Evaluation of the Alere i Influenza A&B assay for rapid identification of influenza A and influenza B viruses

Flavia Cecilia Chiarella,¹ Esther Culebras,¹ Manuel Enrique Fuentes-Ferrer² and Juan José Picazo¹

¹Department of Microbiology, Hospital Clínico San Carlos, 28040 Madrid, Spain
²Department of Preventive Medicine, Hospital Clínico San Carlos, 28040 Madrid, Spain

The Alere i Influenza A&B assay is a novel isothermal nucleic acid amplification assay capable of detecting and differentiating influenza A and B viruses in approximately 15 min with minimal hands-on time. This study was conducted in order to assess the performance of the Alere i Influenza A&B assay compared to molecular techniques, considered to be gold standard methods, to evaluate the results. A total of 119 nasopharyngeal swabs collected from inpatients with influenza-like illness were included in the study using both archived and prospectively collected samples from adults and children. Prospectively collected samples were also compared to the Alere BinaxNOW® Influenza A & B Card. The overall sensitivity for detection of influenza A and B viruses compared to those of molecular techniques were 65.96 % and 53.33 % respectively, while the specificity was 98.51 % and 95.96 %. Compared to the Alere BinaxNOW® Influenza A & B Card, the Alere i assay is considerably more sensitive for detection of influenza A and B viruses, although both tests demonstrated excellent specificity for diagnosis of influenza viruses.

INTRODUCTION

Influenza, commonly known as ‘flu’, is a viral infection caused by influenza viruses. Influenza infection can cause mild to severe illness and is a major economic burden in terms of both health care cost and lost income and productivity of workers (WHO, 1980).

Since the 2009 pandemic, a strain of influenza A virus (H1N1pdm09) has established in human populations as a seasonal influenza virus and it has become a dominant influenza virus circulating along with seasonal influenza virus A H3N2 and influenza virus B (Mosnier et al., 2015). In addition, respiratory infections are associated with significant morbidity and mortality and are a major economic burden in terms of both health care costs and lost income and productivity of workers (Neuzil et al., 2000a, b).

Rapid diagnosis of influenza infections is crucial in reducing mortality and morbidity by the administration of antiviral therapy within 48 h of symptom onset (Moscona, 2005). Molecular tests have become the gold standard to detect influenza viruses in clinical laboratories due to their high level of sensitivity and specificity (Kumar & Henrickson, 2012). One of the biggest limitations of these tests is that they are technically demanding, laborious, and usually have a slow turnaround time to results (Ginocchio et al., 2009). On the other hand, rapid tests have limited sensitivity to detect influenza virus infection and false negative results are common, especially when disease prevalence is high (Chartrand et al., 2012).

The Alere i Influenza A&B assay is a rapid molecular diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection and differentiation of influenza A and influenza B from nasal swab and viral transport media specimens. Some benefits are that it does not require expensive thermal cyclers (which are time consuming), no sophisticated laboratories are needed, results are obtained quickly (within 15 min from specimen receipt) and high sensitivity and specificity have been reported when compared to rapid influenza diagnostic tests (RIDTs) (Hurtado et al., 2015).

The purpose of this study was to evaluate the significance of the Alere i Influenza A&B assay as a rapid test for influenza virus detection. Frozen and prospective respiratory samples

Abbreviations: CDC, Centers for Disease Control and Prevention; FDA, Food and Drug Administration; IQR, interquartile range; iNAT, isothermal nucleic acid amplification technology; NPV, negative predictive value; PPV, positive predictive value; RIDTs, rapid influenza diagnostic tests; RT-PCR, real-time reverse transcription-polymerase chain reaction; UTM, viral transport medium.
were tested using both the Alere i Influenza A&B assay and molecular techniques and the results were compared. Additionally, a certain number of samples were simultaneously tested by the use of Alere i Influenza A&B assay and immunochromatographic virus antigen detection assay (Alere BinaxNOW® Influenza A & B Card).

**METHODS**

**Clinical specimens**

A prospective/retrospective study was conducted in a tertiary care level hospital in Madrid using 119 nasopharyngeal-swab specimens. Samples were collected in 3 ml of viral transport medium (UTM) from inpatients presenting with flu-like symptoms between 31 December 2013 and 16 April 2015 at Hospital Universitario Clínico San Carlos during the influenza season.

