Technical Brief - January 2021

BinaxNOW™ COVID-19 Ag Card
Product Insert Updates

The initial product insert (August 2020) contained interim data from the BinaxNOW™ COVID-19 Ag Card clinical trial. These interim data were provided to the FDA for Emergency Use Authorization (EUA). The clinical trial is now complete, additional data have been submitted and the product insert has been updated accordingly.

Updated product insert data represent a larger trial that assessed performance across more sites, users and patient samples, representing a more robust and representative data set for the acute setting.

<table>
<tr><th>Product Inserts</th><th>Original- August 2020</th><th>Updated- January 2021</th></tr>
<tr><td>Intended Use</td><td>Negative results from patients with symptom onset beyond seven days, should be treated as presumptive and confirmation with a molecular assay, if necessary, for patient management, may be performed.</td><td>Negative results should be treated as presumptive and confirmation with a molecular assay, if necessary, for patient management, may be performed.</td></tr>
<tr><td>Nasal Swab Sampling</td><td>• Rotate the swab 5 times or more against the nasal wall then slowly remove from the nostril. Using the same swab, repeat sample collection in the other nostril.</td><td>• Firmly sample the nasal wall by rotating the swab in a circular path against the nasal wall 5 times or more for a total of 15 seconds, then slowly remove from the nostril. Using the same swab, repeat sample collection in the other nostril.</td></tr>
<tr><td>Study Data</td><td>• 7 clinical trial sites
• Testing was conducted by 32 test operators
• 102 patient specimens</td><td>• 10 clinical trial sites
• Testing was conducted by 62 test operators
• 460 patient specimens</td></tr>
<tr><td>Performance Characteristics</td><td>
<table>
<tr><th>BinaxNOW™ COVID-19 Ag Card</th><th colspan="3">Comparator method</th></tr>
<tr><th></th><th>Positive</th><th>Negative</th><th>Total</th></tr>
<tr><td>Positive</td><td>34</td><td>1</td><td>35</td></tr>
<tr><td>Negative</td><td>1</td><td>66</td><td>67</td></tr>
<tr><td>Total</td><td>35</td><td>67</td><td>102</td></tr>
<tr><td colspan="4">Positive Agreement: 34/35 97.1% (95% CI: 85.1% - 99.9%)</td></tr>
<tr><td colspan="4">Negative Agreement: 66/67 98.5% (95% CI: 92.0% - 100%)</td></tr>
</table>
</td><td>
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<tr><th>BinaxNOW™ COVID-19 Ag Card</th><th colspan="3">Comparator method</th></tr>
<tr><th></th><th>Positive</th><th>Negative</th><th>Total</th></tr>
<tr><td>Positive</td><td>99</td><td>5</td><td>104</td></tr>
<tr><td>Negative</td><td>18*</td><td>338</td><td>356</td></tr>
<tr><td>Total</td><td>117</td><td>343</td><td>460</td></tr>
<tr><td colspan="4">Positive Agreement: 99/117 84.6% (95% CI: 76.8% - 90.6%)</td></tr>
<tr><td colspan="4">Negative Agreement: 338/343 98.5% (95% CI: 96.6% - 99.5%)</td></tr>
</table>
*14 of the discrepant samples had high Ct values (>33) when tested by the comparator method.
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<tr><td>Performance Characteristics by Ct value</td><td>
<table>
<tr><th>BinaxNOW™ COVID-19 Ag Card</th><th colspan="2">Comparator Method (POS by Ct Category)</th></tr>
<tr><th></th><th>POS (Ct < 33)</th><th>POS (Ct ≥ 33)</th></tr>
<tr><td>Positive</td><td>29</td><td>5</td></tr>
<tr><td>Negative</td><td>0</td><td>1</td></tr>
<tr><td>Total</td><td>29</td><td>6</td></tr>
<tr><td>Positive Agreement (95% CI)</td><td>100.0% (88.1, 100.0)</td><td>83.3% (35.9, 99.6)</td></tr>
</table>
</td><td>
<table>
<tr><th>BinaxNOW™ COVID-19 Ag Card</th><th colspan="2">Comparator Method (POS by Ct Category)</th></tr>
<tr><th></th><th>POS (Ct < 33)</th><th>POS (Ct ≥ 33)</th></tr>
<tr><td>Positive</td><td>116</td><td>17</td></tr>
<tr><td>Negative</td><td>12</td><td>28</td></tr>
<tr><td>Total</td><td>128</td><td>45</td></tr>
<tr><td>Positive Agreement (95% CI)</td><td>90.6 (84.2, 95.1)</td><td>37.8 (23.8, 53.5)</td></tr>
</table>
*In patients presenting within 7 days of symptom onset, BinaxNOW COVID-19 Ag Card achieved 95.6% (86/90) positive percent agreement for samples with Ct < 33
</td></tr>
</table>

The BinaxNOW™ COVID-19 Ag Card positive agreement in the entire population, as obtained by test operators with no laboratory experience, is 84.6% (95% CI: 76.8% - 90.6%). When results are stratified by the Ct count, as a surrogate for the amount of virus present in the clinical sample, the positive agreement becomes 90.6%. When the results are limited to

just those patients presenting within 7 days of symptom onset, the positive agreement reaches 95.6%.

Specificity remained unchanged at 98.5%.

Understanding Technology Differences and Cycle Threshold (Ct)

There are 2 different types of COVID-19 diagnostic tests -- molecular tests (also referred to as PCR tests) and antigen (Ag) tests. In this study, BinaxNOW COVID-19 Ag Card was compared to a molecular test. Molecular tests detect the virus that causes COVID-19 whereas, antigen tests detect specific proteins made by the virus.[1] Both antigen and molecular tests perform best when a person is tested during the time period of highest viral load.[2]

PCR amplifies viral RNA through a process involving temperature cycles. Ct counts are the number of times a PCR instrument must cycle through to amplify enough genetic material of the SARS CoV-2 virus for it to be detectable. The greater the amount of virus present (viral load), the fewer cycles required to detect the virus. A person with a higher viral load (and lower Ct count) is more likely to be infectious.

There is a growing body of scientific literature[3] and experience focused on the correlation between infectiousness, Ct counts and viral load. Specifically, scientific evidence suggests that at Ct counts in the 30s[4], the SARS-CoV-2 virus no longer replicates, meaning people are no longer infectious. Molecular tests can detect low levels of viral nucleic acid that cannot be cultured, suggesting that the presence of viral nucleic acid does not always indicate contagiousness.[2]

Summary

The value of rapid antigen testing is to quickly and easily identify individuals during the infectious phase of the virus for appropriate isolation/quarantine and to avert disease transmission.

The test performance demonstrates a high positive agreement of 95.6% with PCR in patients within 7 days of symptom onset and with high viral loads.

1. https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-frequently-asked-questions#devices
2. https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html
3. This article is a pre-print and has not been peer-reviewed. The article reports new medical research that has yet to be evaluated and so should not be used to guide medical practice.
4. La Scola B, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. Eur J Clin Microbiol Infect Dis. 2020 Jun;39(6):1059-1061.