Proficiency Testing and SARS-CoV-2

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1 Introduction

Diagnostic testing for the SARS-CoV-2 virus, the etiologic agent of the COVID-19 pandemic, evolved rapidly. Tests were developed in response to the World Health Organization (WHO) declaration of a public health emergency of international concern on January 30, 2020. Development and implementation of scalable diagnostic tools was needed globally and led to a vast array of options for laboratory and non-laboratory (point of care) testing.

Proficiency testing, often referred to as external quality assessment (EQA) provides laboratories with a tool to monitor and improve the quality of their analytical measurements. As the COVID-19 pandemic spread and the development of numerous types of diagnostic testing methods increased, a need for proficiency testing samples arose. LGC and the American Proficiency Institute (API) partnered together to develop proficiency testing for the detection of SARS-CoV-2 by PCR testing. These schemes were launched in May of 2020 to assure the quality and overall participant performance for detection of the virus. As testing evolved, additional proficiency schemes were developed for serological and antigenic testing platform to ensure accuracy.

Data from the proficiency testing samples and available testing systems were closely monitored. A review of participant laboratory data shows sample adaptation and testing trends as the pandemic reached across the globe.

A review of the following information will be presented:

SARS-CoV-2 - Diagnostic Testing
- Types of tests available
- Role of SARS-CoV-2 testing
- Variant monitoring
- Impact of SARS-2 CoV-2 mutations on diagnostic assays

PT for SARS-CoV-2 Testing
- Primary aim
- Sample development timeline

PT Participation Review
- Laboratory enrolment changes
- Global coverage

2 SARS-CoV-2 – Diagnostic Testing

There are three main types of diagnostic tests used for SARS-CoV-2 testing.

MOLECULAR
RT PCR and other Nucleic Acid Amplification methods to detect current infection. High specificity and sensitivity.

ANTIGEN
Solid phase EIA and other immunoassay methods to detect current infection. High specificity, lower sensitivity than NAAT testing.

ANTIBODY
EIA, ELISA, bead-based antibody detection for late current or past infection. Variable sensitivity and specificity.

Role of SARS-CoV-2 Testing

- Diagnosis of Infection
  - Treatment and medical management
  - Isolation precautions
- Epidemiology
  - Case discovery and contact tracing
  - Control transmission rate
- Surveillance
  - Resource distribution
  - Evaluate effectiveness of current policies

SARS-CoV-2 - Variants

- SARS-CoV-2 mutations created distinct variants of the virus, adding complexity to surveillance of the virus during the pandemic.
- Variants were monitored and classified using criteria including transmissibility, severity of symptoms, and available treatment options.
- The classification system was developed by the SARS-CoV-2 Interagency Group (SIG). More information can be found on the CDC COVID-19 website.

Variant of Interest (VOI)	• Specific genetic markers that are predicted to affect transmission, diagnostics, therapeutics, or immune escape. • Evidence that it is the cause of an increased proportion of cases or unique outbreak clusters. • Limited prevalence or expansion in the US or in other countries.
Variant of Concern (VOC)	• Evidence of impact on diagnostics, treatments, or vaccines. • Evidence of increased transmissibility. • Evidence of increased disease severity.
Variant of High Consequence (VOHC)	• Demonstrated failure of diagnostic test targets • Possible reduction in vaccine effectiveness, a disproportionately high number of infections in vaccinated persons, or very low vaccine-induced protection against severe disease • Significantly reduced susceptibility to multiple (EUA) or approved therapeutics • More severe clinical disease and increased hospitalizations
Variants Being Monitored (VBM)	• May include variants previously designated as a (VOI) or (VOC) that are no longer detected or are circulating at very low levels. • May include variants designated by other organizational committees that have substitutions of concern but that have not been deemed a public health threat within the United States at this time.

SARS-CoV-2 Variants – Impact on Testing Assays

- The omicron variant, B.1.1.529 and its subvariants have significantly more mutations than previous SARS-CoV-2 variants, most notably in its S gene.
- Testing systems must be evaluated to determine performance for viral mutations. Various testing systems that were developed did not incorporate enough portions of the virus's genome resulting in false negative results. As a result, a policy was put into place requiring test developers to evaluate the impact of viral mutations on test performance.
- Information regarding viral mutation and the impact on COVID-19 testing assays is available on the U.S. Food and Drug administration website at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-evaluating-impact-viral-mutations-covid-19-tests-revised

3 PT for SARS-CoV-2 Testing

Primary Aim: External Quality Assurance (EQA)
In response to the EQA needs for various testing systems during the pandemic, samples were developed and continuously refined as the virus variants evolved and testing systems changed.

PT Sample Development Timeline

May 2020 – SARS-CoV-2 Liquid (molecular)
Original samples contained genomic RNA sequences, ORF1a, part of RdRp, E gene, N gene, and S gene.
- Modified to contain whole genome (minus replicative sequences) with the ability to specify variant and viral load.

July 2020 – SARS-CoV-2 Serology
API and LGC collaborated with LGC Clinical Diagnostics (SeraCare) to provide non-infectious plasma-based samples derived from patients recovered from COVID-19.
- Collaborated with the European Organization for External Quality Assurance Providers (EQALM) in Laboratory medicine in 2022 for serology schemes.

