DiaSorin-LIAISON® SARS-CoV-2 Antigen Test

Massimo Rosa
Regional Director (Europe/Central Asia and Africa)

Gian Antonio Ginipro
Global Export Application

Verna Ndongeni
sSA Area Manager

Jan 2021

DiaSorin

Agenda

DiaSorin worldwide

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.

With over **50** *years of experience,*

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)

CLIA Systems

LIAISON®XL

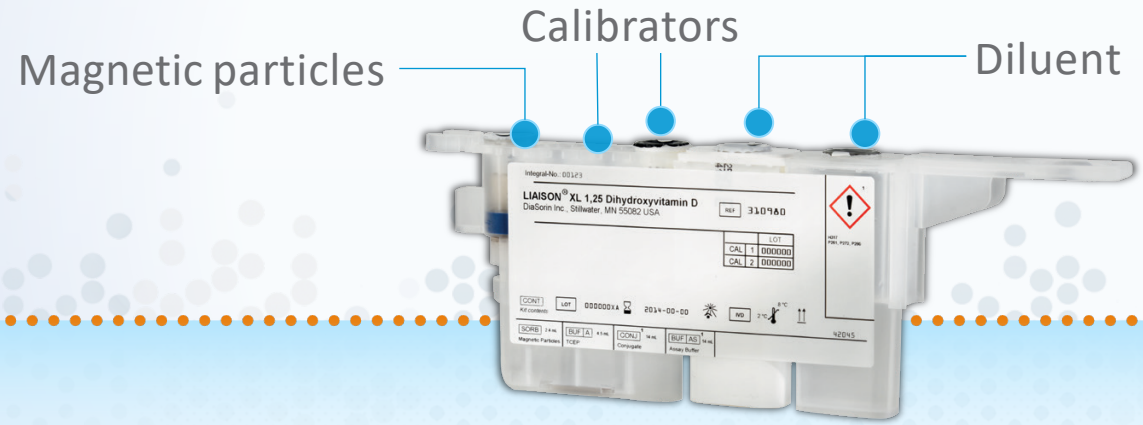
LIAISON®

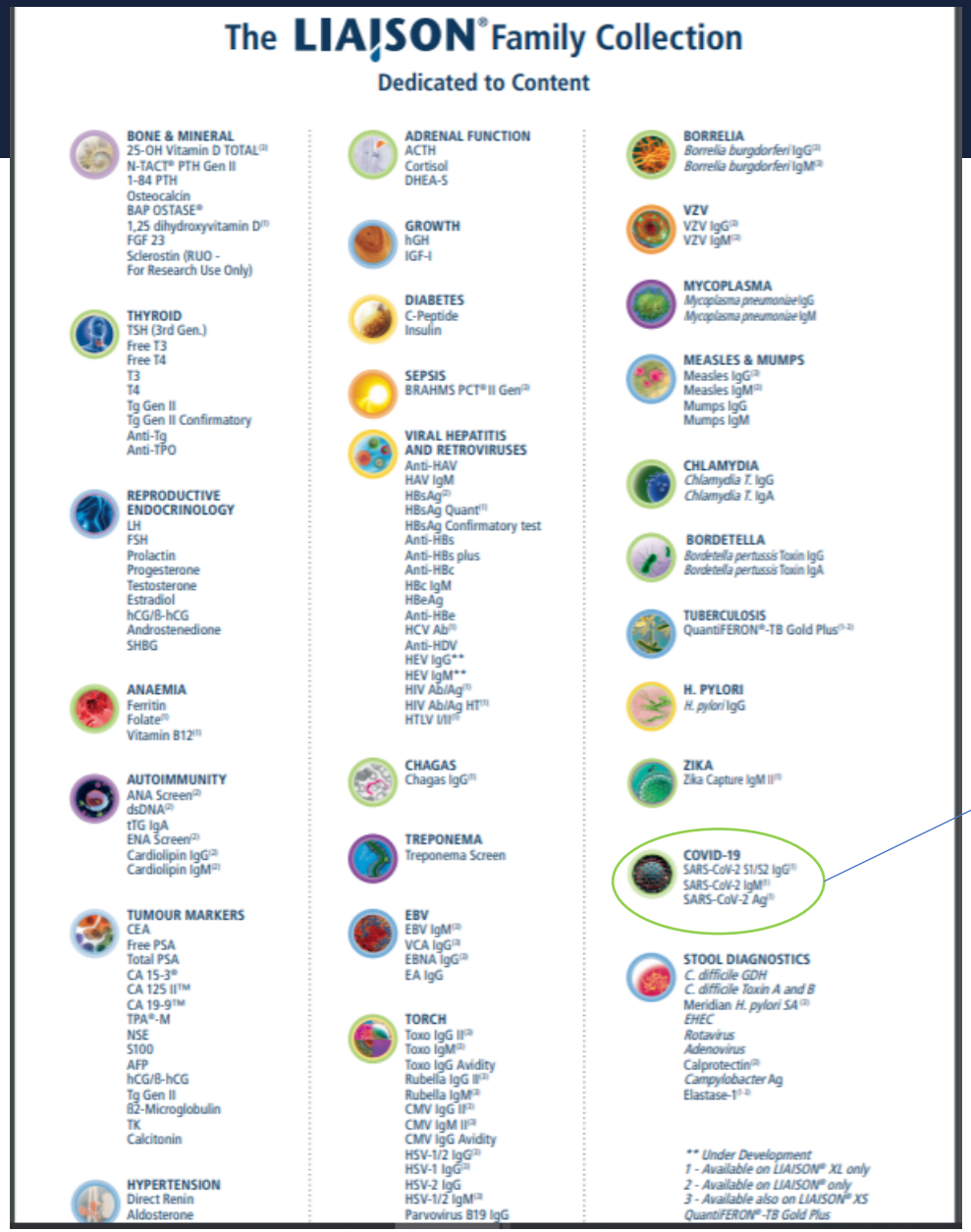
ELISA Systems

ETI-MAX3000

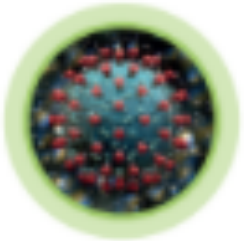
LIAISON family platforms

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





Diasorin CLIA COVID PANEL



COVID-19
SARS-CoV-2 S1/S2 IgG(1)
SARS-CoV-2 IgM(1)
SARS-CoV-2 Ag(1)

SARS – CoV-2 Trimeric IgG (new)

