



ASLM Special COVID19 LabECHO Session

BIO-RAD

Bio-Rad Laboratories

Presenters : Dr Marcus Neusser & Mr Richie Petronis

April 30th, 2020 – 4pm EAT

Summary

- Bio-Rad Laboratories : Who we are
- Bio-Rad in the context of SARS-COV-2 / COVID-19
- Our comprehensive technical solutions :
 - Molecular
 - Standards
- What's next ? (new solution)
- Links to documentation & resources

About Bio-Rad

Leading global provider of sophisticated products for life science research & clinical diagnostics markets:

- Founded in 1952
- Develop, manufacture, & market products that enable discovery
- Diversified and complimentary mix of products & technologies
- Continuous innovation
- Sales exceeded \$2 billion in 2019
- Nearly 65 years of strong performance
- Offices and facilities around the world
- More than 8,000 employees worldwide
- Listed on the NYSE (BIO)

Clinical Diagnostics

The number one specialty diagnostics company in the world



Life Science Research

Complete solutions to accelerate scientific discovery



Bio-Rad in the context of SARS-CoV-2

Coronavirus
SARS-CoV-2 / COVID-19
Assay and Research Solutions

Bio-Rad offers solutions to enable scientists to address the 2019 novel coronavirus outbreak.

[Learn More](#)

Real-Time PCR

Method of choice for routine SARS-CoV-2 testing. CFX Dx, CFX Touch used for 2019-nCoV detection tests.



Droplet Digital PCR

2 recent articles authored by Wuhan clinicians, conclude that *ddPCR* shows superiority for clinical detection of SARS-CoV-2 reducing false negatives.



Bio-Plex

Serum level of inflammatory cytokines is a main clinical parameters monitored in COVID-19 patients and human cytokine panels.



ELISA/EIA

Qualitative detection of total anti-SARS-CoV nucleocapsid antibodies.



Emerging infectious diseases

Vaccine development

Clinical assay development and trial execution.

Need for standardized reagents, sample panels, controls, and assays.

Clinical research

Better understanding of:

- genetic factors influencing clinical outcomes.
- other epidemiologic factors.
- immunopathogenesis of disease.

New or improved treatment.

Diagnostic testing

Once the infectious pathogen has been identified.

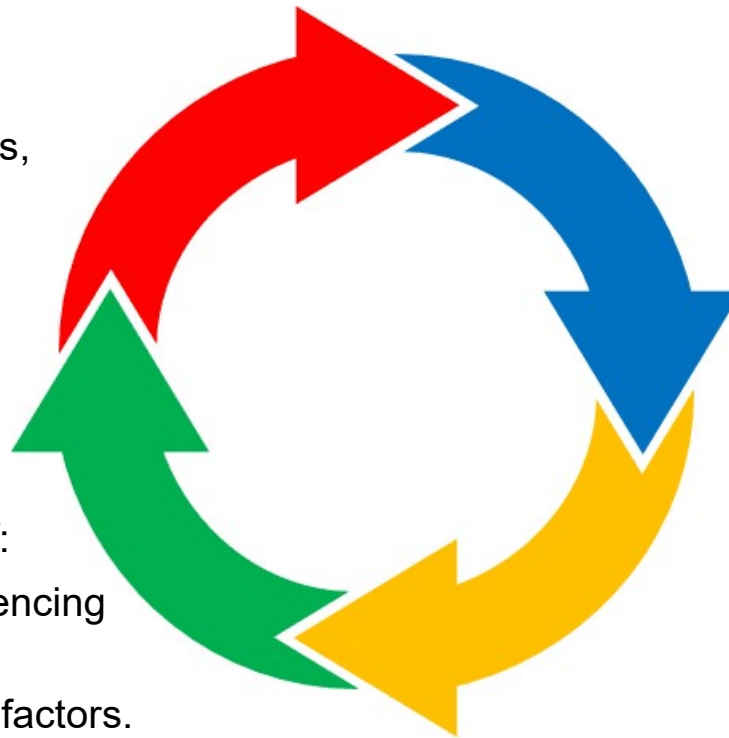
- Nucleic acid tests
- Serological tests

Clinical characterisation

Understand the clinical spectrum of the disease.

Disease progress and correlation to clinical outcomes.

Best course of treatment.



Where do Bio-Rad technologies fit?

Vaccine development



Diagnostic testing



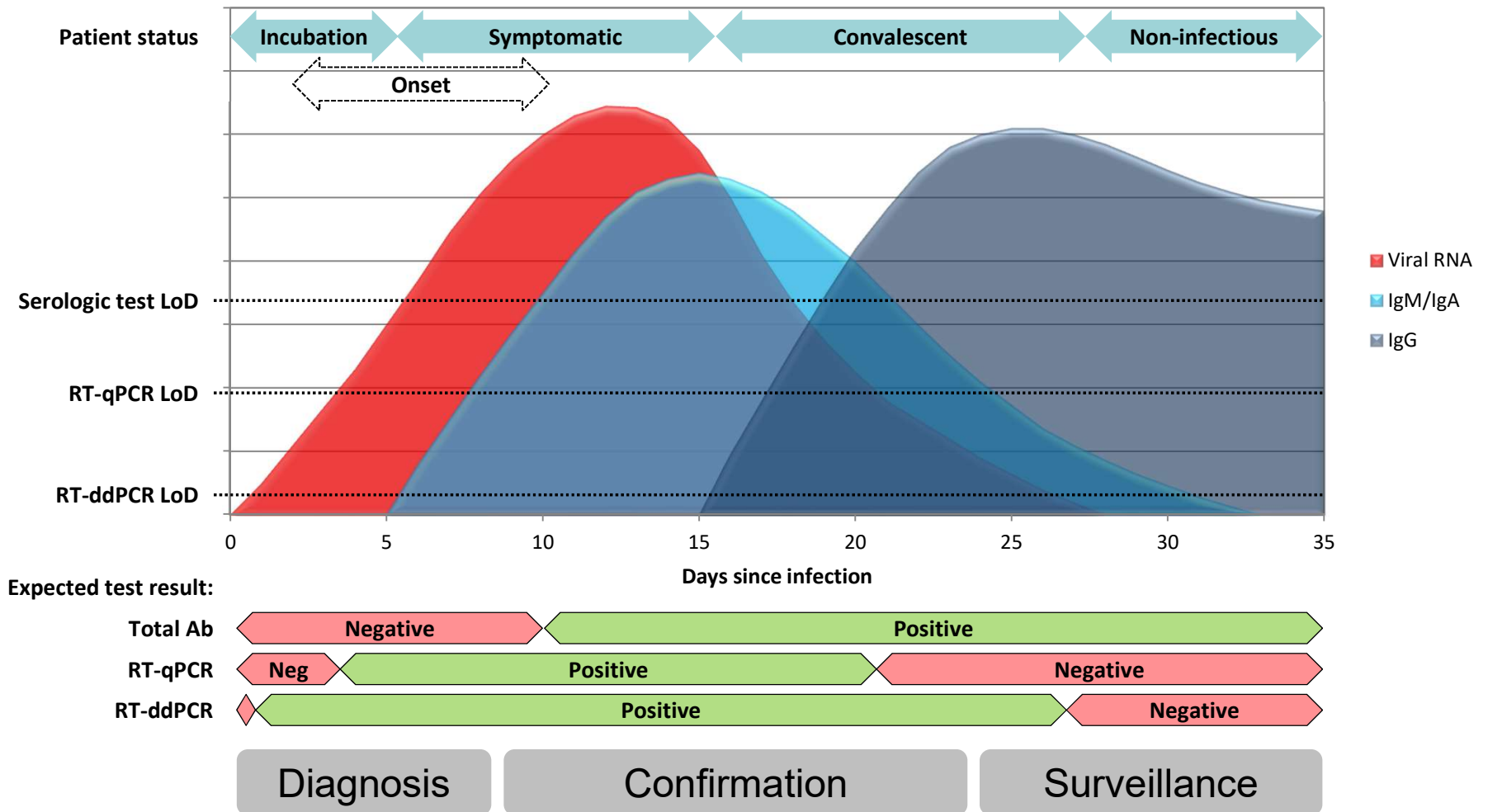
Clinical research



Clinical characterisation

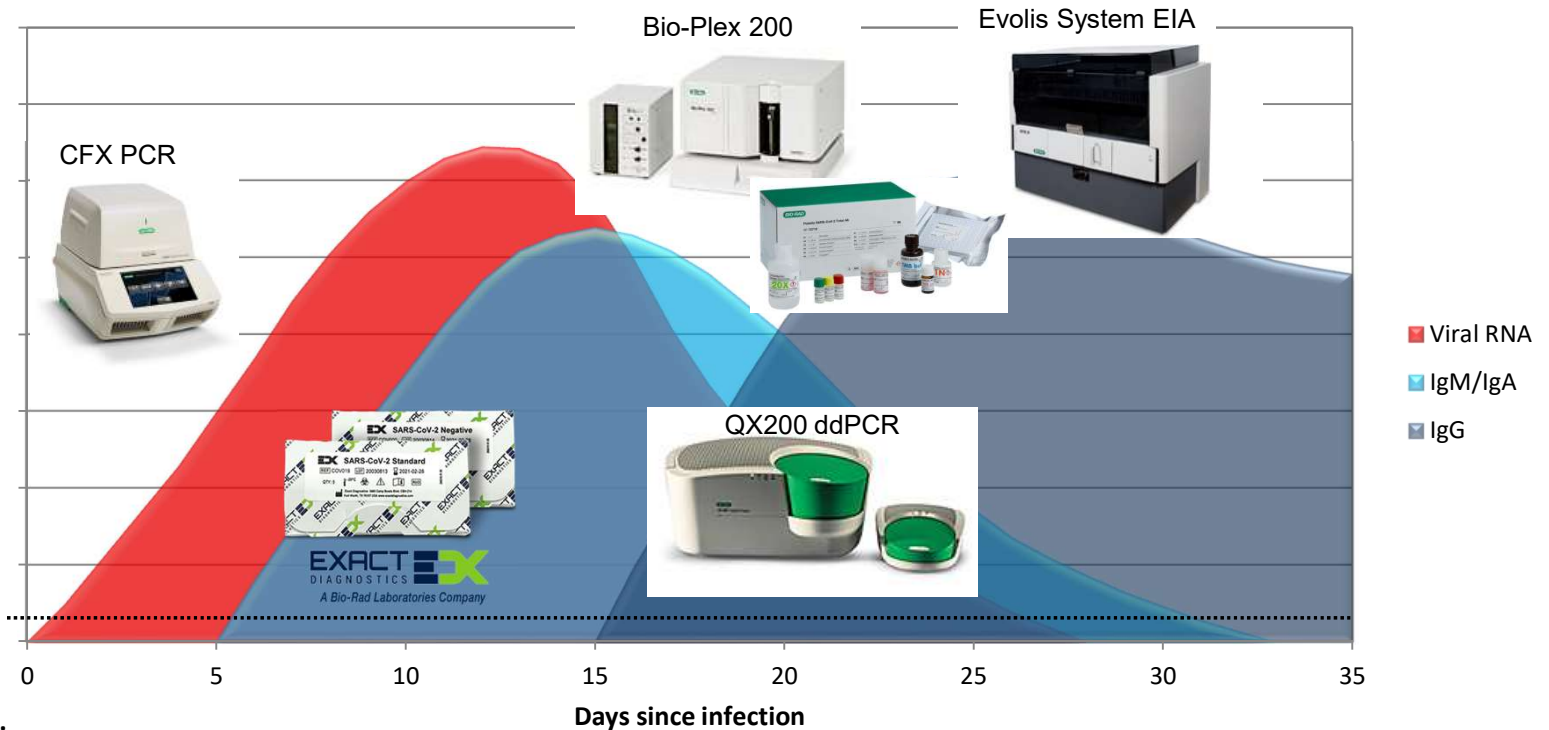


Viral RNA and Ab response profile SARS-CoV-2

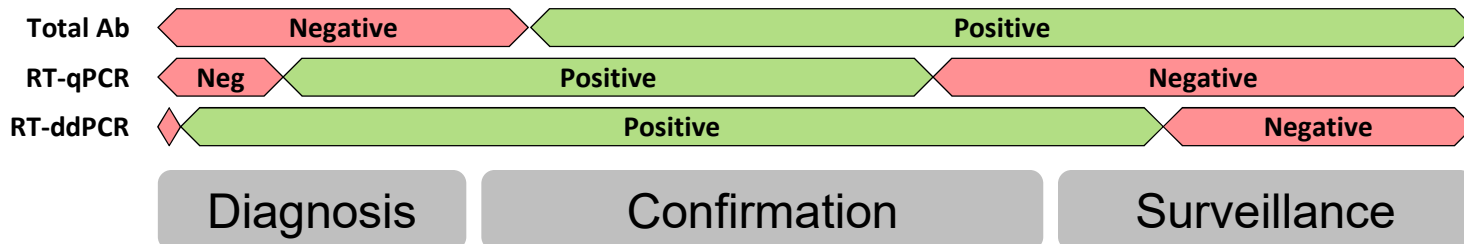


*Times and levels indicated (including LoD) are just estimates and vary amongst patients. The graph describes one of many potential scenarios based on limited published data (see notes for publication details)
 Expected test result section depicts an ideal scenario that considers false negative rate is 0.*

Viral RNA and Ab response profile SARS-CoV-2



Expected test result:



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SARS-CoV-2: Bio-Plex

Bio-Plex

Serum level of inflammatory cytokines is one of the main clinical parameters monitored in COVID-19 patients. Bio-Plex 200 and human cytokine panels appear cited in several publications.

Instrumentation



Bio-Plex 200



Reagents and Consumables

- Bio-Plex 200 and the human cytokine 27- or 48-plex panels appear in several publications as the tool to measure the serum level of inflammatory cytokines:
 - [Clinical features of patients infected with 2019-nCoV](#)
 - [Coronavirus disease in hemodialysis patients](#)
 - [Clinical characteristics of death cases with COVID-19](#)
 - [Cytokines associated with disease severity](#)
- Leading labs interested in deeper understanding of the clinical characteristics of the COVID-19 disease will be monitoring cytokine levels.
- For example, it seems that high levels of IP-10, MCP-3 and IL-1ra are associated with disease deterioration.

SARS-CoV-2: Real-Time PCR

Real-Time PCR

Method of choice for routine SARS-CoV-2 testing, as recommended by FDA and WHO.

Instrumentation

RUO



CFX96 Touch
CFX 384 Touch
CFX Connect

IVD/FDA



CFX96 Dx

Reagents and Consumables

RUO



iTaq one-step mix
Reliance one-step mix



Hard-Shell plates

- Most [commercially available kits](#) are compatible with CFX Real-Time PCR detection systems.
- Validation of CFX96 in *in-house* testing protocols is mentioned in clinical literature (e.g. [Bavarian Health and Food Safety Authority, Germany](#))

- Multiple testing laboratories are utilizing Bio-Rad's Real-Time qPCR (RT-qPCR) products for the detection of SARS-CoV-2 (COVID-19).

SARS-CoV-2: Droplet Digital PCR

Droplet Digital PCR

Studies from researchers in China¹ reported that ddPCR showed superior sensitivity and precision for clinical detection of SARS-CoV-2 compared to existing qPCR test methods.

Instrumentation

RUO



QX200
QX200 AutoDG
QX ONE

IVD/FDA



QXDx
QXDx AutoDG

Reagents and Consumables

RUO



ddPCR supermixes
ddPCR consumables

IVD/FDA



QXDx supermix
QXDx consumables



EUA COVID-19 ddPCR kit

- ddPCR improves diagnostic detection accuracy of SARS-CoV-2 from 28.2% to 87.4%, thereby reducing false negatives.
- Biodesix, a US diagnostic company, has begun SARS-CoV-2 Droplet Digital PCR (ddPCR) testing after submitting for EUA from the FDA.
- ddPCR is used to quantitate SARS-CoV-2 Standards and Controls (Bio-Rad's and others).

The importance of controls in COVID-19 PCR testing

- WHO¹ advises that “each Nucleic Acid Amplification Test (NAAT) run should include both external and internal controls.”
- According to Dr. Bustin (a world-known authority in PCR)²:
 - “Cq values are subject to inherent inter-run variation and should not be used without appropriate calibration standards.”
 - “The inclusion of known negative and positive control samples with each test run is an essential quality control parameter.”

Validate the Entire Process of a Molecular Assay

SARS-CoV-2 Standard

The EDX SARS-CoV-2 Standard is manufactured with synthetic RNA transcripts containing 5 gene targets (E, N, S, ORF1a, and RdRP genes of SARS-CoV-2, 200,000 copies/mL each). The product is formulated in a synthetic matrix and contains human genomic DNA (75,000 copies/mL).

