Luminex®
complexity simplified.

ARIES® SARS-CoV-2 Assay Package Insert

Rx Only

IVD For *In Vitro* Diagnostic Use.

For use under an Emergency Use Authorization (EUA) only.

89-30000-00-865 Rev D
10/2020

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Symbols Glossary

You will encounter these symbols throughout this manual. They represent warnings, conditions, identifications, instructions, and regulatory agencies.

Symbol	Meaning	Symbol	Meaning
5.4.4* 	Caution. Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.	5.1.4* 	Use-by date. Indicates the date after which the medical device is not to be used.
5.1.5* 	Batch Code. Indicates the manufacturer's batch code so that the batch or lot can be identified.	5.1.1* 	Manufacturer. Indicates the medical device manufacturer, as defined in EU Directives 90/385/EEC, 93/42/EEC and 98/79/EC.
5.5.5* 	Contains Sufficient for <n> Tests. Indicates the total number of IVD tests that can be performed with the IVD.	5.3.7* 	Temperature Limit. Indicates the temperature limits to which the medical device can be safely exposed.
5.4.3* 	Consult instructions for use. Indicates the need for the user to consult the instructions for use.	5.1.6* 	Catalog(ue) Number. Indicates the manufacturer's catalogue number so that the medical device can be identified.
5.5.1* 	*In vitro* diagnostic medical device Indicates a med-ical device that is intended to be used as an in vitro diagnostic medical device.	5.2.8* 	Do not use if package is damaged. Indicates a medical device that should not be used if the package has been damaged or opened.
5.4.2* 	Do not re-use. Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure.	BC	Build Code

Symbol	Meaning	Symbol	Meaning
5.1.7* SN	Serial Number. Indicates the manufacturer's serial number so that a specific medical device can be identified.	GHS02 ‡ 	Danger. Highly flammable liquid and vapor.
† Rx Only	Caution: Federal Law restricts this device to sale by or on the order of a licensed practitioner(U.S. Only)		

* ANSI/AAMI/ISO 15223-1:2016, Medical devices—Symbols to be used with medical device labels, labeling, and information to be supplied—Part 1: General requirements.

† 21 CFR 809 (FDA Code of Federal Regulations).

‡ ST/SG/AC.10/30/Rev.7 Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Seventh revised edition

Luminex Technical Support

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This manual can be updated periodically. To ensure that you have a current version, contact Technical Support.

Intended Use

ARIES® SARS-CoV-2 Assay is a Real-Time reverse-transcriptase polymerase chain reaction (RT-PCR) based qualitative *in vitro* diagnostic test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasopharyngeal swab specimens collected from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate and high complexity tests.

Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in nasopharyngeal swab specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient 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. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

The ARIES SARS-CoV-2 Assay is intended for use by trained clinical laboratory personnel specifically instructed and trained on Luminex® ARIES Systems and *in vitro* diagnostic procedures. The ARIES SARS-CoV-2 Assay is only for use under the Food and Drug Administration's Emergency Use Authorization.

The ARIES SARS-CoV-2 Assay is indicated for use with the ARIES Systems.

Summary and Explanation of the Test

There is currently an outbreak of respiratory disease caused by a novel coronavirus that was first detected in Wuhan City, Hubei Province, China, which has now been designated a pandemic by the World Health Organization (WHO) and which has been detected internationally, including cases in the United States. The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). SARS-CoV-2 has demonstrated the capability to spread rapidly, leading to significant impacts on healthcare systems and causing societal disruption. The potential public health threat posed by COVID-19 is high, both globally and to the United States. To respond effectively to the COVID-19 outbreak, rapid detection of cases and contacts, appropriate clinical management and infection control, and implementation of community mitigation efforts are critical. On February 4, 2020, the Secretary of Health and Human Services (HHS) determined that there is a public health emergency and that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection and/or diagnosis of the novel coronavirus (2019-nCoV). Rapid detection of COVID-19 cases in the United States requires wide availability of diagnostic testing to control the emergence of this rapidly spreading, severe illness. [FDA - Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency, March 16, 2020].

The ARIES® SARS-CoV-2 Assay is intended for qualitative detection of SARS-CoV-2 RNA in nasopharyngeal swab specimens from individuals suspected of COVID-19 by their healthcare provider. The specimens can be collected in Universal Transport Medium (UTM-RT®, Copan Diagnostics, Inc, Catalogue 328C) or equivalent. The collection media are not included in the test kit.

Principles of the Procedure

Primary sample (NPS specimen in universal transport medium) is added directly to the ARIES® SARS-CoV-2 Assay cassette sample chamber. The cassette is then placed into an ARIES magazine which can hold up to six cassettes. The magazine is inserted into an ARIES instrument. A barcode on top of the ARIES SARS-CoV-2 Assay cassette is automatically scanned by the ARIES instrument, associating a preloaded ARIES SARS-CoV-2 Assay protocol file with the cassette. The ARIES SARS-CoV-2 Assay protocol file contains the necessary parameters to run the cassette, analyze data, and generate reports.

Sample lysis, as well as isolation and purification of nucleic acids, are automated within the ARIES Systems and the ARIES SARS-CoV-2 Assay cassette. Purified nucleic acids are automatically transferred to the cassette's PCR tube that contains the lyophilized Master Mix for the PCR amplification step. The lyophilized Master Mix contains three sets of primers: one primer/probe set for the internal Sample Processing Control (SPC) target (RNase P), and an independent primer/probe set for each SARS-CoV-2 target. Total assay time, including extraction and PCR cycling, takes approximately two hours.