The retrospective arm of the study was conducted on a total of 73 frozen clinical respiratory specimens collected between 31 December 2013 and 16 February 2015. These specimens were stored at −80 °C after the initial analysis. The historical results were obtained by rapid antigen testing and molecular techniques and included positive Influenza A virus specimens [14 FluA(H3N2), 13 FluA(H1N1pm09), 23 FluA non-typed], ten positive influenza B virus specimens, two positive influenza C viruses, seven specimens that were negative for influenza but positive for other respiratory viruses and four historically true negative specimens. A single Alere i Influenza A&B assay was performed within 24 h of thawing a specimen.

Forty-six respiratory nasal swab specimens that were prospectively collected from 17 February 2015 to 16 April 2015 were also included in the study. All these samples were refrigerated between 2 and 8 °C if immediate testing was not possible and processed in the routine virology laboratory within 24 h of collection. The Alere i Influenza A&B assay was performed alone or in combination with an immunochromatographic virus antigen detection assay (Alere BinaxNOW® Influenza A & B Card). Results were confirmed by one or both reference standards for laboratory confirmation of influenza virus infection: Real time RT-PCR (Roche rRT-PCR, Madrid, Spain) and the CLART® Pneumovir DNA array assay (Genomica, Coslada, Madrid, Spain).

**Detection methods**

**Reference standard methods**

**Nucleic acid extraction.** Total nucleic acids were extracted from 250 μl of clinical specimen and eluted in 25 μl elution buffer using automated EasyMAG system (bioMérieux, Marcy l’Étoile, France), according to the manufacturer’s instructions. Nucleic acid was used immediately or stored at −80 °C until used.

**Real time RT-PCR.** Real-time RT-PCR was performed using the Roche rRT-PCR according to the manufacturer’s instructions. The primer/probe sets used have been described previously (Tham et al., 2012). For amplification, 5 μl of extracted nucleic acids was added to each reaction mix (M2 and HA), thermal cycling was performed in a LightCycler 480 II instrument (Roche Diagnostics GmbH, Mannheim, Germany) using the following conditions for both PCRs: 50 °C for 8 min (reverse transcriptase step), 95 °C for 30 s, followed by 45 cycles of 95 °C for 1 s, 60 °C for 20 s, 72 °C for 1 s, cooling to 40 °C for 30 s. Results were interpreted as positive if the Ct (crossing point) value was ≤40, and as negative if no value or Ct >40.

**CLART® Pneumovir assay.** Human respiratory viruses were detected and identified using the CLART® Pneumovir assay in three steps, according to the manufacturer’s protocol (Genomica, 2015). Briefly, nucleic acids from samples were obtained with automatic extraction in an EasyMag system as described above. A specific 120–380 bp fragment of the viral genome was then amplified using RT-PCR. Five microlitres of the EasyMag elution solution was manually transferred into two amplification tubes. Following amplification, hybridization occurred in a low-density microarray containing triplicate DNA probes specific to the respiratory viruses studied.