DiaSorin

ANTIGEN TEST

LIAISON® SARS-CoV-2 Ag

DiaSorin

Press Release

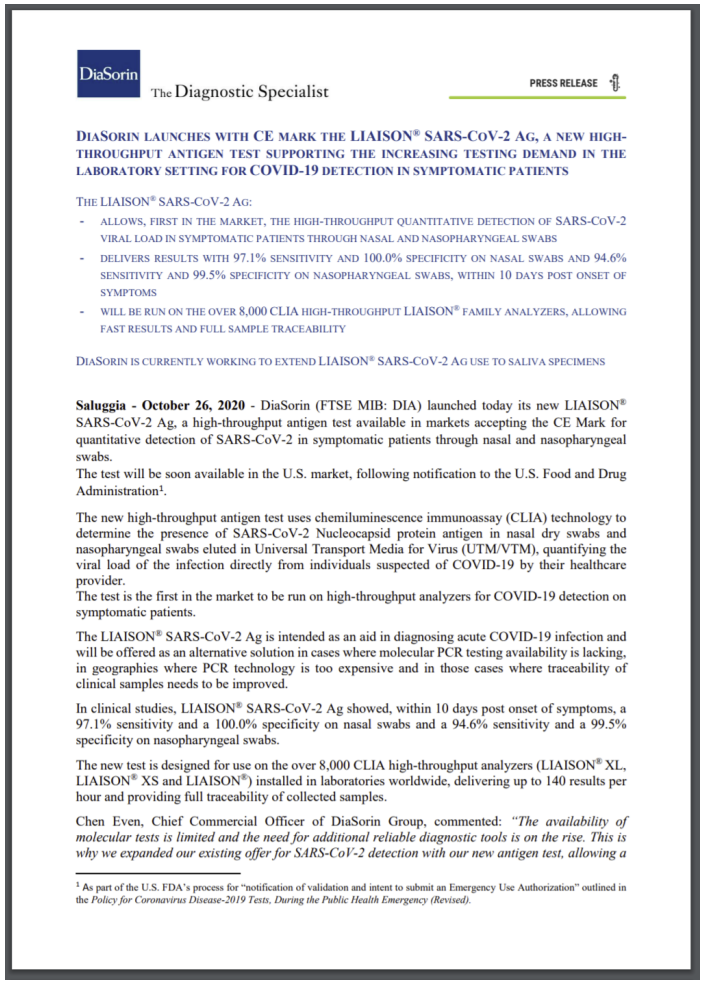
DIASORIN LAUNCHES THE LIAISON®

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.



DiaSorin The Diagnostic Specialist

PRESS RELEASE

DIASORIN LAUNCHES WITH CE MARK THE LIAISON® SARS-COV-2 AG, A NEW HIGH-THROUGHPUT ANTIGEN TEST SUPPORTING THE INCREASING TESTING DEMAND IN THE LABORATORY SETTING FOR COVID-19 DETECTION IN SYMPTOMATIC PATIENTS

THE LIAISON® SARS-COV-2 AG:

- ALLOWS, FIRST IN THE MARKET, THE HIGH-THROUGHPUT QUANTITATIVE DETECTION OF SARS-COV-2 VIRAL LOAD IN SYMPTOMATIC PATIENTS THROUGH NASAL AND NASOPHARYNGEAL SWABS
- DELIVERS RESULTS WITH 97.1% SENSITIVITY AND 100.0% SPECIFICITY ON NASAL SWABS AND 94.6% SENSITIVITY AND 99.5% SPECIFICITY ON NASOPHARYNGEAL SWABS, WITHIN 10 DAYS POST ONSET OF SYMPTOMS
- WILL BE RUN ON THE OVER 8,000 CLIA HIGH-THROUGHPUT LIAISON® FAMILY ANALYZERS, ALLOWING FAST RESULTS AND FULL SAMPLE TRACEABILITY

DIASORIN IS CURRENTLY WORKING TO EXTEND LIAISON® SARS-COV-2 AG USE TO SALIVA SPECIMENS

Saluggia - October 26, 2020 - DiaSorin (FTSE MIB: DIA) launched today its new LIAISON® SARS-CoV-2 Ag, a high-throughput antigen test available in markets accepting the CE Mark for quantitative detection of SARS-CoV-2 in symptomatic patients through nasal and nasopharyngeal swabs.
The test will be soon available in the U.S. market, following notification to the U.S. Food and Drug Administration[1].

The new high-throughput antigen test uses chemiluminescence immunoassay (CLIA) technology to determine the presence of SARS-CoV-2 Nucleocapsid protein antigen in nasal dry swabs and nasopharyngeal swabs eluted in Universal Transport Media for Virus (UTM/VTM), quantifying the viral load of the infection directly from individuals suspected of COVID-19 by their healthcare provider.
The test is the first in the market to be run on high-throughput analyzers for COVID-19 detection on symptomatic patients.

The LIAISON® SARS-CoV-2 Ag is intended as an aid in diagnosing acute COVID-19 infection and will 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.

In clinical studies, LIAISON® SARS-CoV-2 Ag showed, within 10 days post onset of symptoms, a 97.1% sensitivity and a 100.0% specificity on nasal swabs and a 94.6% sensitivity and a 99.5% specificity on nasopharyngeal swabs.

The new test is designed for use on the over 8,000 CLIA high-throughput analyzers (LIAISON® XL, LIAISON® XS and LIAISON®) installed in laboratories worldwide, delivering up to 140 results per hour and providing full traceability of collected samples.

