Q-POC SARS-CoV-2 Assay (Q27001) Clinical Performance Study Plan

CONFIDENTIAL

1 Scope

This document details the testing plan to determine the clinical performance of the Q-POC SARS-CoV-2 Assay (Q27001) in accordance with FDA requirements.

2 Referenced Documents

Document ID	Title
QQA-8	Document Control Procedure
QTEM-270	Deviation Record Template Form
QQA-14	Control of non-conforming product

3 Device Intended Use

The Q-POC SARS-CoV-2 Assay is a real-time PCR test intended for use on the Q-POC instrument for the qualitative detection of nucleic acids from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), in nasal mid-turbinate swabs (MTSW) obtained 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, that meet requirements to perform high complexity or moderate complexity tests.

Results are for the detection of SARS-CoV-2 RNA. SARS-CoV-2 RNA is generally detectable in nasal mid-turbinate swabs (MTSW) during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 and aids in the diagnosis of COVID-19 if used in conjunction with other clinical and epidemiological information. Positive results do not rule out bacterial infection or co-infection with other viruses.

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, recent exposures and epidemiological information. Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

The Q-POC SARS-CoV-2 Assay is intended for use by laboratory personnel who have received specific training on the use of the Q-POC SARS-CoV-2 Assay in conjunction with the Q-POC instrument (Q29001).

4 Sponsor

Sponsor Name	QuantuMDx Group Ltd

Sponsor Address	Lugano Building, 57 Melbourne Street, Newcastle upon Tyne, NE1 2JQ, United Kingdom

5 Clinical Research Organisation

Sponsor Name	EDP Biotech
Sponsor Address	6701 Baum Drive Suite 110 Knoxville, TN 37919

6 Principle Investigator and Study Site(s)

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Principle Investigator Professional Position	Lead Scientist
Name and Address of Study Site(s)	Poplar Healthcare 3495 Hacks Cross Road Memphis, Tennessee 38125
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7 Study Synopsis

Title	Q-POC SARS-CoV-2 Assay Clinical Performance Study Plan
Primary Objective	To evaluate the clinical diagnostic performance (positive percent agreement [PPA] and negative percent agreement [NPA]) of QuantuMDx's Q-POC SARS-CoV-2 Assay when running mid-turbinate nasal swab (MTSW; also known as nasal mid-turbinate, NMT) compared to Roche Cobas 6800 SARS-CoV-2 Comparator Test.
Study Design	Prospective clinical study enrolling patients with signs and symptoms that are consistent with SARS-CoV-2. Positive and negative specimens will be run on the Q-POC SARS-CoV-2 Assay in comparison with an FDA-approved reference standard. The reference standard will be the Roche Cobas 6800 SARS-CoV-2. Three clinical testing sites, located in different geographical locations of the U.S., will be used to collect SARS-CoV-2 positive and negative specimens. Testing sites may be independent from sample collection sites – i.e., there can be multiple sample specimen collection sites that feed into the three testing sites.
Study Population	Prospectively enrolled patients >18 years of age with signs and symptoms that are indicative of SARS-CoV-2 infection. Subject populations must be from the U.S. to be representative of the intended patient population(s).

Intended Sample Type	Nasal mid-turbinate swab specimens (MTSW)
Sample Size	Nasal mid-turbinate swab (MTSW) swab samples from sufficient participants to achieve a minimum target at the end of the study of: 50 comparator test-confirmed SARS-CoV-2 positive samples 500 comparator test-confirmed SARS-CoV-2 negative samples.
Eligibility Criteria	Inclusion Criteria Participants must: Be over the age of 18 years. Present with symptoms indicative of SARS-CoV-2 infection, within 0-5 days of symptom onset. Have capacity to give informed consent. Exclusion Criteria Under the age of 18. No symptoms of SARS-CoV-2 infection. Lack of capacity to give informed consent.
Study Duration	The study period will start on 07NOV22 and will continue until sample collection is complete.
Study Personnel	The study should include 1-3 operators at each of 3 sites to run Q-POC tests. Trained professionals at clinical diagnostic testing sites will collect the specimens and run the comparator test.

