Reviewer's report

Title: Performance of Commercial Dengue NS1 ELISA and Molecular Analysis of NS1 Gene of Dengue Viruses Obtained during Dengue Surveillance in Indonesia

Version: 3 Date: 26 October 2013

Reviewer: Linda Hueston

Reviewer's report:

Thank you for the opportunity of reviewing this very interesting article. Given the increasing availability of commercial NS1 antigen detection kits and IgM and IgG antibody kits for dengue fever across the globe there is a real and on-going need to assess not only the accuracy, sensitivity and specificity of such assays but to consider these in light of geography. It is extremely important to understand that how one approaches the laboratory diagnosis of dengue in Indonesia may well be different to how one approaches laboratory diagnosis in countries like Australia or the USA. Indeed the usefulness of these kits will vary among nations with high dengue burdens - it will also vary over time and this suggests that on-going evaluation is needed. The authors have attempted to do this and have largely succeeded in doing so.

One concern I have is that the authors only examined the use of the PanBio kits, therefore the question I have is do all NS1 antigen kits and Dengue IgG and IgM kits give the same results or would other kits have a better performance. Perhaps PanBio is the only kit available for purchase in Indonesia and if this is true then the authors results very valuable and would be of great interest to clinicians. If it is not true and other kits are available then knowing how other kits perform could be even more useful to clinicians. If the authors cannot add results using different manufacturers products then it is important that the authors make a statement to the effect that other products may perform differently.

There are numerous language corrections which need addressing and I have made some suggestions below. Also I would suggest the author's specify NS1 antigen when they are referring to the kits, they mention NS1 sometimes referring to antigen, sometimes referring to the proteins themselves. Also some kits for antibody detection use NS1 antigen rather than whole native antigens or recombinant antigens - this can affect the sensitivity and specificity of antibody assays. So some clarification of the type of antigen used in the kits under study would be helpful.

Line 36 - mention the total number of collected samples used.

Line 44 - should read "the sensitivity increased to 89.4%" and "NS1 antigen sensitivity varied when correlated...."

Line 54 - should read "..........the low sensitivity of NS1 antigen detection did not relate to NS1 genetic diversity."
Line 55 - should read "the performance of the NS1 antigen test............"

Line 56 - what do you mean by "infectious status of patients"? Do you mean primary or secondary infection, do you mean the time following onset of symptoms or do you mean severity of disease presentation. You need to explain this.

Line 61 - should read "......... with a large global burden"

Line 62 - should read "There are an estimated 50 million infections..........."

Line 70 - should read".........within each serotype"

Line 84 - should read "High level early viremia........"

Line 88 - should read "plasma/serum samples have been described"

Line 96 - should read "...... and are becoming the tool of choice....."

Line 108 should read ".........during dengue surveillance in 2010-2012.

Line 117 - Alere is the manufacturer not Inverness.

Line 141 - should read "Detection and serotyping were confirmed......"

Line 143/144 - should read "The Simplexa Dengue assay was performed according to the manufacturer's instructions."

Line 148 - you mention inoculating C6/36 monolayers but don't mention the size of the flasks used.

Line 164 - should read "......using the method described by the manufacturer"

Line 193/194 delete ".......for NS1 antigen"

Line 205 - change "assessed" for assess

Line 208 - do you mean the difference between NS1 antigen and IgM ELISA kit or do you mean an IgM test kit that uses NS1 antigen?

Line 232 - delete "Result of....." should read "Comparing the sensitivities......."

Line 242 - should read "IgM sensitivity appeared to be affected by geographical regions"

Line 304 - should read ".....NS1 antigen kit evaluated here showed higher sensitivity......."

Line 372 - should read "The non-structural (NS) proteins .........."

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.