DiaSorin-LIAISON® SARS-CoV-2 Antigen Test

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Agenda

- Company Overview
- Product Portfolio
- SARS-CoV-2 Antigen
We are an Italian multinational Group, listed on the stock exchange in the FTSE MIB. Owned by DiaSorin S.p.A., it consists of 24 Companies, 5 foreign branches, offices on the 5 Continents and 5 manufacturing facilities throughout the world.

We are one of the leading hi-tech players in the invitro diagnostic market and, in particular, in the immunodiagnostic and molecular diagnostic segments.
Immunodiagnostics

Technology based on the detection of antibodies to highlight the presence of diseases in a sample of human fluids loaded on proprietary platforms based on **CLIA technology** (Chemiluminescence) and **ELISA technology** (Colorimetry).
LIAISON family platforms

- Same cartridge for each test
- 100 test samples for each cartridge
- Same raw materials

Magnetic particles → Calibrators → Diluent

New in 2021

LIAISON

LIAISON

LIAISON LAS

LIAISON
Diasorin CLIA COVID PANEL

SARS – CoV-2 Trimeric IgG (new)
DIASORIN LAUNCHES THE LIAISON® SARS-COV-2 AG: October 26, 2020

- A high-throughput antigen test available for quantitative detection of SARS-CoV-2 in symptomatic patients through nasal and nasopharyngeal swabs

- The new high-throughput antigen test uses chemiluminescence immunoassay (CLIA) technology to determine the presence of SARS-CoV-2 Nucleocapsid protein antigen, quantifying the viral load of the infection directly from individuals suspected of COVID-19 by their healthcare provider

- The antigen test can be offered as an alternative solution in cases where molecular PCR testing availability is lacking, in geographies where PCR technology is too expensive and in those cases where traceability of clinical samples needs to be improved.
Rethinking Covid-19 Test Sensitivity — A Strategy for Containment

Michael J. Mina, M.D., Ph.D., Roy Parker, Ph.D., and Daniel B. Larremore, Ph.D.

It's time to change how we think about the sensitivity of testing for Covid-19. The Food and Drug Administration (FDA) and the scientific community are currently almost exclusively focused on test sensitivity, a measure of how well an individual can detect viral proteins or RNA molecules. Critically, this measure ignores the context of how the test is being used. Yet when it comes to broad screening that the United States so desperately needs, context is fundamental. The key question is not how well molecules can be detected in a single sample but how effectively infections can be detected in a population by the repeated use of a given test as part of an overall testing strategy — the sensitivity of the testing regimen.

A regime of regular testing works as a sort of Covid-19 filter, by identifying, isolating, and thus blocking new community infections, including those who are asymptomatic. Measuring the sensitivity of a testing regimen or filter requires us to consider a test in context: how often it's used, to whom it's applied, when in the course of an infection it works, and whether its results are returned in time to prevent spread.

Thinking about impact in terms of repeated cases is a familiar concept to clinicians and regulatory agencies: it's involved every time we measure the efficacy of a treatment regimen rather than a single dose. With Covid-19 cases occurring at such a rate throughout much of the world, we urgently need to shift our attention from a narrow focus on the analytic sensitivity of a test (the lower limit of its ability to correctly detect small concentrations of molecules in a sample) to the more relevant measure of a testing regimen's sensitivity to detect infections (the probability that infected persons learn they're infected in time to be filtered out of the population and prevent spread).

A prescreening test that was insensitive enough to be used frequently would have a high sensitivity for detecting infections in time to act without having to meet the benchmark analytic limit of detection (see diagram).

The tests we need are fundamentally different from the clinical tests currently being used, and they must be evaluated differently. Clinical tests are designed for use with symptomatic people, do not need to be low-cost, and require high analytic sensitivity to return a definitive result within a single opportunity to test. In contrast, tests used in effective surveillance regimens tend to reduce the population prevalence of a respiratory virus two surveillance regimens can be adopted (circles) with different analytic sensitivity.

For an effective Covid filter that will stop this pandemic, we need tests that can enable regimes that will capture most infections while they are still infectious.
WHO Guidelines on Ag tests September 11th

Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunosassays
Interim guidance 11 September 2020

**Background**

Since the beginning of the COVID-19 pandemic, laboratories have been using nucleic acid amplification tests (NAATs), such as real-time reverse transcription polymerase chain reaction (RT-PCR) assays, to detect SARS-CoV-2, the virus that causes the disease. In many countries, access to this form of testing has been challenging. The search is on to develop reliable but less complex tests that can be used in a variety of settings, including resource-poor settings.

Ag tests are designed to directly detect SARS-CoV-2 proteins produced by replicating virus in respiratory secretions and have been developed in both laboratory-based tests, and for point-of-care use, so-called rapid diagnostic tests, or RDTs. The diagnostic development landscape is dynamic, with nearly a hundred companies developing or manufacturing rapid tests for SARS-CoV-2 antigen detection.

