Reviewer’s report

**Title:** The use of microbead-based spoligotyping for Myobacterium tuberculosis complex to evaluate the quality of the conventional method: Providing guidelines for Quality Assurance when working on membranes

**Version:** 1 **Date:** 16 December 2010

**Reviewer:** Igor Mokrousov

**Reviewer’s report:**

This paper of Abadia et al. is timely and interesting contribution to the field of molecular typing of M. tuberculosis.

**Major Compulsory Revisions**

Page 9 (last line). The reference method should be not microbead-spoligotyping but direct sequencing of this region in these problematic strains.

Additional variables (not discussed in the article) related to the quality of spoligoprofiles should be presented and discussed:

1. Different Taq polymerases used and PCR conditions as a whole (buffer, MgCl2 concentration etc).
2. For laboratories that made their own membranes, the source of oligonucleotides may be important, I mean that these oligos were likely synthesized in different companies. In fact, speaking about the quality of the membranes produced by Ocimumbio, it would also be interesting to know if and what were the problems of the home-made membranes.

**Minor Essential Revisions**

Abstract, Results: please mention in parentheses what spacers were problematic:

“Few centers shared the same problematic spacers and these problematic spacers were scattered over the whole CRISPR locus (##....................).”

Abstract/Conclusion: last sentence. I would say “to give occasionally weak signals”, as in this reviewer’s lab the home-made membrane never had problem with #15.

Page 5. end of the 1st paragraph: one should also keep in mind a possibility of the convergent evolution thus making spoligotyping results phylogenetically uninformative.

Page 9. Regarding spacer 15 and reference [18], it would be appropriate to explain if this 5 bp deletion occurred only in some strains or was a more general case?
Line numbering of the manuscript would be helpful.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests.