Reviewer's report

Title: Evaluation of Microscopic Observation Drug Susceptibility assay for diagnosis of multidrug-resistant tuberculosis in Viet Nam

Version: 2 Date: 17 September 2011

Reviewer: Howard Takiff

Reviewer's report:

All comments are Major compulsory revisions, because in addition to the major problems, there are so many minor problems that they constitute a major problem.
Until the presentation and writing are improved, it's difficult to completely evaluate the substance of the manuscript.

The manuscript by Dang et al compares the MODS method for detecting tuberculosis to Lowenstein Jensen and MGIT, and detecting resistance to INH and RIF to Lowenstein Jensen.
The question is fairly well defined, and the methods appropriate. The comparison of the methods in a high burden real-life setting would be valuable were it presented better.

1. The data is probably sound, but the three tables described in the text were not included in the material to review, so it is difficult to assess completely the adequacy of the data in supporting the conclusions. The introduction and discussion are a bit long.
2. The intro reviews other techniques, which is appropriate but could be more concise.
3. The discussion also needs to be shortened, focused and tightened
4. The authors should state why MGIT wasn’t also used for detection of resistance.
5. The results of sequencing should be shown in detail. Perhaps this data is in the missing tables.
6. Besides promoter mutations, mutations in the inhA coding region also confer resistance.
7. Without the tables it is hard to follow how the discrepant results were resolved.
8. More data on the cross contamination would be helpful…if two isolates had the same spoligotype, but it’s one of the most common ST’s in the population, it might not be cross contamination.
9. If the gold standard is LJ, how was the performance of LJ evaluated? Compared to MGIT?
10. H37Rv is used as a control but not mentioned in the Methods section
11. The section “DST results by MODS” and the following section should be combined. The way the results are separated makes it more confusing, and not only in this section.

12. The Results section could be written more concisely to make it more easily understood. The way it is written makes the reader have to work to figure out what the authors wish to say, especially in the section on discrepant results. Having the tables should make this easier, but even with them, the writing in the results needs to be improved and tightened.

13. Were discrepant results repeated on LJ?

14. How is it that some isolates weren’t available to test again? What about the control wells without antibiotics?

15. In comparing time to results, do the authors really intend to use the median time (half of the tests were completed in a shorter time, half longer), or is it the mean (average) time they wish to indicate?

16. In the last paragraph of the Results, “The final fungal contamination rate of MGIT and LJ” should be “rates”. There are many examples of errors like this.

17. In the last sentence before the discussion, what is the meaning of “nonsense mutation on ropB gene by sequencing and resistant by DST-LJ”? A nonsense mutation generally means a stop for translation (UGA, UAG or UAA), but that couldn’t be possible because ropB is essential. Do the authors mean a mutation that doesn’t alter the amino acid encoded? The sentence is incomprehensible.

18. The principal problem is that the manuscript is very sloppily assembled. There are all manner of typing mistakes, awkward prose, bad grammar, verb agreement mistakes, plurals that should be singular and visa versa, and other outright errors (ropB should be rpoB). Also the three tables were not included.

19. For example, the first sentence of the Results section “Detection of drug-resistance”… “Although there were 373 samples positive by either MGIT or LJ, 9 samples were identified as Myco other than TB (MOTT: M.fortuitum or M. Chelonae) which were identified by standard biochemical tests and therefore DST-LJH was not done for these samples.”

This sentence has so many errors it’s hard to know where to begin:
“there were 373 samples…, 9 sample were identified as ….which were identified”

Not all MOTT are M. fortuitum or M. cheloneae. If they were identified as these, that should be stated. Why include the abbreviation MOTT if it is the only time it is used, except in Figure 1, where it is defined again in the legend?

If biochemical tests were performed, mention of these belong in the Materials and Methods section.

20. Perhaps some of the awkward syntax could be explained by English not being the author’s mother tongue, but that doesn’t explain or justify the sloppy preparation of the ms. Some of the co-authors have names that suggest they might be native English speakers who should be able to resolve some of the awkwardness of language.
21. For example, in Methods, “Exclusion criteria….or a prior DOSE of TB therapy.” Does that mean prior treatment, or having taken even a single dose of TB therapy?

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

I recently published a paper on a different technique for low-cost drug sensitivity testing in TB, but that’s presumably why I was asked to review this ms. I believe the MODS study is valuable, and that our study of a different method, on which my lab is no longer working, has not biased my comments.

I have no competing financial interests.