8 Objectives of the Clinical Performance Study

To evaluate the clinical diagnostic performance (PPA and NPA) of QuantuMDx's Q-POC SARS-CoV-2 Assay when compared to the Roche Cobas 6800 SARS-CoV-2 in compliance with FDA requirements.

9 IVD Medical Device Under Investigation and Comparator(s)

Table 1: Information on the IVD Medical Device Under Investigation

Device Under Test	Manufacturer	Product Number
Q-POC	QuantuMDx Group Ltd	Q29001
Q-POC SARS-CoV-2 Assay	QuantuMDx Group Ltd	Q27001

Table 2: Information on the comparator assay

Comparator Device	Manufacturer	Product Number
Roche cobas SARS-CoV-2 (Assay for 6800)	Roche	SARS-CoV-2-192T P/N: 09175431190, cobas® SARS-CoV-2-480T P/N: 09343733190
cobas® SARS-CoV-2 Control Kit	Roche	P/N: 09175440190
cobas® 6800/8800 Buffer Negative Control Kit	Roche	P/N: 07002238190
Roche cobas 6800 system	Roche	P/N: 05524245001

10 Testing Sites

The study will be conducted at three external collection and testing sites located in the U.S. (in different geographical locations).

Testing sites may be independent from sample collection sites – i.e., there can be multiple sample collection sites that feed into the three testing sites. If some non-U.S. testing/collection sites are chosen, the relevance of this patient population to a U.S. population will be documented.

11 Operators

The study will include 1-3 operators at each site and at least nine (9) operators across all sites. The operator study participants enrolled must represent anticipated operators of the Q-POC SARS-CoV-2 Assay within the use-case environment. They should be laboratory personnel who

have received specific training on the use of the Q-POC SARS-CoV-2 Assay in conjunction with the Q-POC instrument (Q29001). Operators must be suitably trained to work in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high complexity or moderate complexity tests.

Operators should be personnel currently employed in the selected intended use sites and testing should be integrated into the daily workflow of the facility.

Education (including experience and training) and the occupation of each operator will be recorded and tabulated for each operator enrolled in the study. Study sites will be required to provide CVs and a filled in information form for potential operators prior to approval for their inclusion in the study. This will ensure that the participants meet the definition of intended operators.

The operators who participate in the study will be provided with the test kit in the form that will be made available in the actual intended use settings when the test is marketed. The operators should also be provided with the instructions for use and the training that is intended for such operators.

12 Specimen Information

12.1 Specimen Type to be Tested

Table 3: Claimed specimen type to be validated in this Clinical Performance Study Plan (QVTP-39)

Anatomical Location/Sample type	Common/Uncommon Respiratory Sample Type	Diluted into Liquid?	Type of Liquid/Transport medium
Mid-turbinate nasal swab (MTSW)	Common	Yes	MSwab preservation medium

The comparator test, Roche Cobas 6800 SARS-CoV-2 Test is validated for testing nasopharyngeal swab samples (NPS); therefore, an additional set of this specimen type will be collected for the comparator test in Copan UTM.

Sample Categories:

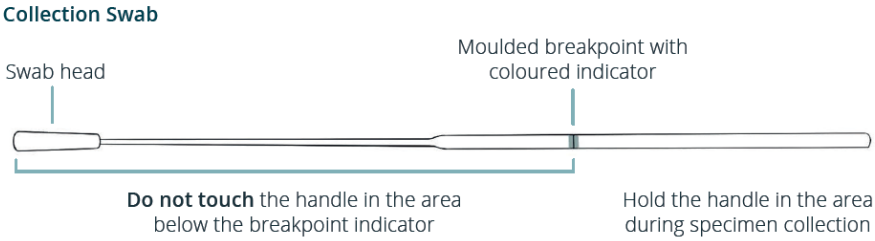
- Category I: Fresh samples, prospectively collected and tested in an ‘all comers’ fashion.
- Category II: Archived samples prospectively collected, frozen, and retrospectively tested. All samples are collected and tested in an ‘all comers’ fashion.

Ideally, Category II samples should be limited to no more than 30% of the total prospective samples enrolled in the clinical study.

