UK NEQAS
Microbiology

SARS-CoV-2 Point of Care: UK NEQAS for Microbiology New EQA Scheme

Heather Crowton, Katie Minns, Rhiannon Weale, Sanjiv Rughooputh

UK NEQAS for Microbiology, National Infection Service, UK Health Security Agency, London

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is an RNA virus that causes respiratory illness through human-to-human transmission[1].

Rapid Point of Care (PoC) tests, such as antigen tests and molecular assays, have been commercialised to support diagnosis of SARS-CoV-2 infection; detecting antigens or nucleic acids in samples taken during active infection[2]. With varying sensitivities between brands, further testing to confirm diagnosis using polymerase chain reaction (PCR) would be considered until recently[3]. In addition, a national systematic evaluation of lateral flow device (LFD) sensitivity and specificity concluded LFD test performance varied by viral load and whether the operator of the test was laboratory-trained[4].

Due to these factors, along with the increasing use of these tests, an external quality assessment (EQA) to assess the performance of SARS-CoV-2 PoC testing completed by various organisations is required.

Objectives

- To understand participant demographic.
- To assess participant performance across the six distributions.
- To monitor the popularity and performance of various SARS-CoV-2 PoC kits/assays used.

Keywords

SARS-CoV-2, Point of Care (PoC), antigen, External Quality Assessment.

Methods

Four simulated specimens were prepared for each of the six distributions (two pilots and four live distributions) (Figure 1) and sent out to participants between February to November 2021. The content of these specimens were unknown to participants, however clinical details of each specimen were provided.

Specimen Preparation

Each positive specimen was prepared using either X-ray irradiated SARS-CoV-2 or recombinant SARS-CoV-2 nucleocapsid protein expressed in *Escherichia coli*, human epithelial (HEp-2) cells and viral transport medium. Specimens containing recombinant nucleocapsid protein were not distributed beyond the pilot schemes as this material was unsuitable for molecular testing platforms.

Each negative specimen was prepared using HEp-2 cells and viral transport medium.

Figure 1: Specimens from a SARS-CoV-2 PoC distribution.

Participant Scoring and Result Collation

Participants were given the opportunity to report results using two methods of detection and asked to submit these results within two weeks from dispatch. Participants were scored based on their ability to correctly identify SARS-CoV-2 positive/negative specimens.

Wolfson EQA Software (WES), an EQA specialist online tool, was used to record and collate results from participants.

Method performance analysis

Test kit performance was analysed by compiling data queries from WES which identified which kits provided discrepant results in each of the six distributions. All results with no method recorded were placed in the 'Unspecified' category.

