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis*) should be a priority, in particular the development of a *N. meningitidis* serogroup *X* RDT.

The group also emphasized that the delivery of RDTs should include programmatic elements such as training, organized transmission of results and related information, and quality control.

The Target Product Profile described in this document should be met by a new generation of Rapid Tests for the diagnosis of bacterial meningitis, as per the Group recommendations. These RDTs should be planned for use as a surveillance tool guiding public health control measures -the vaccine response- during outbreaks of meningococcal meningitis, but also at individual level as an easy to use method to confirm the diagnosis of bacterial meningitis. These tests should not require other testing methods before action is triggered.

World Health Organization

Target Product Profile for the development of a new generation of rapid test for the diagnosis of bacterial meningitis

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The specific requirements should be met by a test to be used in the following context:

Meningitis surveillance in the African meningitis belt: confirmation of acute bacterial meningitis in a number of individuals during the investigation of meningococcal meningitis outbreaks, in order to orientate a vaccine response

In addition, the test can be used inside and outside the African meningitis belt to orientate the *individual clinical management of meningitis*: detection of bacterial meningitis infection for confirmation of diagnosis and specific treatment orientation

TARGET POPULATION / PATIENT

Patient meeting the suspect case of meningitis clinical definition presenting to health care facility and to whom a lumbar puncture is performed

TARGET USE SETTING

- Decentralized health care facilities with no laboratories infrastructure available. The test is performed at point of care where suspect cases are presenting.
- Decentralized laboratory where a Cerebrospinal Fluid (CSF) sample from a suspect patient is brought within one hour from the time of collection

EXPECTED SCALE OF MANUFACTURE

Between 15 000 to 30 000 tests per year for the African belt countries

Executive summary Table

KEY FEATURES	DESIRED	ACCEPTABLE
SCOPE		
Target pathogens	***Neisseria meningitidis*** **serogroup A, B, C, X, Y, W** ***Streptococcus pneumoniae*** ***Haemophilus influenzae***	***Neisseria meningitidis*** **serogroup A, C, X, Y, W**
Target analyte	**Any bacterial material**	**Polysaccharide**
Sample type	**CSF**	**CSF**
Presentation/Format	**Cassette - visual reading technical platform**	**Dipstick**
Type of analysis	**Qualitative (positive/negative)**	**Qualitative (positive/negative)**
Reading system	**Visual reading by the operator**	**A reader device**
PERFORMANCE REQUIREMENT		
Species differentiation	**Species and serogroup**	**Serogroup**
Sensitivity [a]	**> 90% for each pathogen**	**> 90% for each pathogen**
Specificity	**> 95% for each pathogen No cross reaction**	**> 90% for each pathogen No cross reaction**
Limit of detection	**0.5ng of the corresponding capsular polysaccharide or 10^2 CFU/ml**	**1 ng of the corresponding capsular polysaccharide or 10^3 CFU/ml**
Throughput	**More than 5 tests per hour**	**2 tests per hour**
TEST PROCEDURE		
Number of steps to be performed by operator (use of different reagents/incubation steps, excluding waste disposal)	**1**	**1**
Precision pipetting Need to use a precise volume of reagent/sample	**No need**	**No need**
Volume of sample required	**One drop of CSF (around 30-40 microliter)**	**2-3 drops**
Sample preparation Need to process the sample prior to performing the test	**None**	**None**
Time to result	**< 10 minutes**	**< 20 minutes**

Internal control	**Included**	**Included**
OPERATIONAL CHARACTERISTICS		
Stability (reagent storage)	**18 months at 40°C and 80% humidity**	**12 months at 40°C and 80% humidity**
Storage conditions Specific conditions for the test to be transported and stored prior utilization	**No cold chain required**	**No cold chain required**
In use stability (under tropical conditions)	**>1 hour for single use test after opening the pouch**	**>1/2 hour for single use test after opening the pouch**
Reagents reconstitution Need to prepare the reagents (diluent) prior utilization of the test	**All reagents ready for use**	**Reconstitution acceptable if very simple to do.** **All liquids, including water, already in kit**
Biosafety requirement Level of protection to be made available for the staff and the samples	**None apart waste management and use of non-sterile gloves**	**None apart waste management and use of non-sterile gloves**
Need for additional equipment	**None**	**Simple equipment acceptable :** **small, table top device, portable**
USER REQUIREMENT		
End user profile Level of education of the person in charge of the test	**Any level heath care worker**	**Any level heath care worker**
Training needs Time dedicated to training session for end users	**User able to conduct test correctly after brief review of instructions -** **job aid provided**	**Half a day -** **job aid provided**
COMMERCIALIZATION REQUIREMENT		
Target pricing per test	**Less than 5 USD**	**< 8 USD**
Certification	**ISO 13485 certified and authorized for use by a credible regulatory authority (European Union, FDA)**	**ISO 13485** **WHO pre-qualification**

[a] Laboratory conditions, reference test: Lab validated quantitative PCR assay on CSF