**Rapid molecular diagnostic test**

**Alere i Influenza A&B assay.** Alere i Influenza A&B assay is the first molecular diagnostic test for the differential and qualitative detection of influenza A and influenza B virus nucleic acids that delivers actionable, lab-accurate results in less than 15 min on a user-friendly platform (ALERE Healthcare S.L.U.). The Alere i Influenza A&B assay utilizes the NEAR technology (Nicking Enzyme Amplification Reaction) which uses enzymes to drive the amplification process and works at a single constant temperature. It is comprised of a Sample Receiver, containing elution buffer, a Test Base, consisting of two sealed reaction tubes each containing a lyophilized pellet, a Transfer Cartridge for transfer of the eluted sample to the Test Base, and the Alere i Instrument. The reaction tubes in the Test Base contain the reagents required for amplification of influenza A and influenza B, respectively, as well as an internal control. The templates (similar to primers) designed to target influenza A RNA amplify a unique region of the PB2 segment while the templates designed to amplify influenza B RNA target a unique region of the PA segment. Fluorescently-labelled molecular beacons are used to specifically identify each of the amplified RNA targets. To perform the assay the Test Base was inserted into the appropriate colour-coded receptacle, followed by placing the sample receiver into the corresponding colour-coded receptacle. The sample receiver and buffer inside was heated for 3 min. Following the heating step, 200 μl of thawed specimen in UTM was directly added to the buffer in the sample receiver. Two 0.1ml aliquots of the eluate from the sample receiver were then manually transferred via the Transfer Cartridge to the Test Base to rehydrate the lyophilized NEAR InflA and InflB reaction mixes and initiate target amplification and detection. Heating, agitation and detection by fluorescence were performed automatically by the instrument. Alere i Influenza A&B assay contains an internal control that has been designed to control sample inhibition, amplification and assay reagent function (Alere-Iberia Sales Scientific Liaison, personal communication). It consists of an RNA oligonucleotide that is used as a target for amplification/detection in the Alere i Influenza A&B assay confirming proper reagent function and monitoring sample inhibition. The internal control results were automatically checked by the reader to ensure that the test result is valid. The test proceeds and results are available within 10 min.

**Immunochromatographic virus antigen detection assay**

**Alere BinaxNOW® Influenza A & B Card.** The BinaxNOW® influenza test was carried out according to the manufacturer’s instructions. Briefly, 100 μl of sample was added to the test device. Each device was read by visual inspection after 15 min of incubation at room temperature. A positive test result was indicated by a pink to purple test line and a pink to purple control line on a white background. A negative test result as indicated by a pink control line only.

**Statistical analysis**

Results obtained with the Alere i Influenza A&B assay were compared to those obtained by immunochromatographic virus antigen detection assay and molecular techniques (Real time RT-PCR/CLART® PneumoVir assay) as a reference method. The statistical analyses included all valid results obtained by the Alere i Influenza A&B assay and the comparator methods.
RESULTS

During the study period 119 nasopharyngeal specimens were tested using the Alere i Influenza A&B assay. Samples were collected from 99 adults (range 15–99 years) and 20 children (range 0–11 years) with 58 female and 61 male patients. The median patient age was 59 years (IQR: 35–77). Thirty-three patients (27.7%) consulted the emergency department, 82 (68.9%) were hospitalized and four (3.6%) were outpatients that visited a doctor’s office. Among the 82 hospitalized patients, 19 (23.8%) were in the internal medicine department, 15 (18.3%) in the nephrology department, 15 (18.3%) were admitted to the intensive care unit and 13 (15.8%) to the paediatric department. Finally, 20 patients (24.4%) were hospitalized in other medical departments (endocrinology, haematology, pulmonology, oncology, geriatric and gastroenterology).

Among the 119 enrolled specimens, 46 were processed for Real time RT-PCR, 82 for CLART® PneumoVir assay and nine samples were tested using both molecular techniques (the same results were obtained in nine samples tested simultaneously using both gold standard methods).

Considering both molecular techniques as gold standard methods for laboratory diagnosis of influenza viruses, the results obtained from both tests showed 51 positive samples for influenza A virus (13 influenza A virus H1N1-2009, 14 influenza A virus H3N2 and 24 untypeable influenza A viruses) and 15 positive samples for influenza B virus.

Among the 53 negative samples for influenza A and B viruses tested by CLART® PneumoVir, 20 were positive for one non-influenza A/B virus, three samples showed two non-influenza A/B viruses and one presented three non-influenza A/B viruses. Non-influenza A and B viruses detected by this method included: two adenoviruses, three bocaviruses, two influenza C viruses, five rhinoviruses, two metapneumoviruses type A, five metapneumoviruses type B, one parainfluenza virus type 3, one parainfluenza virus type 4, three respiratory syncytial viruses type A and four respiratory syncytial viruses type B. Finally, 29 specimens were negative for all tested respiratory viruses.

