Protocol Title:	Clinical Validation of the Aptitude Medical Systems Metrix COVID/Flu Test for Detection of SARS-CoV-2 and Influenza A/B in Point-of-Care and Non-Laboratory Settings
Protocol ID:	TP-23-003 NCT06191393
Version	0
Date:	23 OCT 2023
Sponsor:	Aptitude Medical Systems, Inc. 125 Cremona Drive, Ste. 100 Goleta, CA 93117
Sponsor Contact:	Tyler Chozinski, PhD Aptitude Medical Systems, Inc. Head of Scientific and Medical Affairs tyler.chozinski@aptitudemedical.com 125 Cremona Drive, Ste. 100 Goleta, CA 93117

The **Metrix COVID/Flu Test** is intended for 510(k)/De Novo submission.
FOR INVESTIGATIONAL USE ONLY and has not been FDA cleared/market authorized
The performance characteristics of this product have not been established.

1. Protocol Summary

Protocol Title	Clinical Validation of the Aptitude Medical Systems Metrix COVID/Flu Test for Detection of SARS-CoV-2 and Influenza A/B in Point-of-Care and At-Home/Non-Laboratory Settings
Investigational Device(s)	Metrix COVID/Flu Test Metrix Reader (Gen 2)
Primary Objective(s)	To evaluate the clinical performance (Positive Percent Agreement, Negative Percent Agreement, and 95% confidence intervals) of the Metrix COVID/Flu Test in detecting SARS-CoV-2, Influenza A, and Influenza B compared to an FDA-cleared comparator assay.
Primary Endpoint(s)	For each target: • PPA ≥95% (lower bound 95% CI ≥85%) • NPA ≥98% (lower bound 95% CI ≥95%)
Study Design and Procedures	This is a multi-site, prospective, cross-sectional study. Enrollment will occur in an "all-comers"/sequential manner after written informed consent (and/or verbal assent, in the case of minors) and confirmation of eligibility. All standard-of-care specimens will be collected prior to any study specimens. Participants will be asked to complete a self-test (or assisted for those under 14 years) using the investigational devices. Participants will execute all steps necessary to complete the test, including result interpretation, without any guidance or aid from study coordinators. After testing with the investigational devices, a healthcare professional will collect a nasopharyngeal swab specimen for comparator assay analysis by an external reference laboratory. Comparator results will not be provided to participants. Results from the investigational device will not be used to make patient healthcare decisions. Healthcare management will be determined by the healthcare provider and their patient without any involvement of the Sponsor.
Study Population	Individuals aged 2+ years with signs and symptoms of respiratory infection. Intended users of the investigational device include lay-users (OTC/home use) with no prior laboratory experience with the investigational device. Participants aged 14 years and up will perform self-testing and participants below 14 years will be assisted by an adult.

Number of Participants	Enrollment and testing will continue until a minimum of 500 negative specimens, 50 positive SARS-CoV-2 specimens, 50 positive Flu A specimens, and 30 positive Flu B specimens are collected.
Inclusion/Exclusion Criteria	**Inclusion Criteria:** 1. Participant or guardian understands and is able and willing to provide written informed consent, and assent where applicable, prior to study enrollment. 2. Male or female aged 2 years or older 3. Participant is currently exhibiting fever, or one or more symptoms of respiratory tract infection (such as, but not limited to, chills, cough, shortness of breath or difficulty breathing, fatigue, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting or diarrhea). Participant must still be exhibiting symptoms on the day of specimen collection. 4. Participant or guardian agrees to read, and is able to read with understanding, the AN swab QRI prior to beginning the operation of each of the Metrix COVID/Flu Test. 5. Participant or guardian is able and willing to contribute the required swab specimens for testing and understands and is able and willing to sign the study informed consent. **Exclusion Criteria:** 1. Participant does not understand and/or is not able and willing to sign the study informed consent and/or assent. 2. Participant or guardian is not able to comply with nasal swab collection requirements following the QRI. 3. Participant has previously provided a specimen for the study. 4. Participant is not able to tolerate specimen collection. 5. Participant is currently undergoing antiviral treatment such as baloxavir marboxil (trade name Xofluza®), oseltamivir (Tamiflu®), zanamivir (Relenza®), and peramivir (Rapivab®). 6. Participant is currently underoing, and/or has undergone within the past 30 days, treatment with prescription medication to treat novel Coronavirus SARS-CoV-2 infection, which may include but is not limited to Remdesivir (Veklury), Paxlovid, molnupiravir or receiving convalescent plasma therapy for SARS-CoV-2. 7. Participants who have had a nasal wash or aspirate as part of their standard of care treatment on day of study visit prior to the study specimen collection.
Study Sites	The study will be conducted at a minimum of three investigational sites located within the United States. Additional sites may be added to the study to meet minimum subject/specimen enrollment requirements and geographic prevalence of respiratory virus

	infections. This may include utilizing one or more investigational sites outside of the US (at which participants are required to be fluent in English), depending on enrollment needs and geographical/seasonal prevalence of respiratory virus infections. This study will be conducted in simulated home environments set up within or near clinical settings (*e.g.*, urgent care clinics).
Study Duration	The study is to take place during the 2023 respiratory season. The estimated length of the specimen collection and testing phase is expected to be up to 24 weeks with an additional 2 to 3 weeks of study preparation and 2 weeks of final study closeout. Therefore, the total estimated study duration is up to 29 weeks. If the prevalence for any of the candidate analytes is low (such that enrollment targets are not met), the study may be extended into the next respiratory season to facilitate collection of additional specimens.

2. Reference Documents

1. Premarket Validation Recommendations for Developers of SARS-CoV-2 Molecular Single Analyte In Vitro Diagnostic Tests and Multi-Analyte Molecular Respiratory Panels that Include SARS-CoV-2 (Feb 2021)

3. Statistcal Analysis

3.1. Clinical Performance Analysis

For each target, the following analysis will be performed to obtain a measure of clinical performance of the Metrix COVID/Flu Test versus the FDA-cleared comparator assay. Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) will be calculated as shown below. The PPA and NPA will be presented in separate 2x2 tables for each target with comparator vs investigational test (test device).

		Comparator Test	
		Positive	Negative
Test Device	Positive	A	B
	Negative	C	D

Positive percent agreement = 100% x A/(A+C)
Negative percent agreement = 100% x D/(B+D)

The two-sided 95% Confidence Interval (CI) will be calculated using the Wilson Score method.

The study will also report participant demographics, percentage of invalid test results and investigational test performance on days from symptom onset (if applicable).

3.2. Clinical Validation Acceptance Criteria

The study results will be reported in 2×2 tables to calculate the estimated positive and negative percent agreements with the comparison device/method. Wilson two-sided 95% confidence intervals will also

be constructed for the positive percent agreement and negative percent agreement statistics. The study will also report participant demographics and invalid test results. Success criteria are defined as a PPA ≥95% (lower bound 95% CI ≥85%) and an NPA ≥98% (lower bound 95% CI ≥95%).

4. Good Clinical Practices (GCP), Ethical Considerations, and Administrative Issues

4.1. Study Oversight

Each enrollment site may be subject to monitoring or auditing to ensure that study procedures are being appropriately followed and records have been maintained according to requirements. Data collected during the study must be provided to the Study Monitor on a regular basis (at least monthly or at the discretion of the Sponsor) and will be reviewed for accuracy and consistency. At the discretion of the Sponsor, this protocol may be prematurely terminated. Reasons may include, but are not limited to, meeting enrollment minimum requirements and acceptance criteria, new regulatory pathway information, business and/or market information/changes.

4.2. Institutional Review Board (IRB) Approval

This protocol will be reviewed by an approved central or local institutional review board (IRB) prior to the start of the study. A copy of the IRB approval(s) will be maintained by the study Sponsor and each participating study site Principal Investigator prior to and during the study.

4.3. Informed Consent and Withdrawal

Participant participation is voluntary. Participants must provide written consent (and verbal assent, in the case of minors) as part of the informed consent process. The Investigator will ensure that each study participant, or thier legally acceptable representative, is fully informed about the nature and objectives of the study and possible risks of participation prior to signing the ICF. Consent may be obtained electronically in accordance with local requirements. The Investigator will retain the original of each signed ICF.

Participants may be withdrawn from the study by any of the following mechanisms:

- Voluntary withdrawal by the participant at any time.
- Determination by the Investigator that withdrawal is in the best interest of the participant.
- Determination by the Sponsor that withdrawal is in the best interest of the participant or study.
- Determination after review that the participant was not eligible for the study.

All data collected from enrollment until withdrawal will be retained and used. Data may be collected from participants who voluntarily withdraw before completing specimen collection. All specimens will be collected, retained, and used unless the participant withdraws or is withdrawn for any reason. Participants who withdraw or are withdrawn may be replaced.

4.4. Confidentiality and Specimen/Data De-Identification

The identity of study participants and collected information will remain confidential. All study participants and associated specimens including demographic and test result information will be

identified by a Study Participant ID code. All participant confidential identifiers will be removed from study specimens and the integrity of all protected health information (PHI) will be maintained in accordance with the IRB approved informed consent form. Only coded test results with minimal clinical information will be provided to the Sponsor. Investigational results (candidate assay) will not be made part of the participant's medical record.

4.5. Participant Risks and Benefits

Collection of upper respiratory swab specimens represents minimal risk to each participant but may cause some discomfort and/or minor bleeding.

There are no personal benefits to the study participants for participation in the study other than the knowledge gained by the Sponsor to help develop a new diagnostic test.

4.6. Protocol Deviations

The protocol described for this study will only be changed or altered on the express written approval of the PI, Study Manager, Sponsor, and IRB (when applicable).

4.7. Safety

4.7.1. Adverse Event (AE)

An adverse event is any unanticipated medical occurrence, unintended disease or injury or any untoward clinical signs (including any abnormal medical finding) in participants, users, or other persons whether or not related to the investigational medical device.

4.7.2. Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

4.7.3. Unanticipated Serious Adverse Device Effect (USADE)

Unanticipated adverse device effect is any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants or users of the investigational medical device.

A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

4.7.4. Adverse Event Reporting Requirements

The Investigator will report all Serious Adverse Events to the Sponsor within 24 hours of discovery and must be followed by a report within 10 days. Reports can be sent via email to the sponsor contact listed at the start of this protocol. The AE must also be reported to the Investigator's IRB.