Assay Controls

- **Internal Sample Processing Control** – RNase P primers and probes are included in the ARIES® SARS-CoV-2 Assay. In the absence of a positive SARS-CoV-2 target, this positive sample processing control verifies that nucleic acid is present in every sample. For negative samples, failure to detect RNase P indicates a failure at either the extraction step, or the reverse-transcription step, or the PCR step.
- **Negative and Positive Controls** – A negative and positive control (not provided with the test kit) should be run as a good laboratory practice. External negative and positive controls should be used in accordance with local, state, and federal accrediting organizations, as applicable.

Materials Provided

The ARIES® SARS-CoV-2 Assay Kit (Part Number 50-10047) contains 24 assay cassettes.

The assay protocol file and a package insert ship separately on a USB as part of the ARIES SARS-CoV-2 Assay Protocol File Kit (CN-0499-01) or can be requested from Luminex Technical Support.

Table 1. ARIES SARS-CoV-2 Assay Contents Provided by Luminex

Item	Part Number	Description
ARIES® SARS-CoV-2 Assay Kit	50-10047	24 ARIES® SARS-CoV-2 Assay cassettes which contain necessary reagents for sample extraction, nucleic acid purification, and amplification.
ARIES® SARS-CoV-2 Assay Protocol File Kit	CN-0499-01	An assay protocol file and a package insert, are provided on a USB.

Materials Required but not Provided

- Reagents for sample collection:
    - Nasopharyngeal swab (NPS) (flocked or polyester swab)
    - Universal Transport Medium (UTM)
- Equipment:
    - -65°C to -95°C freezer
    - 2°C to 8°C refrigerator
    - Luminex® ARIES® Systems (either an ARIES System or an ARIES M1 System can be used) and accessories
        - ARIES magazines
        - Sample Prep Tray
        - Hand-held barcode reader
    - Vortex mixer
    - Appropriately sized pipettor
- Plasticware and Consumables:
    - Nuclease-free aerosol-barrier pipette tips

Reagent Storage, Handling, and Stability

Store assay cassettes at room temperature (15°C to 30°C) after receipt.

Always check the expiration date on the kit box and cassettes.

Warnings and Precautions

1. For Use under the FDA Emergency Use Authorization (EUA) only.
2. For *In Vitro* Diagnostic Use.
3. For prescription use only.
4. Do not eat, drink, smoke, or apply cosmetic products in the work areas.
5. ARIES® SARS-CoV-2 Assay protocol is unique and will not run concurrently with other ARIES Assay Cassettes in the same magazine.
6. Positive results are indicative of SARS-CoV-2 RNA.
7. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.
8. Always use pipette tips with aerosol barriers. Tips that are used must be sterile and free of DNases and RNases. Use only supplied or specified required consumables to ensure optimal test performance.
9. All human-sourced materials should be considered potentially infectious and should be handled with universal precautions. If spillage occurs, immediately disinfect with a freshly prepared solution of 0.5% sodium hypochlorite in distilled or deionized water (dilute household bleach 1:10) or follow appropriate site procedures.
10. Fresh clean gloves must be worn in each area and must be changed before leaving that area.

11. Do not pipette by mouth.
12. Perform the procedure given in this package insert as described. Any deviation from the outlined protocols may result in assay failure or cause erroneous results. Modifications to assay reagents, assay protocol, or instrumentation is not permitted, and are in violation of the product Emergency Use Authorization.
13. Do not use the kit or any kit components past the expiration date indicated on the kit carton label. Do not interchange kit components from different kit lots. Lot numbers are identified on the kit label.
14. Handle all samples as if infectious using safe laboratory procedures such as those outlined in CDC/ NIH *Biosafety in Microbiological and Biomedical Laboratories*, and in the CLSI Document M29 *Protection of Laboratory Workers from Occupationally Acquired Infections*.
15. Thoroughly clean and disinfect all surfaces with 10% household bleach.
16. Avoid contamination from positive controls and samples by following good laboratory practices.
17. Wear appropriate personal protective equipment (PPE), including a lab coat and disposable gloves, when performing procedures. Wash your hands thoroughly after performing the test.
18. Follow your institution's safety procedures for working with chemicals and handling biological samples.
19. Do not use cassettes, kits, or reagents beyond their expiration date.
20. The cassettes are single-use. Do not reuse cassettes.
21. Store cassettes at the temperatures recommended on the cassette label. Do not freeze.
22. Only use the extraction protocol file provided by Luminex on the USB drive.
23. Only use ARIES® Systems that have been properly maintained according to the manufacturer's recommendations.
24. ARIES cassettes contain guanidinium thiocyanate. Refer to the Safety Data Sheet (SDS) regarding safe handling practices for any spills.
25. In the event that a PCR tube falls off the cassette or a cassette leaks inside the ARIES instrument, you should perform appropriate decontamination procedures to reduce the risk of contamination. Immediately clean all surfaces of the ARIES magazine and the surrounding bench top with water. Wipe the surfaces with a lint-free cloth. Follow that with a fresh 10% household bleach solution. Allow the bleach solution to sit for a minimum of 10 minutes. Thoroughly rinse bleached surfaces with deionized water. Dispose of all lint-free cloths in the appropriate waste container. Immediately contact Luminex Technical Support in order to retrieve the PCR tube from the ARIES instrument. Do not throw away the cassette before you contact Technical Support. Do not attempt to retrieve the tube or put your hands inside the ARIES instrument at any time. Do not proceed with additional testing until the PCR tube has been removed from the ARIES instrument. Discard the cassette in accordance with the procedures defined by appropriate biohazard safety guidelines or regulations.
26. Do not let the ARIES Systems get wet or allow standing water to pool under the instrument.
27. Refer to the appropriate ARIES system operation manual for electrical warnings.
28. In the event of damage to the protective packaging, consult the Safety Data Sheet (SDS) for instructions.
29. Safety Data Sheets (SDS) are available by contacting Luminex Corporation or visiting our website at www.luminexcorp.com.

Assay Procedure

Sample Collection

NOTE: Standard precautions should be taken with regard to sample collection, handling, and storage prior to extraction (refer to the latest edition of the CLSI MM13-A Guideline[1]; and Farkas et al. (1996)[2]).

The recommended sample type for ARIES® SARS-CoV-2 Assay is a nasopharyngeal swab in Universal Transport Media (UTM™) or equivalent transport media.

Software Setup

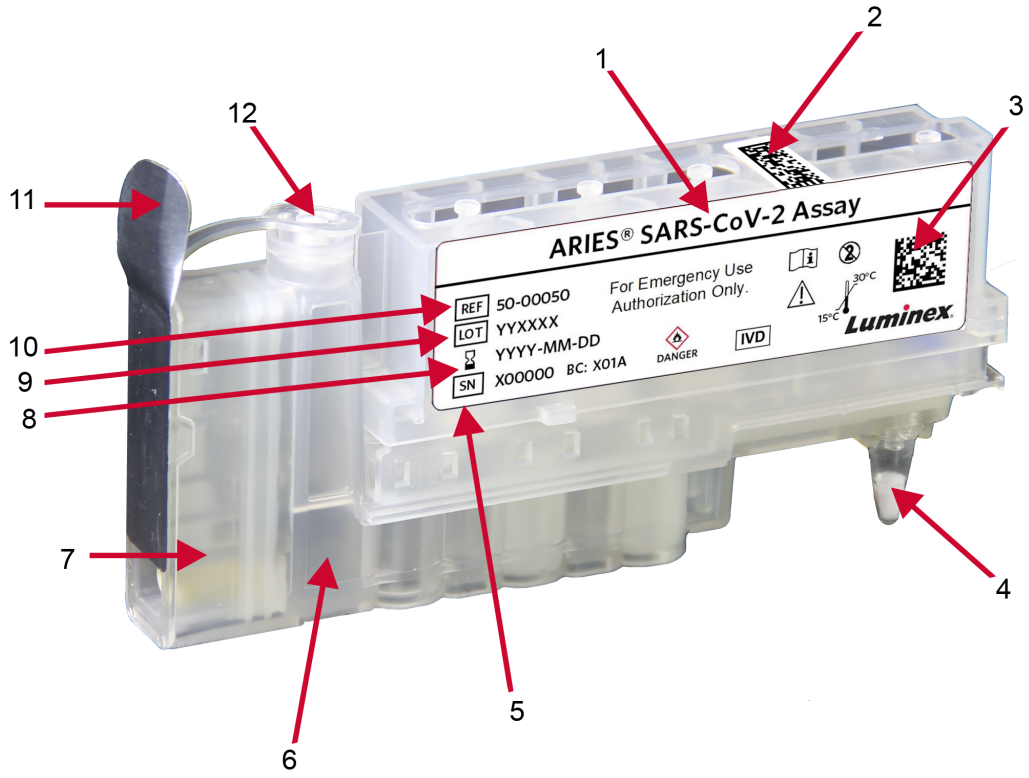
Import Assay Files to ARIES® Systems

The ARIES® SARS-CoV-2 Assay protocol file is provided on the USB flash drive. The assay protocol file only needs to be imported to the ARIES Systems once.

To import the assay protocol file, complete the following:

1. Insert the USB flash drive into one of the five USB connectors (one in the front and four in the back).
2. Select ☰ in the upper left-hand corner of the screen and navigate to **Assay Management**.
3. Select **Import Assay** from the Page Action bar. The **Import File** dialog box displays.
4. Choose the **Location** and **File Name** of the assay file. Select **OK**.

   NOTE: The ARIES System can start runs automatically or manually. To ensure that the ARIES System will begin a run automatically, check that Auto run upon Magazine Insertion is toggled to Yes in the Run Options dialog box located on the Run > Settings page. For information on how to start runs manually, refer to the applicable ARIES system operation manual.



1. Assay type	7. Side cassette
2. Cassette barcode (top)	8. Cassette expiration date
3. Cassette barcode (side)	9. Cassette lot number
4. PCR tube	10. Cassette part number
5. Cassette serial number	11. Back Seal
6. Cassette sample chamber	12. Cassette cap

Add Samples to the Cassettes

1. Remove the assay cassette from its packaging and visually inspect the cassette for any damage.

   NOTE: Once the cassette is removed from its packaging, it is stable for up to 10 hours at room temperature (15°C to 30°C).

If the cassette(s) or its packaging appears damaged in any way or if you see any leaks, DO NOT USE THE CASSETTE. Immediately contact Luminex Technical Support to report the damage.

2. Close the cassette cap to seal the cassette sample chamber.

3. Pull the tab to remove the foil seal from the cassette.

⚠	Use caution when pulling the back seal off the cassettes. The foil is sharp and may cause injury.