SKU: COV019

5 Vials, 0.3 mL Fill Volume, -20°C or below Storage



SARS-CoV-2 Negative

The EDX SARS-CoV-2 Negative is negative for SARS-CoV-2. The product is formulated in a synthetic matrix and contains human genomic DNA (75,000 copies/mL)

SKU: COV000

5 Vials, 0.3 mL Fill Volume, -20°C or below Storage

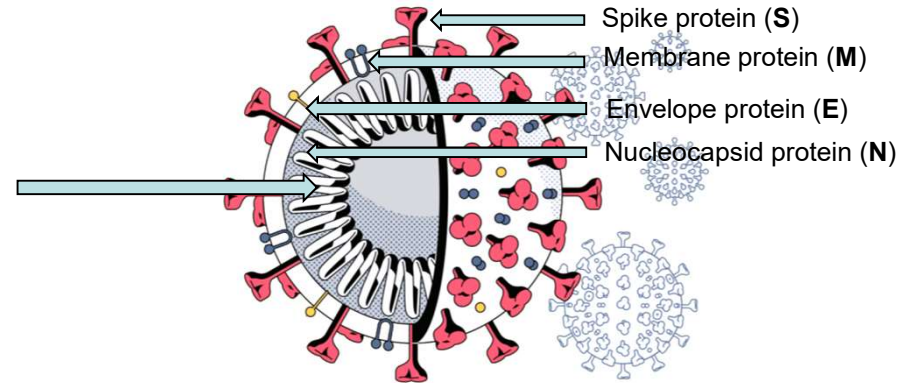


LIMITATIONS: For research use only. Not for use in diagnostic procedures.

5 Gene Targets for COVID-19



Single-stranded
RNA genome



(E) Envelope Gene 200,000 copies/mL	(N) Nucleocapsid Gene 200,000 copies/mL	(O) OrF1a* Gene 200,000 copies/mL *Open Reading Frame	(R) RdRP* Gene 200,000 copies/mL *RNA-dependent RNA polymerase	(S) Spike Protein Gene 200,000 copies/mL
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Advantages of SARS-CoV-2 Standard

- **This is a new coronavirus standard with In-Vitro transcript RNA quantified by ddPCR against a human genomic DNA background**
- Advantages to use the SARS-CoV-2 Standard:
- Includes all relevant RNA gene targets to cover a wide range of assay targets (E, N, ORF1a, RdRP, and S) to confirm that your test detects target genes
- It can be validated for use as an independent control and is provided at high enough concentration to allow effective dilutions for Limit of detection studies (200,000 cps/mL, using negative as diluent)
- Matrix includes Human Genomic DNA (especially useful for CDC assay)
- Designed to validate the entire process of a molecular assay

Platelia SARS-CoV2 Total Ab assay



Diagnosis

In conjunction with clinical presentation and testing with other methods, Platelia SARS-CoV-2 Total Ab can be used to help diagnose COVID-19 disease

Surveillance

To be used as a screening tool for detecting the presence of anti-SARS-CoV-2 total antibodies in order to determine individuals' immune status regarding exposition to SARS-CoV-2

Bio-Rad solutions to the support COVID-19 battle

Coronavirus SARS-CoV-2 / COVID-19 Assay and Research Solutions

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EXACT DX
DIAGNOSTICS
A Bio-Rad Laboratories Company

Droplet Digital PCR

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Links to resources

- **Website** : <https://www.bio-rad.com/>
- **Bio-Rad SARS-CoV-2 / COVID-19 Assay and Research Solutions:**
[https://www.bio-rad.com/featured/en/coronavirus-covid-19-assay-development-vaccine-research.html?hplink=\[Hero\]%20\[COVID19-MAR2020%20-%2020200319%20-%201\]](https://www.bio-rad.com/featured/en/coronavirus-covid-19-assay-development-vaccine-research.html?hplink=[Hero]%20[COVID19-MAR2020%20-%2020200319%20-%201])
- **Webinar** : “Corona Virus outbreak: The Singapore Story”
<https://info.bio-rad.com/Coronavirus-Outbreak-The-Singapore-Story-Webinar.html>
- **Exact Diagnostics SARS-COV-2 Standards**
<http://www.exactdiagnostics.com/sars-cov-2-standard.html>
- **Exact Diagnostics SARS-COV-2 Negative Controls**
<http://www.exactdiagnostics.com/sars-cov-2-negative.html>
- **Platelia SARS-COV-2 Total Ab assay** (*press releases*):
[https://www.bio-rad.com/fr-fr/corporate/newsroom/bio-rad-announces-launch-serology-assay-detect-coronavirus-covid-19-antibodies?ID=Bio-Rad-Announces-th_1586243352&tlp-link=\[News%20&%20Media\]%20\[Serology%20Assay%2004/07/20\]=](https://www.bio-rad.com/fr-fr/corporate/newsroom/bio-rad-announces-launch-serology-assay-detect-coronavirus-covid-19-antibodies?ID=Bio-Rad-Announces-th_1586243352&tlp-link=[News%20&%20Media]%20[Serology%20Assay%2004/07/20]=)



Q&A