INSTRUCTIONS FOR USE

CV2Ag

VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack	REF	619 9949
VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator	REF	619 9950

Rx ONLY
For *in vitro* diagnostic and laboratory professional use.

Intended Use

VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack

The VITROS Immunodiagnostic Products SARS-CoV-2 Antigen test is a chemiluminescent immunoassay intended for the qualitative detection of SARS-CoV-2 nucleocapsid antigens in nasopharyngeal (NP) and anterior nasal swab specimens collected in CDC's formulation of VTM, WHO's formulation of VTM, COPAN Universal Transport Media (UTM)®, Hardy R99 VTM, FlexTrans™ Transport Media, saline or phosphate buffered saline (PBS) from individuals who are suspected of COVID-19 by their healthcare provider within seven days of the onset of symptoms using the VITROS 3600 Immunodiagnostic System and the VITROS 5600/XT 7600 Integrated Systems.

Results are for the identification of SARS-CoV-2 nucleocapsid antigen. This antigen is generally detectable in upper respiratory samples during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. The VITROS SARS-CoV-2 Antigen test does not differentiate between SARS-CoV and SARS-CoV-2. Laboratories are required to report all positive results to the appropriate public health authorities. Negative results from patients with symptom onset outside of one to seven days should be treated as presumptive. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19.

VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator

For use in the calibration of the VITROS 3600 Immunodiagnostic System and the VITROS 5600/XT 7600 Integrated Systems for the qualitative detection of the SARS-CoV-2 nucleocapsid antigen.

Summary and Explanation of the Test

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a novel beta coronavirus and is the causative agent of Coronavirus Disease 2019 (COVID-19) and the pandemic. SARS-CoV-2 is mainly transmitted through droplets and contact routes, and people who are infected with SARS-CoV-2 may express signs and symptoms of acute respiratory illness, such as fever, cough, shortness of breath, etc., but can also be asymptomatic.[1-2] The median incubation time is estimated to be 5.1 days with symptoms expected to be present within 12 days of infection.[3] Symptomatic, pre-symptomatic and asymptomatic SARS-CoV-2 carriers all can be potential sources for viral transmission.[4]

Real-time reverse transcription polymerase chain reaction (rRT-PCR) detecting viral genes is the current gold standard for the diagnosis of COVID-19. Upper respiratory specimen, such as nasopharyngeal swab and oropharyngeal swab, are commonly used for diagnostic testing.[2] SARS-CoV-2 produces multiple viral antigens with the nucleocapsid antigens being the most abundant.[5] Immunoassays detect the SARS-CoV-2 nucleocapsid antigen and are also used for the diagnosis of active infection.[6]

Principles of the Procedure

The VITROS Immunodiagnostic Products SARS-CoV-2 Antigen test is performed using the VITROS SARS-CoV-2 Antigen Reagent Pack and the VITROS SARS-CoV-2 Antigen Calibrator on the VITROS 3600 Immunodiagnostic System and the VITROS 5600/XT 7600 Integrated Systems. An immunometric technique is used; this involves a two stage reaction. In the first stage SARS-CoV-2 nucleocapsid antigen present in the sample binds with biotinylated monoclonal anti-SARS-CoV-2 coated on the well. Unbound sample is removed by washing. In the second stage horseradish peroxidase (HRP)-labeled monoclonal anti-SARS-CoV-2 is added in the conjugate reagent. The conjugate binds specifically to any SARS-CoV-2 nucleocapsid captured on the well in the first stage. Unbound conjugate is removed by the subsequent wash step.

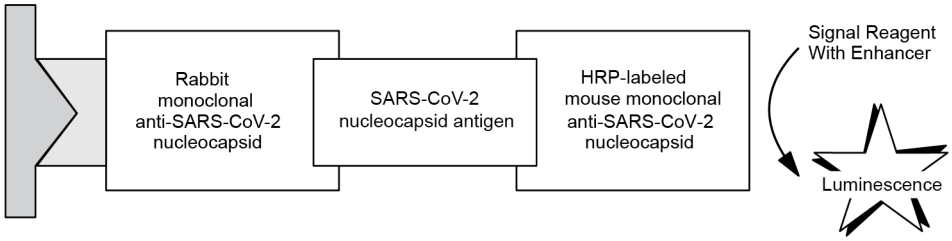
The bound HRP conjugate is measured by a luminescent reaction.[7] A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs its emission. Signal to cutoff numerical values will increase as the amount of SARS-CoV-2 antigen present in the sample increases.

