Siemens Healthineers
Molecular Diagnostic Response to COVID-19

16 September 2021

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MDX, Siemens Healthineers, MESA
Agenda

1. Siemens Healthineers Molecular Dx Approach & Portfolio
2. Siemens Healthineers Dx: COVID-19 Testing Solutions
4. Q&A
Siemens Healthineers
Molecular Diagnostics
Approach & Portfolio
Molecular Diagnostics Laboratories: Challenges and Needs
Siemens Healthineers Molecular Dx Approach

- Syndromic approach
- Large assay menu
- Multiplexing
- Same protocol for all kits
- Compatibility

Siemens Healthineers offers flexible and easy workflow solutions and innovations to help you overcome your laboratory challenges!
Siemens Healthineers Molecular Portfolio
Toward Precision Medicine

**KPCR**
- Extraction and PCR Set up

**LiPA**
- VERSANT® HCV Genotyping LiPA Market leader in HCV genotyping

**TPS**
- Tissue Preparation System Fully-automated nucleic acid extraction from FFPE and fresh frozen tissues

**FTD**
- Broad range of Multiplex Syndromic PCR assays

Product availability varies and is subject to country-specific regulatory requirements.
Siemens Healthineers DX COVID-19 Testing Solutions
COVID-19 patient pathway

- **Diagnosis**
  - COVID-19 infection?
    - Antigen POC test
    - Molecular lab test

- **Prognosis**
  - How severe is it?
    - Immunochemistry lab tests
    - Hematology Morbidity tests
    - Blood gas tests
    - CT
    - X-ray
    - C-arm
    - Ultrasound

- **Therapy**
  - How to treat?
    - Immunochemistry lab tests
    - Hematology Morbidity tests
    - Blood gas tests
    - CT
    - X-ray
    - C-arm
    - Ultrasound

- **Follow-up**
  - When recovered?
    - CT
    - X-ray
    - C-arm
    - Ultrasound
    - Immunochemistry lab tests
    - Hematology lab tests
    - Molecular lab test
    - Antibody POC test*
    - Antibody lab test*

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* To help indicate an immune response
This pathway is for illustration purposes only. (Status Nov. 20, 2020)
The path to normalcy: COVID-19 testing options

From the lab to the point of care, a full portfolio of COVID-19 testing solutions that consistently delivers sensitivity and performance—to get us to what’s next

Satellite Testing
Near-patient testing can be used to identify and isolate infected people more quickly.

Large-scale Testing and Diagnosis
Clinicians use diagnostic tests to determine if people have current COVID-19 infections, enabling patient management decisions.

Management and Monitoring
Management and monitoring are critical in determining the full scope of the disease, combating the pandemic, and rebuilding public confidence.
FTD SARS-CoV-2 Assay

Assay design

- Single-tube dual target assay covering highly conserved regions ORF1ab and N gene
- Same dye/channel for the two target regions
  - Increased signal
  - Lower chance for inconclusive results
- Optimized detection of possible mutants

<table>
<thead>
<tr>
<th>Target</th>
<th>Detection dye/channel</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>FAM/Green</td>
</tr>
<tr>
<td>ORF1ab</td>
<td>FAM/Green</td>
</tr>
<tr>
<td>IC (Equine Arteritis Virus)</td>
<td>Cy5/Red</td>
</tr>
</tbody>
</table>

*CE-IVD labelled for diagnostic use in the EU. This test has not been FDA cleared or approved. This test has been authorized by FDA under an EUA for use by authorized laboratories. This test has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens. This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21. U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
Different systems and laboratory space
Platform – agnostic workflow

Extraction

PCR set up

Amplification detection

Analysis Interpretation

Different compatible extractors and manual methods*

* refer to compatibility list

SARS-CoV-2  FLU/HRSV

Same PCR cycling profile for all FTD assays

Different compatible thermocyclers*
VERSANT kPCR molecular system with FTD SARS CoV-2 assay: Siemens automation solution for sample-to-result

VERSANT® kPCR Molecular System
Nucleic Acid Extraction + PCR Set up + PCR run + Analysis

VERSANT® kPCR SP Module
VERSANT Sample Preparation 1.0 Reagent kit

VERSANT kPCR AD Module (QS5 DX MiPLX SWv2.0)
FTD SARS-CoV-2 Kit

Sample Collection

Result Analysis and Interpretation
Proficiency study for sensitivity with FDA Reference Panel

• FDA provided protocol and reference SARS-CoV-2 sample panel to document and publish comparable analytical sensitivity or limit of detection (LOD) performance among all EUA manufacturers.