Over the course of the study, of a total of 119 enrolled specimens, the Alere i Influenza A&B assay reported 31 influenza virus A, 11 influenza virus B, one positive result for both influenza A and B viruses and 71 negative results (Table 1). Five invalid results were obtained, probably because of handling errors at the beginning of test use, of which four were positive for influenza A virus and one negative for both influenza A and B viruses but positive for influenza C virus by PCR (Real time RT-PCR and/or CLART® PneumoVir assay). All five invalid results were excluded from the statistical analysis, leaving a total of 114 valid samples. The results from all collected specimens were confirmed by Real time RT-PCR and/or CLART® PneumoVir assay as reference methods. During the study period, the Alere i Influenza A&B assay showed five discordant results which have been processed for molecular confirmation (Real time RT-PCR and/or CLART® PneumoVir assay) revealing three untypeable influenza A viruses, one influenza AH3N2 virus and one influenza B virus. We found that all five discordant results obtained by Alere i Influenza A&B assay corresponded to samples with high Ct values (Ct >25). We also found that in comparison to molecular techniques (Real time RT-PCR and/or CLART® PneumoVir assay), which is considered to be one of the reference standards for laboratory confirmation of influenza virus infection together with viral culture (CDC, 2014), the overall sensitivity of the Alere i Influenza A&B assay was 65.96% for the detection of influenza A virus and 53.33% for the detection of influenza B virus. The specificities were 98.51% and 95.96% for influenza A and B viruses respectively. The PPV of the Alere i Influenza A&B assay was 96.88% for influenza A and 66.67% for influenza B. The NPV was 80.49% for influenza A virus and 93.14% for influenza B virus.

Table 1. Performance of the Alere i Influenza A&B assay compared to reference results

<table>
<thead>
<tr>
<th>Virus</th>
<th>Genotype</th>
<th>No. detected (Arele/reference)*</th>
<th>Sensitivity (%) (95 % CI)</th>
<th>Specificity (%) (95 % CI)</th>
<th>PPV (95 % CI)</th>
<th>NPV (95 % CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+/-</td>
<td>+/−</td>
<td>−/+</td>
<td>−/−</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza A</td>
<td>Total</td>
<td>31</td>
<td>16</td>
<td>66.96 (57.26–74.66)</td>
<td>98.51 (96.28–100.73)</td>
<td>98.88 (93.68–100.07)</td>
</tr>
<tr>
<td></td>
<td>H1N1pdm09</td>
<td>8</td>
<td>4</td>
<td>78</td>
<td>76.47 (68.68–84.26)</td>
<td>25.00 (17.05–32.95)</td>
</tr>
<tr>
<td></td>
<td>H3N2</td>
<td>10</td>
<td>2</td>
<td>78</td>
<td>71.43 (63.14–79.72)</td>
<td>78.00 (70.40–85.60)</td>
</tr>
<tr>
<td></td>
<td>Untypeable</td>
<td>13</td>
<td>8</td>
<td>66</td>
<td>61.90 (51.76–72.05)</td>
<td>98.51 (95.97–101.04)</td>
</tr>
<tr>
<td>Influenza B</td>
<td>8</td>
<td>4</td>
<td>7</td>
<td>95</td>
<td>53.33 (44.18–62.49)</td>
<td>95.96 (92.35–99.57)</td>
</tr>
</tbody>
</table>

*Five invalid Alere i Influenza A&B assay results were excluded from the statistical analysis, leaving a total of 114 samples. +, positive; −, negative.
Additionally, 57 of the 119 samples were simultaneously tested with the Alere i Influenza A&B assay and immuno-chromatographic virus antigen detection assay (Alere BinaxNOW® Influenza A & B Card). The Alere i Influenza A&B assay showed 25 negative results for influenza A and B viruses, 23 positive results for influenza A virus and nine positive results for influenza B virus. Results obtained by BinaxNOW® Influenza A & B Card revealed 50 negative results for influenza A and B viruses and seven positive results for influenza A virus (Table 2).

In order to confirm the results obtained by both methods (Alere i Influenza A&B assay and Alere BinaxNOW® Influenza A & B Card) samples were processed for CLART® PneumoVir assay and/or Real time RT-PCR (Roche rRT-PCR).