Test Type	System*	Incubation Time	Time to first result	Test Temperature	Reaction Sample Volume
Immunometric	3600, 5600, XT 7600	37 minutes	48 minutes	37 °C	Extracted 80 µL**

* Not all products and systems are available in all countries.

** 80 µL of extracted sample (see Specimen Collection and Preparation)

Reaction Scheme



Warnings and Precautions

WARNING: *Potentially Infectious Material*

Treat as if capable of transmitting infection.

Handle, use, store and dispose of solid and liquid waste from samples and test components, in accordance with procedures defined by appropriate national biohazard safety guideline or regulation (e.g. CLSI document M29).[8]

WARNING: *Contains EDTA (CAS 10378-23-1) and ProClin 300*[9]

The VITROS SARS-CoV-2 Antigen Reagent Pack contains 1.9% EDTA and 1.0% ProClin 300. H317: May cause an allergic skin reaction. H319: Causes serious eye irritation. P280: Wear protective gloves, Eye Protection. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P362 + P364: Take off contaminated clothing and wash before reuse.

WARNING: *Contains 2-methyl-3(2H) isothiazolone (MIT) (CAS 2682-20-4)*[9]

The VITROS SARS-CoV-2 Antigen Calibrator contains 0.0475% 2-methyl-3(2H)isothiazolone (MIT). H317: May cause an allergic skin reaction. P261: Avoid breathing dust/fume/gas/mist/vapors/spray. P272: Contaminated work clothing should not be allowed out of the workplace. P280: Wear protective gloves. P302 + P352: IF ON SKIN: Wash with plenty of water and soap. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P363: Wash contaminated clothing before reuse. P501: Dispose of contents/ container to an approved waste disposal plant.

Refer to www.orthoclinicaldiagnostics.com for the Safety Data Sheets and for Ortho Clinical Diagnostics contact information.

WARNING

Safe Disposal

Follow local disposal regulations based on your location along with recommendations and content in the Safety Data Sheet to determine the safe disposal of this product.

Reagents

Reagent Pack Contents

1 reagent pack containing:

- 100 coated wells (rabbit monoclonal anti-SARS-CoV-2 nucleocapsid, 1.0 µg/mL)
- 6.0 mL assay reagent (buffer with bovine protein stabilizers and antimicrobial agent)
- 16.2 mL conjugate reagent (HRP-mouse monoclonal anti-SARS-CoV-2 nucleocapsid, 2.0 µg/mL) in buffer with protein stabilizers and antimicrobial agent)

Reagent Pack Handling

- The reagent pack is supplied ready for use.
- The reagent pack contains homogeneous liquid reagents that do not require shaking or mixing prior to loading onto the system.
- Handle the reagent pack with care. Avoid the following:
  - allowing condensation to form on the pack
  - causing reagents to foam
  - agitation of the pack

Reagent Pack Storage and Preparation

Reagent	Storage Condition		Stability
Unopened	Refrigerated	2–8 °C (36–46 °F)	expiration date
Opened	On system	System turned on	≤4 weeks
Opened	Refrigerated	2–8 °C (36–46 °F)	≤4 weeks

- The VITROS SARS-CoV-2 Antigen Reagent Pack is suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- Do not freeze reagent packs.
- Load reagent packs directly from refrigerated storage to minimize condensation.
- Opened reagent packs are moisture/humidity sensitive. Store opened refrigerated reagent packs in a sealed VITROS Immunodiagnostic Products Reagent Pack Storage Box with desiccant.

Calibrator Contents

- 2 vials of VITROS SARS-CoV-2 Antigen Calibrator (recombinant SARS-CoV-2 nucleocapsid antigen in buffer with bovine serum albumin and antimicrobial agent, 1.0 mL)
- 8 calibrator bar code labels

Calibrator Handling

- Use only with reagent packs of the same lot number. Mix thoroughly by inversion and bring to 15–30 °C (59–86 °F) before use.
- Handle calibrators in original stoppered containers to avoid contamination and evaporation. To avoid evaporation, limit the amount of time calibrators are on the system. Refer to the operating instructions for your system. Return to 2–8 °C (36–46 °F) as soon as possible after use, or load only sufficient volume for a single determination.

