Reviewer's report

Title: Zika vaccines and therapeutics: landscape analysis and challenges ahead

Version: 0 Date: 21 Jan 2018

Reviewer: David Freedman

Reviewer's report:
Well-written organized, and comprehensive synthesis of the current considerations and landscape for Zika vaccine development from a number of existing WHO reports available on the WHO and clinicaltrials.gov websites by a group of eminent authors who appear to have been involved in the series of WHO meetings that led to the source documents. As WHO should be a main driver in coordination of the many Zika vaccine efforts worthwhile, exposing thoughts and the landscape widely may be worthwhile.

The review largely overlaps a series of similar and slightly more expansive articles just published in a supplement to J Inf Dis in December 2017.

The important hurdles posed by the limitations of current diagnostics are underplayed here, just a brief statement without elaboration in an ending paragraph. If laboratory endpoints in clinical trials are to be paramount as suggested by the authors, this warrants more discussion.

The history of flavivirus vaccine development is much in the news these days with the challenges of dengue vaccine becoming more apparent. This needs a full and separate section for discussion.

More is now known of biology and impact of infection in pregnant women (CZS) and populations (GBS). A numerical impact ballpark that would drive vaccine development strongly or not might be stated. Any adverse effects of live virus vaccines might then be put in context of levels of sexual transmission and levels of CZS in future epidemics.
Should the discussion of the possible vaccine platforms be re-ordered in order of likelihood of success? Seems unusual to lead with nucleic acid vaccines, a platform that has yet to see success for any infectious disease.

The non-vaccine therapeutics and prophylaxis seem the least promising, do they need so much coverage or do they belong in another paper?

There is too little discussion on sample size of necessary clinical trials, period of follow-up (given the antibody-dependent enhancement issues with flaviviruses), need for multiple trials in multiple regions, and cost.

Fatigue by industry for development of vaccines for newly emerging viruses has been evident recently and needs discussion.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable
**Declaration of competing interests**

Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?
5. Do you have any other financial competing interests?
6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I was a member of the WHO Zika Emergency Committee but have not been involved with any WHO Zika activities since November 2016 and have had no involvement in the vaccine strategic planning group.

**Statement on potential review bias**

Please complete a statement on potential review bias, considering the following questions:

1. Did you co-author any publication with an author of this manuscript in the last 5 years?
2. Are you currently or recently affiliated at the same institution as an author of this manuscript?
If you can answer no to all of the above, write ‘I declare that I did not publish with these authors in the last 5 years and also meet the affiliation criteria”. If your reply is yes to any, please give details below.

I consult for WHO (uncompensated) on various un-related issues concerning the International Health Regulations.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal