Reviewer's report

Title: Point-of-care detection of lipoarabinomannan (LAM) in urine for diagnosis of HIV-associated tuberculosis: a state of the art review

Version: 1 Date: 27 February 2012

Reviewer: Andy Ramsay

Reviewer's report:

Overall this is an excellent review. Well-written and informative.

Major Compulsory Revisions: None

Minor essential revisions:

1. There are a few sentences where the meaning is not so clear. It is recommended that these are re-worded:
   a) 3rd paragraph under "What is lipoarabinomannin (LAM)" - "In addition to ManLAMs in pathogenic species, LAM capped with phosphoinositol (PILAMs) are typically found in non-pathogenic species such as Mycobacterium smegmatis".
   b) 3rd paragraph under "How does LAM enter the urine?" - "A more detailed analysis of this issue found that LAM antigenuria was not associated with heavy proteinuria that would be required to permit glomerular filtration of immune-complexed LAM".
   c) 6th paragraph under "Potential utility of Determine TB-LAM point-of-care assay" - "In a study in Cape Town, South Africa, where Xpert MTB/RIF is being rolled out in centralised laboratories, only 76.6% of patients diagnosed as having Xpert-positive TB during pre-ART screening started TB treatment after a median of 9 days (interquartile range, 6 - 18 days)".

2. A reference to Figure 3 is, in my opinion, mis-placed. Instead of being referred to in paragraph 3 under "Clinical evaluation of a point-of-care LAM assay" it would be better at the end of the first sentence of paragraph 1 (under the same heading).

3. There are a few typos:
   a) End of paragraph 1 under "What is lipoarabinomannin (LAM)" - "The presence OF mannose capping allows ....."
   b) 1st paragraph under "Clinical evaluation of a point-of-care LAM assay" - "Patients were classified as either having TB (based ON a diagnostic gold-standard OF culture-based detection......")"

4. A mention of the utility of LAM antigen detection in HIV-positive children
suspected of having TB, or the need for research, would address an obvious gap in the review.

5. Those familiar with earlier versions of the LAM assays would be aware of the earlier need for specimen processing (boiling the urine) which adversely affected their utility at point-of-care. A brief explanation of the assay’s transition from using processed to unprocessed specimens would address this.

Discretionary revisions

1. The author refers to two studies from Tanzania: one by Boehme et al which reports a high specificity (99%) and another by Reither et al, reporting a much lower specificity (88%). In the 4th paragraph under "Clinical evaluation of commercial ELISAs" the Boehme et al paper is included with the 5 South African studies reporting high specificity, while studies from the other countries report lower specificity. In the second paragraph under the same heading the Boehme et al paper is described as reporting "a very high specificity" among HIV-positive and negative ambulatory patients with TB. The paragraph ends stating that "No study has since replicated these data and the reasons for this remain unclear". Research on this issue is called for later in the review. From reading the Boehme et al paper it seems that study design issues may explain the findings - perhaps, if the author agrees, this deserves comment.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No competing interests