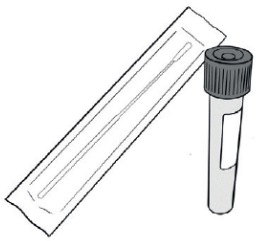
Please note that Category I and II samples must be collected sequentially from all patients meeting study inclusion criteria and representing the assay's intended use population (i.e., not pre-selected) presenting at a clinical facility between two pre-determined dates. This minimizes bias and prevalence of infection in the population can be evaluated. The Category II samples should be appropriately stored (e.g., frozen at -70˚C to -80˚C).

It is anticipated that within this clinical study both the comparator and candidate samples will be tested under the Category I conditions.

12.2 Method of Specimen Collection



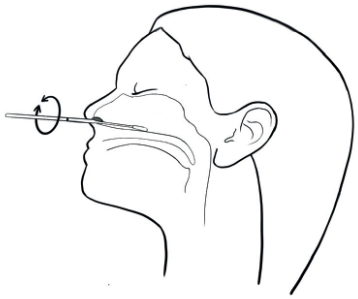
1. Open the kit package and remove the tube of MSwab™ reagent and the inner pouch containing the sterile swab applicator.



2. Remove the swab applicator from its peel pouch and use it to collect the clinical specimen.

3. Using gentle rotation and tilting patient's head back 70 degrees, insert the swab about 2 cm into the nostril without tipping the swab head up or down.

The nasal passage runs parallel to the floor, not parallel to the bridge of the nose.



4. Leave the swab in place for a few seconds, then slowly rotate the swab as it is being withdrawn.

DO NOT USE FORCE while inserting the swab. It should travel smoothly with minimal resistance. If resistance is encountered, withdraw the swab a little bit, without taking it out of the nostril, then elevate the back of the swab and move it forward.

At all times when handling the swab applicator, the operator must **NOT** touch the area below the breakpoint line, as this may result in contamination.

5. Unscrew the cap of the MSwab™ tube and insert the swab until the marked breaking point.
6. Bend and break the swab at the marked breaking point holding the tube away from your face.

Hold the tube away from your face while breaking the swab handle to prevent potential exposure to biological material.

DO NOT place the swab on a bench. Use of aseptic technique is recommended to avoid contamination.

7. Discard the broken handle into an approved biohazard disposable container.
8. Replace cap on the tube and secure tight to prevent leaks.
9. Invert the tube five (5) times.

12.3 Inclusion and Exclusion Criteria

Inclusion Criteria:

Participants must:

- Be over the age of 18 years.
- Present with any symptoms indicative of SARS-CoV-2 infection within 0 to 5 days of symptom onset.

- Have capacity to give informed consent.

Exclusion Criteria:

Participants must not:

- Be under the age of 18.
- Have no symptoms indicative of SARS-CoV-2 infection.
- Lack capacity to give informed consent.

Required patient and sample data to be recorded:

- Collection testing date and time
- Age
- Sex
- Country of residence
- Ethnicity
- Clinical signs and symptoms
- Time since onset of symptoms
- Clinical history
- Co-morbidities
- Medications taken or administered
- Vaccination status (SARS-CoV-2 and Influenza)
- Other relevant diagnostic data e.g., indications for testing
- Time taken between specimen collection and sample processing on Q-POC

12.4 Number of Specimens

Nasal mid-turbinate swab (MTSW) samples from sufficient participants to achieve a minimum target at the end of the study of:

- 50 comparator test-confirmed SARS-CoV-2 positive samples
- 500 comparator test-confirmed SARS-CoV-2 negative samples

Sample numbers chosen are in alignment with FDA recommendations in response to QuantuMDx's pre-submission Q220638.

An adequate number of subjects (N=550) will be enrolled to achieve a minimum 50 symptomatic positive and 500 negative cases confirmed via Roche Cobas 6800 SARS-CoV-2, a FDA approved reference standard.

12.5 Specimen Storage, Handling, Transport, and Disposal

Once recruited, a healthcare professional will take a sample per subject for the comparator test, following the manufacturer's Instructions For Use (IFU) in one nostril. MTSW samples will be taken from the opposite nostril (that was not swabbed for the comparator NPS sample), using Copan FLOQ Swabs and placed into MSwab buffer (Q14-116-P02), for the test under investigation. In instances where opposite nostrils cannot be swabbed for both the comparator and the test under investigation, a 15 minute wait period to allow for viral reloading must occur between collecting both the comparator and the test samples on the same nostril.

