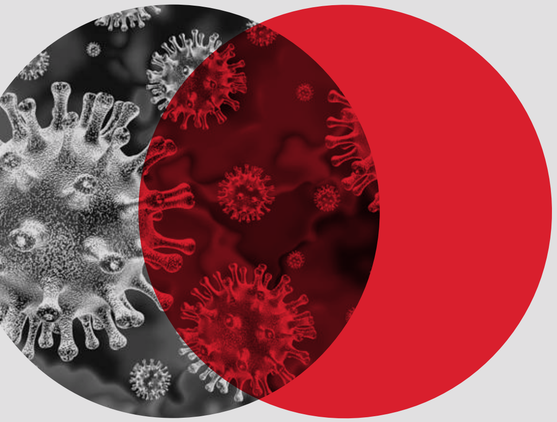
External Quality Assurance Program for Coronavirus SARS CoV-2 Antibodies – the first 12 months

Elizabeth Marland, Louise Wienholt and Peter Graham



Introduction

As Anti-SARS-CoV-2 serological assays became available to the market in 2020, the RCPAQAP developed an EQA program for interlaboratory comparison of SARS-CoV-2 antibody testing. Given the rapid deployment of new assays in 2020, we reviewed the initial submissions from 2020 compared to 2021 as a possible indicator of market trends and performance.

Method

We compared the % consensus for each measurand, the number of participants and the available assays in 2020 compared to 2021. The initial EQA program was introduced in August 2020 comprising two surveys distributed to a total of 73 Australian and international laboratories for SARS-CoV-2 antibody testing (IgA, IgG, IgM, total antibody and Point of Care IgG and IgM). In 2021, four surveys have been distributed to 110 Australian and international laboratories.

For the Serology program, qualitative targets are based on ≥ 80% of participants returning the same qualitative value (provided there are 6 or more results). Participants who return the expected value are assessed as "Concordant". Participants in the minority group are assessed as inconsistent from the consensus and their results are listed as "Discordant". When < 6 laboratories agree, the uncertainty of the results increases so no assessment is made and all results are reported as "Not Assessed".

Results

% Consensus

Laboratories use a mixture of commercial and in-house assays for testing. Comparison of data from 2020 and 2021, shows that there has been a high concordance in reporting SARS-CoV-2 IgG, Total Antibody and Point of Care IgG results. Discrepant reporting was seen for SARS-CoV-2 IgA and IgM antibodies, and Point of Care IgM.

The measurands with the highest number of participant result submissions in Survey 3 2021 are IgG (n=73), Total Antibody (n=43) and IgM (n=34).

Table 1. Consensus achieved and number of participants per measurand for SARS-CoV-2 2020 Survey samples

2020	Sample 01			Sample 02			Sample 03			Sample 04		
SARS-CoV-2 Measurand	Result	Consensus %	N	Result	Consensus %	N	Result	Consensus %	N	Result	Consensus %	N
IgG	Neg	97.7	43	Pos	100	43	Pos	95.7	47	Neg	87	46
IgM	Neg	100	17	Pos	70.6	17	Neg	47.1	17	Neg	100	17
IgA	Neg	100	7	Pos	85.7	7	Pos	60	5	Neg	60	5
Total Antibody	Neg	100	17	Pos	100	17	Pos	100	20	Neg	100	20
Point of Care IgG	Neg	100	5	Pos	100	5	Pos	90	10	Neg	100	10
Point of Care IgM	Neg	100	5	Pos	80	5	Pos	60	10	Neg	100	10

Table 2. Consensus achieved and number of participants per measurand for SARS-CoV-2 2021 Survey samples