Results

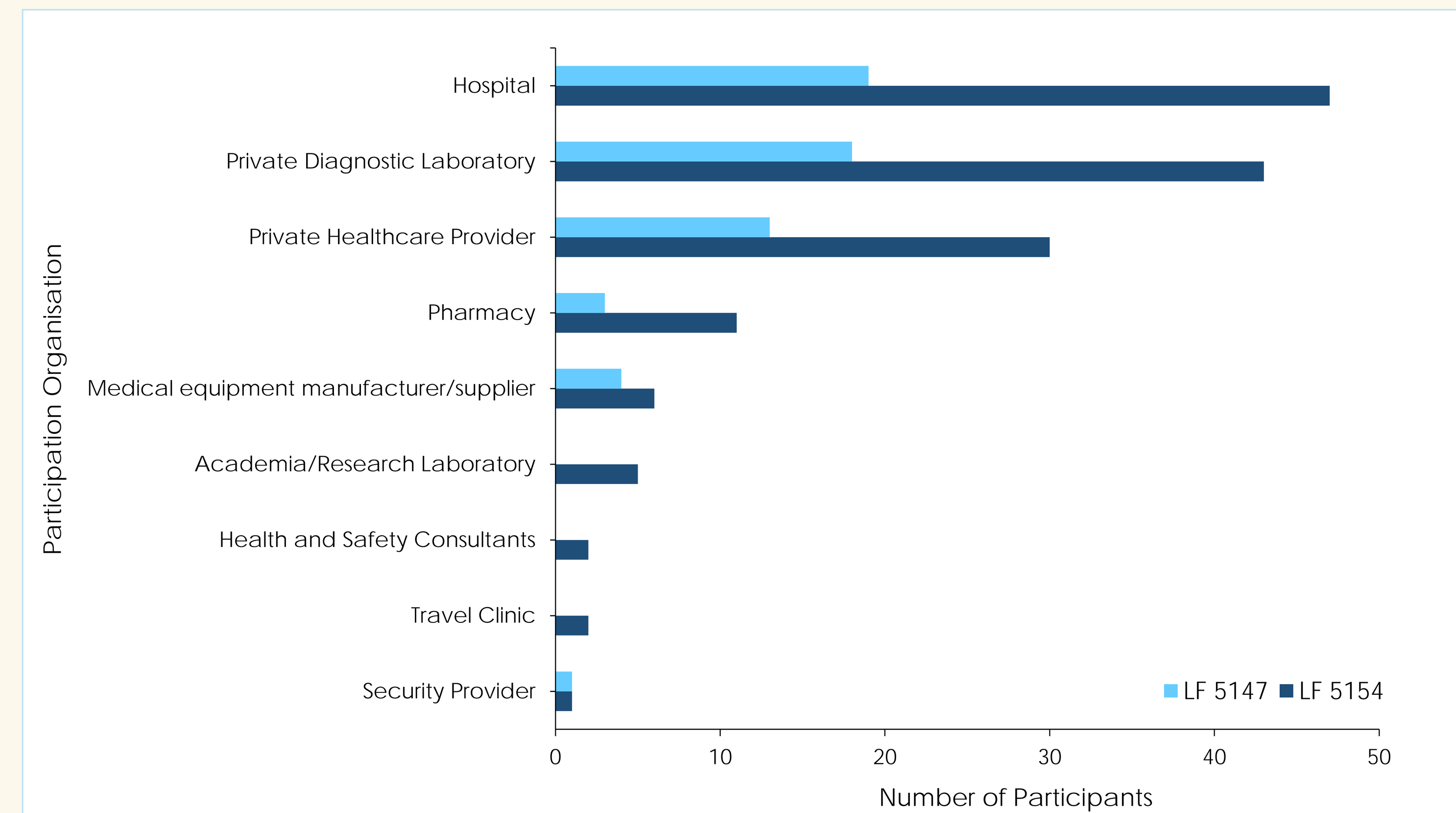

Figure 2: Type of participant organisation registered for the first live distribution (LF 5147) and the November distribution (LF 5154).

The number of participants, as well as the variety of participant organisations, registered for the SARS-CoV-2 PoC scheme have increased over the past four live distributions (Figure 2).

The majority of participants were either hospitals (LF 5147 32.8%, LF 5154 32.0%) or private diagnostic laboratories (LF 5147 31.0%, LF 5154 29.3%) in both the first and the November distribution.

Table 1: The effect of variation in positive material concentration on participant concordance.

Distribution	Specimen	Positive Material	Concentration	Participant Concordance (%)
LF 5145	6446	Recombinant SARS-CoV-2 nucleocapsid protein	12.5µg/mL	94.7
	6445		5µg/mL	94.7
	6490		5µg/mL	93.0
	6489	None	N/A	98.2
LF 5146	6541	X-ray irradiated SARS-CoV-2 (England strain)	2.0×10^5 PFU/mL	88.9
	6601		1.1×10^5 PFU/mL	88.3
	6600		5.0×10^4 PFU/mL	84.4
	6542	Recombinant SARS-CoV-2 nucleocapsid protein	5µg/mL	87.7
LF 5147	6695	X-ray irradiated SARS-CoV-2 (England strain)	3.17×10^5 genome copies/mL	95.0
	6647		2.42×10^5 genome copies/mL	96.9
	6694		2.38×10^5 genome copies/mL	95.0
	6648	None	N/A	94.0
LF 5148	6747	X-ray irradiated SARS-CoV-2 (England strain)	1.98×10^5 genome copies/mL	98.7
	6799		1.98×10^5 genome copies/mL	98.7
	6798		2.2×10^4 genome copies/mL	96.6
	6746	None	N/A	97.9
LF 5153	7077	X-ray irradiated SARS-CoV-2 (England strain)	3.3×10^4 genome copies/mL	98.4
	7076		2.2×10^4 genome copies/mL	94.4
	7078		2.2×10^4 genome copies/mL	91.3
	7079	None	N/A	96.8
LF 5154	7083	X-ray irradiated SARS-CoV-2 (Delta variant)	2.2×10^5 genome copies/mL	97.9
	7080	X-ray irradiated SARS-CoV-2 (England strain)	2.2×10^4 genome copies/mL	95.9
	7082		2.0×10^4 genome copies/mL	93.7
	7081	None	N/A	96.8