4. Place the cassette in the Sample Prep Tray next to the sample.

5. Vortex the sample for 5 to 10 seconds to homogenize the mixture.
6. Using an appropriately sized pipettor and aerosol barrier pipette tip, aspirate 200 µL of processed specimen from the Sample Processing Tube.
7. Open the cassette cap and place the specimen in the cassette sample chamber by inserting the pipette tip near the bottom of the chamber before expelling the processed specimen.

⚠	Ensure the correct amounts of sample are used.
	Use care to avoid contamination of the pipettor during transfer of the sample from the sample tube to the cassette.

8. Close the cassette cap to seal the cassette sample chamber.

⚠	Ensure the correct amounts of sample are used.Failure to ensure the cassette cap is fully closed may cause a delay or failure in results and expose you to buihazards.
	Do not vortex or shake the cassette.

Entering Orders on ARIES® Systems

When entering orders, the Sample ID and Assay are required for an order to be valid.

NOTE: The order should be created prior to placing the cassette in the magazine. If you scan the cassette while the cassette is in the magazine, it is possible to scan the incorrect cassette barcode.

1. Select ☰ in the upper left-hand corner of the screen and navigate to **Order Management** > **Sample Orders**.
2. Select **New Order** from the Page Action bar. The **New Order** dialog box displays.
3. Pick up and scan the barcode on the top (or side) of the cassette with the hand-held barcode reader or enter the required cassette information manually. A touch screen keyboard or a drop-down menu displays.

   NOTE: If the keyboard does not automatically appear, toggle the keyboard icon to Yes. The keyboard will appear when you click in a field.

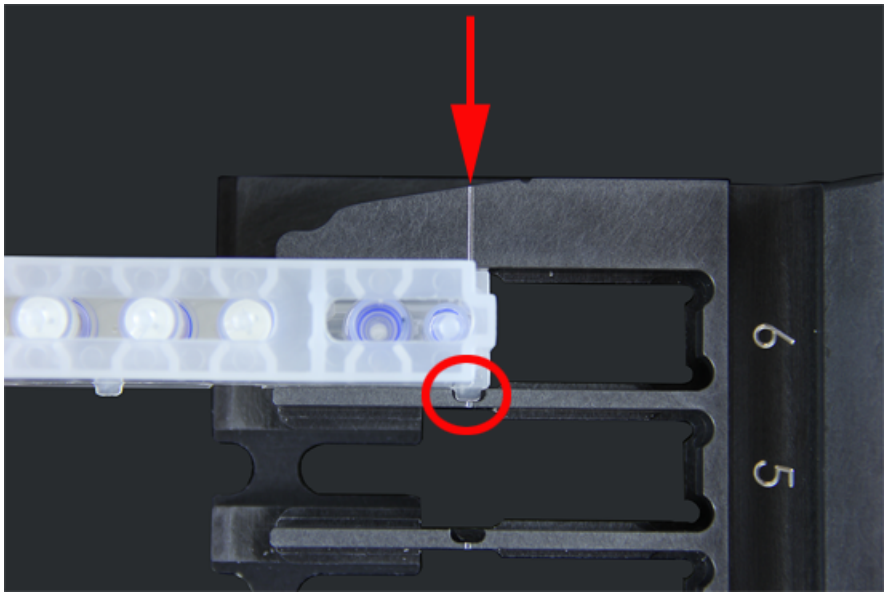
   NOTE: If manually entering the Cassette Lot Expiration, select the calendar icon and choose the date using the calendar. The date is shown in the YYMMDD format.

   a. If applicable, to add a control, choose **Control** in the **Sample Type** drop-down menu.
   b. In the **Control** field, click the magnifying glass to select a control from the **Controls** dialog box.
   c. Select the type of control in the **Control Type** drop-down menu.

      NOTE: You can define the controls on the Assay Management > Controls page. Refer to the applicable ARIES® System operation manual for more information on controls.

4. Pick up and scan the Sample ID on the sample tube or enter the required information manually.
5. Scan the Data Matrix barcode on the screen next to Save, or manually select **Save**.

6. Place the cassette into the magazine by lining the cassette up with the first notch (a tab on the cassette fits into the notch).



7. Gently insert the cassette into the magazine.
8. Gently slide the cassette all the way back toward the numbers. Repeat for all other cassettes.

⚠	Do not use your index finger to push the cassette into the magazine. You may indirectly dispense the reagent. Luminex recommends using the palm of your hand or holding the cassette and sliding the cassette into the proper position.

Run the Assay

1. Select ☰ in the upper left-hand corner of the screen and navigate to **Run > Run**.

2. Insert the magazine into the ARIES® Instrument. The ARIES Instrument automatically scans the barcode printed on the top of the ARIES SARS-CoV-2 Assay cassettes, identifies associated orders, and the proper assay protocol files before starting the run.

   NOTE: Ensure that the Auto run upon Magazine Insertion is toggled to Yes in the Run Options dialog box, located on the Run Settings page. The instrument automatically scans the cassettes once the magazine is inserted and starts the run.

3. If there are any errors, the ARIES Instrument displays the specific error (for example, cassettes that cannot be run together, cassette IDs that have not been read, or assay files not loaded on to the ARIES Instrument). These errors must be corrected in order for the run to begin.

   a. If **Auto run upon Magazine Insertion** is enabled and no errors occur, the instrument will automatically scan and start the run for you. The magazine state then indicates **PLEASE DO NOT REMOVE THE MAGAZINE** and an orange lock icon displays on the left-hand side of the magazine state. The Run Status bar, located at the bottom of the **Run** page, displays an orange progress bar next to the estimated time to completion, colored purple. If you do not have the Auto Run feature enabled, you can start the run manually by selecting **Start Run** from the Page Action bar.

