lumiraDx™ SARS-CoV-2 Ag Ultra Pool

For Professional Use Only
For *In Vitro* Diagnostic Use Only **IVD**

SPEC-35986 R1 ART-02764 R1 Date of Rev 2022/07

Product Name	Product Description	REF	Σ
LumiraDx SARS-CoV-2 Ag Ultra Pool	EN, FR,DE,IT,NL,ES Test Strips	L016000701048	48
LumiraDx SARS-CoV-2 Ag Ultra Pool	EN/NO/FI/DA/SE Test Strips	L016000702048	48
LumiraDx SARS-CoV-2 Ag Ultra Pool	EN/ES/PT-EU/PT-BR Test Strips	L016000704048	48
LumiraDx SARS-CoV-2 Ag Ultra Pool	EN/TR/GR/FR/Arabic Test Strips	L016000705048	48
LumiraDx SARS-CoV-2 Ag Ultra Pool	EN/ID/VN/KR/TH Test Strips	L016000706048	48
LumiraDx SARS-CoV-2 Ag Ultra Pool	EN/CZ/RO/PL/HU/BG Test Strips	L016000708048	48

ENGLISH

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The LumiraDx Severe Acute Respiratory Syndrome (SARS) CoV-2 Antigen (Ag) Ultra Pool test strips (hereafter referred to as Test Strips) are to be used with the LumiraDx Platform. The LumiraDx Platform is a point of care system for professional use which is used for *in vitro* diagnostic tests. It comprises a portable LumiraDx Instrument and a LumiraDx Test Strip for the required test. This test is for **HEALTHCARE PROFESSIONAL USE ONLY** and allows users to perform tests using small sample volumes and to view results quickly on the Instrument touchscreen.

Intended use:

The LumiraDx SARS-CoV-2 Ag Ultra Pool test is an automated rapid microfluidic immunofluorescence assay for use with the LumiraDx Platform intended for the qualitative detection of the nucleocapsid protein antigen to SARS-CoV-2 in 1 to 5 individual samples from professionally supervised & self-collected nasal swab samples or professionally collected nasal samples which are then pooled for testing. Samples should be collected from 1 to 5 individuals suspected of COVID-19 infection within the first twelve days of symptom onset or from asymptomatic individuals.

Positive results indicate the presence of viral antigens from infective virus in one of the pooled samples, but clinical correlation with each individual's history and other diagnostic information is necessary to confirm infection status. If the pool is positive, then each individual should be re-tested as a separate and newly collected individual sample before reporting a result.

Negative results do not rule out SARS-CoV-2 infection and should be considered in the context of an individual's recent exposures, history and presence of clinical signs and symptoms consistent with COVID-19.

Results should not be used as the sole basis for treatment or case management decisions, including infection control decisions.

The LumiraDx SARS-CoV-2 Ag Ultra Pool test is intended for use by individuals trained in point of care settings and proficient in performing tests using the LumiraDx Platform.

Caution: For *in vitro* diagnostic use.

Before you start testing, if you are new to the LumiraDx Instrument and LumiraDx Platform, you must read the LumiraDx Platform User Manual and this entire Product Insert. In addition, please watch the LumiraDx Platform Training Video available at lumiradx.com

Summary and explanation of the Test:

The World Health Organization (WHO) have named the disease caused by SARS-CoV-2 virus as coronavirus 2019 or COVID-19[1]. The most common symptoms of COVID-19 are fever, tiredness, and dry cough. Some patients may have aches and pains, nasal congestion, headache, conjunctivitis, sore throat, diarrhoea, loss of taste or smell, or a rash on skin or discoloration of fingers or toes. These symptoms are usually mild and begin gradually. Some people become infected but do not develop any symptoms and do not feel unwell. However, the disease can develop rapidly and have high morbidity in certain populations, especially those with underlying health conditions. The disease can spread from person to person through small droplets from the nose or mouth which are spread when a person with COVID-19 coughs or exhales. Most estimates of the incubation period for COVID-19 range from 2-14 days[2].

The use of a LumiraDx SARS-CoV-2 Ag Ultra Pool test will enable the physician to verify infection quickly among a pool of 1 to 5 patients, begin proper treatment and initiate isolation precautions helping prevent further spread of infection.

Principle of the assay:

The LumiraDx SARS-CoV-2 Ag Ultra Pool test is a fluorescence immunoassay device designed to detect the presence of the nucleocapsid protein antigen from SARS-CoV-2 in nasal swab samples. The Test Strip is single use.

The LumiraDx SARS-CoV-2 Ag Ultra Pool test is performed by taking nasal swab samples from up to five individuals and combining into one pool by eluting each individual sample sequentially into a single vial containing extraction buffer. One drop of this sample is then added to the sample port at the bottom of the test strip. The LumiraDx Instrument is programmed to perform the Pooled Test Protocol when the specimen has reacted with the reagents. The analysis is based on the amount of fluorescence the Instrument detects within the measurement area of the test strip. The concentration of the analyte in the specimen is directly proportional to the fluorescence detected. The results are displayed on the Instrument touchscreen within 5 minutes from the addition of the pooled sample. If the pool is positive, then each individual should be re-tested as a separate and newly collected individual sample. If the pool is negative, then each constituent sample is reported as negative.

Materials provided:

- LumiraDx Test Strips packed individually in sealed desiccant foil pouches.
- LumiraDx Test Product Insert
- RFID (Radio frequency ID) Tag held inside the Test Strip carton
- Extraction Buffer Vials
- Dropper Lids

Materials required but not provided:

- LumiraDx Instrument
- LumiraDx SARS-CoV-2 Ag Ultra Pool Quick Reference Instructions
- LumiraDx SARS-CoV-2 Ag Quality Controls (as required to meet local and organisational compliance)
- LumiraDx Connect if connectivity required (refer to LumiraDx Connect User Manual)
- Standard nasal swab collection equipment. Please visit lumiradx.com for information on validated swabs for use with the LumiraDx SARS-CoV-2 Ag Ultra Pool test.

Warnings and precautions:

- For *in vitro* diagnostic use only
- Do not open the Test Strip until ready for immediate use.
- Discard and do not use any damaged or dropped Test Strips or other materials.
- To avoid sample contamination avoid touching the swab sampling head before and after sample collection.
- The Test cannot be visually interpreted; the LumiraDx Instrument must be used to generate results.
- Do not use the kit components beyond the expiration date
- Do not reuse any kit components.
- Samples must be processed as indicated in the Sample Extraction and Performing a Test sections of this Product Insert. Failure to follow the instructions for use can result in inaccurate results.
- All components of this kit should be discarded as biohazard waste according to local regulations and procedures.
- Exercise the normal precautions required for handling all laboratory reagents. Wear protective clothing such as laboratory coats, disposable gloves, and eye protection when samples are collected and evaluated.
- Proper laboratory safety techniques should be followed at all times when working with SARS-CoV-2 patient samples. Patient swabs, used Test Strips, and used Extraction Buffer vials may be potentially infectious. Proper handling and disposal methods should be established by the laboratory in accordance with local regulations and procedures.
- For additional information on safety, handling, and disposal of the components within this kit, please refer to the Safety Data Sheet (SDS) located at lumiraDx.com

Storing the Test Kit:

Store the Test Strips in their original carton. You can store the Test Strips at a temperature between 2°C and 30°C (36°F and 86°F). Avoid freezing or storing in any area that could exceed 30°C. When stored properly, the Test Strips can be used until the expiration date printed on the Test Strip foil pouch and the Test Strip carton. Discard the Test Strips if they are passed the expiration date.