Comparator RT-PCR samples will be shipped overnight with ice packs as they are collected and processed for testing within 48 hours of collection. Comparator RT-PCR samples will be stored frozen at -70°C to -80°C after testing; they will be defrosted and brought up to room temperature immediately before re-testing, if required. Test MTSW samples will tested as soon as possible following collection, however if time is required between specimen collection and testing, the samples must be stored at 2-8 °C for up to 24 hours. Test samples must also be stored at 2-8 °C whilst the Q-POC test is running.

Following testing (and any subsequent re-testing), residual samples will be stored between -70°C to -80°C for retesting of any discordant results. Once the study is completed, the samples will be disposed of within biohazardous waste.

13 Clinical Performance Study Procedures

NPS samples will be tested on the Roche Cobas 6800 SARS-CoV-2 Test. A 400 µL aliquot of MTSW sample will be inserted into the Q-POC SARS-CoV-2 Assay test cassette and run on the Q-POC instrument.

Test and comparator assays will be run on their respective sample types.

13.1 Data Validity

Upon completion of each Q-POC run, the instrument should display the test status as 'VALID'. If any other test status is displayed, the run should be discarded.

The comparator RT-PCR assay, Roche cobas® SARS-CoV-2, uses two SARS-CoV-2 nucleocapsid targets. Target 1 is specific to the SARS-CoV-2 virus, but Target 2 is a pan-Sarbecovirus region of the nucleocapsid that is conserved and detects both SARS-CoV-1 and SARS-CoV-2. This comparator RT-PCR assay considers samples which are positive for Target 1 as positive for SARS-CoV-2 virus regardless of the status of Target 2 which can be invalid, negative, or positive

and the sample is still SARS-CoV-2 positive if Target 1 is positive. If Target 2 is positive and Target 1 is either negative or invalid, then the result is a presumptive positive due to Target 2's promiscuity among Sarbecovirus members. The decision has been made to consider all presumptive positive results as invalid for this clinical performance study. Only the result of "SARS-CoV-2 RNA detected", according to the manufacturer's instructions for use, will be counted as positive in the clinical performance evaluation data analysis.

Any problems encountered during testing must also be communicated to the relevant facilitator(s) and to QuantuMDx.

Any invalid tests should be repeated at least once.

External Quality Controls will be run as per the Q-POC SARS-CoV-2 Assay product IFU and Roche cobas® SARS-CoV-2 IFU. External positive control runs must return positive results. External negative control runs must return negative results. If the incorrect result is returned, or the Q-POC™ instrument displays one of these test statuses as 'INVALID', the controls should be re-run. If repeats also fail, contact the facilitator(s) or QuantuMDx.

13.2 Discordance Analysis

Any discrepant results will be investigated via repeat testing using an alternative FDA approved RT-PCR test. Discrepant analysis will not be used to adjust PPA and NPA calculations. These results can only be used to provide further information in the product IFU or academic publications. Statistical analysis of test assay performance will be conducted to determine PPA and NPA. This will be based solely on comparison of Q-POC SARS-CoV-2 Assay and Roche Cobas 6800 SARS-CoV-2 Test results.

14 Monitoring Plan and Data Management

Study monitoring shall ensure

a) investigators adhere to the CPSP,

b) study data are accurate and complete, and

c) ethical conduct of the study, e.g. the rights and well-being of study subjects are protected.

One or more qualified monitors shall be appointed. Monitors shall be:

- qualified through training and experience as well as scientific or clinical knowledge,
- knowledgeable on the specific activities to be monitored, the CPSP, and any other relevant requirements, and
- trained on the relevant quality assurance procedures as well as any special procedures for monitoring a specific clinical performance study. Training shall be documented in the study master files.

Study data will be captured in the case report forms (CRFs) by the study staff. Paper forms will be filled in during the study and transcribed into electronic forms (smartsheet) which will feed into a spreadsheet. The paper forms will also be scanned and uploaded to the spreadsheet. Access to the data collection system will be provided to members of the study site who have been delegated data collection and entry responsibilities by the site PI and who have completed training on the EDC system.

