National Laboratories Programme

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Report produced by NHS Lothian Laboratories on behalf of National Services Scotland

Extended evaluation report POCT COVID Antibody Tests

Kit name and manufacturer: Biomerica

Aim

To perform an extended evaluation of the test against the minimally acceptable clinical performance requirements described by the MHRA[1]. The scope of this evaluation extends to performance characteristics only.

The intended use of these assays is to determine if the individual being tested has been exposed to SARS-CoV-2 and has mounted an antibody response. It is envisaged that these tests could be used in patients who have not had a previous PCR test. Accordingly, the specificity requirements are stringent, since the consequence of a false positive result is incorrectly informing the person tested that they have antibodies.

Evaluation

The desired target analyte is IgG subtype antibodies to SARS-CoV-2. MHRA acceptable target criteria are as follows:

>98% clinical specificity from testing at least 200 confirmed negative cases or from testing of specimens collected at least 6 months before the known appearance of the virus (including prepandemic samples, other hCoV epitopes, respiratory viruses and bacterial pathogens)

>98% clinical sensitivity on specimens collected ≥ 20 days post symptom onset.

Evaluation panel

Clinical sensitivity:
Serum samples from hospitalised patients with a positive SARS-CoV2 PCR test and patients with a positive PCR test who did not require hospital admission. Time between symptom onset and the sample was determined from clinical notes or patient questionnaires (see Table 1).

[1] https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/target-product-profile-antibody-tests-to-help-determine-if-people-have-recent-infection-to-sars-cov-2-version-2

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Clinical specificity:
All serum samples were taken prior to December 2019, prior to the appearance of the virus in the UK and were stored following routine serology or immunology investigations and a panel of serum samples from blood donors. A panel of confounder samples was also included to look for cross reactivity. These were from patients who had received a positive PCR for respiratory pathogens including human coronaviruses (hCoV) strains. Patients with elevated Rheumatoid Factor, Cyclic Citrullinated Peptide, anti-Nuclear antigen or positive for CMV IgG, IgM or EBV IgM were also included (see Table 1).

PCR positive	n (134)
Hospitalised patients (5-38 days post symptom onset)	86
Non-hospitalised patients (35-58 days post symptom onset)	48
Uninfected controls	n (327)
Samples stored for routine immunological analyses (antenatal screening (32) and sexual health clinic (55))	87
PCR positive for human coronavirus [9-308 days post PCR] (47), Other respiratory panel PCR positives [7-77 days post PCR] (20)	67
CMV IgG, EBV IgG, EBV IgM positive (40), RF/CCP/ANA positive (33)	73
Anonymised serum samples from blood donors.	100

Table 1. Samples used in the evaluation panel.

Results

Tests were performed according to insert instructions. Results were scored as negative, positive or weak positive for IgG and IgM. The variability in signal strength between the positives could lead to issues around interpretation. Weak positives or strong positives were both scored as positive.

Batch variation in results was assessed by running 5 positive and 5 negative samples using the two kit batches. No difference was observed in the results.

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Sensitivity

Sensitivity was calculated for IgG and IgM and samples ≥ 20 days post symptom onset. Results are shown in Table 2. We note that IgG sensitivity improved when samples at least 20 days post symptom onset were analysed from 86.6% to 95.2%.

Total sensitivity (n = 108)					
IgG weak positive	11	IgM weak positive	26	Antibody positive	116
IgG strong positive	105	IgM strong positive	17		
Total sensitivity (%)	86.6		32.1		86.6
Sensitivity ≥ 20 days post symptom onset (n = 83)					
IgG weak positive	5	IgM weak positive	16	Antibody positive	79
IgG strong positive	74	IgM strong positive	10		
Total sensitivity (%)	95.2		31.3		95.2

Table 2. Sensitivity results

Specificity

Results are shown in Table 3. Overall 12 from 327 known negative samples showed antibody positivity, giving a specificity of 96.3%. 3/327 samples were positive for IgG (2 weak positives and one strong positive) giving an IgG specificity of 99.1%. These samples were all in the immune confounders category of RF, CCP or ANA antibody positive. The strong false positive was IgM positive, and was also positive in the Abbott IgG immunoassay. Importantly none of the respiratory confounding panel were IgG positive. 10/327 samples were positive for IgM – 1 was also IgG positive, and the other 9 were IgM only positive.

Specificity (n = 327)					
IgG weak positive	2	IgM weak positive	6	Antibody positive	12
IgG strong positive	1	IgM strong positive	4		
Specificity (%)	99.1		96.9		96.3

Table 3. Specificity results.

Summary

IgG specificity of 99.1% has met the MHRA specificity criteria of 98%, although the IgG sensitivity of 95.2% ≥ 20 days post symptom onset is lower than the 98% target. However, the high specificity of the kit means it warrants further investigation, including field trials.