Calibrator Storage and Preparation

Calibrator	Storage Condition		Stability
Unopened	Frozen	≤-20 °C (≤-4 °F)	expiration date
Opened	Refrigerated	2–8 °C (36–46 °F)	≤24 hours
Opened	Ambient	15–30 °C (59–86 °F)	≤4 hours

- VITROS SARS-CoV-2 Antigen Calibrator is supplied frozen. DO NOT REFREEZE.
- The VITROS SARS-CoV-2 Antigen Calibrator is suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- The VITROS SARS-CoV-2 Antigen test uses 80 µL of calibrator for each determination. Transfer an aliquot of each calibrator into a sample container (taking account of the minimum fill volume of the container). For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.

Caution:	**Do not add extraction buffer to calibrator.**

- The VITROS SARS-CoV-2 Antigen Calibrator is automatically processed in duplicate.

Specimen Collection, Preparation and Storage

Patient Preparation

No special patient preparation is necessary.

Specimens Recommended

- Nasopharyngeal and anterior nasal swab specimens, collected from symptomatic individuals, stored in transport media

Special Precautions

IMPORTANT:	*Certain transport media have been reported to affect other analytes and tests.* [10] *Owing to the variety of transport media available, Ortho Clinical Diagnostics is unable to provide a definitive statement on the performance of its products with these solutions. Confirm that your transport media are compatible with this test.*

Specimen Collection and Preparation

- Collect specimens using standard procedures for respiratory specimens. [10]
- Follow the instructions provided with your transport media for use and processing of the sample. [10]
- The VITROS SARS-CoV-2 Antigen test uses 80 µL of extracted sample for each determination. This is in addition to the minimum fill volume of the chosen sample container. For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.
- Sample Preparation and Testing:

1. Prepare Sample for Extraction
   - Receive sample swab in transport media.
   - Mix transport tube well (e.g., vortex approx. 3-5 seconds).
2. Add Extraction Buffer to Sample
   - Transfer 100 µL VITROS SARS-CoV-2 Antigen Extraction Buffer into a labeled new sample tube.
   - Add 400 µL viral sample into the same sample tube.
   - Mix well (e.g. cover sample container with cap/plug and vortex approx. 3-5 seconds).

IMPORTANT:	*Care should be taken on opening sample tubes prior to the addition of the extraction buffer as the sample should be considered potentially infectious.*

3. Load to Instrument
   - Load and process samples in the same manner as other testing on your VITROS System.
   - Refer to the operating instructions for your system.

Note:	An alternate sample volume may be used if desired, using 4 parts media to1 part VITROS SARS-CoV-2 Antigen Extraction Buffer. It is recommended to have a minimum of 250 µL of sample/extraction buffer loaded on the VITROS system. If programming samples on the system manually, process samples by selecting the CV2Ag test button on system.

Handling and Storage Conditions

Extraction	Storage Condition	Stability
Pre- or Post-	Room Temperature (up to 30 °C [86 °F])	24 hours
Pre- or Post-	Refrigerated 2–8 °C (36–46 °F)	48 hours

- Handle samples in stoppered containers to avoid contamination and evaporation.
- Follow procedures within your laboratory to avoid cross contamination of patient specimens.
- The amount of time samples are on the system prior to analysis should be limited to avoid evaporation. Refer to the operating instructions for your system.
- Return unused sample (pre- or post-extraction) to 2–8 °C (36–46 °F) as soon as possible after use or load sufficient volume for a single determination.
- Samples (pre- or post-extraction) that will not be tested within the time frames outlined above should be stored at ≤-20 °C [≤-4 °F] and may be subjected to 5 freeze-thaw cycles.
- As an alternative to the above, sample stability may be established by each laboratory.

