Reviewer’s report

Title: A novel detection device for Mycobacterium tuberculosis antigen in breath

Version: 1 Date: 19 February 2010

Reviewer: Matthias Frank

Reviewer’s report:

In this article, the authors describe the use of the TB Breathalyzer device (a commercial system by Rapid Biosensor Systems LTD) in a field test conducted in Ethiopia where 60 patients were screened. The authors provide some background on the problem of tuberculosis and tuberculosis transmission and briefly describe their device. The methods and results are described in more detail. Overall, the results with this device seem very promising, although there are some false positives and some false negatives. To the authors’ credit it should be noted that they are not trying to oversell those results, but advertise further study of the device and the relationship between excreted antigen and smear positivity. They are also not advocating their device as a replacement, but rather a complement to the smear test. From the reported results it appears that this device should have some usefulness in the early identification of TB cases and this paper should be of great interest to readers in this field.

The reviewer has some issues and suggestions that should be addressed by a revision.

1. The title reads “A novel detection device …..”, but the actual device is described only very briefly and cursory under methods on pg. 5/6. – Suggestion: consider making the title more congruent with what is described in the paper (i.e., the field test or performance evaluation). - Discretionary Revision

2. The only reference to the actual device is a reference to the U.S patent and/or the European patent application. (adding those patent numbers may be helpful for the readers). The reviewer could not find any peer-reviewed or other technical publication on this device (other than the some information on the companies webpage). If there is a publication, it should be referenced. If not, this seems to be a major weakness in presenting this work in a scientific peer-reviewed journal (that could be fixed, in part, by providing some more actual technical details on this device right here in this article). - Major Compulsory Revision

3. The reviewer also wonders why the authors call the device “novel” where the patent applications were submitted in 2002 – almost 8 years ago. - Discretionary Revision

4. In the introduction, the authors claim that there is “…little data available regarding the exhalation of M. tuberculosis.” (pg. 4) and that “Rapid, real time methods of assessing whether an individual is expelling M. tuberculosis in their
breath have not previously been reported.” (pg. 5). These statements are, in their absoluteness, not correct. There has been some relevant published work in these areas. E.g.


And a simple Google search will yield additional references. Not including any of this previous work is somewhat of a shortcoming of this paper in the present version. Add some more references - Major Compulsory Revision.

Discretionary Revision: There are other real-time methods under evaluation, such as breath trace gas analysis, that may not have made it into a commercial device yet, but have been evaluated with TB patients and could be mentioned, too. E.g.,


5. Methods, page 7: It is unclear to the reviewer (and probably also to other readers) what a “…reduction in signal greater than 20 units…” really means. Is that 20 units out of 100, i.e. a reduction by 20%? What fraction of the fluorescently labeled analogue molecules needs to be replaced by TB antigen to cause this kind of signal? How many antigen molecules does this correspond to in absolute numbers and how many intact TB bacilli would have to bind to cause this signal? (i.e. from the information given it is unclear what the sensitivity (in terms of number of TB bacilli coughed out) of the device is.) - Major Compulsory Revision

Level of interest: An article of importance 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:

I have no competing interests.

[In the interest of full disclosure, I have worked on LLNL’s patented technology on
single particle aerosol mass spectrometry (SPAMS) as a potential detection device for pathogens. Some of this work included evaluating the potential of this technology for TB detection - see, e.g., Kristl L. Adams, et al., Anal. Chem. 80: 5350-5357, 2008. I do not believe this constitutes a competing interest, since these were only very basic studies not involving actual patients and, to my knowledge, there is no commercial interest in further developing this SPAMS technology for a TB detector by us or the licensee of our patents, at this time and the foreseeable future.]