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 across the U.S. 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 SARS-CoV-2. As variant schemes were developed for serological and antigen 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.

## 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.

## 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 past current or past infection. Variable sensitivity and specificity.

## 3 PT for SARS-CoV-2 Testing

### PT Sample Development Timeline

- **May 2020 – SARS-CoV-2 Liquid (molecular)**
- **June 2020 – SARS-CoV-2 Antigen**
- **July 2020 – SARS-CoV-2 Rapid (molecular)**
- **October 2020 – SARS-CoV-2 Antigen**
- **February 2021 – Respiratory Multiplex Panel**
- **May 2022 – SFR 4plex Panel**

### PT Participation Review

- **SARS-CoV-2 – Diagnostic Testing**

#### Role of SARS-CoV-2 Testing

- Diagnosis of Infection
- Treatment and medical management
- Isolation precautions
- Epidemiology
- Case discovery and contact tracing
- Control transmission rate

### 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 U.S. or in other countries.

### Variant of Concern (VOC)

- Evidence of impact on diagnostic, treatments, or vaccines.
- Evidence of increased transmissibility.
- Evidence of increased disease severity.

### Variant of High Consequence (VHC)

- Demonstrates 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 submissions of concern but that have not been deemed a public health threat within the United States at this time.

## 4 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 variants.

**TESTING SYSTEMS**

- The liquid molecular program has begun to decline largely due to a handful of kit manufacturers only offering 4plex 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.

## 5 References