      NOTE: If you are using an ARIES System with two modules, highlight the module you want before selecting Start Run.

Monitor the Run

From the Run page, select **Status** on the Page Action bar to display the status of the magazine(s), the estimated time to completion, and the customizable name of the ARIES® Instrument. This status screen is intended to be visible from across the room, allowing you to monitor your runs while you are working on other projects.

NOTE: On the Run > Settings page, you can customize whether the estimated completion time or estimated time remaining displays.

Reports and Results

Refer to the applicable ARIES® system operation manual regarding reports and results.

Interpretation of Results

External controls are automatically analyzed and interpreted by the ARIES® software. If the external controls are not valid, patient results should not be interpreted until valid external control results are achieved.

The ARIES SARS-CoV-2 Assay detects targets using primers and probes specific to SARS-CoV-2. The ARIES software determines results for the sample and the sample processing control (SPC) based on the amplification cycle (Ct) value provided in the assay protocol file. All assay outcomes are listed in *Table 2*.

Table 2. Interpretation of Sample Results

SARS-CoV-2_ORF1ab	SARS-CoV-2_N	Sample Processing Control (SPC)	Result Interpretation
+	+	+/-	SARS-CoV-2 positive
+	-	+/-	SARS-CoV-2 positive
-	+	+/-	SARS-CoV-2 positive
-	-	+	SARS-CoV-2 negative
-	-	-	Invalid

* In case of an "Invalid" result, re-test the sample with a new assay cassette. If the problem is unresolved, please contact Luminex Technical Support.

Invalid Results

In case of an "Invalid" result, re-test beginning with the primary sample. Start at "Assay Procedure" and use a new assay cassette. If the problem is unresolved, contact Luminex Technical Support.

Quality Control

Quality control procedures intended to monitor ARIES® Systems and assay performance are outlined below.

Table 3. Controls to Monitor Quality

Control Type	Use
External Negative Control	Monitors for environmental contamination.
External Positive Control	Monitors the ARIES® System, cassettes, and assay protocols to ensure proper function.
Internal Sample Processing Control	Verifies proper nucleic acid extraction, and proper reagent, cassette, ARIES instrument, and assay protocol performance.

Each ARIES® SARS-CoV-2 Assay cassette contains a sample processing control, which is processed with the sample and analyzed during the amplification reaction. Positive and Negative control samples should be tested in accordance with appropriate federal, state, and local guidelines or accreditation requirements, as applicable.

Limitations

1. This device may not be able to differentiate newly emerging SARS–CoV-2 subtypes.
2. Performance of the ARIES® SARS-CoV-2 Assay has only been established in nasopharyngeal swab specimens.
3. The use of Amies transport medium and PBS with this device is not recommended.
4. Analyte targets (viral sequences) may persist *in vivo*, independent of virus viability. Detection of analyte target(s) does not imply that the corresponding virus(es) are infectious, or are the causative agents for clinical symptoms.
5. All results from this and other tests must be considered in conjunction with the clinical history, epidemiological data and other data available to the clinician evaluating the patient.
6. The detection of pathogen nucleic acids is dependent upon proper specimen collection, handling, transportation, storage and preparation (including extraction). Failure to observe proper procedures in any one of these steps can lead to incorrect results. There is a risk of false negative values resulting from improperly collected, transported, or handled specimens.
7. This test is a qualitative test and does not provide the quantitative value of detected organisms present.
8. There is a risk of false positive values resulting from cross-contamination by target organisms, their nucleic acids or amplified product, or from non-specific signals in the assay.
9. There is a risk of false negative values due to the presence of sequence variants in the pathogen targets of the assay, procedural errors, amplification inhibitors in specimens, or inadequate numbers of organisms for amplification.
10. A specimen yielding a negative result may contain respiratory pathogens not probed by the assay.
11. The performance of this assay was not established in immunocompromised patients.
12. The performance for some viruses and subtypes may vary depending on the prevalence and population tested.
13. The performance of this test has not been established for screening of blood or blood products.
14. This test cannot rule out infections caused by other viral or bacterial pathogens not present on this panel.
15. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.
16. This device has been evaluated for use with human specimen material only.
17. The performance of this device has not been evaluated for patients without signs and symptoms of infection.
18. The performance of this device has not been evaluated for monitoring treatment of infection.
19. There is a risk of false negative results when at low concentration and in the presence of a high concentration co-infection.
20. The effect of interfering substances has been evaluated only for those listed within the labeling. Interference by substances other than those described can lead to erroneous results.
21. *In silico* analysis with SARS coronaviruses (NCBI Accession Numbers AY714217 and AY365036) suggests that these two sequences may be detected with the ARIES SARS-CoV-2 Assay.
22. Cross-reactivity with respiratory tract organisms other than those tested can lead to erroneous results.
23. For use only on the ARIES System or ARIES M1 System.

Conditions of Authorization for Laboratory

The ARIES® SARS-CoV-2 Assay Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: *https://www.fda.gov/MedicalDevices/Safety/ EmergencySituations/ucm161496.htm*.