Chen Even, Chief Commercial Officer of DiaSorin Group, commented: *"The availability of molecular tests is limited and the need for additional reliable diagnostic tools is on the rise. This is why we expanded our existing offer for SARS-CoV-2 detection with our new antigen test, allowing a*

[1] As part of the U.S. FDA's process for "notification of validation and intent to submit an Emergency Use Authorization" outlined in the *Policy for Coronavirus Disease-2019 Tests, During the Public Health Emergency (Revised).*

DiaSorin

REMEMBER....Viral Load «Curve»

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Rethinking Covid-19 Test Sensitivity — A Strategy for Containment

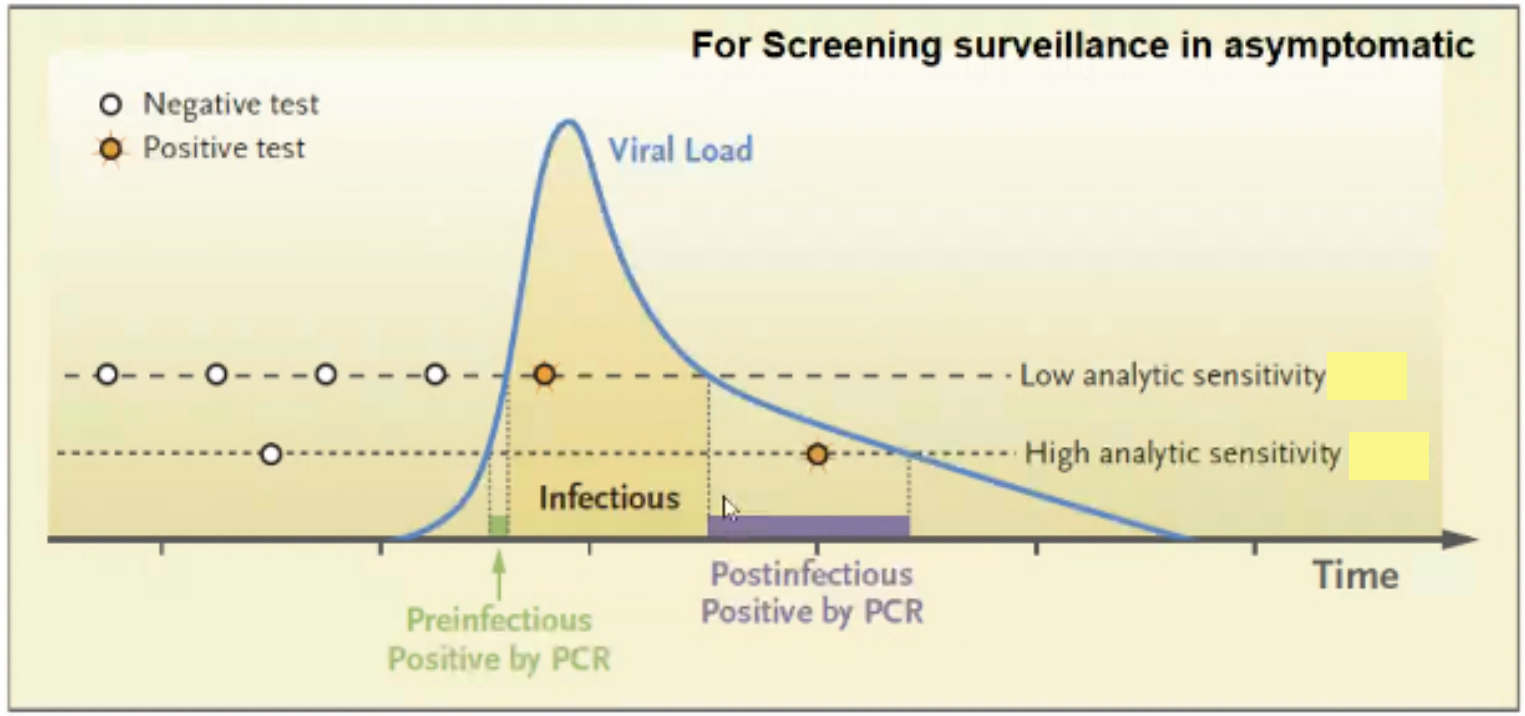
Michael J. Mina, M.D., Ph.D., Roy Parker, Ph.D., and Daniel B. Larremore, Ph.D.