Testing Procedure

Materials Provided

- VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack
- VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator

Materials Required but Not Provided

- VITROS Immunodiagnostic Products Signal Reagent
- VITROS Immunodiagnostic Products Universal Wash Reagent
- Quality control materials such as VITROS Immunodiagnostic Products VITROS SARS-CoV-2 Antigen Controls
- VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Extraction Buffer
- VITROS Immunodiagnostic Products Reagent Pack Storage Box (optional) with desiccant
- Appropriate volume pipette and sample containers for extraction

Operating Instructions

Check the inventory regularly to aid the management of reagents and ensure that sufficient VITROS Signal Reagent, VITROS Universal Wash Reagent and calibrated reagent lots are available for the work planned. When performing panels of tests on a single sample, ensure that the sample volume is sufficient for the tests ordered.
For detailed information refer to the operating instructions for your system.

Note: Do not use visibly damaged product.

Default Test Name

The default test name which will appear on patient reports is SARS-CoV-2 Ag. The default short name that will appear on the test selection menus and laboratory reports is CV2Ag. These defaults may be reconfigured, if required. For detailed information refer to the operating instructions for your system.

Calibration

Calibration Procedure

- Calibration is lot specific; reagent packs and calibrator are linked by lot number. Reagent packs from the same lot may use the same calibration.
- A Master Calibration is established for each new reagent lot by performing multiple tests. This is the process by which a lot-specific parameter [a] which links the signal at the cutoff (cutoff value) to the calibrator signal is determined.
- Cutoff value = (a x Signal of Cal 1)
- Ensure that the Master Calibration for each new reagent lot is available on your system.
- Load sufficient for the automatic duplicate determination. Calibration need not be programmed if bar code labels are used; calibration will be initiated automatically.
- When the calibrator is processed, the validity of the calibration is assessed against quality parameters which compare the actual signal of the calibrator with the expected signal. If the calibration is acceptable the cutoff value is calculated and stored for use with any reagent pack of that lot.

- The quality of calibration cannot be completely described by a single parameter. The calibration report should be used in conjunction with acceptable control values to determine the validity of the calibration.
- Recalibration is required after a pre-determined calibration interval, or when a different reagent lot is loaded.
- Calibration results are assessed against a range of quality parameters. Failure to meet any of the defined quality parameter ranges will be coded in the calibration report. For actions to be taken following a failed calibration refer to the operating instructions for your system.
- Refer to the operating instructions for your system for detailed instructions on the calibration process.

When to Calibrate

- Calibrate when the reagent pack and calibrator lot changes.
- Calibrate every 28 days.
- After specified service procedures have been performed.
- If quality control results are consistently outside of your acceptable range.

For additional information on when to calibrate, refer to the operating instructions for your system.

Traceability of Calibration

Calibration of the VITROS SARS-CoV-2 Antigen test is traceable to an in-house reference calibrator which has been value assigned to optimize clinical sensitivity and specificity.

Calibration Model

Results are calculated as a normalized signal, relative to a cutoff value. During the calibration process a lot-specific parameter is used to determine a valid stored cutoff value for the VITROS Immunodiagnostic and VITROS Integrated Systems.

Quality Control

Quality Control Material Selection

VITROS SARS-CoV-2 Antigen Controls are recommended for use with the VITROS Immunodiagnostic and VITROS Integrated Systems. There are 2 VITROS SARS-CoV-2 Antigen Controls (SARS-CoV-2 Ag negative and SARS-CoV-2 Ag positive).

Appropriate quality control value ranges must be established for all quality control materials used with the VITROS SARS-CoV-2 Antigen test.

Quality Control Procedure Recommendations

- Good laboratory practice requires that controls be processed to verify the performance of the test.
- To verify system performance, analyze control materials:
  - After calibration
  - If the system is turned off for more than 2 hours
  - After reloading reagent packs that have been removed from the MicroWell Supply and stored for later use
  - According to local regulations or at least once each day that the test is being performed
  - After specified service procedures are performed

If quality control procedures within your laboratory require more frequent use of controls, follow those procedures.

- Analyze quality control materials in the same manner as patient specimens.
- If control results fall outside your acceptable range, investigate the cause before deciding whether to report patient results.
- Refer to published guidelines for general quality control recommendations. [11]

For more detailed information, refer to the operating instructions for your system.

Quality Control Material Preparation and Storage

Refer to the manufacturer’s product literature for preparation, storage, and stability information.

Results

Results are automatically calculated by the VITROS Immunodiagnostic and VITROS Integrated Systems.

Result Calculation

$$\text{Result} = \frac{\text{Signal for test sample}}{\text{Signal at Cutoff (Cutoff value)}}$$

Interpretation of Results

Sample results will be displayed with a numerical signal to cutoff (S/C) value and a “Non-reactive" (negative) or “Reactive" (positive) label.

Result (S/C)	<1.00	≥1.00
Result Text	Non-reactive (negative)	Reactive (positive)

Signal to cutoff numerical values will increase as the amount of SARS-CoV-2 antigen present in the sample increases.

Limitations of the Procedure

Known Interferences

The VITROS SARS-CoV-2 Antigen test was evaluated for interference. Commonly encountered substances were tested on one lot of reagent. Of the compounds tested, none was found to interfere with the clinical interpretation of the test. SARS-CoV was not tested using the VITROS assay however it does cross-react in the VITROS SARS-CoV-2 Antigen assay. Refer to “Substances that do not Interfere” for a list of compounds tested that did not show interference.

Other Limitations

- The contents of this kit are to be used for the qualitative detection of SARS-CoV-2 antigens from nasopharyngeal or anterior nasal swab specimens only.
- A negative test result may occur if the level of antigen in a sample is below the detection limit of the test.
- Positive test results do not rule out co-infections with other pathogens.
- Positive test results do not differentiate between SARS-CoV and SARS-CoV-2.
- Negative test results are not intended to rule in other non-SARS viral or bacterial infections.
- If the differentiation of specific SARS viruses and strains is needed, additional testing, in consultation with local public health departments, is required.
- A false-negative test result may occur if the level of viral antigen in a sample is below the detection limit of the test or if the sample was collected or transported improperly; therefore, a negative test result does not eliminate the possibility of SARS-CoV-2 infection.
- The VITROS SARS-CoV-2 Antigen test can detect both viable and non-viable SARS-CoV-2 material. The VITROS SARS-CoV-2 Antigen test performance depends on antigen load and may not correlate with other diagnostic methods performed on the same specimen.
- Use in conjunction with the testing strategy outlined by public health authorities in your area.
- The performance of this device has not been assessed in a population vaccinated against COVID-19.
- Device performance has not been assessed on specimens containing emerging variants of SARS-CoV-2 that are a public health concern.

Performance Characteristics

Limit of Detection

The Limit of Detection (LoD) is defined as the lowest virus concentration at which a minimum of 19 replicates out of 20 generate a Reactive result. Testing was performed across seven transport media types and the resulting LoD ranged from 25 $TCID_{50}$ per swab to 151 $TCID_{50}$ per swab.

LoD Determinations

Transport Medium	$TCID_{50}$ per swab
CDC Viral Transport Medium	25
NewProv Viral Transport Medium	38
COPAN Universal Transport Medium	25
Hardy Viral Transport Medium	38
Bartels FlexTrans™ Transport medium	151
WHO Viral Transport Medium	38
Saline (PBS and 0.9% NaCl)	76

Clinical Performance Characteristics - Nasopharyngeal Specimens

Clinical performance characteristics of the VITROS SARS-CoV-2 Antigen test was evaluated using residual samples from patients suspected of having contracted the SARS-CoV-2 virus within seven days of symptom onset. Nasopharyngeal samples were stored frozen between the time of collection and the time of testing. PCR positive patients in this study had samples collected up to seven days after reporting symptoms. FDA Emergency Use Authorized high sensitivity real-time Polymerase Chain Reaction (RT-PCR) assays for the detection of SARS-CoV-2 were utilized as the comparator methods for this study.

Testing was performed by operators who were blinded to the RT-PCR test result. External control testing, using VITROS SARS-CoV-2 Antigen Controls was performed on each day of VITROS testing.

The performance of VITROS SARS-CoV-2 Antigen test was established with 240 nasopharyngeal specimens collected from individual symptomatic patients (between 1 and 7 days of onset) who were suspected of COVID-19.

VITROS SARS-CoV-2 Antigen Performance in RT-PCR Positive Samples Collected within 7 Days of Symptom Onset Against the Comparator Method

VITROS SARS-CoV-2 Antigen Test	RT-PCR Comparator Method		
	Detected	Not Detected	Total
Reactive	100	2	102
Non-reactive	14	124	138
Total	114	126	240
Positive Percent Agreement: 87.7% (95% CI: 80.3–93.1%)			
Negative Percent Agreement: 98.4% (95% CI: 94.4–99.8%)			

Positive results broken down by days since symptom onset.

Days Since Symptom Onset	Cumulative PCR Positive (+)	Cumulative VITROS Reactive (+)	PPA
0	8	5	62.5%
1	16	13	81.3%
2	30	26	86.7%
3	50	43	86.0%
4	61	53	86.9%
5	97	85	87.6%
6	110	97	88.2%
7	114	100	87.7%

Clinical Performance Characteristics - Anterior Nasal Specimens

Clinical performance characteristics of the VITROS SARS-CoV-2 Antigen test was evaluated using residual samples from patients suspected of having contracted the SARS-CoV-2 virus within seven days of symptom onset. Nasal samples were stored frozen between the time of collection and the time of testing. FDA Emergency Use Authorized high sensitivity real-time Polymerase Chain Reaction (RT-PCR) assays for the detection of SARS-CoV-2 were utilized as the comparator methods for this study.

Testing was performed by operators who were blinded to the RT-PCR test result. External control testing, using VITROS SARS-CoV-2 Antigen Controls was performed on each day of VITROS testing.

The performance below of VITROS SARS-CoV-2 Antigen test was established with 152 nasal specimens collected from individual symptomatic patients (within 7 days of onset) who were suspected of COVID-19 and compared to RT-PCR on a paired anterior nasal swab. Performance compared to a paired RT-PCR on an NP swab is presented in the table below.

VITROS SARS-CoV-2 Antigen Performance in RT-PCR Positive Samples Collected Within 7 Days of Symptom Onset Against the Comparator Method

VITROS SARS-CoV-2 Antigen Test	RT-PCR Comparator Method		
	Detected	Not Detected	Total
Reactive	49	0	49
Non-reactive	10*	93	103
Total	59	93	152
Positive Percent Agreement: 83.1% (95% CI: 71.0–91.6%)			
Negative Percent Agreement: 100.0% (95% CI: 96.1–100.0%)			

* Two non-reactive results were also negative on an alternate RT-PCR method.

Positive results broken down by days since symptom onset.

Days Since Symptom Onset	Cumulative PCR Positive (+)	Cumulative VITROS Reactive (+)	PPA
0	2	1	50.0%
1	8	7	87.5%
2	18	17	94.4%
3	31	29	93.5%
4	35	32	91.4%
5	49	42	85.7%
6	57	47	82.5%
7	59	49	83.1%

Potentially Cross-reacting Subgroups

The VITROS SARS-CoV-2 Antigen test was evaluated for potential microbial cross-reactivity and interference using contrived samples in the absence and presence of SARS-CoV-2. Potentially cross-reactive organisms were spiked into solution at concentrations of greater than or equal to 10^6 CFU/mL for bacteria and greater than or equal to 10^5 pfu/mL for viruses. The results are summarized in the table below.

Sample Category	Non-Reactive Sample	Spiked Reactive Sample	Cross-Reactivity (Y/N)
Human coronavirus 229E	Non-Reactive	Reactive	N
Human coronavirus OC43	Non-Reactive	Reactive	N
Human coronavirus NL63	Non-Reactive	Reactive	N
Influenza A	Non-Reactive	Reactive	N
Influenza B	Non-Reactive	Reactive	N
Adenovirus (e.g., C1 Ad. 71)	Non-Reactive	Reactive	N
Human Metapneumovirus (hMPV)	Non-Reactive	Reactive	N
Parainfluenza virus 1-4	Non-Reactive	Reactive	N
Enterovirus	Non-Reactive	Reactive	N
Respiratory syncytial virus	Non-Reactive	Reactive	N
Rhinovirus	Non-Reactive	Reactive	N
Hemophilus influenzae	Non-Reactive	Reactive	N
Streptococcus pneumoniae	Non-Reactive	Reactive	N
Streptococcus pyogenes	Non-Reactive	Reactive	N
Candida albicans	Non-Reactive	Reactive	N
Bordetella pertussis	Non-Reactive	Reactive	N
Mycoplasma pneumoniae	Non-Reactive	Reactive	N
Legionella pneumophila	Non-Reactive	Reactive	N
MERS-coronavirus	Non-Reactive	Reactive	N
Chlamydophila pneumoniae	Non-Reactive	Reactive	N
Staphylococcus epidermidis	Non-Reactive	Reactive	N
Staphylococcus aureus	Non-Reactive	Reactive	N

