Reviewer’s report

Title: Impact of naturally occurring amino acid variations on the detection of HIV-1 p24 in diagnostic antigen tests

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Reviewer: Valeria Ghisetti

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The Authors show that HIV p24 position 16 and 170 is important in performances of diagnostic tests for HIV p24 antigen-only and 4th generation immunoassays combining antigen and antibidy detection. Their finding appears not to be related to HIV subtype, even is the frequence of polymorphisms at those levels varies according to HIV subtype. The work is well done and well written and the issue is very important for the reason that recently published guidelines from the CDC (July 2014) have clearly stated that 4th generation immunoassays should become the standard of care for the diagnosis of HIV infection. Knowing that key p24-position could affect assay performance is therefore of high value. The design of the experiments including mutagenesis tests are well conducted.

I strongly suggest and recommend the Authors to assess a panel of p24 WHO antigen preparation to study performances of the same immunoassays they have used for their experiments to identify variation in the signal/CUT-off due to polymorphisms at position 16 or 170 or both. Alternatively, they could test a panel of HIV serum samples from HIV recent infection to study if variation in assay performance is due to polymorphisms at those two position. The chance to do this is certainly an added value to their study and further clarify the impact of these two positions for p24 detection for 4th generation immunoassays.

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 I have no competing interests