A positive correlation between viral concentration and participant concordance with the intended result was observed in the second (LF 5146), fourth (LF 5148) and sixth distribution (LF 5154) (Table 1).

Overall concordance values are lower in the distribution using a combination of positive material types.

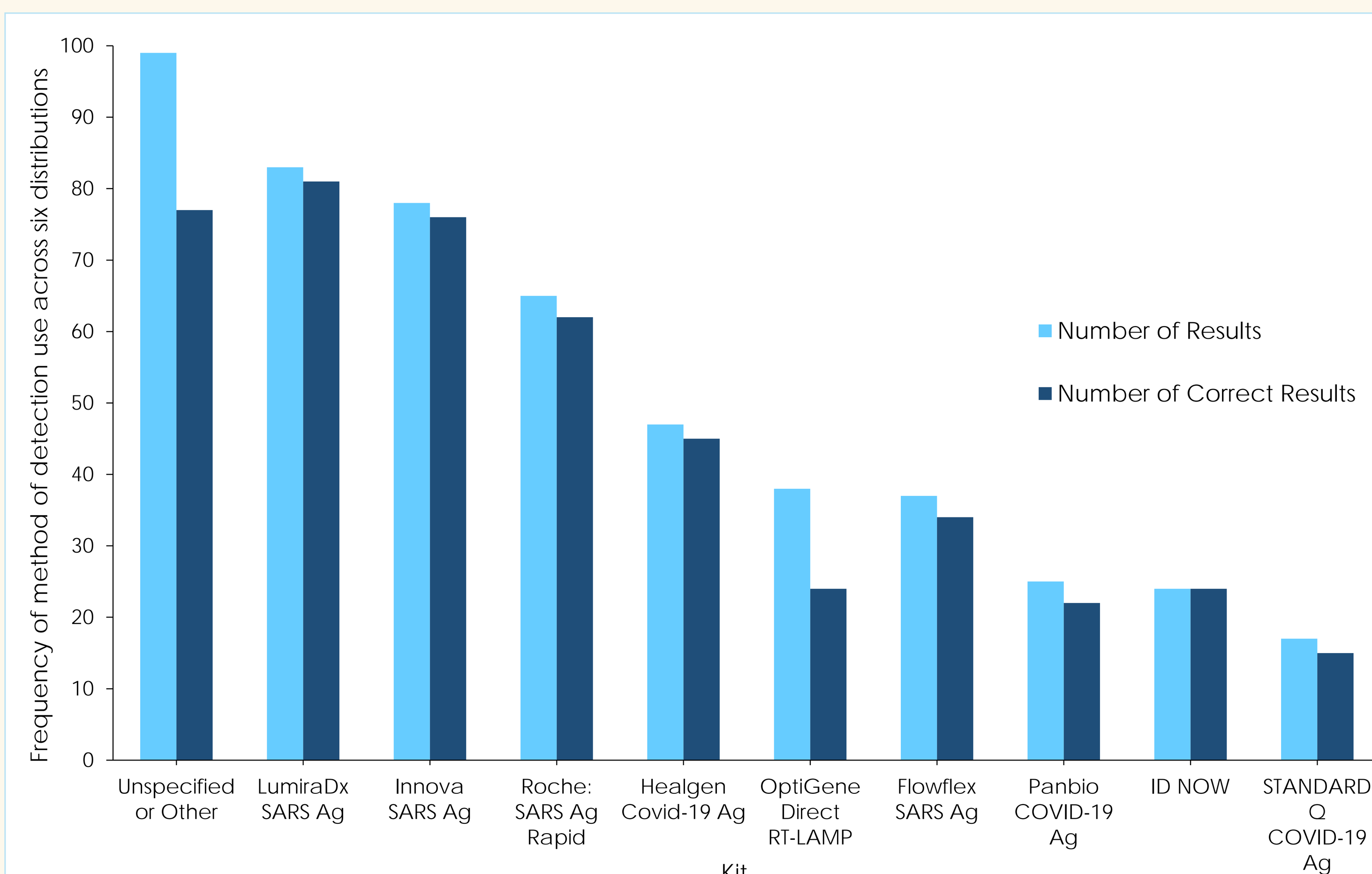

Figure 3: Most frequently used SARS-CoV-2 detection methods across the six distributions.

Over the six distributions sent out, there were 29 named brands of SARS-CoV-2 detection methods recorded, with the LumiraDx kit being the most frequently used named kit (Figure 3).

There was a lower proportion of correct results submitted by OptiGene Direct RT-LAMP kit (36.8%) users compared to other most frequently used kits.

Discussion

The introduction of the SARS-CoV-2 Point of Care scheme is critical for capturing the use of PoC tests and monitoring the correct reporting of SARS-CoV-2 infection, in turn protecting public health.

Participant organisations

Participant organisations were diverse and reflected the use of SARS-CoV-2 PoC tests in both clinical and non-clinical settings.

Increasing diversity of participant organisations highlights the expanding use-cases of these tests. This could be important when assessing participant concordance overall, as not all participants may be laboratory trained or participated in EQAs before.

Participant Concordance

Concordance values remained high in distributions that used the same positive material throughout (see Table 1). Concordance decreased when a combination of positive material had been used, reflecting the appropriateness of the material used over different testing platforms.

Results from half of the distributions are indicative of a relationship between viral concentration and participant concordance. Data from the other distributions could suggest there are reproducibility issues affecting the results submitted.

Participant methods and performance

Use of SARS-CoV-2 detection methods were varied across the six distributions and reflected the use of both rapid antigen test and molecular methods.