To estimate the likelihood of cross-reactivity with SARS-CoV-2 virus in the presence of organisms that were not available for wet testing, *In silico* analysis using the Basic Local Alignment Search Tool (BLAST) managed by the National Center for Biotechnology Information (NCBI) was used to assess the degree of protein sequence homology.

- No protein sequence homology was found between M. tuberculosis, *P. jirovecii* or HCov-HKU1 thus cross-reactivity can be ruled out.
- The comparison between SARS-CoV-2 nucleocapsid protein and SARS-CoV-1 shows homology of 90.52% and suggests that there may be significant cross reactivity in this test.

Specificity

Substances that do not Interfere

The VITROS SARS-CoV-2 Antigen test was evaluated for interference. Of the compounds tested, none was found to interfere with the clinical interpretation of the test in Non-reactive and weakly Reactive samples at the concentrations indicated.

Interfering Substance	Active Ingredient	Concentration
Human Blood	Blood	4%
Hemoglobin	Hemolysate	1000 mg/dL
Biotin	Biotin	3510 ng/dL
Purified mucin protein	Mucin protein	5.0 mg/mL (0.5%)
OTC Nasal Spray 1	Oxymetazoline	15%
OTC Nasal Spray 2	Fluticasone	5%
OTC Nasal Spray 3	Triamcinolone	5%
OTC Nasal Spray 4	Phenylephrine hydrochloride	15%
OTC Nasal Spray 5	Budesonide (Glucocorticoid)	5%
OTC Nasal Spray 6	Saline	15%
OTC Nasal Spray 7	Cromolyn	15%
OTC Nasal Wash	Alkolol	10%
OTC Nasal Gel	Sodium Chloride (NeilMed)	5%
Sore Throat Spray	Benzocaine, Menthol, Phenol	0.7 g/mL (70%)
Throat Lozenge	Menthol	0.8 g/mL (80%)
Anti-viral Drug 1	Oseltamivir	5.0 µg/mL
Anti-viral Drug 2	Zanamivir	282.0 ng/mL
Anti-bacterial, Systemic	Tobramycin	1.25 mg/mL
Hemeopathic Cold Remedy	Galphimia glauca, Luffa operculata, Sabadilla	5%
Antibacterial	Mupirocin	10 mg/mL