Handling the Test Strips:

When you are ready to perform a test, open the Test Strip carton, take out a Test Strip, and remove it from the foil pouch. Hold the Test Strip by gripping the blue label end with the label facing upward. Do not touch Test Strip Sample Application Area. Do not bend or fold the Test Strip. Do not touch Test Strip contacts. After removing the Test Strip from the foil pouch, it should be used immediately. Do not use the Test Strip if there are any visible signs of damage to the foil pouch such as tears or holes.

Sample material:

The following samples can be used with the LumiraDx SARS-CoV-2 Ag Ultra Pool test:

- Anterior Nasal Swab Sample (NS)

The Test device contains:

- Rabbit and Mouse Monoclonal antibodies
- Fluorescent Latex particles
- Magnetic particles
- Buffer and Stabilising agents

Preparing the Instrument to perform a Test:

Power on the Instrument by pressing the power button at the rear of the Instrument. You will hear the Instrument powering on, and the display will be a blank black screen for several seconds before starting up. If the screen is just dimmed tap the touchscreen to wake up the Instrument. Check that "Pooled Test" is available on the Instrument home screen. If it is not, enable "Pooled Test" in the Instrument settings menu.

If performing the SARS-CoV-2 Ag Ultra Pool test with 2-5 patients, select "Pooled Test" from the Platform Home Screen. If performing the SARS-CoV-2 Ag Ultra Pool test with 1 patient, select "Patient Test" from the Platform Home Screen. Please do not insert the Test Strip until prompted to do so.

Refer to the section on **Performing a Test** in this Product Insert for information on how to test a sample. The LumiraDx SARS-CoV-2 Ag Ultra Pool test Quick Reference Instructions (QRI) provides an illustrated step-by-step procedure on how to run a Test. Operate the LumiraDx Platform at room temperature between 15°C and 30°C (59°F and 86°F) and 10% - 75% relative humidity

The Instrument will prompt to install the Lot Calibration File when inserting a new Test Strip Lot for the first time. Once installed, the Instrument will have all the information required to process the test, and any future tests from the same Lot of Test Strips.

Lot Calibration File installation:

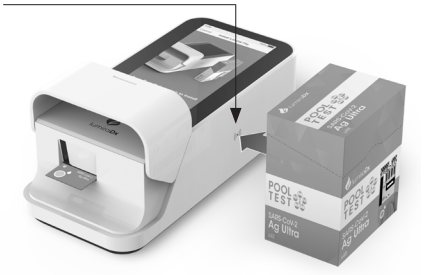
Lot Calibration Files are required to provide the instrument with the information needed to perform diagnostics tests. This only needs to be completed once for each Test Strip Lot. The instrument will prompt to install the Lot Calibration File when inserting a new Test Strip Lot.

RFID strip code reader

Locate ((•)) symbol on Instrument.

Installation

Touch back of Test Strip Carton ((•)) symbol to install.



The Instrument will sound and a confirmation message will be displayed.

When indicated by the touchscreen, open the foil pouch just before use and insert the LumiraDx Test Strip into the LumiraDx Instrument. The Instrument will indicate when it is ready for the sample to be applied.

The LumiraDx SARS-CoV-2 Ag Ultra Pool test results should be evaluated by a Healthcare Professional in the context of all available clinical and laboratory data.

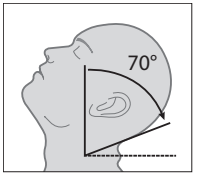
Instructions for sample collection:

When collecting any type of sample, follow universal collection precautions and guidelines according to your organization. For collection of nasal swabs, follow appropriate Swab Collection Guidelines and swab manufacturers' recommendations. Users should be trained in appropriate sample collection and handling procedures.

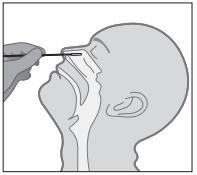
The steps that follow apply to nasal swabs. For information on recommended swabs to use with the LumiraDx SARS-CoV-2 Ag Ultra Pool test, please see the 'SARS-CoV-2 Ag Ultra Pool Test Technical Bulletin – Swabs' available at Lumiradx.com.

Sampling from an anterior nasal swab:

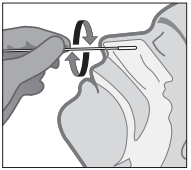
Individual samples should be collected and placed into a dry, clean, and sterile tube separately.



1. Tilt patient's head back 70°



2. A swab sample is needed from both nostrils and this is taken using the same swab. Remove sterile swab from the swab packet. Hold the swab by the shaft, while gently rotating the swab, insert swab less than one inch into the nostril until resistance is met at Turbinates. (Turbinates are the small structures inside the nose).



3. Rotate the swab several times against the nasal wall. Remove and repeat this process by using the same swab into the second nostril. Place swab in dry, clean, and sterile tube or process the swab directly in the extraction buffer vial as per instructions for sample extraction of pooled samples outlined below.

After patient swabbing, process the Swab in the Extraction Vial as soon as possible or place in an individual dry, clean and sterile tube for up to 1 hour before processing in the extraction buffer. Do not place the swab back into the swab packaging sleeve after sample collection.

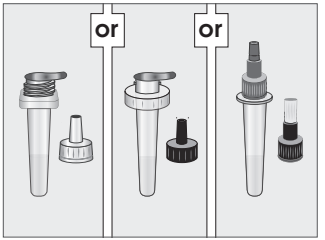
Sample pooling for SARS-CoV-2 Ag Ultra Pool testing:

Pools of 1 to 5 swab samples may be tested using the SARS-CoV-2 Ag Ultra Pool test.

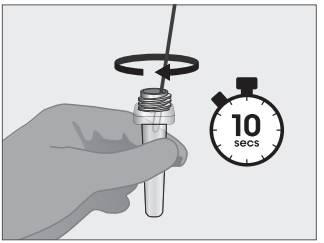
Process pooled samples as described in the instructions below for sample extraction of pooled samples.

Instructions for sample extraction of pooled samples:

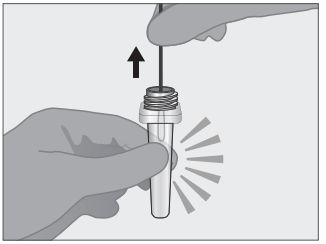
1 to 5 individual swabs can be eluted sequentially into a single Extraction Buffer vial.



1. **Remove the seal or blue screw cap** from the top of the Extraction Vial containing the Extraction Buffer.

