Author’s response to reviews

Title: Nearly half of Ultrio Plus NAT non-discriminated reactive blood donors were identified as occult HBV infection in south China

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Version: 2 Date: 31 May 2019

Author’s response to reviews:

Dear Dr. Antoinette C Van Der Kuyl:

Ref: manuscript INFD-D-19-00121 entitled “Nearly half of Ultrio Plus NAT non-discriminated reactive blood donors were identified as occult HBV infection in south China”.

We would like to re-submit the new version of manuscript before 16 April as the journal required. According to reviewers’ and your comments and questions, the manuscript was carefully revised in the new version with changes highlighted. The explanation or answer has been addressed as indicated below under each question point by point.

If you have any more question regarding to this manuscript, please let me know.

Yours sincerely,

Dr. Tingting Li
Reviewer reports:

Jean-Pierre Allain (Reviewer 1): The revised manuscript by Ye et al, has improved but several areas still need improvement.

1. English and spelling in the revisions need attention. For instance, Discussion is misspelled. There are many other mistakes to be corrected.
   Answer: Thanks, the manuscript has been carefully edited in the new version of text.

2. In the Discussion, the discrepancies between results of this study and those from previous studies have not been appropriately addressed.
   Answer: We are thankful for the reviewer’s suggestion. The discrepancies between this study and previous studies were added in Discussion section, Line 376-378, page 14, which might be related with the alternative NATs and detection times, or different targeting genomic regions.

   In Table 5, aa substitutions known as related to vaccination, those recognized as frequent in OBI are not clearly indicated and the references supporting this type of classification are not specifically indicated.
   Answer: According to your suggestion, vaccination related mutations were indicated by symbol # in Table 5, Page 26, and the references were cited for [14-19, 24] in the footnote.

   The issue of absence of cysteine substitutions in the MHR typical of OBI as well as P120 substitutions has not been clearly addressed.
   Answer: Thank you very much. We added “No cysteine or typical P120L substitutions of OBI in the MHR were found in NDRs.” in Results section, Line 264, Page 10.

3. The issue of absence of difference in anti-HBc and anti-HBs in the NDR DNA pos or neg is not sufficiently addressed in the discussion. Anti-HBc is considered in other studies as a critical marker for confirmation but clearly not in this case. This needs specific discussion.
   Answer: We added “There is no significant difference in anti-HBc and anti-HBs between the NDR DNA pos or neg donations (p>0.05).” in Results section, Line 187-188, Page 8. Further analysis of anti-HBc for confirmation was added in Discussion section, Line 291-293, Page 11 with “Furthermore, anti-HBc was considered in other studies as a critical marker for confirmation [25], but clearly not in this case due to a higher proportion of anti-HBc positive donations involved in NDRs”.

4. The authors should indicate what information and advice they may give deferred donors when they are NDR DNA positive or negative.
   Answer: We are thankful for the reviewer’s suggestion. “Only a donor with confirmation of NDR DNA negative in follow-up detection with an interval of 3-6 months by multiple tests can be informed to be healthy.” was added in Discussion section, Line 333-335, Page 13.

Angelita Silva de Miranda Corrêa (Reviewer 2): - Needs some language corrections before being published
   Answer: Thanks, the manuscript has been carefully edited in the new version.
- The manuscript must be reviewed building a parallel among different scenarios found in high, median and low-income countries.
   Answer: We are thankful for the reviewer’s suggestion. We reviewed anti-HBc screening in different counties according to different prevalence. “In some medium/low endemic countries including Canada, France, Germany, Ireland, the Netherlands, Lebanon, Brazil and USA, anti-HBc was mandatorily implemented in blood donation screening.” was added in Introduction section, Line 56-59, Page 3.

- Review the conclusions based only in your findings.
   Answer: We added “based only on our findings” at the end of Conclusion section, Line 426, Page 15.

- Try to emphasize what is not known about the subject of your research.
  Answer: Considering the limitations of this study, we emphasize the importance of follow-up detection in confirming NDR DNA or OBI in Discussion section, Line 413-414, Page 15. We also added “More sensitive commercial NAT assays such as MPX2.0 ID NAT could interdict more HBV DNA positive NDRs if used in this study.” in Discussion section, Line 414-415, Page 16.