2021	Sample 01			Sample 02			Sample 03			Sample 04			Sample 05			Sample 06		
SARS-CoV-2 Measurand	Result	Consensus %	N	Result	Consensus %	N	Result	Consensus %	N	Result	Consensus %	N	Result	Consensus %	N	Result	Consensus %	N
IgG	Pos	95	60	Neg	96.6	59	Neg	98.5	68	Pos	97.1	70	Neg	100	71	Pos	68.5	73
IgM	Pos	70	30	Neg	93.3	30	Neg	97	33	Pos	66.7	33	Neg	100	34	Neg	85.3	34
IgA	Pos	60	5	Neg	80	5	Neg	75	4	Pos	100	4	Neg	100	4	Neg	100	4
Total Antibody	Pos	100	36	Neg	100	35	Neg	97.6	42	Pos	97.6	42	Neg	100	42	Pos	83.7	43
Point of Care IgG	Pos	92.3	13	Neg	91.7	12	Neg	100	11	Pos	100	12	Neg	100	12	Pos	58.3	12
Point of Care IgM	Pos	78.6	14	Neg	100	13	Neg	100	12	Pos	58.3	12	Neg	100	13	Neg	76.9	13

*Green = ≥ 80% consensus achieved

Note: Where <80% was achieved, the result refers to the qualitative results reported by the majority of laboratories but the result is not assessed for EQA.

Number of participants

There has been an increase in the number of participants for the Coronavirus SARS-CoV-2 program since 2020 except for the IgA measurand. IgA had it's highest number of participants in Survey 1 of 2020 compared to Survey 3 in 2021 (n= 7 vs n=4). All other measurands have an average of 53.2%.

Table 3. Participant % changes between 2020 and 2021

	No. of Reagents	
SARS-CoV-2 Measurand	2020	2021
IgG	15	17
IgM	11	13
IgA	3	3
Total Antibody	6	9
Point of Care IgG	5	7
Point of Care IgM	5	8

Available Assays

The number of available methods used by participants for the listed measurands has increased between 2020 and 2021, except for IgA. However some assays that were used in 2020 are no longer used in 2021.

Table 4. Number of reagents in use by participants in 2020 and 2021

% comparisons			
2020	2021 1st survey	2021 3rd survey	2020 vs 2021
9%	22%	18%	36%
0%	43%	12%	50%
-40%	0%	-25%	-75%
15%	44%	16%	60%
50%	23%	-8%	58%
50%	29%	-8%	62%

Discussion

We have seen very good concordance in our program and expect this to continue in the future. As the world begins to ease lockdown restrictions and increase vaccinations, we expect that samples sourced from vaccinated persons will become the easiest to source and that naive sample sources will become harder to find. As vaccination rates increase, this may lead to problems sourcing samples who have been naturally infected with a history of a PCR positive result. However new mutations of Covid-19 may occur and complicate the availability of some sample antibody types.

Following welcome customer feedback and consultation with our Advisory Committee, we recognised that there are many issues to be considered when interpreting Anti-SARS-CoV-2 serology results. These issues include:

- age and sex of patient
- previous underlying comorbidities
- is the patient immunosuppressed
- have they been previously vaccinated and if so
- which vaccine brand
- how many doses
- country where they were vaccinated
- date of last vaccination
- if previously infected with Covid-19 and if so
- date of PCR positive result
- severity of disease (asymptomatic/symptomatic)
- previous Covid Serology results and dates
- other relevant information.

From this information, we can endeavour to distinguish which assays may be expected to detect antibodies depending on the antigen targets used.

Conclusion

Overall, the surveys in both 2020 and 2021 were performed well, especially for the reporting of SARS-CoV-2 IgG, Total Antibody and POC IgG. The data shows that SARS-CoV-2 Total Antibody testing is the most reliable in comparison to other measurands. In both 2020 and 2021, 80% concordance was not achieved in some surveys for SARS-CoV-2 IgM and/or SARS-CoV-2 IgA and POC IgM testing. The variation in the reporting of IgM and IgA results appears to be related to assay sensitivity and/or specificity.

The data also shows that the number of participants per survey has increased and that the number of methods has steadily increased. We expect both to continue to increase in 2022.

Data comparison as part of EQA helps provide valuable information regarding assay reliability and can help identify poorly performing test kits. The RCPAQAP Coronavirus SARS-CoV-2 antibodies program offers quality assurance that can be an effective tool for verifying the accuracy of testing procedures, reporting and interpretation of results. This program can assist laboratories in evaluating new assays by method comparison using characterised samples and as an educational tool for patient reporting.

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1300 78 29 20 | serology@rcpaqap.com.au
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