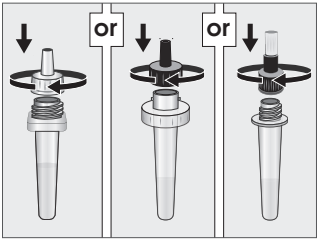


2. **Place and soak the Patient Swab** in the Extraction Buffer for 10 seconds and then stir well by rotating the swab against the side of the vial 5 times.

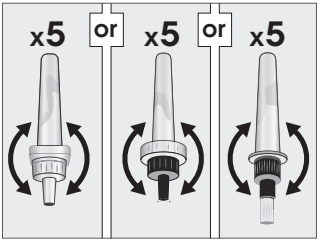


3. **Squeeze Swab** Remove the Patient Swab while squeezing the middle of the Extraction Vial to remove the liquid from the swab. Discard the swab in biohazard waste.

NOTE: For testing of pooled samples of 2-5 individuals, repeat steps 2 and 3 sequentially for up to 4 more swabs. Up to and including a total of 5 samples can be placed into the same Extraction Buffer Vial.



4. **Firmly attach the clear or purple Dropper Lid** to the top of the Extraction Vial. The extracted Pool sample must be used within 5 hours of preparation when stored at room temperature. Extracted nasal swab samples may be frozen at -80°C and used up to 5 days after freezing.



5. **Gently invert the Extraction Vial** five times just before applying the sample to the Test Strip.

Performing a Test (refer to the Quick Reference Instructions to make sure that your Instrument has been prepared before starting this step).

1. **Squeeze and apply the extracted sample from the Extraction Buffer Vial** onto the Sample Application Area of the inserted Test Strip. To do this gently press the sides of the extraction buffer vial until **one whole drop** is visible and allow the drop to touch the Sample Application Area of the Test Strip. The sample will then be drawn by capillary action into the Test Strip. When the sample is detected the Instrument will sound (if sounds are enabled) and a confirmation message will be displayed. The touchscreen of the LumiraDx Instrument will request the user to **immediately close the door (Note: you have 10 seconds only to close the door).**
2. **Do not add more than one drop of sample.** Do not open the door while the test is in progress. The touchscreen will indicate test progress.
3. **The result** will appear on the Instrument touchscreen within 5 minutes of applying the sample and starting the test. For pooled sample testing with 2-5 samples, the results will be displayed as a **"Pooled Positive" or "Pooled Negative" result SARS-CoV-2-Ag** on the Instrument screen. (see Fig 1 and Fig 2). For pooled sample testing with 1 sample, the results will be displayed as a **positive or negative result SARS-CoV-2 Ag** on the Instrument screen.
4. **If retesting is required,** a new Test Strip must be used. Use the same Extraction Buffer Vial and repeat the test. The extracted sample must be used within 5 hours of preparation when stored at room temperature. Extracted nasal swab samples may be frozen at -80°C and used up to 5 days after freezing.
5. **Dispose** of the swabs, Extraction Buffer Vial and Test Strip in the appropriate clinical waste.
6. **Disinfection** of the Instrument with LumiraDx approved materials is recommended if contamination is suspected. Details of approved disinfecting materials is available at lumiradx.com. Allow the Instrument to air dry before testing the next sample. The disinfectant should remain in contact for at least 1 minute.

Result interpretation for individual test:

The results will be displayed on the Instrument screen – **examples are shown below of result screen display for pools of 2-5:**

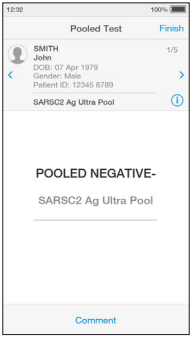


Fig 1: Negative result for SARS-CoV-2 Ag Pool Test of 2-5 patients

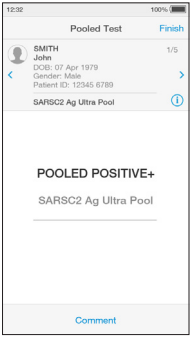


Fig 2: Positive result for SARS-CoV-2 Ag Pool Test of 2-5 patients

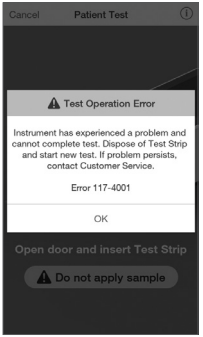
NOTE: A negative result, from patients with symptoms onset beyond twelve days, should be treated as presumptive and confirmation with a molecular assay, if necessary, for patient management, may be performed.

Negative—Negative results from pooled sample testing require no further testing of individuals within the pool and each constituent sample is reported as negative. If the individual's clinical signs and symptoms are inconsistent with a negative result and if results are necessary for individual sample management, then the individual should be considered for individual testing.

Positive— A positive pool means that one or more of the individuals tested in that pool may be positive for SARS-CoV-2 antigen. Individuals included within a positive sample pool with the LumiraDx SARS-CoV-2 Ag Ultra Pool Test should (1) be recalled for testing with individual sample collection or (2) seek follow up care with their physician or healthcare provider for additional testing.

Error Messages:

If an issue occurs, a message will be displayed on the Instrument touchscreen. Alert messages include useful information and are highlighted by an orange banner. Error messages also include a ⚠ symbol. All messages will contain a description of the Instrument status or error and an instruction. Error messages contain an identifying code that may be used for further troubleshooting purposes. Refer to the LumiraDx Platform User Manual if an error message is displayed on the LumiraDx Instrument touchscreen and contact LumiraDx Customer Services on customerservices@lumiradx.com.



Example of an error screen:

If the on board control (OBC) fails, an error message will be shown and no test result will be returned. Follow the on screen instructions to dispose of the Test Strip and start a new test. If the problem persists, contact Customer Services.

Built-in controls:

The instrument reads the 2D bar code on each Test Strip and can identify if the strip has exceeded the expiry date for use, and if the strip Lot Calibration file has not yet been loaded, at which point it will request it.

The LumiraDx Instrument and LumiraDx SARS-CoV-2 Ag Ultra Pool test strips have several quality control functions integrated to ensure validity of each test run. These checks ensure that the volume of sample added is sufficient and the assay sequence of the Test Strip is as expected. The checks also ensure that the Test Strip has not been damaged or used previously. If these checks are not verified, the test run will be rejected, and an error message displayed on the Instrument touchscreen.

The LumiraDx Instrument ensures the quality of test results obtained through the following features:

- Automated checks of the correct functioning of the Instrument at power on and during operation.
- This includes electrical component operation, heater operation, battery charge state, mechanical actuators and sensors and optical system performance.
- Monitoring of Test Strip performance and controls during test run time.
- Ability to perform Quality Control Tests using LumiraDx Quality Control solutions to meet regulatory compliance requirements.

External Quality Controls:

External liquid SARS-CoV-2 Ag Quality Controls are available from LumiraDx and may be used to demonstrate that the Test is functioning properly by demonstrating the expected Quality Control results and correct test performance by the operator.

External Quality Control requirements should be established in accordance with local, state, and federal regulations or accreditations requirements. It is recommended that external control testing be performed with each new operator and before using a new lot or shipment of the LumiraDx SARS-CoV-2 Ag Ultra Pool test. Refer to the LumiraDx SARS-CoV-2 Ag Quality Controls product insert available at www.lumiradx.com for detailed instructions.

LumiraDx SARS-CoV-2 Ag Quality Controls are purchased separately.

If the LumiraDx SARS-CoV-2 Ag Quality Controls do not perform as expected, repeat the QC Test and if the problems persist, do not report patient results and contact LumiraDx Customer Services.

Cleaning and disinfection:

Cleaning and disinfection of the Instrument should follow and be performed according to established site protocols and schedules.

To clean the Instrument wipe the external surfaces with a soft, slightly damp cloth when it appears visibly dirty.

It is recommended to clean and disinfect the Instrument at least once per day if in use, or if contamination is suspected. Details of LumiraDx approved disinfectant materials can be found at lumiradx.com. Allow the Instrument to air dry before testing the next sample. The disinfectant should remain in contact for at least 1 minute.

Excessive liquid may damage the Instrument. It is important for the protection of the Instrument that exposure to excess moisture is prevented. All disinfection cloths and/or wipes should only be slightly damp, with any excess liquid being manually removed from the cloth before use.

Avoid USB ports and power inlet. Do not spray or pour solution directly onto the Instrument. Do not put any objects or cleaning materials into the Test Strip slot.

Limitations:

- This test detects both viable (live) and non-viable, SARS-CoV and SARS-CoV-2. Test performance depends on the amount of virus (antigen) in the sample and may or may not correlate with viral culture results performed on the same sample.
- Failure to follow the instructions for use may adversely affect test performance and/or invalidate the test result.
- Test results should be considered in the context of all available clinical and diagnostic information, including patient history and other test results.
- 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.
- Negative results, from patients with symptom onset beyond twelve days, should be treated as presumptive and confirmation with a molecular assay, if necessary for patient management, may be performed.
- The performance of the Ag Ultra test was established based on the evaluation of clinical specimens collected between July 2020 and May 2022. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.
- If the differentiation of specific SARS viruses and strains is needed, additional testing, in consultation with state or local public health departments, is required.
- Clinical performance was established on frozen samples and performance may be different with fresh clinical samples.
- When considering pooling strategies, the appropriateness of the pooling strategy should be considered based on the positivity rate in the testing population, efficiency of the pooling workflow, and pooled test specificity.
- Users should test samples as quickly as possible after sample collection.
- Extracted nasal samples may be frozen at -80°C and used up to 5 days after freezing.
- Swab samples and Extraction Buffer must be at room temperature before testing.
- Positive test results do not rule out co-infection with other pathogens.
- A false negative 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 inappropriately, therefore a negative test result does not rule out the possibility of SARS-CoV-2 infection.

- The amount of antigen in a sample may decrease as the duration of illness increases. Samples collected after 12 days are more likely to be negative compared to RT-PCR.
- The contents of this kit are for qualitative detection of SARS-CoV-2 antigens from nasal swab samples only.
- For information on swabs have been validated for use with the LumiraDx SARS-CoV-2 Ag Ultra Pool Test please visit lumiradx.com.
- Only dry, clean, and sterile tubes have been validated for use with the LumiraDx SARS-CoV-2 Ag Ultra Pool Test.

Clinical Performance 1 (Performance with samples collected from symptomatic individuals)

The performance of the LumiraDx SARS-CoV-2 Ag Ultra test was established with 81 direct nasal swabs prospectively collected from individual subjects during the COVID-19 pandemic. Samples were collected from sequentially enrolled subjects who presented with symptoms of COVID-19 or Influenza like illness. No positive results were observed from patients without symptoms or beyond 12 days since symptom onset (DSSO). Dual nasal swabs were simultaneously collected and then randomly allocated to testing with the LumiraDx test or an EUA authorized PCR reference method. Samples were collected from 2 sites across the United States.

Swabs were collected and extracted into the LumiraDx Extraction Buffer without transport media.

Samples were frozen within 1h of collection and stored until tested. Samples were thawed and sequentially tested according to the Product Insert, with operators blinded to the PCR result. The performance of the LumiraDx SARS-CoV-2 Ag Ultra test was compared to the results from nasal swabs collected into 3ml universal transport medium (UTM) and tested with an EUA authorized PCR reference method.

Patient demographics

Patient demographics (gender, age) are available for the 81 samples used in the study. The following table shows the number of positive subjects correctly identified by the LumiraDx (LDx) assay.

Age	Total N	LumiraDx and PCR SARS-CoV-2 Positive	Prevalence*
≤ 5 years	1	0	0.0%
6 to 21 years	6	2	33.3%
22 to 59 years	59	29	49.2%
≥ 60 years	15	7	46.7%
Female	49	21	42.9%
Male	32	17	53.1%

** Prevalence here is calculated as LumiraDx correctly identified positives divided by Total N*

Clinical performance

The following table shows the performance measure, and 95% confidence intervals, as calculated with the Wilson Score method for 81 nasal samples collected up to and including 12 DSSO* for the detection of SARS-CoV-2.

Grouping	N	PPA	95% CI
Ct (all)	41	92.7%	(80.6%,97.5%)
Ct < 34 (all)	39	97.4%	(86.8%,99.5%)
Ct < 33 (all)	38	97.4%	(86.5%,99.5%)
Ct < 30 (all)	35	97.1%	(85.5%,99.5%)
Ct < 25 (all)	25	100.0%	(86.7%,100.0%)

Samples with Ct's above 33-34 are generally considered to be non-infectious.[3]

Therefore, the following table shows the agreement between LumiraDx SARS-CoV-2 Ag Ultra and the Reference RT-PCR assay for detection of SARS-CoV-2 in 79 samples collected to Ct 34 and including 12 DSSO*.

	RT-PCR to Ct <34					95% Wilson Score CI		
		POS	NEG	Total	Measure	Estimate	LCI	UCI
LumiraDx SARS-CoV-2 Ag Ultra	POS	38	0	38	PPA	97.4%	86.8%	99.5%
	NEG	1	40	41	NPA	100.0%	91.2%	100.0%
	TOTAL	39	40	79	PPV	100.0%	90.8%	100.0%
					NPV	97.6%	87.4%	99.6%
					Prevalence	49.4%	38.6%	60.2%
					OPA (% Agreement)	98.7%	93.2%	99.8%

PPA - Positive Percent Agreement (Sensitivity)
NPA - Negative Percent Agreement (Specificity)
PPV - Positive Predictive Value
NPV - Negative Predictive Value
OPA - Overall Percent Agreement
CI - Confidence Interval
LCI - Lower Confidence Interval
UCI - Upper Confidence Interval

* DSSO = Days Since Symptom Onset

Clinical Performance 2 (Performance with samples collected from asymptomatic individuals)

The performance of the SARS-CoV-2 Ag Ultra test was further established with 52 anterior nasal swabs prospectively collected from individual asymptomatic subjects between November 2020 and March 2021. Samples were collected from 4 sites across the United States. Swabs were collected and extracted into the LumiraDx Extraction Buffer. Samples were frozen within 1h of collection and stored until tested. The performance of the LumiraDx SARS-COV-2 Ag Ultra Test was compared to the results from paired anterior nasal swab samples collected into 3ml universal transport medium (UTM) and tested with an EUA authorized PCR method.

Patient demographics (gender, age) are available for the 52 samples used in the study. The following table shows the number of positive subjects correctly identified by the LumiraDx (LDx)

Patient demographics

Age	Total N	LumiraDx and PCR SARS-CoV-2 Positive	Prevalence*
≤ 5 years	0	0	0.00%
6 to 21 years	11	7	63.6%
22 to 59 years	31	10	32.3%
≥ 60 years	10	5	50.0%
Female	35	12	34.3%
Male	17	10	58.8%

**Prevalence here is calculated as LumiraDx correctly identified positives divided by Total N*

Clinical performance

The following table shows the performance measure, and 95% confidence intervals, as calculated with the Wilson Score method for groupings of the results below.

Grouping	N	PPA	95% CI
Ct (all)	23	95.7%	(79.0%,99.2%)
Ct < 30 (all)	22	100.0%	(85.1%,100%)
Ct < 25 (all)	18	100.0%	(82.4%,100%)

The following table shows the agreement between LumiraDx SARS-CoV-2 Ag Ultra and the Reference RT-PCR assay for detection of SARS-CoV-2 in samples collected from asymptomatic individuals.

	RT-PCR					95% Wilson Score CI		
LumiraDx SARS-CoV-2 Ag Ultra		POS	NEG	Total	Measure	Estimate	LCI	UCI
	POS	22	0	22	PPA	95.7%	79.0%	99.2%
	NEG	1	29	30	NPA	100.0%	88.3%	100.0%
	TOTAL	23	29	52	PPV	100.0%	85.1%	100.0%
					NPV	96.7%	83.3%	99.4%
					Prevalence	44.2%	31.6%	57.7%
					OPA (% Agreement)	98.1%	89.9%	99.7%

Clinical Performance 3 (SARS-CoV-2 Ag Ultra Pool Test with 5 Nasal Samples)

The performance of the SARS-CoV-2 Ag Ultra Pool Test was established during the 2020-2022 COVID pandemic with 30 positive pools collected from 150 individual subjects, and 36 negative pools collected from 180 individual subjects. Subjects were presenting with symptoms of COVID-19 or assumed negative donors. Samples (anterior nares) were collected by a healthcare provider or by supervised self-collection from sites in the United States, Germany and United Kingdom. Swabs were collected and frozen with 1 hour of collection. Samples were then thawed and extracted into the LumiraDx extraction buffer. One positive swab was included in a randomized sequence with 4 negative swabs for the positive pools. For the negative pools, 5 negative swabs were extracted. The performance of the LumiraDx SARS-CoV-2 Ag Ultra Pool Test was compared to results from nasal or nasopharyngeal swabs from the individual subjects collected into UTM and tested with a PCR method.

Clinical performance (Classification of all evaluable pools)

The following table shows the performance measure, and 95% confidence intervals, as calculated with the Wilson Score method for groupings of the results below.

Grouping	N	PPA	95% CI
Ct (all)	30	90.0%	74.4-96.5%
Ct <34 (all)	29	93.1%	78.0-98.1%
Ct < 33 (all)	28	92.9%	77.4-98.0%
Ct < 30 (all)	26	96.2%	81.1-99.3%
Ct < 28 (all)	22	100%	85.1-100.0%

Performance measures, and 95% confidence intervals, as calculated with the Wilson Score method.

	RT-PCR result for single swab					95% Wilson Score CI		
		POS	NEG	Total	Measure	Estimate	LCI	UCI
LumiraDx Pooled Test	POS	27	1	28	PPA	90.0%	74.4%	96.5%
	NEG	3	35	38	NPA	97.2%	85.8%	99.5%
	TOTAL	30	36	66	PPV	96.4%	82.3%	99.4%
					NPV	92.1%	79.2%	97.3%
					Prevalence	45.5%	34.0%	57.4%
					OPA (% Agreement)	93.9%	85.4%	97.6%

Supplementary Clinical Performance Evaluations

Clinical Performance 4 (SARS-CoV-2 Ag Ultra Test - Expanded data set with Anterior Nasal swab as reference method)

The performance of the LumiraDx SARS-CoV-2 Ag Ultra test was further expanded with additional samples to create a dataset of 477 direct nasal swabs prospectively collected from individual subjects during the COVID-19 pandemic. Samples were collected from sequentially enrolled subjects who presented with symptoms of COVID-19 or from asymptomatic screening. No positive results were observed from patients who presented with symptoms beyond 12 days since symptom onset (DSSO). Dual nasal swabs were simultaneously collected and then randomly allocated to testing with the LumiraDx test or an EUA authorized PCR method. Samples were collected from 11 sites across the United States.

Swabs were collected and extracted into the LumiraDx Extraction Buffer without transport media. Samples were frozen within 1h of collection and stored until tested. Samples were thawed and sequentially tested according to the Product Insert, with operators blinded to the PCR result. The performance of the LumiraDx SARS-CoV-2 Ag Ultra test was compared to the results from nasal swabs collected into 3ml universal transport medium (UTM) and tested with an EUA authorized PCR method.

Patient demographics

Patient demographics (gender, age) are available for the 477 samples used in the study. The following table shows the number of positive subjects correctly identified by the LumiraDx (LDx)

Age	Total N	LumiraDx and PCR SARS-CoV-2 Positive	Prevalence*
≤ 5 years	9	3	33.3%
6 to 21 years	75	25	33.3%
22 to 59 years	306	94	30.7%
≥ 60 years	87	27	31.0%
Female	275	70	25.5%
Male	202	79	39.1%

**Prevalence here is calculated as LumiraDx correctly identified positives divided by Total N*

Clinical performance

The following table shows the number of positive and negative subjects correctly identified by the LumiraDx device vs RT-PCR across days since symptom onset (DSSO):

DSSO	Cumulative PCR+ve	LDx +ve	PPA	LCI	UCI	Cumulative PCR-ve	LDx -ve	NPA	LCI	UCI
0	3	3	100.0%	43.9%	100.0%	8	8	100.0%	67.6%	100.0%
4	109	97	89.0%	81.7%	93.6%	238	237	99.6%	97.7%	99.9%
7	138	122	88.4%	82.0%	92.7%	279	278	99.6%	98.0%	99.9%
12	143	127	88.8%	82.6%	93.0%	282	281	99.6%	98.0%	99.9%

The following table shows the performance measure, and 95% confidence intervals, as calculated with the Wilson Score method for groupings of the results below.

Grouping	N	PPA	95% CI
Ct (all)	166	89.8%	(84.2%,93.5%)
Ct < 35 (all)	149	96.0%	(91.5%,98.1%)
Ct < 34 (all)	144	98.6%	(95.1%,99.6%)
Ct < 33 (all)	141	98.6%	(95.0%,99.6%)
Ct < 30 (all)	128	98.4%	(94.5%,99.6%)
Ct < 25 (all)	91	98.9%	(94.0%,99.8%)

The following table shows the performance measure, and 95% confidence intervals, as calculated with the Wilson Score method for **subjects results above, up to and including 12 DSSO** using an EUA authorized RT-PCR method as the reference.

