Author's response to reviews

Title: Serial counts of Mycobacterium tuberculosis in sputum as surrogate markers of the sterilising activity of rifampicin and pyrazinamide in treating pulmonary tuberculosis

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Reviewer: Prof Leonid Heifets

1. Dr Heifets' comments that a proposal of his to the Global Alliance for TB Drug Development for the collection of weekly sputum samples during the initial phase of chemotherapy might be included in the discussion. I do not really think that it is appropriate to mention this point in the paper. The proposal, which has not yet been accepted, would involve a great deal of additional work and it is far from clear what benefit would result. While it may be a good idea to have more numerous sputum collections during treatment, one cannot introduce the issue without some evidence on the benefits conferred, which we do not have as yet.

2. I have altered the phrase "extended early bactericidal activity" to give the actual periods involved during treatment.

3. I would prefer to leave the conclusion on page 13 as it stands. Although many people in the field understand the concept of sterilising activity, there are those who might prefer it to be more closely defined.

4. I have removed one reference to Table 1, which is not appropriate. Table 3 is referred to on page 7.

5. I think it is appropriate to show the evidence from the mouse model since a text description would only provide partial information.

Reviewer: Michael Cynamon

1. The reference to Table 1 has been removed as the data are not described in it. Neither is a reference to Table 2 appropriate and has been removed.

2. I have deleted "in the following period".

3. Page 8, line 16, "14-28". I am not clear what the reviewer means by this.

4. Page 9, line 2. I would have thought that everyone knows that F is the variance ratio. However, I have indicated in the text that this is what F is.
5. Page 10, last paragraph. I have changed "presumably" to "perhaps" since I agree that the statement is highly speculative.

6. Page 15, line 17. This is a typo. I have changed (1.78 log cfu/ml) to (1.78 log cfu/ml).


8. Table 3. I really feel that everybody knows what F and p mean.

9. Figs 1-4. These figures are only illustrative of the changes, but I doubt whether error bars will help in their interpretation. I have not put them in.