Supplementary evidence submitted by Professor Paul Cosford, Director for Health Protection and Medical Director, Public Health England (EME0019)

At my appearance at the Committee on 24 November, I promised to come back to you on two issues. The first was on my suggestion that the World Health Organisation (WHO) should consider a move to a more descriptive set of incident Levels. This more nuanced approach would allow levels of concern to be expressed without having to choose between the binary options of no emergency and a "public health emergency of international concern", with all of the economic, political and reputational issues they entail. I attach a guide to Public Health England's (PHE) Incident Levels, including the criteria behind them and how we would manage the response at each level. A graded response would enable earlier intervention in a developing health problem and help avert them developing into major crises.

The second issue was the introduction of rapid diagnostic tests for Ebola. PHE constantly evaluates relevant diagnostic products and actively assists in evaluating new technologies, working with companies, academia and where appropriate developing tests in house to tackle unmet needs. PHE is actively involved in projects on rapid diagnostics for Ebola.

The ability to rapidly diagnose Ebola at the point-of-care remains an unmet need. To facilitate the development, assessment and deployment of diagnostic tests, WHO implemented the Emergency Use Assessment and Listing Procedure (EUAL) and drew up a target product profile against which tests were assessed prior to evaluating their performance. As a result, several lateral flow rapid diagnostic tests (RDTs) that detect Ebola, have been evaluated by the Foundation for Innovative Diagnostics and other agencies. The issue is that there has been no clear international consensus on how best to deploy this type of device at point-of-care during the current outbreak response.

As part of the international response to Ebola in West Africa the British Government and PHE have sought to follow the processes and procedures that are internationally acceptable. This has included collaboration with relevant agencies, including the WHO, Sierra Leone Ministry of Health and Sanitation, and other organisations working in the region.

Lateral flow antigen RDT

On the specific lateral flow antigen RDT mentioned by Dr Oliver Johnson, this was evaluated in the field by PHE in collaboration with the King's Sierra Leone Partnership. It performed well in comparison to an established test for effectiveness in one study[1] although the comparator sample test it was subsequently showed it was less than perfect[2]. For the UK Government to be in a position to work with the manufacturer to make the test available of this particular product we would need at least the following in place:

- The device in question to have received the necessary clearance for emergency use by WHO. This particular antigen RDT does not have regulatory clearance for emergency use and has not been through the EUAL process which is, de facto, a prerequisite for wider deployment.
- International consensus on how best to deploy antigen RDTs. In common with other rapid diagnostic tests of this type, it would be unlikely to have been deployed at point-of-care. These antigen rapid tests [3] have not been deployed due to a lack of consensus about where and how they should be used. Indeed, WHO has issued interim guidance to Ministries of Health stating that antigen RDTs 'should not be used in the routine diagnostic management of Ebola virus disease at the current stage of this outbreak', except in certain 'special situations'[4].
- A request to Sierra Leone Ministry of Health and Sanitation. Any interventions would clearly need the approval of the country's health body.

We think antigen RDTs have considerable value as these devices would be very suitable for a rapid assessment, but there need to be agreements in advance encompassing their use and limitations. For example what happens when the

result is negative, when the test is repeated, and what is an acceptable error rate? This all needs to be in place before they are deployed, and PHE are very happy to help develop these requirements with the WHO should they wish to go down that line.

Rapid gene tests

There were two rapid gene tests mentioned at the session. One was the Biofire FilmArray and the second was the Cepheid GeneXpert ebola assay. PHE has been heavily involved in evaluating both of these technologies during the outbreak.

The FilmArray received FDA emergency use approval in the US, but currently does not meet full regulatory approval for use in the UK. It was granted eligibility for WHO procurement through the EUAL mechanism in September 2015. PHE evaluated the FilmArray in collaboration with the Defence Science and Technology Laboratory and MOD in the UK and Sierra Leone[5]. We are satisfied that the FilmArray provides a good platform for detection of Ebola in blood. It has a limitation of only being able to analyse one sample per hour[6] and does not exclude other causes of viral haemorrhagic fever. PHE worked with Medicines and Healthcare Regulatory Agency to obtain temporary UK derogation of the FilmArray to permit its supply and use in the UK, deploying it to its laboratories in the UK[7]. The test was used for rapid exclusion of Ebola in UK patients, in conjunction with specific algorithms co-ordinated through the Imported Fever Service.