	RT-PCR					95% Wilson Score CI		
		POS	NEG	Total	Measure	Estimate	LCI	UCI
LumiraDx SARS-CoV-2 Ag Ultra	POS	149	1	150	PPA	89.8%	84.2%	93.5%
	NEG	17	310	327	NPA	99.7%	98.2%	99.9%
	TOTAL	166	311	477	PPV	99.3%	96.3%	99.9%
					NPV	94.8%	91.8%	96.7%
					Prevalence	34.8%	30.7%	39.2%
					OPA (% Agreement)	96.2%	94.1%	97.6%

Clinical Performance 5 (SARS-CoV-2 Ag Ultra Test - Expanded data set with Nasopharyngeal swab as reference method)

For 346 subjects in the dataset in section "clinical performance 4", an additional Nasopharyngeal swab was collected following the dual nasal collection. The Nasopharyngeal swab was placed into 3ml universal transport medium (UTM) and tested with an EUA authorized PCR method.

Patient demographics

Patient demographics (gender, age) are available for the 346 samples used in the study. The following table shows the number of positive subjects correctly identified by the LumiraDx (LDx)

Age	Total N	LumiraDx and PCR SARS-CoV-2 Positive	Prevalence*
≤ 5 years	8	3	37.5%
6 to 21 years	58	16	27.6%
22 to 59 years	217	55	25.4%
≥ 60 years	63	15	23.8%
Female	192	37	19.3%
Male	154	52	33.8%

**Prevalence here is calculated as LumiraDx correctly identified positives divided by Total N*

The following table shows the number of positive and negative subjects correctly identified by the LumiraDx device vs RT-PCR across days since symptom onset (DSSO):

Clinical performance

DSSO	Cumulative PCR+ve	LDx +ve	PPA	LCI	UCI	Cumulative PCR-ve	LDx -ve	NPA	LCI	UCI
0	3	3	100.0%	43.9%	100.0%	8	8	100.0%	67.6%	100.0%
4	79	69	87.3%	78.2%	93.0%	203	202	99.5%	97.3%	99.9%
7	100	86	86.0%	77.9%	91.5%	241	240	99.6%	97.7%	99.9%
12	103	89	86.4%	78.5%	91.7%	243	242	99.6%	97.7%	99.9%

The following table shows the performance measure, and 95% confidence intervals, as calculated with the Wilson Score method for groupings of the results below.

Grouping	N	PPA	95% CI
Ct (all)	103	86.4%	(78.5%,91.7%)
Ct < 35 (all)	97	90.7%	(83.3%,95.0%)
Ct < 34 (all)	94	92.6%	(85.4%,96.3%)
Ct < 33 (all)	91	93.4%	(86.4%,96.9%)
Ct < 30 (all)	84	96.4%	(90.0%,98.8%)
Ct < 25 (all)	59	98.3%	91.0%,99.7%)

The following table shows the performance measure, and 95% confidence intervals, as calculated with the Wilson Score method for **subjects results above, up to and including 12 DSSO** using an EUA authorized RT-PCR method as the reference.

	RT-PCR					95% Wilson Score CI		
		POS	NEG	Total	Measure	Estimate	LCI	UCI
LumiraDx SARS-CoV-2 Ag Ultra	POS	89	1	90	PPA	86.4%	78.5%	91.7%
	NEG	14	242	256	NPA	99.6%	97.7%	99.9%
	TOTAL	103	243	346	PPV	98.9%	94.0%	99.8%
					NPV	94.5%	91.0%	96.7%
					Prevalence	29.8%	25.2%	34.8%
					OPA (% Agreement)	95.7%	93.0%	97.4%

Limit of Detection - (Analytical sensitivity) with nasal samples:

Limit of Detection (LoD) studies determined the lowest detectable concentration of SARS-CoV-2 at which 95% of all (true positive) replicates test positive. The LoD for the LumiraDx SARS-CoV-2 Ag Ultra Pool test was established using limiting dilutions of Ultraviolet (UV) inactivated SARS-CoV-2 (Zeptometrix 0810622UV). The 0810622UV is a preparation of SARS-Related Coronavirus 2 (SARS-CoV-2), isolate USA/NY-Wadsworth-33126-01/2020, that has been inactivated by ultraviolet irradiation. The material was supplied frozen at a concentration of 1.26×10^6 $TCID_{50}$/mL.

Limit of Detection screening:

An initial LoD screening study was performed using a 5-fold serial dilutions (six dilutions in total) of the UV inactivated virus made in pooled negative human nasal matrix starting at a test concentration of 1.6×10^5 $TCID_{50}$/mL and processed for each study as described above. One swab was spiked with virus and four swabs were spiked with negative human nasal matrix and then extracted individually into the same extraction buffer tube to mimic the Pool Test. These dilutions were tested in triplicate and across 3 LumiraDx SARS-CoV-2 Ag Ultra Pool Lot numbers. The lowest concentration at which all (3 out of 3 replicates) were positive was chosen for LoD Range finding. This was 1600 $TCID_{50}$/mL.

Limit of Detection range finding:

Using the 1600 $TCID_{50}$/mL concentration, the LoD was further refined using a 2-fold dilution series (five dilutions in total) of the UV inactivated virus made in pooled negative human nasal matrix. These dilutions were tested in triplicate. The lowest concentration at which all (3 out of 3 replicates) were positive was treated as the tentative LoD for the LumiraDx SARS-CoV-2 Ag Ultra Pool test. This was 400 $TCID^{50}$/mL.

Limit of Detection confirmation:

The LoD of the LumiraDx SARS-CoV-2 Ag Ultra Pool test was then confirmed by testing 20 replicates with concentrations at the tentative Limit of Detection. The final LoD of the LumiraDx SARS-CoV-2 Ag Ultra Pool test was determined to be the lowest concentration resulting in positive detection of nineteen (19) out of twenty (20) replicates. Based on this testing the LoD for nasal swab samples was confirmed as 400 $TCID_{50}$/mL.

Starting Material Concentration	Estimated LoD	No. Positive/Total	% Positive
1.26 x 10^6 $TCID_{50}$/mL	400 $TCID_{50}$/mL	19/20	95

For comparability, the LumiraDx SARS-CoV-2 Ag Ultra test was also tested using the UV inactivated virus stock to compare LoD. The results in the table below demonstrates that both test strips have an LoD of 400 $TCID^{50}$/mL when using this stock. This confirms that the LumiraDx SARS CoV-2 Ag Ultra Pool test has an equivalent LoD to the LumiraDx SARS-CoV-2 Ag Ultra test.

Previous studies have shown comparable LoD of the SARS-CoV-2 Ag Ultra test with the SARS-CoV-2 Ag 12-minute test.

	LumiraDx SARS-CoV-2 Ag Ultra test (single swab)	SARS-CoV-2 Ag Ultra Pool test
SARS-CoV-2 tested ($TCID_{50}$/mL) using Zeptometrix 0810622UV	**Test Result**	**Test Result**
1600	3/3 positive	3/3 positive
800	3/3 positive	3/3 positive
400	20/20 positive	19/20 positive
200	0/3 positive	0/3 positive
100	0/3 positive	0/3 positive
50	0/3 positive	0/3 positive

Note: $TCID_{50}$/mL levels can vary across batches, preparations and different stock material used. The LumiraDx SARS-CoV-2 Ag Ultra test and SARS-CoV-2 Ag Ultra Pool test were compared with the same stock material preparation at the same time for traceability and showed an equivalent LoD.