The Alere i Influenza A&B assay evaluated in this study has been capable of detecting both influenza A and B viruses. Furthermore, all positive samples detected by Alere BinaxNOW® Influenza A & B Card were also positive by Alere i Influenza A&B assay. Additionally, the Alere i Influenza A&B assay detected 25 true positive samples that were missed by BinaxNOW® Influenza A & B Card. The overall sensitivity of the Alere i Influenza A&B assay and the Alere BinaxNOW® Influenza A&B Card for detection of influenza A and B virus was 66.67 % and 14.58 % respectively, while the specificity was 100 % for both techniques. For influenza A virus, the sensitivity of the Alere i Influenza A&B assay was 62.16 % and for Alere the BinaxNOW® Influenza A & B Card 18.92 % with 100 % specificity for both techniques. No influenza B virus has been detected by Alere BinaxNOW® Influenza A&B Card.

The Kappa index between the two techniques was 0.20, suggesting low agreement. Besides, a McNemar’s test was applied in this study for analysis of correlated proportions revealing significant differences between both assays (p<0.002).

Of the 57 specimens tested by Alere i Influenza A&B assay and BinaxNOW® Influenza A & B Card, 31 (54.4 %) were identified as positive by CLART® PneumoVir assay and 30 (52.6 %) were positive by Real time RT-PCR (Roche rRT-PCR). This last group of samples were further subdivided into two groups: low Ct values (Ct <25) and high Ct values (Ct ≥25). The maximum Ct values for influenza A samples that were detected by Influenza A&B assay and BinaxNOW® Influenza A & B Card were 31.7 and 27 respectively.

Results showed that the samples missed by BinaxNOW® Influenza A & B Card but detected by Alere i Influenza A&B assay had relatively higher Ct rates (Fig. 1). This indicates the Alere i Influenza A&B assay was more capable of detecting low viral loads than BinaxNOW® Influenza A & B Card. Nevertheless, the sensitivity of the Alere i Influenza A&B assay was also affected by the viral load present in each sample explaining the false negative results that can be seen in the groups of low Ct rates and high Ct rates.

Fig. 1. Percentage (%) of Influenza A positive samples by Alere i Influenza A&B assay and Alere BinaxNOW® Influenza A & B Card according to Ct values in Real time RT-PCR.

**DISCUSSION**

The Alere i Influenza A&B assay is the first molecular diagnostic test that delivers actionable, lab-accurate results in less than 15 min on a user-friendly platform (Alere i Influenza A&B Product Insert). This molecular test based on iso-thermal nucleic acid amplification technology (iNAT) which does not require lengthy and complex thermo cycling or nucleic acid purification and can therefore deliver PCR calibre results more quickly and in a broad range of settings (Bell & Selvarangan, 2014). Issues related to RIDTs include the likelihood of giving false negative or positive results. However, due to the limited sensitivities and predictive values of RIDTs, a confirmatory laboratory test must be undertaken (FDA, 2015).

In this study we also evaluated the performance of the Alere BinaxNOW® Influenza A & B Card because of its ability to detect both influenza A and B viruses and because in recent years this test has been one of the RIDTs most widely used in clinical practice. Recent studies have demonstrated similar results and conclusions, and some of these are referenced in the bibliography (Dunn et al., 2014; Hassan et al., 2014). Moreover, no false positive results have been obtained among all tested nasopharyngeal swab samples. RIDTs have differences in accuracy with different specimen collection methods and some distinguish between influenza A or B virus infection while others do not (CDC, 2014).

During the course of the study two different gold standard methods were applied in order to confirm the results obtained by the use of RIDTs (Alere i Influenza A&B assay/Alere BinaxNOW® Influenza A & B Card). When determining the influenza A virus subtype was necessary, a single CLART® PneumoVir assay was performed. This assay was also performed in order to identify co-infection with one or various viral pathogens, especially in those patients presenting poor clinical outcomes.

Several studies about this new molecular rapid test have been published since 2014 (Bell et al., 2014; Chapin & Flores-Cortez, 2015; Hazelton et al., 2015). Although larger
samples have been described in recent published articles, the present study is a retrospective/prospective analysis that includes adults and children from different medical departments. Besides, two standard reference methods were used to confirm the results obtained by Alere i Influenza A&B assay and/or BinaxNOW®Influenza A & B Card.