However, to assist clinical laboratories using the ARIES SARS-CoV-2 Assay, the relevant Conditions of Authorization are listed below and are required to be met by laboratories performing the EUA test:

1. Authorized laboratories* using your product will include with result reports of the ARIES SARS-CoV-2 Assay and all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
2. Authorized laboratories using the ARIES SARS-CoV-2 Assay will use the ARIES SARS-CoV-2 Assay as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use the ARIES SARS-CoV-2 Assay are not permitted.
3. Authorized laboratories that receive the ARIES SARS-CoV-2 Assay will notify the relevant public health authorities of their intent to run the ARIES SARS-CoV-2 Assay prior to initiating testing.
4. Authorized laboratories using the ARIES SARS-CoV-2 Assay will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
5. Authorized laboratories will collect information on the performance of ARIES SARS-CoV-2 Assay and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: *CDRH-EUA-Reporting@fda.hhs.gov*) and Luminex Corporation, Inc. (via email: *support@luminexcorp.com*) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the ARIES SARS-CoV-2 Assay of which they become aware.
6. All laboratory personnel using the ARIES SARS-CoV-2 Assay must be appropriately trained in RT- PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the ARIES SARS-CoV-2 Assay in accordance with the authorized labeling.
7. Luminex, authorized distributors, and authorized laboratories using the ARIES SARS-CoV-2 Assay will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

* The letter of authorization refers to, "United States (U. S.) laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high and moderate complexity tests" as "authorized laboratories."

Disposal

Dispose of hazardous or biologically contaminated materials according to the practices of your institution.

Performance Characteristics

Limit of Detection (LoD)

The Limit of Detection (LoD) study established the lowest SARS-CoV-2 viral concentration (Genomic Copy Equivalents or GCE) that can be detected by the ARIES® SARS-CoV-2 Assay at least 95% of the time using gamma-irradiated SARS-CoV-2 viral fluid (SARS-Related Coronavirus 2, isolate USA-WA1/2020). Negative nasopharyngeal specimens (Negative Clinical Matrix, NCM) collected from 6/29/2019 to 7/14/2019 from a US site were pooled and used for this study. SARS-Related Coronavirus 2 gamma-irradiated viral fluid consists of a crude preparation of cell lysate and supernatant from *Cercopithecus aethiops* kidney epithelial cells (Vero E6; ATCC® CRL-1586™) infected with severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), isolate USA-WA1/2020 (NRC-52281 lot 70033641) and was obtained from Biodefense and Emerging Infections Research Resources Repository (BEI catalog number: NR-52287). SARS-Related Coronavirus 2 gamma irradiated viral fluid was spiked into 200 µL of pooled NCM and subjected to ARIES sample-to-answer processing. A two-phase approach was used to determine the LoD of the ARIES SARS-CoV-2 Assay. In phase I, the preliminary LoD was established by testing 3 replicates at each of 6 serially diluted concentrations (3-fold dilutions).

Table 4. ARIES® SARS-CoV-2 Assay Limit of Detection Results Summary (Phase II)

Concentration (GCE/mL/ $TCID_{50}$/mL)	Replicate	SARS-CoV-2 - ORF1ab		SARS-CoV-2 - N		SARS-CoV-2 Result*	% Positivity
		Ct Value	Result	Ct Value	Result		
1.00E+03/ 1.65E-01	1	31.6	+	37.7	+	Positive	100%
	2	N/A**	-	32.8	+	Positive	
	3	N/A	-	32.9	+	Positive	
	4	N/A	-	32.6	+	Positive	
	5	30.0	+	33.5	+	Positive	
	6	N/A	-	35.8	+	Positive	
	7	29.4	+	33.0	+	Positive	
	8	30.8	+	33.6	+	Positive	
	9	N/A	-	35.9	+	Positive	
	10	N/A	-	36.3	+	Positive	
	11	30.3	+	33.3	+	Positive	
	12	29.6	+	33.1	+	Positive	
	13	N/A	-	36.5	+	Positive	
	14	N/A	-	34.6	+	Positive	
	15	N/A	-	33.9	+	Positive	
	16	N/A	-	33.4	+	Positive	
	17	N/A	-	35	+	Positive	
	18	N/A	-	36.3	+	Positive	
	19	N/A	-	33.5	+	Positive	
	20	27.4	+	33.8	+	Positive	

Concentration (GCE/mL/ $TCID_{50}$/mL)	Replicate	SARS-CoV-2 - ORF1ab		SARS-CoV-2 - N		SARS-CoV-2 Result*	% Positivity
		Ct Value	Result	Ct Value	Result		
3.33E+02/ 5.48E-02	1	N/A	-	N/A	-	Negative	95%
	2	N/A	-	38.5	+	Positive	
	3	N/A	-	36.9	+	Positive	
	4	N/A	-	38.3	+	Positive	
	5	N/A	-	37.4	+	Positive	
	6	N/A	-	36.4	+	Positive	
	7	N/A	-	36.7	+	Positive	
	8	N/A	-	36.8	+	Positive	
	9	N/A	-	36.8	+	Positive	
	10	N/A	-	36.3	+	Positive	
	11	N/A	-	36.1	+	Positive	
	12	N/A	-	37.2	+	Positive	
	13	N/A	-	36.3	+	Positive	
	14	N/A	-	38.6	+	Positive	
	15	N/A	-	35.3	+	Positive	
	16	N/A	-	36	+	Positive	
	17	N/A	-	35.2	+	Positive	
	18	N/A	-	35.5	+	Positive	
	19	N/A	-	35.3	+	Positive	
	20	N/A	-	37.9	+	Positive	

* Positive - At least one of the two targets was positive; Negative - both targets were negative.

** N/A means not available.

FDA SARS-CoV-2 Reference Panel Testing

The evaluation of sensitivity and MERS-CoV cross-reactivity was performed using reference material (T1), blinded samples and a standard protocol provided by the FDA. The study included a range finding study and a confirmatory study for LoD. Blinded sample testing was used to establish specificity and to confirm the LoD. The results are summarized in the *Table 5*.

Table 5. Summary of LoD Confirmation Result using the FDA SARS-CoV-2 Reference Panel

Reference Materials Provided by FDA	Specimen Type	Product LoD	Cross-Reactivity
SARS-CoV-2	nasopharyngeal swab	1.8×10^5 NDU/mL	N/A
MERS-CoV		N/A	ND

NDU/mL = RNA NAAT detectable units/mL

N/A: Not applicable

ND: Not detected

Clinical Performance

The performance of the ARIES® SARS-CoV-2 Assay was established using leftover nasopharyngeal swab clinical specimens collected from patients with signs and symptoms of upper respiratory tract infection. Individual negative nasopharyngeal clinical specimens (Negative Clinical Matrix, NCM) were collected from 01/03/2019 to 04/03/2019 from a U.S. site, by qualified personnel according to the package insert of the collection device. Specimens were handled as described in the package insert of the collection device, aliquoted, and stored frozen until use.

All specimens were shown to be negative for common upper respiratory tract infection pathogens by testing with a commercially available nucleic acid test or an in-house PCR followed by bi-directional sequencing. All samples were also shown to be negative for SARS-CoV-2 by testing with the Luminex ARIES SARS-CoV-2 Assay.

Thirty (30) contrived positives were generated for testing, of which twenty (20) were prepared at 2X LoD, five at 3X LoD, and five at 5X LoD. Gamma-irradiated SARS-CoV-2 viral fluid (USA_WA1/2020 (NRC-52281 lot 70033641)) obtained from Biodefense and Emerging Infections Research Resources Repository (BEI catalog number : NR-52287) was spiked into 200 µL of individual NCM and subjected to ARIES sample to answer processing.

Six (6)† clinical negative specimens were extracted and tested as described above. The positive and negative clinical specimens were tested in a blinded and randomized fashion. The results are summarized in the table below and demonstrated a PPA and NPA of 100%.

Table 6. Clinical Performance of the ARIES® SARS-CoV-2 Assay

Target Concentration	Number of Samples Tested	SARS-CoV-2 - ORF1ab		SARS-CoV-2 - N		SARS-CoV-2 Result	% Positivity
		Mean Ct Value	% Agreement (#Pos or Neg) / Total	Mean Ct Value	% Agreement (#Pos or Neg) / Total		
SARS-CoV-2 - 2x LoD	20	N/A*	25% 5/20**	34.8	100% 20/20	Positive	100%
SARS-CoV-2 - 3x LoD	5	N/A*	20% 1/5**	33.2	100% 5/5	Positive	100%
SARS-CoV-2 - 5x LoD	5	N/A*	40% 2/5**	32.6	100% 5/5	Positive	100%
NCM	6	N/A*	100% 6/6	N/A	100% 6/6	Negative	0%

* A mean ct was calculated for the specimens where ct was available.

** Several replicates were negative for the ORF1ab gene, however the N gene target was detected for these replicates, and the specimens were assigned a positive result.

† An additional 30 contrived clinical positive and 30 clinical negative specimens were tested using purified SARS-CoV-2 viral genomic RNA (USA_WA1/2020 strain) obtained from World Reference Center for Emerging Viruses and Arboviruses (WRCEVA) and there were no changes to the assay performance between the old data and the new.

Analytical Performance

Inclusivity

Based on *in silico* analysis, it is predicted that ARIES® SARS-CoV-2 Assay will detect all analyzed SARS-CoV-2 sequences in NCBI and in GISAID databases.

In silico inclusivity analyses of the primers and probe sequences for the SARS-CoV-2 ORF1ab and N sets were performed against all SARS-CoV-2 sequences available in the GISAID database as of March 5, 2020, as well as the SARS-CoV-2 reference sequence from GenBank. The analysis included 177 sequences in the ORF1ab gene region and 188 sequences in the N gene region. SARS-CoV-2 ORF1ab gene assay had 100% homology to all 177 sequences analyzed and SARS-CoV-2 N gene assay had 100% homology to all 188 sequences analyzed, with exception to six recently submitted sequences in the GISAID database. These six sequences (EPI_ISL_412912, EPI_ISL_412972, EPI_ISL_413021-EPI_ISL_413024) showed three contiguous mismatches at the 5′ end of the N gene forward primer (23 nt length) corresponding to 86.4% homology. These mismatches are not expected to affect assay performance since they are located at the 5' end of the primer sequence.

Analytical Specificity (Cross-Reactivity)

An *in silico* cross-reactivity analysis was performed with all primer and probe sequences in ARIES® SARS-CoV-2 Assay against sequences from GenBank nt database available as of February 24, 2020 for organisms listed in *Table 7*. Based on *in silico* analysis, it is predicted that the assay will not cross-react with any organisms listed in *Table 7*.

Results from the *in silico* cross-reactivity analysis showed the only organism in *Table 7* with oligo-hit sequence homology ≥80% is SARS-coronavirus. All hits to SARS-coronavirus sequences involve the forward and reverse primers and probe from the N gene. *Table 8* shows the forward primer, reverse primer, and probe homology. Based on low % homology, mismatch pattern, and predicted Tm change, it is predicted that the ARIES SARS-CoV-2 Assay will not cross-react with SARS-coronavirus.

