Target Product Profile for *Zaïre ebolavirus* rapid, simple test to be used in the control of the Ebola outbreak in West Africa

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Background:

As of 01 October 2014, a total number of 7,203 cases including 3,340 deaths from Ebola virus disease (EVD) were reported from West Africa (Guinea, Liberia, Sierra Leone, Senegal, Nigeria). Unless Ebola control measures in West Africa are enhanced quickly, experts from WHO and Imperial College, London predict numbers could continue to climb exponentially, and that more than 20 000 people may be infected by early November (NEJM 2014). The US CDC estimates that by January 2015, without any additional interventions, the total number of cases could reach 550,000 in Liberia and Sierra Leone or 1.4 million if corrections are made for underreporting (MMWR 2014; 63).

While effective intervention strategies such as new treatment and vaccines are being explored, accurate diagnosis of EVD is a key element in responding to the outbreak.

Controlling the epidemic relies heavily on laboratory testing to appropriately direct patients to either an Ebola Treatment Centre or another setting. Current laboratory capacity relies on mobile laboratory units and other designated laboratories to run molecular assays such as RT-PCR assays to confirm EVD. These laboratories are connected to Ebola Treatment Centres. There is growing recognition that while these laboratories are very important, they cannot address all the diagnostic needs of the current EVD outbreak. There is thus an urgent need for new rapid, point of contact/care EVD tests to be used in decentralized health care facilities and not requiring extensive biosafety requirements.

Such rapid EVD tests will allow for early diagnosis and referral to Ebola Treatment Centres or other settings for care, enhancing patient and community outcomes through earlier support of patients and families, contact tracing and isolation.

The fear of contracting EVD in the affected areas greatly affects healthcare delivery for other conditions in particular if their symptoms are similar to EVD (e.g. non EVD febrile patients and maternal hemorrhage). The availability of

rapid, EVD diagnostics that are highly predictive of EVD not being present would also reduce that fear and thus reduce the impact that EVD is currently having on other medical needs.

The current method of choice for diagnosis of EVD is based on molecular techniques using RT-PCR assays. However, numerous methods based on different technologies and biomarkers can potentially be used for the detection of EVD. For example, antigen detection tests in an RDT format may play a useful role in the control of this EVD outbreak if they can be highly sensitive. A number of automatic semi-portable NAAT platforms have also been developed for other diseases such as HIV, TB and malaria and may potentially be used for EVD detection if adapted to the appropriate biosafety requirements. However, whatever the technologies and biomarkers chosen, the type of specimen to be used and the collection requirements will be crucial in achieving tests feasible for use in disseminated locations. The amount of training required for local staff to conduct the testing should also be kept to a minimum.

In addition to this Target Product Profile document, an Emergency Assessment Mechanism for EVD diagnostic has been set up to help inform procurement of all assays available to diagnose EVD. The web link is given below:
http://www.who.int/diagnostics_laboratory/en/

KEY FEATURES	DESIRED	ACCEPTABLE
PRIORITY FEATURES		
Target population	Patients presenting with fever to health care facilities for assessment.	
Target use setting	Decentralized health care facilities with no laboratories infrastructure available	Decentralized health care facilities with minimum laboratory infrastructures available.
Intended Use	In Ebola outbreak setting, distinguish between symptomatic patients with acute Ebola virus infection and non-Ebola virus infection without the need for confirmatory testing	In Ebola outbreak setting, distinguish between symptomatic patients with acute Ebola virus infection and non-Ebola virus infection with the need for confirmatory testing
Clinical sensitivity[a, b]	> 98%	>95%
Analytical specificity	>99%	>99%
Type of analysis	Qualitative or Quantitative	Qualitative
Sample type	• Capillary whole blood from finger stick once/if the use of this type of samples has been validated. • Other less invasive sample types (e.g.., saliva, buccal) once/if their use has also been validated	Whole blood from phlebotomy, in particular if collection is simple and automated to reduce biosafety requirements
TEST PROCEDURE		
Number of steps to be performed by operator (use of different reagents/incubation steps)	< 3 0 timed steps	<10 1 timed step
Biosafety[c]	No additional biosafety in addition to Personal Protective Equipment [c]	No additional biosafety in addition to Personal Protective Equipment [c]
Need for operator to transfer a precise volume of sample	No	Acceptable if adequate disposable blood transfer device is provided
Time to result	< 30 minutes	< 3 hours
Internal control	included	included

Sample preparation Need to process sample prior to performing the test	None or fully integrated	None or fully integrated
OPERATIONAL CHARACTERISTICS		
Operating conditions	5- 50°C 90% RH	5 – 40°C 90% RH
Reagent storage (stability)	24 months at 40°C + 90% RH; no cold chain should be required. Should be able to tolerate stress during transport (3 days at 50°C)	12 months at 30°C + 70% RH including 3 months at 40°C, no cold chain should be required. Should be able to tolerate stress during transport (3 days at 50°C)
In use stability (under tropical conditions)	>1 hour for single use test after opening the pouch	>½ hour for single use test after opening the pouch
Reagents reconstitution Need to prepare the reagents prior utilization	All reagents ready to use	Reconstitution acceptable if very simple to do. All liquids, including water, already in kit
Training needs Time dedicated to training session for end users	Less than half a day for any level health care worker. Job aid provided.	Less than 2 days for any level of health care worker. Job aid provided
Equipment (if needed)	Small and portable, handheld instrument Weight <2 kg	Small, table top device, portable
Power Requirements	None required Optional: 110-220 V AC current DC power with rechargeable battery lasting up to 8 hours of testing	110-220 V AC current DC power with rechargeable battery lasting up to 8 hours of testing
Need for maintenance/spare parts	None	1 annual calibration ideally by operator
PRICING (To be discussed)		
Cost per consumables (e.g. cartridges, strips,..) (for procurement)		
Cost per equipment (if needed) (for procurement)		

[a] clinical sensitivity in first 10 days of presentation. Allow for repeat testing as per WHO guidelines
[b] reference test: Lab validated quantitative PCR assay on blood sample (whole blood or plasma) drawn by phlebotomy
[c] biosafety resources for Ebola: http://www.who.int/csr/disease/ebola/en/;
http://www.who.int/csr/resources/publications/ebola/filovirus_infection_control/en/

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