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Development of an External Quality Assessment (EQA) Programme for Point of Care (POCT) Respiratory Viruses

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Introduction

A number of POCT devices used for rapid screening of respiratory viruses and seasonal influenza are now widely available in the UK. The viral testing targets in POCT platforms can be single, dual or multiplex, the commonest being SARS-CoV-2 alone, with Influenza A and B (and/or subtypes) or with respiratory syncytial virus (RSV). Platforms tend to be based on nucleic acid amplification technologies (NAAT), which generally have improved sensitivity compared to first generation Antigen based lateral flow devices. Studies have shown that their use in well designed and defined settings with appropriate governance arrangements can lead to improved patient triage, better use of isolation rooms during periods of winter pressure, more targeted use of antivirals, reduction in unnecessary antibiotic use and a reduced length of hospital stay.

With the increased utilisation of these platforms, in January 2021, Weqas developed an EQA programme to assess and monitor the performance of these tests.

Method

Ten hospital organisations in the UK were recruited to take part in the initial study representing 28 different POCT sites. Two to three samples were sent monthly with each site receiving 30 samples over the 18 month period. The platforms enrolled in the programme included; Roche Cobas Liat (n=18), Abbott ID NOW (n=9) and Cepheid GeneXpert Xpress (n=1). The pilot was run from January 2021 to July 2022. The initial pilot focused on Flu and RSV with the addition of SARS-CoV-2 Ag in 2022 bringing an additional number of sites undertaking this test to 52, with 12 sites using the Cobas Liat and 40 sites using the Abbott ID NOW.

The material was prepared by the addition of inactivated viruses; Influenza A/B, RSV and SARS-CoV-2 into a solution of phosphate buffer, dispensed into 1mL aliquots and stored at -20°C until dispatch.

A range of samples were prepared, both as single and as mixed viruses; single virus samples included 10 positive samples containing Flu A, 4 with Flu B, 5 with RSV, 4 with SARS-CoV-2 and 2 samples contained a mix of Flu A/B and Flu A/RSV. Both H1N1 and H3N2 were used for Influenza A. The samples were prepared at a range of viral loads.

Stability

The material was found to be stable for 3 and 2 weeks at room temperature for Flu A and B respectively. Long term storage at -20°C was found to be 3.5 months.

Results

The results received for all participants for all the samples distributed, with a breakdown of the methods used, are shown in Table 1 for Influenza A/B and RSV, and Table 2 for SARS-CoV-2 Ag respectively.

98% (200/204) of participants correctly identified the positive samples for Influenza A, 84.7% (72/85) for Influenza B and 90% (117/130) for RSV respectively. For RSV, 95% sensitivity was observed at high and 'normal' viral loads with decreased sensitivity of 36% for one sample (IF0421 S2) at a low viral load. 85% (125/147) of participants correctly identified the positive samples for SARS-CoV-2.

99% (151/153) of participants correctly identified the Negative samples for Influenza A, 99% (282/285) for Flu B, 99% (272/274) for RSV, and 99% for SARS CoV-2 Ag respectively. All users correctly identified the 1 sample with no virus present (all other samples had at least 1 virus present). The specificity and sensitivities of the individual methods are detailed in Table 3.

Table 1 Reported results for Influenza A/B & RSV for each sample distributed in the study