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 assay can detect viral protein or RNA molecules. Critically, this measure neglects the context of how the test is being used. Yet when it comes to the broad screening 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 regimen of regular testing works as a sort of Covid-19 filter, by identifying, isolating, and thus filtering out currently infected persons, 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.[1-3]

Thinking about impact in terms of repeated uses is a familiar concept to clinicians and regulatory agencies; it's invoked every time we measure the efficacy of a treatment regimen rather than a single dose. With Covid-19 cases accelerating or plateauing 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 to others). A point-of-care test that was inexpensive enough to use 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 clinical diagnosis given a single opportunity to test. In contrast, tests used in effective surveillance regimens intended 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 regimens that will capture most infections while they are still infectious.

DiaSorin

WHO Guidelines on Ag tests September 11th

Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays

Interim guidance

11 September 2020

World Health Organization

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 (rRT-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 expensive and faster diagnostic tests that detect antigens specific for SARS-CoV-2 infection. Antigen-detection diagnostic tests are designed to directly detect SARS-CoV-2 proteins produced by replicating virus in respiratory secretions and have been developed as both laboratory-based tests, and for near-patient 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 (1).

This document offers advice on the potential role of antigen-detecting RDTs (Ag-RDT) 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 point of care immunodiagnostics test 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 immunodetection 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 buffer wells, a nitrocellulose matrix strip, with a test line with bound antibody specific for conjugated target antigen-antibody complexes and a control line with bound antibody specific for conjugated-antibody. In the case of SARS-CoV-2 RDTs the target analyte is often the virus' 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 use of a reader standardizes interpretation of test results, reducing variance in assay interpretation by different operators, but requires ancillary equipment. Most of the currently manufactured 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, oral fluid 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 decrease in sensitivity compared to NAAT. Very few of the SARS-CoV-2 Ag-RDTs have undergone stringent regulatory review. Only four tests have received United States Food and Drug Administration (FDA) Emergency Use Authorization (EUA), and another two tests 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 brands being evaluated. They have shown that sensitivity compared to NAAT in samples from upper respiratory tract (nasal or nasopharyngeal swabs) appears to be highly variable, ranging from 0-94% (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 loads (Ct values ≤25 or >10^6 genomic virus copies/mL) which usually appear in the pre-symptomatic (1-3 days before symptom onset) and early symptomatic phases of the

-1-

- Target 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.**

DiaSorin

WHO Guidelines September 11th

To diagnose SARS-CoV-2 infection where NAAT is unavailable

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

USE OF Ag Test

To support outbreak investigations (e.g. in closed or semi-closed groups including schools, care-homes, cruise ships, prisons, work-places and dormitories)

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.

DiaSorin

LIAISON® SARS-CoV-2 Ag in a nutshell

FDA

- 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

DiaSorin

Technical Specification

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

10 Days onset symptoms

DiaSorin

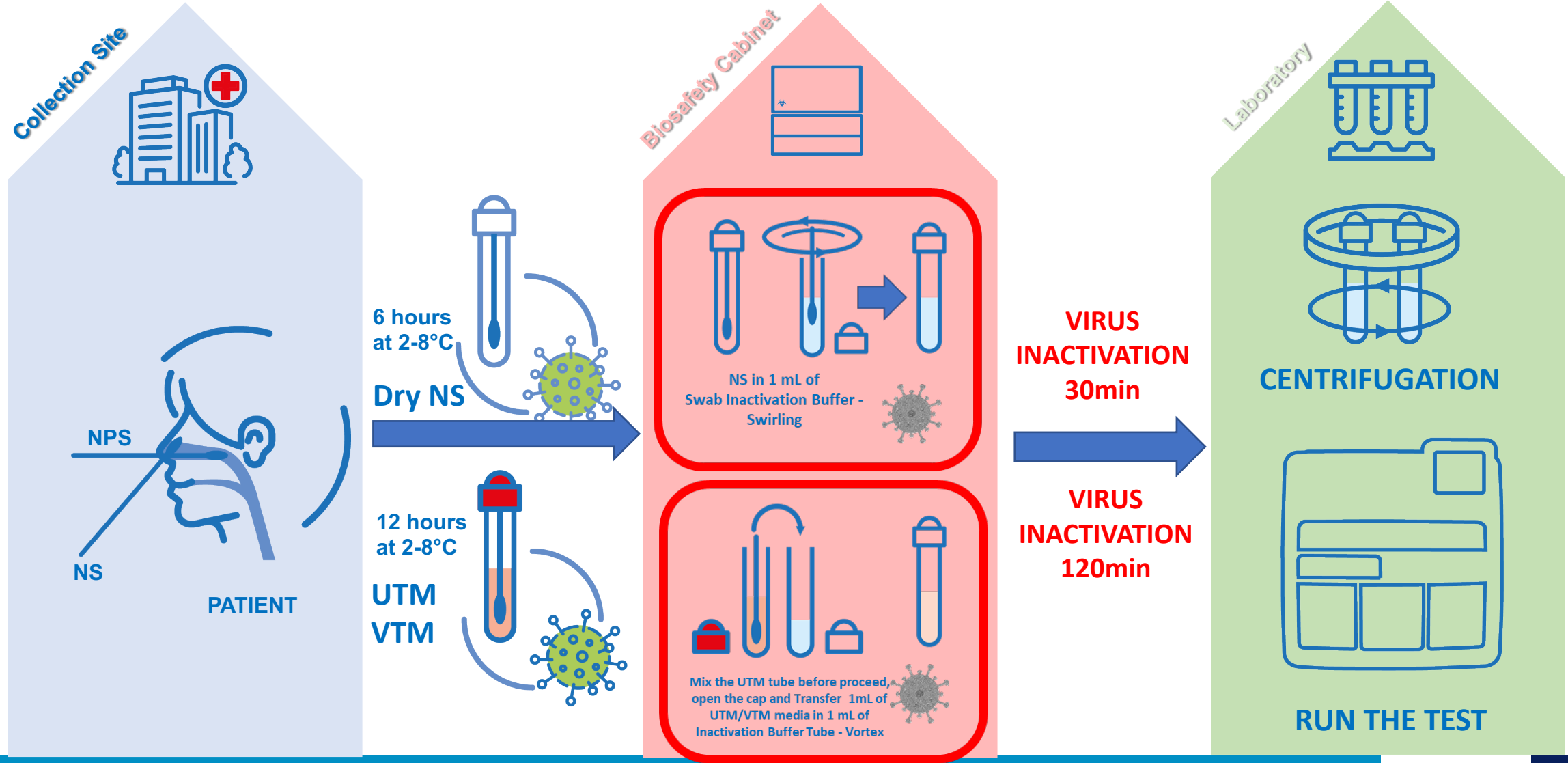
Results Interpretation

LIAISON® SARS-CoV-2 Ag assay		
$TCID_{50}$/mL	**Result**	**Rules and interpretation**
< 100.00	Negative	A result below 100 $TCID_{50}$/mL may indicate the absence of SARS-CoV-2 antigen in the specimen.
100.00 - 199.99	Equivocal	A result ranging between 100 and 199.99 $TCID_{50}$/mL may indicate the presence of SARS-CoV-2 antigen at low titer and should be confirmed with molecular testing.
≥ 200.00	Positive	A result above or equal to 200 $TCID_{50}$/mL generally indicates presence of the SARS-CoV-2 antigen in the specimen.

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.