Endogenous and Exogenous interference studies with 1 nasal sample

A study was performed to demonstrate that potentially interfering substances that may be found in the upper respiratory tract in symptomatic subjects (including over the counter medications) do not cross-react or interfere with the detection of SARS-CoV-2 with the LumiraDx SARS-CoV-2 Ag Ultra test. Each substance was tested in triplicate in the absence or presence of SARS-CoV-2 at 2-3 x LoD. The final concentration of the substances tested are documented in the following table.

Following risk assessment, no substances were deemed higher risk for repeat testing with 5 nasal swabs.

Interfering substance	Concentration	Interference (Yes/No)
Blood (human)*	4% v/v	No (3/3 Negative, 3/3 Positive)
HAMA*	44 ng/mL	No (5/5 Negative, 5/5 Positive)
Mucin*	500 mg/dL	No (3/3 Negative, 3/3 Positive)
Acetylsalicylic Acid**	3 mg/dL	No (3/3 Negative, 3/3 Positive)
Afrin (Oxymetazoline)**	15% v/v	No (3/3 Negative, 3/3 Positive)
Biotin**	0.35 mg/dL	No (3/3 Negative, 3/3 Positive)
Budesonide**	0.00063 mg/dL	No (3/3 Negative, 3/3 Positive)
CVS Nasal Drops (phenylephrine)**	15% v/v	No (3/3 Negative, 3/3 Positive)
CVS Nasal Spray (Cromolyn)**	15% v/v	No (3/3 Negative, 3/3 Positive)
Dexamethasone**	1.2 mg/dL	No (3/3 Negative, 3/3 Positive)
Dextromethorphan**	0.00156 mg/dL	No (3/3 Negative, 3/3 Positive)
Diphenhydramine**	0.0774 mg/dL	No (3/3 Negative, 3/3 Positive)
Fluticasone Propionate**	0.000126 mg/dL	No (3/3 Negative, 3/3 Positive)
Homeopathic(Alkalol)**	10% v/v	No (3/3 Negative, 3/3 Positive)
Menthol/Benzocaine**	150 mg/dL	No (3/3 Negative, 3/3 Positive)
Methanol**	5% v/v	No (3/3 Negative, 3/3 Positive)
Mupirocin**	10 mg/dL	No (3/3 Negative, 3/3 Positive)
Naso GEL (NeilMed)	5% v/v	No (3/3 Negative, 3/3 Positive)
Salbutamol**	0.0045 mg/dL	No (3/3 Negative, 3/3 Positive)
Sore Throat Phenol Spray**	15% v/v	No (3/3 Negative, 3/3 Positive)
Tamiflu (Oseltamivir phosphate)**	500 mg/dL	No (3/3 Negative, 3/3 Positive)
Tobramycin**	0.4 mg/dL	No (3/3 Negative, 3/3 Positive)
Zicam Cold Remedy**	5% v/v	No (3/3 Negative, 3/3 Positive)

* Endogenous substances
** Exogenous substances

Cross-reactivity (analytical specificity) and microbial interference studies with 1 nasal sample

Cross-reactivity and interference of the LumiraDx SARS-CoV-2 Ag Ultra Test was evaluated by testing a panel of related pathogens, high prevalence disease agents and normal or pathogenic flora including various microorganisms and viruses and negative matrix that are reasonably likely to be encountered in the clinical sample and could potentially cross-react or interfere with the LumiraDx SARS CoV-2 Ag Ultra Pool Test. Each organism and virus were tested in the absence or presence of heat inactivated SARS-CoV-2 at 2-3 x LoD and results are shown below.

Microorganism	Source	Concentration	Cross-reactivity (Yes/No)	Interference (Yes/No)
Adenovirus (eg. Type 1)	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Adenovirus (eg. Type 5)	LGC Limited	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Adenovirus (eg. Type 7)	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Acinetobacter Baumannii	LGC Limited	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Bordetella pertussis	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Burkholderia cepacia	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Candida albicans	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Chlamydia pneumoniae	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Cytomegalovirus	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Enterovirus (EV70)	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Eikenella corrodens	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Escherichia.coli	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Epstein-Barr Virus	Zeptometrix	1 x 10^5 cp/mL	No (3/3 negative)	No (3/3 positive)
Haemophilus influenzae	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Haemophilus parainfluenzae	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Herpes Simplex Virus	LGC Limited	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Human coronavirus 229E	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Human coronavirus NL63	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)

Microorganism	Source	Concentration	Cross-reactivity (Yes/No)	Interference (Yes/No)
Human coronavirus OC43	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Human echovirus 3	LGC Limited	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Human Metapneumovirus	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Influenza virus A H1N1 Brisbane	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Influenza virus B (Victoria/2/87)	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Legionella pneumophila	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Lactobacilus acidophilus	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Measles	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
MERS-coronavirus	Helvetica Care Sarl	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Moraxella Catarrhalis	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Mycobacterium tuberculosis	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Mycoplasma pneumoniae	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Nocardia asteroides	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Parainfluenza virus Type 1	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Parainfluenza virus Type 2	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Parainfluenza virus Type 3	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Parainfluenza virus Type 4a	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Pneumocystis jirovecii	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Pooled Human Nasal Wash	In-house donors	14%v/v	No (3/3 negative)	No (3/3 positive)
Proteus mirabilis	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Proteus Vulgaris	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)

Microorganism	Source	Concentration	Cross-reactivity (Yes/No)	Interference (Yes/No)
Pseudomonas aeruginosa	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Respiratory syncytial virus (type A)	LGC Limited	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Respiratory syncytial virus (type B)	LGC Limited	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Rhinovirus (eg. type 1A)	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Rhinovirus (eg. Type 2A)	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Mumps	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Serratia marcescens	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Staphylococcus aureus	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Staphylococcus epidermis	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Streptococcus mitis	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Streptococcus mutans	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Streptococcus pneumoniae	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Streptococcus pyogenes	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Streptococcus salivarius	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Streptococcus oralis	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Varicella Zoster Virus	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)

To estimate the likelihood of cross-reactivity with SARS-CoV-2 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.

- For Human Coronavirus HKU1, homology exists between the SARS-CoV-2 nucleocapsid protein and Human Coronavirus HKU1. BLAST results showed 30 sequence IDs, all nucleocapsid protein, showing homology. Sequence ID AGW27840.1 had the highest alignment score and was found to be 39.1% homologous across 76% of the sequences, this is relatively low but cross-reactivity cannot be fully ruled out.

- For SARS-Coronavirus, high homology exists between the SARS-CoV-2 nucleocapsid protein and SARS-Coronavirus. BLAST results showed 68 sequence IDs, mostly nucleocapsid protein, showing homology. Sequence ID AAR87518.1, had the highest alignment score isolated from a human patient and was found to be 90.76% homologous across 100% of the sequence. This is high and cross-reactivity is likely.

Cross-reactivity (analytical specificity) and microbial interference studies with 5 nasal samples

Cross-reactivity and interference of the LumiraDx SARS-CoV-2 Ag Ultra Pool Test was evaluated by testing a panel of higher risk pathogens that are reasonably likely to be encountered in the clinical sample and could potentially cross-react or interfere with the LumiraDx SARS CoV-2 Ag Ultra Pool Test. Each organism or virus testing concentration was tested in the absence or presence of heat inactivated SARS-CoV-2 at 2-3 x LoD (by extracting one positive swab and four negative swabs into a single Tauns extraction buffer vial). The results are shown below.

Microorganism	Source	Concentration	Cross-reactivity (Yes/No)	Interference (Yes/No)
Burkholderia cepacia	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Chlamydia pneumoniae	LGC Limited/ATCC	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Cytomegalovirus	Zeptometrix	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Haemophilus parainfluenzae	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Human echovirus 3	LGC Limited/ATCC	1 x 10^5 PFU/mL	No (3/3 negative)	No (3/3 positive)
Human Metapneumovirus 3*	Zeptometrix	8138 PFU/mL	No (3/3 negative)	No (3/3 positive)
Legionella pneumophilia	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Varicella Zoster Virus	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)
Mycobacterium tuberculosis	Zeptometrix	1 x 10^6 CFU/mL	No (3/3 negative)	No (3/3 positive)

* For Human Metapneumovirus, the stock concentration was lower than or equal to the recommended testing concentration. In this case, it was only possible to test it at the stock concentration.

High dose hook effect with 5 nasal samples

High Dose Hook Effect studies determine the level at which false negative results can be seen when very high levels of target are present in a tested sample. To determine if the LumiraDx SARS-CoV-2 Ag Ultra Pool test suffers from any high dose hook effect, increasing concentrations of UV inactivated SARS-CoV-2 virus (Zeptometrix 0810622UV) were tested up to a concentration of 6.3 x 10^5 $TCID_{50}$/mL. In this study, the starting material was spiked into a volume of pooled human nasal matrix obtained from healthy donors and confirmed negative for SARS-CoV-2. At each dilution, 50 µL samples were added to swabs and the swabs processed for testing on the LumiraDx SARS-CoV-2 Ag Ultra Pool test as per the Product Insert using the procedure appropriate for patient nasal swab samples.

There was no impact on test performance or high dose hook effect observed up to a concentration of 6.3 x 10^5 $TCID_{50}$/mL of SARS-CoV-2.

Test Dilution	Concentration ($TCID_{50}$/mL)
1	0
2	4921.88
3	9843.75
4	19687.5
5	39375
6	78750
7	157500
8	315000
9	630000

Variants of Concern

LumiraDx actively monitors new mutations in the SARS-CoV-2 viral genome as they arise. The reactivity of the LumiraDx SARS CoV-2 Ag Ultra Pool test will be assessed against all variants of concern as they arise. The up to date results of this testing program can be found on our SARS-CoV-2 Variants Technical Bulletin on our website lumiradx.com.

References:

1. World Health Organization www.who.int
2. Centers for Disease Control and Prevention www.cdc.gov
3. La Scola B., Le Bideau M., Andreani J., Hoang V.T., Grimaldier C., Colson P. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. Eur J Clin Microbiol Infect Dis. 2020:39(6): 1059-1061

Symbols glossary

Symbol	Meaning
	Temperature limitation
	Manufacturer
	*In vitro* diagnostic medical device
	Catalogue Number
	Lot Number
	Use-by Date – indicates the date after which the unopened IVD/Quality Control Material cannot be used
	Refer to instructions for use
	Do not re-use
	For near patient testing
	Importer
	"CE Mark ". This product fulfils the requirements of the European Directive 98/79/EC on *in vitro* diagnostic medical devices.
	Indicates the presence of the Radio Frequency Identification (RFID) reader/ tag.
	Indicates the total number of IVD tests that can be performed with the IVD medical device.
	Indicates a carrier that contains unique device identifier information.
	Indicates the authorized representative in the European Community/ European Union.

LumiraDx customer services:

For product enquiries please contact LumiraDx Customer Services at customerservices@lumiradx.com or find telephone contact details at lumiradx.com.

Any adverse results experienced with the use of this product, and/or quality problems should also be reported to LumiraDx Customer Services by email: customerservices@lumiradx.com or at lumiradx.com.

If during the use of the device or as a result of its use, a serious incident has occurred, please report it to the manufacturer and/or its authorized representative and to your national authority.

For return policy:

If there is a problem with the **LumiraDx SARS-CoV-2 Ag Ultra Pool Test Strips** you may be asked to return them. Before returning tests please obtain a return authorization number from LumiraDx Customer Services. This return authorization number must be on the shipping carton for return. For ordinary returns following purchase, please contact LumiraDx Customer Services for terms and conditions.

Limited warranty

LumiraDx SARS-CoV-2 Ag Ultra Pool Test Strips – As per shelf life.

Unused strips must be stored according to the required storage conditions as printed in this product insert and they can be used only up to the expiry date printed on the Test Strip pouch and Test Strip box. For the applicable warranty period, LumiraDx warrants that each product shall be (i) of good quality and free of material defects, (ii) function in accordance with the material specifications referenced in the product insert, and (iii) approved by the proper governmental agencies required for the sale of products for their intended use (the "limited warranty"). If the product fails to meet the requirements of the limited warranty, then as customer's sole remedy, LumiraDx shall either repair or replace, at LumiraDx's discretion, the Test Strips. Except for the limited warranty stated in this section, LumiraDx disclaims any and all warranties, express or implied, including but not limited to, any warranty of merchantability, fitness for a particular purpose and non-infringement regarding the product. LumiraDx's maximum liability with any customer claim shall not exceed the net product price paid by the customer. Neither party shall be liable to the other party for special, incidental or consequential damages, including, without limitation, loss of business, profits, data or revenue, even if a party receives notice in advance that these kinds of damages might result. The Limited Warranty above shall not apply if the customer has subjected the LumiraDx SARS-CoV-2 Ag Pool Test to physical abuse, misuse, abnormal use, use inconsistent with the LumiraDx Platform User Manual or Product Insert, fraud, tampering, unusual physical stress, negligence or accidents. Any warranty claim by Customer pursuant to the Limited Warranty shall be made in writing within the applicable Limited Warranty period.

Intellectual property:

The LumiraDx Instrument, Test Strips and all provided LumiraDx documentation ('Products') are protected by law. The Intellectual Property of the LumiraDx Products remains at LumiraDx. Details of relevant Intellectual Property regarding our products can be found at lumiradx.com/IP.

Legal notices:

Manufacturer information:

LumiraDx UK Ltd
Dumyat Business Park, Alloa
FK10 2PB, United Kingdom
Registration number: 09206123

CE Mark applies to LumiraDx Instrument, Test Strips, Quality Controls, and Connect Hub only

EC REP LumiraDx AB, Västra Vägen 5A, 16961 Solna, Sweden

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