Reviewer’s report

Title: Biosafety and biosecurity requirements for Orientia spp. diagnosis and research: Recommendations for risk-based biocontainment, work practices and the case for reclassification to Risk Group 2.

Version: 0 Date: 08 Aug 2019

Reviewer: Ratree Takhampunya

Reviewer's report:

The recommendation to reclassify Orientia spp. pathogen from RG3 to RG2 is appropriated. Considering the information we have so far that it is not an airborne pathogen and do not spread via person-to-person contact, therefore the risk to community is very low. The only recognized natural route of transmission is via chigger bite. An increasing public health concerns in several regions not only limited to Asia Pacific has garnered much attentions from many scientists, public health personnel, and government research institutes to work on this area. Reclassification of the Orientis spp. to RG2 would allow for an extensive research to develop a better clinical diagnostic assay or even vaccine in the future or to understand the underlying mechanism of disease pathogenesis in human.

Comments

1) P8, line50 to P9, line21: Under recommended risk assessments for Orientia spp. research activities. The scale of scrub typhus culture from clinical specimen/animal/arthropod: When stating the small-scale of the in vitro culture to be considered as LOW risk activities, more definition (maybe volume or quantity of viable rickettsia pathogens) should be added. This can be used as guidelines or reference for research lab (not clinical lab) when assessing risk-management.

   - Likewise, when stating that the significantly increase the volume and concentration of the culture materials (ml? or viable cells) such as in the case of reagent production then the risk would increase to MEDIUM or HIGH. If possible, please clearly define the volume and concentration.

   - Adding which group the risk is referring to when stating the "risk" in this paragraph, on what (environment/community) or whom (laboratory personnel) the risk would have impact?

   - Again in Table 4: Please define "low concentration, low volume" and "high concentration, high volume". These criteria can be used to distinguish in-house reagent production (such as for IFA or ELISA) and industrial production (mass production).

2) BSL-3 biocontainment cannot prevent the incident of parental inoculation (bite, cut, and inoculation), so the requirement of BSL-3 biocontainment for some research work such as cultivation or some small animal work (even the works performed under class II BSC) seems to be overstated. Although high volume, high concentration production can generate an infectious aerosol; however, working under class II BSC should successfully prevent the transmission to laboratory personnel who works with Orientia spp. Therefore, defining the scale of cultivation should allow some in-house antigen production activity be performed in class II BSC under BSL-2 facility.
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 declare that I have no competing interests.

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