According to a recent report, a polymorphism within segment PA of the influenza B genome was identified in influenza B/Russia, Wisconsin and Texas lineages which could explain the lower sensitivity obtained in this study for influenza B virus. This polymorphism results in a product/template mismatch determined to be moderately destabilizing that can significantly reduce assay sensitivity (Alere i Influenza A&B Product Insert). Hopefully this aspect will be improved, according to the manufacturer (Alere-Iberia Sales Scientific Liaison, personal communication). Overall, these results indicated that the Alere i Influenza A&B assay was more sensitive than the Alere BinaxNOW® Influenza A & B Card in detection of Influenza A and B viruses in respiratory specimens with similar time consuming. Nevertheless, the Alere i Influenza A&B assay showed poorer specificity values due to samples determined positive for both influenza A and B viruses. In general, the Alere i Influenza A&B assay provided an acceptable sensitivity, although this assay did show poorer sensitivity with samples determined to have low influenza A virus titres by RT-PCR [a mean real-time PCR threshold cycle (CT) value ≥31], which included the majority of the samples called influenza A virus ‘no subtype detected’ by CLART® PneumoVir assay.

The prevalence of influenza infection during the retrospective analysis was high due to the large number of collected specimens included in this part of the study. Meanwhile, the prevalence in the prospective study was low. This occurred because the prospective study took part when the Alere i Influenza A&B assay had first been introduced at the Hospital Universitario Clínico San Carlos (February/2015), and contained a smaller number of samples. Besides, the vast majority of samples prospectively studied included influenza B virus positive specimens, which has been the most frequently isolated Influenza virus type in our environment in the past influenza season. Indeed, we believe that this retrospective/prospective study allowed simultaneous targeted analysis of both types of samples: fresh and frozen nasopharyngeal specimens.

Considering that the manufacturer recommends using fresh specimens when analyzing influenza viruses by Alere i Influenza A&B assay, one of the limitations of this study is the use of salvaged frozen nasopharyngeal swabs. Among the 51 positive specimens for influenza A virus, 50 were salvaged frozen nasopharyngeal swabs included in the retrospective part of the study which clearly contains the majority of studied specimens. Other limitations of this study include the selection of positive specimens for the majority of testing and the poorer sensitivity with samples determined to have low Influenza A virus titres by Real time RT-PCR which included the majority of the samples called ‘untypeable’ by CLART® PneumoVir. On the other hand, the overall low number of influenza B cases results in a lower sensitivity for this type of virus. Indeed, compared to recent studies, sensitivity rates of the current study are lower than those described in the literature.

Based on the results of this study, we can conclude that the Alere i Influenza A&B assay is considerably more sensitive than Alere BinaxNOW® Influenza A & B Card for detection of influenza A and B viruses, although both tests demonstrated excellent specificity for diagnosis of influenza viruses.

As many authors reported in the literature (Bell & Selvarangan, 2014; Chapin & Flores-Cortez, 2015; Hazelton et al.,

**Table 2. Overall agreement (%) of Alere i Influenza A&B assay compared to Alere BinaxNOW® Influenza A & B Card**

<table>
<thead>
<tr>
<th></th>
<th>Binax</th>
<th>Kappa</th>
<th>% Agreement</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any influenza virus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alere +</td>
<td>7</td>
<td>0.197</td>
<td>56.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza A virus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alere +</td>
<td>7</td>
<td>0.343</td>
<td>71.93</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza B virus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alere +</td>
<td>0</td>
<td>84.21</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The agreement (%) value for detection of influenza B virus is not real, this occurred principally because of data distribution during the study period (no influenza B virus has been detected by BinaxNOW® Influenza A & B Card).
2015; Hurtado et al., 2015; Nie, et al., 2014), we consider that the Alere i Influenza A&B assay has the potential to serve as an alternative to RIDTs for the diagnosis of influenza A and B viruses as a point-of-care test with significantly improved sensitivity.

ACKNOWLEDGEMENTS

The authors are very grateful to M José Solis, Emilia Vazquez and Maribel Treviño for technical assistance. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES


