Reviewer's report

Title: Comparison of two dengue NS1 rapid tests for sensitivity, specificity and relationship to viraemia and antibody responses

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Reviewer: Philippe Dussart

Reviewer's report:

This manuscript compares the sensitivity and specificity of the Bio-Rad NS1 Ag Strip and SD Dengue Duo (NS1/IgM/IgG) lateral flow rapid tests in a panel of human samples from Vietnamese patients with RT-PCR confirmed dengue (n=245) and with other febrile illnesses (n=47).

The authors have observed that the NS1 rapid tests had similar diagnostic sensitivities (respectively 61.6% and 62.4%) in confirmed dengue cases but were 100% specific. Moreover, inclusion of the IgM and/or the IgG parameter(s) in the interpretation of the SD Duo test increased the diagnostic sensitivity over NS1 alone. They confirmed previous statements: (i) NS1 detection rates were significantly lower in patients with secondary dengue than primary dengue, (ii) viremia levels were significantly higher in patients who were NS1 positive versus those who were NS1 negative. This prospective study is mainly based on DENV-1. No DENV-4 has been tested.

In this study authors had two samples from each patient: the first one during the acute phase of the disease (enrolment) and the second 7-14 days after fever onset. All acute sera were dengue confirmed using dengue RT-PCR. Then, these acute sera were tested with the Bio-Rad NS1 Ag Strip and the SD Dengue Duo (NS1/IgM/IgG) lateral flow rapid tests.

Major Compulsory Revisions:

I agree with these findings and conclusions of this paper. However, the presentation of the results in tables 2, 3, 4 and in the text is not very clear. The authors compare sensitivity of dengue RDT’s in these tables: BR-NS1, SD-NS1, SD NS1 and/OR IgM, SD NS1 and/OR IgG and/OR IgG. If the authors use the statement “SD NS1 OR IgM OR IgG”, I understand that they consider a patient with a positive result for IgM detection with negative NS1 detection as a dengue confirmed case. The same comment could be underline for a positive IgG detection.

IgM can persist several weeks/months and this is well underlined in the discussion. IgG persist after a primary infection: an isolated positive detection of IgG cannot be associated with a confirmed diagnosis of dengue infection. Moreover antibody cross-reactivities with other flaviviruses exist.

The exact significance of “SD NS1 and/OR IgM” and “SD NS1 and/OR IgM
and/OR IgG” must be clearly defined in the manuscript. It refers to algorithm previously published in ref 11, but did the authors use the second serum for general conclusion on dengue status? The authors must clarify.

**Minor Essential Revisions**

1- Introduction, line 2:

Line 2: replace (DENV1-4) by (DENV-1 to DENV-4)

At the end of the introduction, the sentence “Our findings suggest that…” is a summary of the results. This part should be removed from the introduction.

2- Discussion, page 12:

“It is possible these factors might account for the differences between the study findings, It may also reflect chance differences associated with relatively small sample sizes.”

Replace the comma by a point after “findings”.

3- Page “figure 3”, replace figure 3 by figure 3A and page “figure 4” replace figure 4 by figure 3B to be consistent with the text.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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.