This document offers advice on the potential role of antigen-detecting RDTs (Ag-RDTs) in the diagnosis of COVID-19 and the need for careful test selection. The information on Ag-RDTs in this document updates guidance that was included in the Scientific Brief entitled WHO Advice on use of some rapid immunodiagnostic tests for COVID-19 published on 8 April 2020. Guidance on the use of Ag-RDTs will be regularly updated as new evidence becomes available.

Most Ag-RDTs for COVID-19 use a sandwich immunomodulatory method employing a simple-to-use lateral flow test format commonly employed for HIV, malaria and influenza testing. Ag-RDTs are usually comprised of a plastic cassette with sample and control wells, a microporous matrix strip, with a test line with antibody specific for conjugated target protein and a control line with antibody specific for unmodified antibody. In the case of SARS-CoV-2 RDTs the target antigen is often the viral ‘nucleocapsid protein’, preferred because of its relative abundance. Typically, all materials that are required to perform the test, including sample collection materials, are provided in the commercial kit, with the exception of a timer.

After collecting the respiratory specimen and applying it to the test strip, results are read by the operator within 10 to 30 minutes with or without the aid of a reader instrument. The ease of a reader substantially contributes to the speed of results, allowing for the rapid interpretation by different operators, but requires auxiliary equipment. Most of the currently manufactured tests require nasal or oropharyngeal swab samples, but companies are carrying out studies to assess the performance of their tests using alternative sample types such as saliva, and field and sample collection systems to potentially expand options for use and to facilitate safe and efficient testing. Generally, the ease-of-use and rapid turnaround time of Ag-RDTs offers the potential to expand access to testing and decrease delays in diagnosis by shifting to decentralized testing of patients with early symptoms. The trade-off for simplicity of operation of Ag-RDTs is a lower in sensitivity compared to NAATs. Various lines of the SARS-CoV-2 Ag-RDTs have undergone antigen regulatory review. Only four lines have received United States Food and Drug Administration (FDA) Emergency Use Authorization (EUA), and another two test lines have been approved by Japan’s Pharmaceutical and Medical Devices Agency. Only three companies have submitted documents toward WHO’s Emergency Use Listing (EUL) procedure (2, 3).

Data on the sensitivity and specificity of currently available Ag-RDTs for SARS-CoV-2 have been derived from studies that vary in design and in the test formats being evaluated. They have shown that the sensitivity compared to NAAT in samples from upper respiratory tract (nasal or oropharyngeal swabs) appears to be highly variable, ranging from 0-90% (4-13) but specificity is consistently reported to be high (>97%). Although more evidence is needed on real-world performance and operational aspects, Ag-RDTs are most likely to perform well in patients with high viral load (Ct values ≤25 or >107 genomes per ml), which usually appear in the pre-symptomatic (1-3 days before symptom onset) and early symptomatic phases of the disease. However, positive results from these tests should be confirmed by NAAT.

An Ag test is the virus’ “nucleocapsid protein”, preferred because of its relative abundance.

**Results** are read by the operator within 10 to 30 minutes with or without the aid of a reader instrument.

Tests require nasal or nasopharyngeal swab samples, but companies are carrying out studies to assess the performance of their tests using alternative sample types such as saliva.

**Performance requested:**

- Sensitivity ≥80% and have very high specificity (≥97-100%).

- To optimize performance, testing with Ag test should be conducted within the first 5-7 days following the onset of symptoms.
To diagnose SARS-CoV-2 infection where NAAT is unavailable

Where prolonged TAT of Real Time PCR can preclude clinical utility of the test

In case of widespread community transmission, Ag may be used for early detection and isolation of positive cases in health facilities, COVID-19 testing centres/sites, care homes, and for contact tracing.

To support outbreak investigations (e.g. in closed or semi-closed groups including schools, care-homes, cruise ships, prisons, workplaces and dormitories)
This assay is a unique quantitative solution to detect suspected COVID-19 patients, do contact tracing and rapidly implement isolation procedures for those patients who have been infected and might be able to spread SARS-CoV-2. LIAISON® SARS-CoV-2 Ag assay could help to keep the COVID-19 pandemic at bay, because specimens can be tested out rapidly in a great numbers.

The pre-analytic processing of the new assay requires a specific training to be aware about the important steps that the customer need to strictly follow to work safely and to obtain the best performance from the test.