LIAISON® SARS-CoV-2 Ag

Sample Workflow



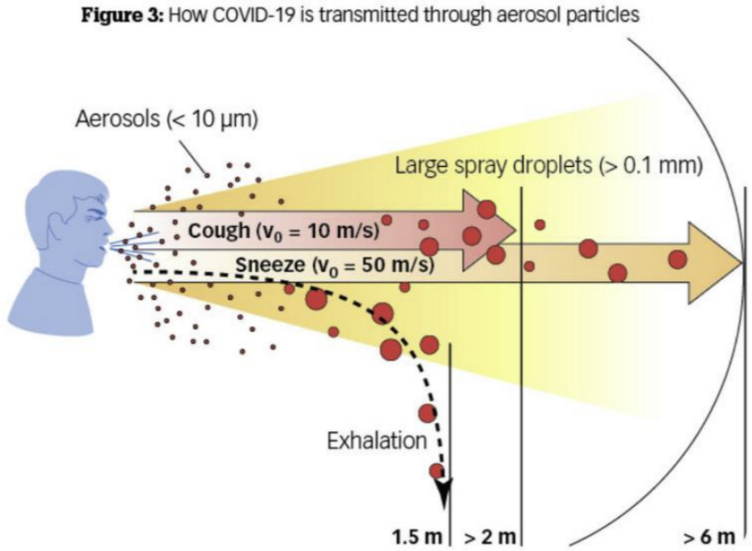
DiaSorin

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.

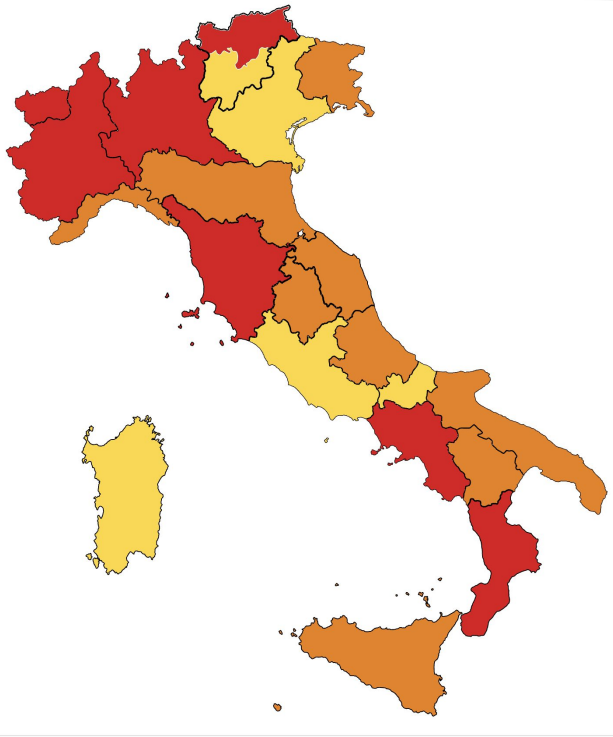


In order to reduce risk of exposure to live viral particles and increase operator safety, DiaSorin has developed a Sample Inactivation Buffer which decreases the viral load in dry swab and UTM samples.

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*



ROMAGNA: organization of labs	
AUSL (Ravenna, Rimini, Forlì, Cesena)	4
Laboratories on site	7
Tests performed/year	21.000.000 /1.050.000 Micro)
Population	1.200.000

Daily Routine in Area Vasta Romagna	
N° of Samples Collection Sites	93
Out patients	4500
Access Sites	400
In Patients	1500
Hospitals in Area Vasta Romagna	15

COVID-19 7000 swabs/day

DiaSorin

Surveillance Routine example

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale della Romagna

Finding
Routine November –December 2020

	PCR +	PCR -	Total
Ag +	232	28	260
Ag -	0	13.267	13.267
Total	232	13.295	13.527

- 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)

Schools

Nursing Home

DiaSorin

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.**

DiaSorin

DiaSorin

THANK YOU!

Massimo and Gian