Table 7. Organisms Assessed in *In Silico* Cross-Reactivity Analysis

Human coronavirus 229E	Respiratory syncytial virus A
Human coronavirus OC43	Respiratory syncytial virus B
Human coronavirus HKU1	Rhinovirus
Human coronavirus NL63	*Chlamydia pneumoniae*
SARS-coronavirus	*Haemophilus influenzae*
MERS-coronavirus	*Legionella pneumophila*
Adenovirus	*Mycobacterium tuberculosis*
Human Metapneumovirus (hMPV)	*Streptococcus pneumoniae*
Parainfluenza virus 1	*Streptococcus pyogenes*
Parainfluenza virus 2	*Bordetella pertussis*
Parainfluenza virus 3	*Mycoplasma pneumoniae*
Parainfluenza virus 4	*Pneumocystis jirovecii* (PJP)
Influenza A	*Candida albicans*
Influenza B	*Pseudomonas aeruginosa*
Enterovirus	*Staphylococcus epidermis*
	Streptococcus salivarius

Table 8. Percent Homology for Primers and Probe

Strain	Oligo	Percent Identity
SARS Coronavirus CDC#200301157	SARS-CoV-2 - N Forward Primer	90.9%
	SARS-CoV-2 - N Probe	80.0%
	SARS-CoV-2 – N Reverse Primer	90.9%

Strain	Oligo	Percent Identity
SARS coronavirus HB	SARS-CoV-2 - N Forward Primer	90.9%
	SARS-CoV-2 - N Probe	80.0%
	SARS-CoV-2 - N Reverse Primer	86.4%

Cross-reactivity for the ARIES SARS-CoV-2 Assay was assessed with 31 potential cross-reactive microorganisms evaluated in the cross-reactive wet-testing study. All results were in agreement with the expected results for SARS-CoV-2 demonstrating the microorganisms tested do not interfere with the ARIES SARS-CoV-2 Assay at the concentrations tested.

Table 9. Organisms Tested for Potential Cross-Reactivity

Organism	Concentration Tested		SARS-CoV-2 Results
Human coronavirus - SARS-CoV-1	Undiluted*	$TCID_{50}$/mL	Negative
Human coronavirus - MERS	Undiluted*	$TCID_{50}$/mL	Negative
Human coronavirus - HKU1	4.20E+04 $TCID_{50}$/mL		Negative
Human coronavirus - NL63	3.50E+04$TCID_{50}$/mL		Negative
Human Coronavirus - 229E	8.40E+03$TCID_{50}$/mL		Negative
Human coronavirus - OC43	8.40E+04$TCID_{50}$/mL		Negative
Adenovirus Type 14 - 2006 isolate	1.41E+05	$TCID_{50}$/mL	Negative
Influenza A H1N1 - Brisbane /59/07	3.55E+05	$TCID_{50}$/mL	Negative
Influenza B - Florida/04/06	1.26E+05	$TCID_{50}$/mL	Negative
Human Metapneumovirus (hMPV)- IA10 - 2003 A1	8.51E+05	$TCID_{50}$/mL	Negative
Parainfluenza virus 1 - C35	1.60E+05	$TCID_{50}$/mL	Negative
Parainfluenza virus 2 - Greer	5.90E+05	$TCID_{50}$/mL	Negative
Parainfluenza virus 3 - C 243	1.58E+05	$TCID_{50}$/mL	Negative
Parainfluenza virus 4A	4.57E+05	$TCID_{50}$/mL	Negative

Organism	Concentration Tested		SARS-CoV-2 Results
Parainfluenza virus 4B	3.55E+05	$TCID_{50}$/mL	Negative
Respiratory syncytial virus A - A2	4.40E+05	PFU/mL	Negative
Respiratory syncytial virus B - 18537	5.01E+05	$TCID_{50}$/mL	Negative
Rhinovirus 1A	1.51E+05	$TCID_{50}$/mL	Negative
Enterovirus (Type 71) - 2003 isolate	3.80E+05	$TCID_{50}$/mL	Negative
Bordetella pertussis - E431	1.17E+06	CFU/mL	Negative
Chlamydia pneumoniae - TW-183	1.58E+04	$TCID_{50}$/mL	Negative
Haemophilus influenzae - MinnA	5.33E+06	CFU/mL	Negative
Legionella pneumophila - Philadelphia	1.75E+06	CFU/mL	Negative
Mycoplasma pneumoniae - M129	5.62E+06	CFU/mL	Negative
Mycobacterium tuberculosis - H37Ra-1	1.36E+06	CFU/mL	Negative
Pseudomonas aeruginosa - ATCC35554	1.90E+06	CFU/mL	Negative
Staphylococcus epidermis - MRSE; RP62A	3.60E+06	CFU/mL	Negative
Streptococcus pneumoniae - Z022; 19F	8.73E+06	CFU/mL	Negative
Streptococcus pyogenes - Z018	2.60E+06	CFU/mL	Negative
Staphylococcus salivarius - Z127	7.47E+06	CFU/mL	Negative
Candida albicans - Z006	1.53E+06	CFU/mL	Negative
Pooled Human Nasopharyngeal	N/A	N/A	Negative

* Highest concentration available. Concentration is unknown.

References

1. MM13-A Collection, Transport, Preparation and Storage of Specimens for Molecular Methods; Approved Guideline, 1st Edition.
2. Specimen collection and storage for diagnostic molecular pathology investigation. Farkas DH, Kaul KL, Wiedbrauk DL, Kiechle FL Arch Pathol Lab Med. 1996 Jun;120(6):591-6.

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