10 Days onset symptoms
## Technical Specification

<table>
<thead>
<tr>
<th>Name</th>
<th>LIAISON® SARS-CoV-2 Ag Assay</th>
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<tbody>
<tr>
<td>Intended Use</td>
<td>CE</td>
</tr>
<tr>
<td>Sample Type</td>
<td>Quantitative determination of SARS-CoV-2 Nucleocapsid protein antigen in upper respiratory specimens</td>
</tr>
<tr>
<td>Sample Type</td>
<td>Nasal Swab (NS), Nasopharyngeal Swab (NPS) eluted in Viral Transport Media (UTM/VTM).</td>
</tr>
<tr>
<td>Platforms</td>
<td>LIAISON® XL</td>
</tr>
<tr>
<td>Time to first result</td>
<td>36 min</td>
</tr>
<tr>
<td>Throughput</td>
<td>136 tests/h – approx. 700 tests/working shift</td>
</tr>
<tr>
<td>Clinical Sensitivity (NS)</td>
<td>98.6% (95% CI: 92.5– 99.7%) on samples positive for Real time PCR (within 10 days onset symptoms)</td>
</tr>
<tr>
<td>Clinical Specificity (NS)</td>
<td>100% (95% CI: 96.5 – 100%) on samples positive for Real time PCR (within 10 days onset symptoms)</td>
</tr>
<tr>
<td>Clinical Sensitivity (NPS)</td>
<td>98.9% (95% CI: 90.3 – 98.8%) on samples positive for Real time PCR (within 10 days onset symptoms)</td>
</tr>
<tr>
<td>Clinical Specificity (NPS)</td>
<td>99.5% (95% CI: 97.3 – 99.9%) on samples positive for Real time PCR (within 10 days onset symptoms)</td>
</tr>
</tbody>
</table>

10 Days onset symptoms
**Assay range:** The analyzer directly calculates SARS-CoV-2 viral concentration up to $10^5$ TCID50/mL. Samples containing antigen levels above the assay range may be pre-diluted by the Dilute function of the instrument and retested (the recommended dilution factor is 1:10). The results will then be automatically multiplied by the dilution factor to obtain the antibody levels of the neat specimens. The specimen diluent excess available in the reagent integrals allows up to 10 samples pre-dilutions to be performed.
Inactivation buffer: Why is this needed?

NS and NPS samples can contain live SARS-CoV-2 virus

Instruments that perform automatic pipetting, like most automated Immunology platforms, have the potential to create aerosol particles

Spread of SARS-CoV-2 viral particles through aerosol is well documented.

In order to reduce risk of exposure to live viral particles and increase operator safety, DiaSorin has developed a Sample Inactivation Buffer which decreases the viral load in dry swab and UTM samples.

The use of the inactivation buffer also aids in sample stabilization allowing storage of NS samples for up to 5 days at 2-8°C and of NPS samples in UTM of up to 4 days at 2-8°C. By inactivating the sample at collection site (NS only), it is possible to extend time of transport and optimize sample logistics.
Evaluation 1 Italy

The Greater Romagna Area: organization of *Hub and spoke laboratory model*

<table>
<thead>
<tr>
<th>ROMAGNA: organization of labs</th>
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<tbody>
<tr>
<td><strong>AUSL (Ravenna, Rimini, Forli, Cesena)</strong></td>
</tr>
<tr>
<td>Laboratories on site</td>
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<tr>
<td>Tests performed/year</td>
</tr>
<tr>
<td>Population</td>
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</table>

<table>
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<tr>
<th>Daily Routine in Area Vasta Romagna</th>
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<tbody>
<tr>
<td>N° of Samples Collection Sites</td>
</tr>
<tr>
<td>Out patients</td>
</tr>
<tr>
<td>Access Sites</td>
</tr>
<tr>
<td>In Patients</td>
</tr>
<tr>
<td>Hospitals in Area Vasta Romagna</td>
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COVID-19 7000 swabs/day
Finding
Routine November – December 2020

<table>
<thead>
<tr>
<th></th>
<th>PCR +</th>
<th>PCR -</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ag +</td>
<td>232</td>
<td>28</td>
<td>260</td>
</tr>
<tr>
<td>Ag -</td>
<td>0</td>
<td>13.267</td>
<td>13.267</td>
</tr>
<tr>
<td>Total</td>
<td>232</td>
<td>13.295</td>
<td>13.527</td>
</tr>
</tbody>
</table>

• Screening n = 13,527 individuals tested
• Total positive Ag n=260
• Truth Positive confirmed by PCR n= 232
• Ag False Positive n=28
• Overall Specificity of the Ag test 99.8%
• Increased Frequency of surveillance (from every 45 to 15 days)
Our Assay VALUE Proposition

- **Rapid diagnostic answer** (36 min) in a **high throughput platform** 136 tests/h.
- **STOP COVID-19 transmission** through targeted isolation and cohorting of the most infectious cases and their close contacts.
- **Expand access to testing** and **guarantee traceability**.
- **Identification individuals suspected to have COVID-19** by their healthcare provider within the **first ten days from the onset of symptoms**.
THANK YOU!

Massimo and Gian