Reviewer's report

**Title:** High background rates of positive tuberculosis-specific interferon-gamma release assays in a low prevalence region of UK: a surveillance study

**Version:** 1  **Date:** 19 March 2012

**Reviewer:** Roland Diel

**Reviewer's report:**

**Major comments:**

Page 4, Background, first para: “Such data would be valuable for interpreting the significance of a positive IGRA result, and guiding cost-benefit analyses of new diagnostics.[1]”

This sentence needs some improvement because “significance” of a positive IGRA result has already been shown e.g. for exposed contacts of infectious TB source cases. Further, some cost-benefit analyses have been performed with respect to the topic of implementing the IGRA tools.

Page 5, Results, first para: “Testing was not performed in 168 exposed patients because they had died (n=66), or testing was declined or considered inappropriate (n=102).” If the 102 individuals were real contact persons how could testing considered to be inappropriate? Please clarify!

Page 8, Methods, first para: “Contact tracing identified 445 potential contacts of the index case, comprising 142 staff and 303 patients.”

What about the progression rate within the 15 months of the contacts scored IGRA positive?

Page 8, Methods, second para: “These comprised a further 191 individuals with a similar age distribution recruited from staff and adult patients on the same respiratory and general medical wards where exposure had previously occurred, but who had not been exposed to any of the 9 cases.”

Why was only a total of 191 individuals taken as control group of the 445 contacts? Was the reason, if the matching took place in the same time frame, that only 191 individuals were available? Was the matching performed by random? Please clarify!

Figure 1: A total of 34 contacts were T-Spot positive and 4 were “borderline”

Do the authors add the contacts scored “borderline” to the IGRA-positive or to the IGRA-negative contacts? Given 34 positive contacts, at least 6 out them progressed to active TB, i.e. the progression rate was 6/34 (17.6%). It may be helpful to add the progression rate to the text because it reflects that the selection of contacts was valid.

**Minor Comments:**
Page 4, Background, first para: “Rates of 6.7-9.9% IGRA-positivity have been observed in healthcare workers in low prevalence countries.[4]”

The information referenced lacks any significance, thus I suggest qualifying this statement, perhaps as follows “The few studies that have reported on IGRA positivity in healthcare workers place the figure in the 6.7-9.9% range.”

Page 4/page 8, general comment: It is common practice that the Method section should be placed before the Result section!

Page 5, Results, second para: “The rates of IGRA positivity were: unexposed patients 8.7% (95%CI, 4.2-13, n=149), unexposed staff 9.5%(3.0-22, n=21), exposed patients 22%(14-29, n=130), exposed staff 11%(6.1-16, n=142). Please add the number of positives, not only the number of tested persons, and the term “95%CI” into each bracket!

Page 5, Discussion: “All these unexposed individuals were white-Caucasians...”. The sentence should read “presumably not recently exposed individuals...” because they must have been exposed to TB patients at least once in the past to acquired MTB infection (as evidenced by their IGRA positivity)!

Page 9, Acknowledgements: The name of the company correctly spells “Oxford Immunotec” instead of “Oxford Immunotech.”

**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:**

In the past five years R.D. has received travel reimbursements and/or a fee for speaking at symposia sponsored by Oxford Immunotec Ltd., Cellestis Ltd. or Pharmore Ltd. (exclusive supplier of RT 23 TST for Germany).