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CASE STUDY

BEST IN CLASS PERFORMANCE FOR

EUROFINS COVID-19 TESTING SOLUTIONS

Method Validation of Surrogate Virus Neutralizing Antibody Test Kit and RT-PCR Lab Developed Test (LDT)

Client:

Large Pharmaceutical company

Therapeutic Area:

COVID-19 Vaccine Development

Study Phase:

Phase 3, High Patient Volume

Services:

- Method Transfer
- Method Validation
- Sample Analysis

PROJECT AT A GLANCE

Early in the global pandemic, Eurofins BioPharma Services was at the forefront of addressing an unmet need for a Client conducting a Phase 3 clinical trial for COVID-19 Vaccine Development. One of the requirements was the need for reliable RT-PCR Testing to detect the SARS-CoV-2 virus in a clinical trial setting. In addition, Client expressed their need to monitor the SARS-CoV-2 Neutralizing Antibody status of clinical trial patients.

Prior to March 2020, there did not exist any commercial SARS-CoV-2 testing kit globally. As a world leader in laboratory science, Eurofins deployed their scientific expertise to develop analytical solutions meeting their Client needs with best in class performance, whilst reducing cost and timelines.

Eurofins BioPharma Services, Laboratory Testing has been the partner of choice for the world's most innovative Biopharmaceutical companies to advance timely vaccines and therapeutics to patients in need. As the Go-To Global Laboratory CRO, we work diligently with our Clients to get vaccines and therapeutics to market, in the best and safest way possible.

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#1 Performance in RT-PCR Testing

SITUATION

Prior to March 2020, there did not exist any commercial COVID-19 testing kit globally. During the early months of the Coronavirus Disease 2019 (COVID-19) pandemic, clinical specimens were not readily available to developers of In Vitro Diagnostic [IVD] tests to detect SARS-CoV-2 virus. Therefore, the FDA authorized IVDs based on available data from contrived samples generated from a range of SARS-CoV-2 material sources (for example, gene specific RNA, synthetic RNA, or whole genome viral RNA) for analytical and clinical performance evaluation. Also, FDA has been granting Emergency Use Authorizations (EUA) to laboratory organizations that developed COVID-19 RT-PCR assays (Laboratory Developed Tests or LDT) in house.

CHALLENGES

With limited availability of commercial, high performance SARS-CoV-2 RT-PCR testing kits resulting in false negatives and -positives, the Client wanted to mitigate risks in their high patient volume Phase 3 clinical trial.

SOLUTIONS

Eurofins was granted an Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA) for its Clinical Diagnostics' molecular laboratory-developed test (LDT) on April 8, 2020. Whilst offering the SARS-CoV-2 RT-PCR test in clinical diagnostics laboratories throughout the world, in order to extend its use to support clinical trials for COVID-19 vaccine and therapeutics development, Eurofins BioPharma Services, Laboratory Testing performed method transfer and validation for use in clinical trials, and received a bridging EUA, using the same LDT methodology.

While validation IVDs and LDTs using the before-mentioned contrived specimens provided a measure of confidence in test performance at the beginning of the pandemic, it is not feasible to precisely compare the performance of various tests because each test's validated performance was using samples derived from different sources. The FDA obtained live virus in February to develop a reference panel. Reference panels are a fundamental tool for performance assessment of molecular tests, and the use of the same reference material across different tests allows a direct comparison of analytical sensitivity performance across these tests.

In October 2020, the FDA sent their reference panel to developers of 181 EUA authorized assays to conduct performance characteristics on their IVD and LDT tests, with their results being analyzed and compared by the FDA. Confirmed results of the relative sensitivity of EUA authorized assays are available for 117 labs, and a summary is displayed in the table on the next page:

Product LoD [NDU/ml]	Assay Developer	Test Name
180	**Viracor Eurofins Clinical Diagnostics (Eurofins)**	**Viracor SARS-CoV-2 assay**
1800	Roche Molecular Systems, Inc. (RMS)	cobas SARS-CoV-2
1800	Quest Diagnostics Infectious Disease, Inc.	Quest SARS-CoV-2 rRT-PCR
2700	Abbott Molecular	Abbott RealTime SARS-CoV-2 assay
5400	Illumina, Inc.	Illumina COVIDSeq Test
18000	Centers for Disease Control and Prevention (CDC)	CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel (CDC)
54000	TNS Co., Ltd (Bio TNS)	COVID-19 RT-PCR Peptide Nucleic Acid (PNA) kit
180000	Thermo Fisher Scientific, Inc.	TaqPath COVID-19 Combo Kit
LoD = limit of Detection NDU/ml = NAAT Detectable Units/mL Matrix: Nasopharyngeal swabs		