• FTD SARS-CoV-2 Assay on the VERSANT kPCR Molecular System is ranked as one of the **TOP FIVE most-sensitive tests** out of **117 manufacturers** listed on the FDA website.

• Limit of detection of **540 NDU/mL** provides better sensitivity than most other kit manufacturers

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*NAAT detectable units/mL (NDU/mL): calibration unit of FDA reference sample delivered by FDA to all manufacturers for LoD determination.
Emergence of variants: A fast response from FTD...

- **In silico** analysis on a large number of sequences was performed to investigate any possible change in detection of these 2 emerging variants with the FTD SARS-CoV-2 Assay.

- The **in silico** analysis has shown that the emergent variants are detected with a **100% detection rate** by both N gene and ORF1ab assays.*

- **Customer letter** issued on December 28, 2020

- **In silico** analysis is an ongoing process by FTD to determine assay performance on new variants as they emerge. So far, over 1.2 million complete sequences of SARS-CoV-2 have been tested giving similar (100%) detection rate.

- Another **customer letter**: June 2021

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* Data on file

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Unrestricted © Siemens Healthineers, 2020
### FTD SARS-CoV-2 assay

#### WHO listed assays

<table>
<thead>
<tr>
<th>Supplier</th>
<th>CE</th>
<th>FDA</th>
<th>WHO</th>
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</thead>
<tbody>
<tr>
<td><strong>FTD-114 SARS-CoV-2</strong></td>
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<td>✔</td>
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<td>Siemens/FTD</td>
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<td>✔</td>
<td>✔</td>
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<td><strong>Cobas SARS-CoV-2 Qualitative</strong></td>
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<td>✔</td>
<td>✔</td>
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<tr>
<td>Roche</td>
<td>✔</td>
<td>✔</td>
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<td>Abbott</td>
<td>✔</td>
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<tr>
<td><strong>PerkinElmer® SARS-CoV-2 Real-time RT-PCR</strong></td>
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<td>Perkin Elmer</td>
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<td><strong>Real-time fluorescent RT-PCR kit for detecting 2019-nCoV</strong></td>
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<tr>
<td>BGI</td>
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<td>✔</td>
<td>✔</td>
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<tr>
<td>Da An Gene Co</td>
<td>✔</td>
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<tr>
<td><strong>Multiple Real-Time PCR Kit for Detection of 2019-nCoV</strong></td>
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<tr>
<td>Beijing ABT Co</td>
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**WHO Emergency Use Listing (EUL) - Product eligible for listing**

- **Product name:** FTD SARS-CoV-2 (FTD-114-32)
- **Application number:** EUL 0502-193-00
- **Product code:** 11416300
- **Regulatory version:** CE marked version

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*For more information, visit [https://www.who.int/diagnostics_laboratory/eual/listing/en/](https://www.who.int/diagnostics_laboratory/eual/listing/en/)*
Molecular Diagnostics: COVID-19 Variants Response
## Variants of Concern (VOC) and Variants of Interest (VOI)*

<table>
<thead>
<tr>
<th>WHO label</th>
<th>Country first identified</th>
<th>Common name</th>
<th>Next strain</th>
<th>GISAID</th>
<th>Lineage (Pango)</th>
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<tr>
<td>Alpha</td>
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<td>20I/501Y.V1</td>
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<td>Gamma</td>
<td>BRA</td>
<td>P.1</td>
<td>20I/501Y.V3</td>
<td>GR/484K.V2</td>
<td>P.1 /B.1.1.28.1</td>
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<td>Delta</td>
<td>India</td>
<td>20A/S:478K</td>
<td>20A/S:478K</td>
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<td>B.1.617.2</td>
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<table>
<thead>
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<td>India</td>
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<tr>
<td>Iota</td>
<td>USA (NY)</td>
<td></td>
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<td>202102/03</td>
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<td>Eta</td>
<td>UK</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lambda</td>
<td>Peru</td>
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<thead>
<tr>
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<tr>
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<td>20A/S:478K</td>
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<td>B.1.617.2</td>
</tr>
</tbody>
</table>