The Cepheid GeneXpert ebola test, similarly, has Ebola emergency use authorisation approval from the US Food and Drug Administration and has been granted eligibility for WHO procurement[8]. This became available towards the end of the outbreak, and the test now has regulatory approval for use in the UK. PHE has been involved the evaluation in the PHE-led laboratories in Sierra Leone. It has performed well compared to existing tests for blood samples, but has been more problematic on other samples types such as post-mortem mouth swabs[9]. There is now a programme to deploy this test in government laboratories in Sierra Leone and PHE has started to use the test in its in-country laboratories and to provide surge capacity to supplement the existing tests.

Neither of these rapid gene tests are considered as true point of care devices but have their uses in specific situations.

Conclusion

As you will appreciate, adoption and implementation of any diagnostic test is a complex process and requires a large number of factors to be considered, ranging from clinical benefit, cost, ease of use, sensitivity, specificity, place of use and others. PHE continues to evaluate rapid diagnostic products and translate innovations into practice after due consideration of the relevant requirements and in line with the evidence base.

I hope this is helpful. If you have any further questions please don't hesitate to come back to me.

December 2015

---

[1] Walker, N. F., C. S. Brown, D. Youkee, P. Baker, N. Williams, A. Kalawa, K. Russell, A. F. Samba, N. Bentley, F. Koroma, M. B. King, B. E. Parker, M. Thompson, T. Boyles, B. Healey, B. Kargbo, D. Bash-Taqi, A. J. Simpson, A. Kamara, T. B. Kamara, M. Lado, O. Johnson and T. Brooks (2015). "Evaluation of a point-of-care blood test for identification of Ebola virus disease at Ebola holding units, Western Area, Sierra Leone, January to February 2015." Euro Surveill 20(12): pii=21073. doi:10.2807/1560-7917.ES2015.20.12.21073

[2] Broadhurst, M. J., J. D. Kelly, A. Miller, A. Semper, D. Bailey, E. Groppelli, A. Simpson, T. Brooks, S. Hula, W. Nyoni, A. B. Sankoh, S. Kanu, A. Jalloh, Q. Ton, N. Sarchet, P. George, M. D. Perkins, B. Wonderly, M. Murray and N. R. Pollock (2015). "ReEBOV Antigen Rapid Test kit for point-of-care and laboratory-based testing for Ebola virus disease: a field validation study." The Lancet Published Online June 26, 2015 http://dx.doi.org/10.1016/S0140-6736(15)61042-X

[3] Broadhurst, M. J., J. D. Kelly, A. Miller, A. Semper, D. Bailey, E. Groppelli, A. Simpson, T. Brooks, S. Hula, W. Nyoni, A. B. Sankoh, S. Kanu, A. Jalloh, Q. Ton, N. Sarchet, P. George, M. D. Perkins, B. Wonderly, M. Murray and N. R. Pollock (2015).

"ReEBOV Antigen Rapid Test kit for point-of-care and laboratory-based testing for Ebola virus disease: a field validation study." The Lancet Published Online June 26, 2015 http://dx.doi.org/10.1016/S0140-6736(15)61042-X

[4] WHO. (March 2015). Interim guidance on the use of rapid Ebola antigen detection tests WHO Doc ref WHO/EVD/HIS/EMP/15.1 [http://www.who.int/csr/resources/publications/ebola/ebola-antigen-detection/en/]

[5] Simon A Weller, Daniel Bailey, Steven Matthews, Sarah Lumley, Angela Sweed, Derren Ready, Gary Eltringham, Jade Richards, Richard Vipond, Roman Lukaszewski, Phillippa M Payne, Emma Aarons, Andrew J Simpson, Emma J Hutley, and Tim Brooks (2015) Evaluation of the Biofire FilmArray Biothreat E-test (v2.5) for rapid identification of Ebola virus disease in heat-treated blood samples obtained in Sierra Leone and United Kingdom. J. Clin. Microbiol. Accepted manuscript posted online 4 November 2015. doi:10.1128/JCM.02287-15

[6] For context in Sierra Leone at the peak laboratories were processing 200 samples a day.

[7] located at Porton Down, London and Newcastle.

[8] WHO Public report. WHO Emergency Use Assessment and Listing for EVD IVDs. Product: Xpert® Ebola Assay Number: EA 0020-019-00 [http://www.who.int/diagnostics_laboratory/procurement/150508_pr_expert_ebola_test_usa.pdf?ua=1]

[9] Amanda Semper, M. Jana Broadhurst, Jade Richards, Geraldine M. Foster, Andrew Simpson, Elisabetta Groppelli, Julie Johnson, J. Dan Kelly, Tim Brooks, Christopher H. Logue, Ann Miller, Megan B. Murray and Nira R. Pollock, Field Laboratory Evaluation of the GeneXpert Ebola Assay for Diagnosis of Ebola Virus Disease in Sierra Leone. [https://idsa.confex.com/idsa/2015/webprogram/Paper54137.html]