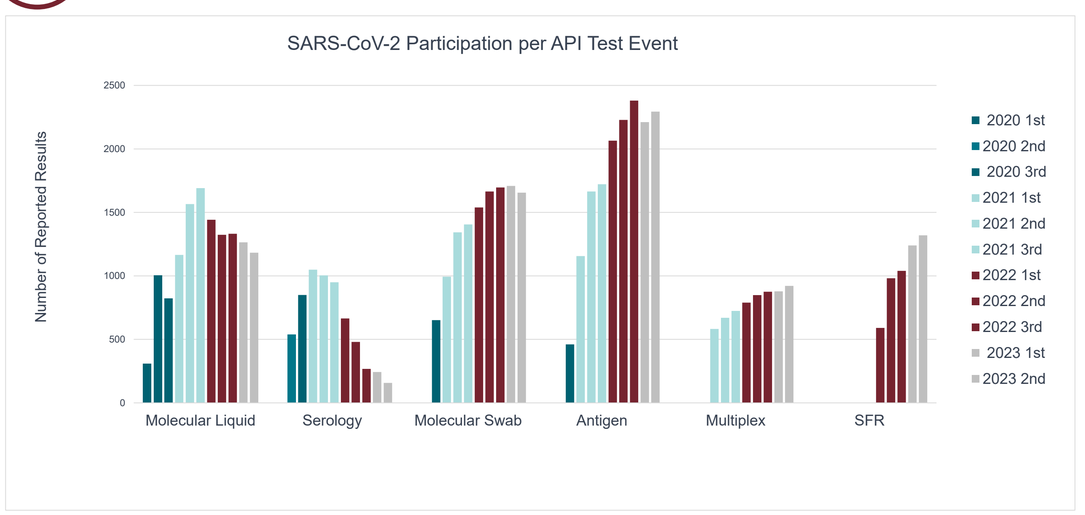
October 2020 – SARS-CoV-2 SWAB (molecular)
Created specifically for commercial assays requiring testing directly from a swab. Contained inactivated whole genome cDNA of SARS-CoV-2, human fibroblast cells, and viral nucleic acid.
- Variants of concern added as the virus mutated

October 2020 – SARS-CoV-2 Antigen
Antigen testing became prevalent testing method for a screening test. Sample developed and has continuously improved to ensure variants of concern were included.

February 2021 – Respiratory Multiplex Panel
Various multiplex testing systems began adding SARS-CoV-2 capability to their panels. In response, SARS-CoV-2 target added to API's Respiratory Multiplex Panel samples.

May 2022 – SFR 4 plex Panel
New Respiratory screening panel testing platforms required introduction of a compatible sample that contained targets for SARS-CoV2, Influenza A & B, and RSV.

4 PT Participation Review

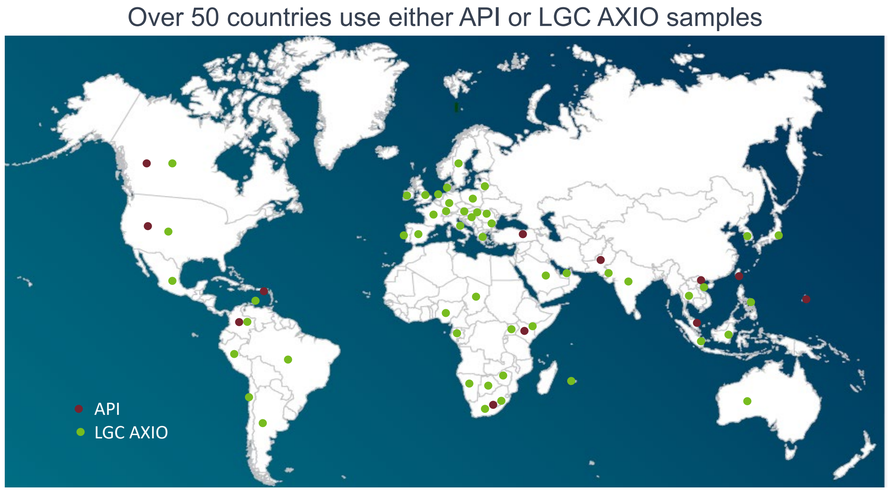


RAPID EVOLUTION OF EQA SAMPLES - As the SARS-CoV-2 virus mutated, samples were and continue to be refined, including relevant variants to ensure testing platforms can detect concerning strains.

TESTING SYSTEMS - Since the introduction of the programs, there has been changes in the growth based on the type of testing available.

- The liquid molecular program has begun to decline largely due to a handful of kit manufacturers only offering 4 plex testing (not stand alone) which has caused laboratories to shift to using the 4plex SFR samples.
- Serology testing peaked in early 2021 and has been steadily declining.
- Antigen testing displays the steepest growth.
- Testing systems for "seasonal respiratory" viruses – Influenza A&B and Respiratory Syncytial Virus began implementing SARS-CoV-2 as a target, thus the introduction of the 4plex SFR sample in 2022.

Over 50 countries use either API or LGC AXIO samples



5 References

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