		Correct Results					Correct Results					Correct Results			
Sample Code	Flu A	All results	ID NOW	Cobas Liat	GeneXpert Xpress	Flu B	All results	ID NOW	Cobas Liat	GeneXpert Xpress	RSV	All results	ID NOW	Cobas Liat	GeneXpert Xpress
IF0522 S1	Positive	17/17	-	16/16	1/1	Negative	17/17	-	16/16	1/1	Positive	12/13	3/4	8/8	1/1
IF0522 S2	Positive	17/17	-	16/16	1/1	Negative	17/17	-	16/16	1/1	Negative	13/13	4/4	8/8	1/1
IF0422 S1	Positive	12/13	-	11/12	1/1	Negative	12/13	-	11/12	1/1	Negative	17/17	7/7	9/9	1/1
IF0422 S2	Positive	13/13	-	12/12	1/1	Negative	13/13	-	12/12	1/1	Positive	17/17	7/7	9/9	1/1
IF0322 S1	Positive	17/17	-	17/17	-	Positive	12/17	-	12/17	-	Negative	22/22	6/6	16/16	-
IF0322 S2	Negative	17/17	-	17/17	-	Positive	15/17	-	15/17	-	Negative	22/22	6/6	16/16	-
IF0222 S1	Negative	18/18	1/1	16/16	1/1	Negative	18/18	1/1	16/16	1/1	Positive	18/19	4/5	13/13	1/1
IF0222 S2	Positive	18/18	1/1	16/16	1/1	Negative	18/18	1/1	16/16	1/1	Negative	19/19	5/5	13/13	1/1
IF0122 S1	Positive	15/16	1/1	14/14	0/1	Negative	16/16	1/1	14/14	1/1	Negative	19/20	6/6	13/13	0/1
IF0122 S2	Negative	15/16	1/1	14/14	0/1	Negative	16/16	1/1	14/14	1/1	Positive	16/20	6/6	13/13	1/1
IF1221 S1	Negative	15/15	1/1	13/13	1/1	Negative	15/15	1/1	13/13	1/1	Positive	15/18	1/4	13/13	0/1
IF1221 S2	Positive	15/15	1/1	13/13	1/1	Negative	15/15	1/1	13/13	1/1	Negative	18/18	4/4	13/13	1/1
IF1121 S1	Positive	14/15	1/1	13/13	0/1	Negative	14/15	1/1	13/13	0/1	Negative	14/14	1/1	12/12	1/1
IF1121 S2	Positive	14/15	1/1	13/13	0/1	Negative	14/15	1/1	13/13	0/1	Negative	14/14	1/1	12/12	1/1
IF1021 S1	Negative	14/14	1/1	13/13	-	Positive	13/14	0/1	13/13	-	Negative	16/16	3/3	13/13	-
IF1021 S2	Negative	14/14	1/1	13/13	-	Negative	14/14	1/1	13/13	-	Positive	16/16	3/3	13/13	-
IF0921 S2	Negative	15/15	1/1	13/13	1/1	Positive	12/15	0/1	12/13	0/1	Negative	15/15	1/1	13/13	1/1
IF0421 S1	Positive	11/11	1/1	9/9	1/1	Negative	11/11	1/1	9/9	1/1	Negative	11/11	1/1	9/9	1/1
IF0421 S2	Negative	11/11	1/1	9/9	1/1	Negative	11/11	1/1	9/9	1/1	Positive	4/11	0/1	4/9	0/1
IF0421 S3	Negative	10/11	1/1	8/9	1/1	Positive	10/11	0/1	9/9	1/1	Negative	10/11	1/1	8/9	1/1
FL3 S1	Negative	12/12	1/1	10/10	1/1	Negative	12/12	1/1	10/10	1/1	Positive	12/12	1/1	10/10	1/1
FL3 S2	Negative	12/12	1/1	10/10	1/1	Negative	12/12	1/1	10/10	1/1	Negative	12/12	1/1	10/10	1/1
FL3 S3	Positive	12/12	1/1	10/10	1/1	Negative	12/12	1/1	10/10	1/1	Negative	12/12	1/1	10/10	1/1
FL2 S1	Negative	11/11	1/1	9/9	1/1	Positive	10/11	0/1	9/9	1/1	Negative	11/11	1/1	9/9	1/1
FL2 S2	Positive	11/11	1/1	9/9	1/1	Negative	11/11	1/1	9/9	1/1	Negative	11/11	1/1	9/9	1/1
FL1 S1	Positive	7/7	1/1	6/6	-	Negative	7/7	1/1	6/6	-	Negative	7/7	1/1	6/6	1/1
FL1 S2	Positive	7/7	1/1	6/6	-	Negative	7/7	1/1	6/6	-	Negative	7/7	1/1	6/6	1/1

Table 2 Reported results for SARS-CoV 2 Ag for each sample distributed in the study

		Correct Results			
Sample Code	SARS CoV-2 Ag	All results	ID NOW	Cobas Liat	CT
RV0622 S1	Negative	26/26	16/16	10/10	n/a
RV0622 S2	Positive	24/25	14/15	10/10	n/a
RV0722 S1	Positive	28/34	21/27	7/7	28.9
RV0722 S2	Positive	20/34	14/27	7/7	30.1
RV0822 S1	Positive	53/54	39/40	14/14	28.2
RV0822 S2	Negative	53/54	40/40	13/14	n/a

Table 3 Sensitivity and Specificity by method (% true positive and negative samples correctly identified)

Flu A	All results	ID NOW	Cobas Liat	GeneXpert Xpress	Flu B	All results	ID NOW	Cobas Liat	GeneXpert Xpress
Pos/ Tru Pos	200/204	10/10	181/182	9/12	Pos/ Tru Pos	72/85	0/4	70/78	2/3
Sensitivity (%)	98.04	100	99.45	75	Sensitivity (%)	84.71	0	89.74	75
Neg/Tru Neg	151/153	11/11	132/133	8/9	Neg/Tru Neg	282/285	17/17	249/250	16/18
Specificity (%)	98.69	100	99.25	88.9	Specificity (%)	98.89	100	99.60	88.9

RSV	All results	ID NOW	Cobas Liat	GeneXpert Xpress	SARS CoV-2 Ag	All results	ID NOW	Cobas Liat
Pos/ Tru Pos	117/130	29/35	83/88	5/7	Pos/ Tru Pos	125/147	87/109	38/38
Sensitivity (%)	90.00	82.86	94.3	71.43	Sensitivity (%)	85.03	79.8	100
Neg/Tru Neg	272/274	52/52	205/206	15/16	Neg/Tru Neg	79/80	56/56	23/24
Specificity (%)	99.27	100	99.5	93.75	Specificity (%)	98.75	100	95.83

Discussion and Conclusions

The number of participants for Flu A/B and RSV varied throughout the year with the majority of participants providing a service for autumn and winter only. For this reason no samples were distributed over the summer. The Cobas Liat was the predominant analyser used for POCT Flu and RSV, with only 1 participant using the Abbott ID NOW and Gene Xpert Xpress for Flu A and B. The method data for these 2 analytes should therefore not be relied upon as it represents only one laboratory. However, the Abbott ID NOW was used by the majority for SARS CoV-2 Ag. Consistent performance was observed for participants using the Cobas Liat for all 3 viruses. Lower sensitivities were observed for the Abbott ID NOW compared with the Cobas Liat at low viral loads (High Ct values). Additional studies are ongoing to determine cross reactivity including the effects of positive SARS-CoV-2 virus on the performance of the other respiratory viruses.

References

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