* https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/
Current Testing Strategies and Algorithms for SARS-CoV-2 Mutations and Variants*

**GOLD STANDARD**
- Comprehensive mutation information
- New mutations/variants discovery
- Long TAT
- Potential sensitivity issue especially for samples with low viral load

**FIRST LINE ASSAY**
- Replaces the routine diagnostics assay
- Faster TAT
- Limited number of mutations
- Detects known mutations
- Complex development

**REFLEX ASSAY**
- High sensitivity for diagnosis
- Easy to implement
- Flexible approach with evolution of new mutations/variants
- Detects known mutations

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Siemens Healthineers Strategy for SARS-CoV-2 Mutation Detection and Variant Identification

The Siemens Healthineers approach provides molecular laboratories an add-on, flexible workflow solution for the surveillance of critical SARS-CoV-2 mutations and the identification of variants without affecting routine testing for SARS-CoV2 diagnosis.

- **Reflex testing approach**
- **Cost effective**
  - Fast and easy to implement
- **SNPs assays** for mutation profiling
- **Detection of critical mutations** that might appear due to convergent evolution
- **Flexible** and regionalized solution to detect variants
- **High sensitivity** and broad testing infrastructure vs. sequencing approach
Reflex Testing Approach for Detection of SARS-CoV-2 Mutations/Variants

Sample collection

RT-PCR Diagnostic SARS-CoV-2 Workflow

Testing algorithm

Reflex test

Reflex SNP assay

- RT-PCR based RUO SNP assays for detection of SARS-CoV-2 mutations
- Each assay is specific for one mutation
- Combinations of mutations provide for variant identification
- Lab selects specific SNP assay(s) for regional needs

FTD SARS-CoV-2 Kit*

SARS-CoV-2 Detection

Mutation detection assay(s)

WT

Mutant

Mutation Profiling

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# SARS-CoV-2 Mutation Detection Assays

## VOC (Variants of Concern) and VOI (WHO) of Critical Mutations

<table>
<thead>
<tr>
<th>WHO label</th>
<th>Alpha</th>
<th>Beta</th>
<th>Gamma</th>
<th>Delta</th>
<th>Kappa</th>
<th>Iota</th>
<th>Eta</th>
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<tr>
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<td>X</td>
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<tr>
<td>L452R</td>
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<tr>
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</tbody>
</table>

## Diagnovital Kits

- Diagnovital SARS-CoV-2 del HV69/70 Mutation Detection Kit (RUO*)
- Diagnovital SARS-CoV-2 K417N Mutation Detection Kit (RUO*)
- Diagnovital SARS-CoV-2 L452R Mutation Detection Kit (RUO*)
- Diagnovital SARS-CoV-2 E484K Mutation Detection Kit (RUO*)
- Diagnovital SARS-CoV-2 E484Q, Mutation Detection Kit (RUO*)
- Diagnovital SARS-CoV-2 N501Y Mutation Detection Kit (RUO*)

### Notes

- Six single mutation reflex RT-PCR assays selected for the detection of critical mutations and the identification of Variants of concern (VOC) and major variants of interest (VOI)

*For Research Use Only.*
Siemens Healthineers Total Solution for SARS-CoV-2 Diagnosis, Mutation Detection, and Variant Identification

Uses highly sensitive FTD SARS-CoV-2 Assay* for initial diagnosis with subsequent reflex testing of residual eluates from positive samples only. Does not disrupt SARS-COV-2 routine testing.

Offers broad range of single mutation RT-PCR assays, covering emerging critical mutations and variants.

Tailored and flexible approach that is adaptable to uncertain variant evolution and regional needs.

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Thank you for your enthusiasm!

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