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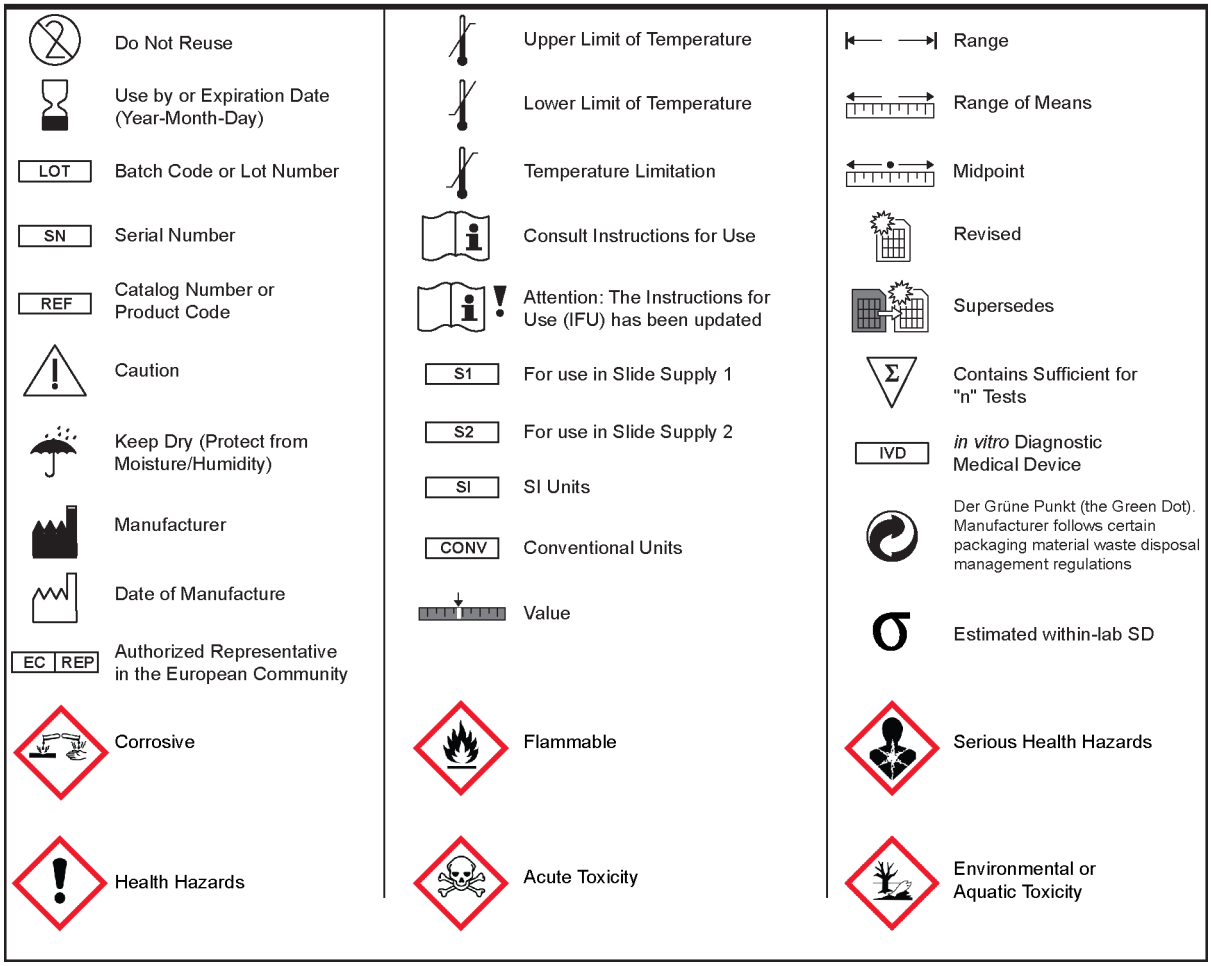
10. Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19. (https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html)
11. CLSI. *Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline - Fourth Edition*. CLSI guideline C24, Wayne, PA: Clinical and Laboratory Standards Institute; 2016.
12. https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html

Glossary of Symbols

The following symbols may have been used in the labeling of this product.



Revision History

Date of Revision	Version	Description of Technical Changes*
2022-03-31	2.0	• Intended Use: – Added nasal specimens and additional VTMs – Changed symptom onset to seven days • Warnings and Precautions: Updated Precaution statements to align with the Safety Data Sheets • Calibrator Storage Section: Added storage for ambient temperature ≤4 hours • Specimens Recommended: Added anterior nasal specimen • Specimens Not Recommended: Removed section • Special Precautions: Updated Important statement • Other Limitations: Added 'or anterior nasal' • Limit of Detection: Updated LoD range and added VTMs to LoD table • Clinical Performance Characteristics – Nasopharyngeal Specimens: – Updated data to 240 specimens, 7 day onset – Removed information regarding cycle threshold (Ct) • Clinical Performance Characteristics – Anterior Nasal Specimens – Added new anteriror nasal specimens – Updated the table header • Specificity: – Corrected typographical error for concentration of Purified mucin protein from 5% to 0.5% – Corrected typographical error for concentration of OTC Nasal Spray 4 from 5% to 15%

* The change bars indicate the position of a technical amendment to the text with respect to the previous version of the document.

When this Instructions For Use is replaced, sign and date below and retain as specified by local regulations or laboratory policies, as appropriate.

Signature

Obsolete Date

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