Data from the FDA SARS-CoV-2 Reference Panel demonstrates that Eurofins truly offers best in class solutions in the laboratory services marketplace, outperforming well respected IVD reagents kit manufacturers and other laboratories that developed LDTs in house. The FDA SARS-CoV-2 Reference Panel Comparative Data can be reviewed in full here: **https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data**

#1 Performance in Surrogate Neutralizing Antibody Testing (sVNT)

SITUATION

Current testing methods for SARS-CoV-2 virus either confirm the presence of viral material or the presence of an immune response caused by exposure to the virus rather than detecting the virus itself. Where binding antibodies are responsible for binding to the virus and alerting the immune system of its presence, neutralizing antibodies help to stop the virus to actually enter cells in the body. Neutralizing antibodies are triggered both by infections and vaccinations against infections. Client requested Neutralizing antibody COVID-19 testing to expedite timelines for their vaccine development.

CHALLENGES

The conventional method, using a live virus, requires strict safety conditions in a BSL3 laboratory, would take days to perform and would be very expensive. Eurofins was tasked with finding a fast and automatable solution that would cut timelines and reduce costs to detect the presence of binding and blocking antibodies induced by immune response from exposure to the SARS-CoV-2 virus.

SOLUTIONS

Eurofins BioPharma Services, Laboratory Testing reviewed several potential analytical methods to meet the Client's requirements to monitor COVID-19 Neutralizing Antibody status of clinical trial patients that they wished to evaluate for protection from COVID-19 from either vaccination, treatment, or post-infection. Rather than take the time to develop a de novo method using live virus, Eurofins chose to perform a validation of the GenScript cPASS surrogate virus neutralization test (sVNT).

Adhering to the current scientific best practice recommendations for method validation, and where applicable, regulatory guidelines1, Eurofins successfully demonstrated 100% performance compared to Genscript's validated method that was fast and automatable. Being an ELISA methodology, the in-house, fully validated surrogate virus neutralization test (sVNT) is amenable to high-throughput testing, at a lower analytical cost and requires no extended validation timelines for our Client base. It also removes the requirement for a biosafety level 3 containment. The advantage over historic antibody IgG/IgM tests is that this new assay tests for neutralizing antibodies (versus binding antibodies), by confirming neutralizing function without the need for a secondary antibody and is isotype and species independent.

METHOD PERFORMANCE

- Mean assay sensitivity is 575.02 ng/mL
- Precision of 10.2% CV at LPC, 3.9% CV at HPC and 14.2% CV at NC
- Control Acceptance ranges of: >1.045 OD for NC, 0.256-0.148 OD for LPC and 0.081-0.043 OD for HPC.
- Selectivity passed for 100% of all normal, hemolytic and lipemic matrix lots assessed.
- Titer precision of known positive samples showed a maximum of 25.1% CV across plates and reproducible titer point across plates and analysts.

Data from the FDA, EUA Authorized Serology Test Performance demonstrates that 4 out of 62 antibody kit manufacturers, including Eurofins partner GenScript, delivered 100% of the estimated performance in selectivity and sensitivity performance.

Assay Developer	Antibody	Sensitivity	Selectivity	PPV at prevalence = 5%	NPV at prevalence = 5%
GenScript/Eurofins	**Pan-Ig**	**100%**	**100%**	**100%**	**100%**
Abbott	IgM	95%	99.6%	92%	99.7%
Beckman	IgG	96.8%	99.6%	93.5%	99.8%
Biorad	Pan-Ig	98%	99.3%	88.6%	99.9%
Luminex	IgG	96.3%	99.3%	88.4%	99.8%
Euroimmun	IgG	90%	100%	100%	99.5%
ThermoFisher	Pan-Ig	96.7%	97.5%	67.1%	99.8%

PVV = Positives Predictive Values
NPV = Negative Predictive Values

The full details of the FDA, EUA Authorized Serology Test Performance can be reviewed here: **https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance**

[1] **https://www.fda.gov/media/119788/download**