The high number of results reported under the 'unspecified' or 'other' category limits the ability to identify the true range of test kits used. This emphasises the breadth of SARS-CoV-2 PoC tests available, as well as the requirement for an EQA scheme to monitor the introduction of new kits and their performance.

The reduced performance from the OptiGene Direct RT-LAMP kit users may be attributable to kit sensitivity issues.

Conclusions

- Registered participants reflected the use of SARS-CoV-2 Point of Care tests in the community.
- Further testing should be conducted to determine the relationship between viral concentration and participant concordance.
- Both rapid antigen tests and molecular methods were used and overall kit performance was good.

References

1. Centers for Disease Control and Prevention. 2021. COVID-19 Overview and Infection Prevention and Control Priorities in non-U.S. Healthcare Settings [online] Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/non-us-settings/overview/index.html#background> [Accessed 13 January 2022].

2. GOV.UK. 2020. Target Product Profile: Point of Care SARS-CoV-2 Detection Tests [online] Available at: <https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/target-product-profile-point-of-care-sars-cov-2-detection-tests#target-product-profile-point-of-care-sars-cov-2-detection-tests-1> [Accessed 13 January 2022].

3. Dinnes J, Deeks JJ, Berhane S, Taylor M, Adriano A, Davenport C, Dittrich S, Emperador D, Takwoingi Y, Cunningham J, Beese S, Domen J, Dretzke J, Ferrante di Ruffano L, Harris IM, Price MJ, Taylor-Phillips S, Hooft L, Leeflang MMG, McInnes MDF, Spijker R, Van den Bruel A. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013705.

4. T. Peto et al., 2021. COVID-19: Rapid antigen detection for SARS-CoV-2 by lateral flow assay: A national systematic evaluation of sensitivity and specificity for mass-testing. EClinicalMedicine. Volume 36, pp1-7.

Acknowledgements

Thank you to the UK NEQAS for Microbiology team for their hard work on the implementation of the scheme, and the Sayers' laboratory at the University of Sheffield Institute for Nucleic Acids, National Institute for Biological Standards and Control (NIBSC), UKHSA Porton and High Containment Microbiology for the provision of isolates.

Thank you to the WES team for their exceptional work in the development of the EQA software for the delivery of this EQA.