The data recorded in the CRFs will be source-verified from study-related source documents. Quality Control checks will take place to verify that the smartsheet MDF matches the scans of the paper source CRFs. The investigator shall ensure that all data on the CRFs are complete, accurate, and consistent with source documentation. A monitor from the Sponsor (or designee) will review the CRFs for completeness and accuracy.

The investigator will anonymise patient data so that no identifiable information is kept. Data arising from the administration of the index and reference tests, e.g. graphs and other outputs will be collected. All data related to the evaluation will be stored; raw and unanalysed data files will be shared with QuantuMDx.

15 Statistical Considerations

The diagnostic performance of the Q-POC SARS-CoV-2 Assay (in terms of PPA and NPA) will be determined using the Roche Cobas 6800 SARS-CoV-2 Test, as an FDA-approved reference standard comparator assay. This will be done for the entire dataset and also for subsets classified by comparator Ct-banding (Ct≤25, 25<Ct≤30, Ct>30) for SARS-CoV-2. Diagnostic performance will be assessed as follows:

- Positive Percent Agreement (PPA) will be calculated as 100% × (TP/(TP + FN)).
- Negative Percent Agreement (NPA) will be calculated as 100% × (TN/(TN + FP)).
- PPA and NPA will include 95% CI.

Where:

- True Positive (TP) indicates that both the Q-POC SARS-CoV-2 Assay and comparator assay returned a positive result for the target.
- False Negative (FN) indicates that the Q-POC SARS-CoV-2 Assay returned a negative result for the target, while the comparator assay returned a positive result.
- True Negative (TN) indicates that both the Q-POC SARS-CoV-2 Assay and comparator assay returned a negative result for the target.
- False Positive (FP) indicates that the Q-POC SARS-CoV-2 Assay returned a positive result for the target, while the comparator assay returned a negative result.

The performance of the Q-POC SARS-CoV-2 Assay will be presented based on the overall study (all specimens of a claimed specimen type combined) as well as stratified by site and time since symptom onset.

The rate of invalid/indeterminate results observed during the clinical study by site and overall will be reported. The prevalence of infection observed at each clinical site as determined by the comparator and the detection rate by the Q-POC SARS-CoV-2 Assay separately will be reported.

16 Deviations from the Clinical Performance Study Plan

The investigator is not allowed to deviate from the CPSP, except when a deviation is necessary to protect subject's rights, safety and well-being, or the scientific integrity of the clinical performance study.

Should a deviation from the clinical performance study plan be required, this will be communicated to QuantuMDx, QuantuMDx will record the deviation in a Deviation Record Template Form (QTEM-270) and circulated for approval with the relevant stakeholders. All deviations will be explained and referenced in the Clinical Performance Study Report. Should there be any major and/or repeated deviations, these will be recorded and corrective and preventative actions implemented via the Control of Non-Conforming Product Procedure (QQA-14).

17 Accountability of the IVD Medical Devices under Investigation

Access to IVD medical devices under investigation shall be controlled and these devices shall be used only in the clinical performance study according to this Clinical Performance Study Plan (QVTP-39).

The sponsor shall keep records to document the physical location of all IVD medical devices under investigation from shipment of the devices to the study site until return or disposal.

The principal investigator or an authorized designee shall keep records documenting the receipt, use, return and disposal of the IVD medical devices under investigation, which shall include, when applicable:

a) The date of receipt
b) The identification of each Q-POC instrument via serial number and Q-POC SARS-CoV-2 Assay Test cassettes via batch number
c) The expiry date of the Q-POC SARS-CoV-2 Assay Test Cassettes
d) The dates of use
e) The date on which the devices under investigation were returned or disposed of
f) The date of return of unused, expired or malfunctioning devices under investigation

18 Statements of Conformity

The clinical performance study outlined in this plan (QVTP-39) shall be conducted in accordance with relevant local and national ethical principles.

The clinical performance study outlined in this plan (QVTP-39) should comply with the Federal Food, Drug, and Cosmetic Act (FD&C Act) and its implementing regulations and should ensure compliance with all other pertinent laws and regulations, including Occupational Health and Safety Administration (OSHA) regulations pertaining to biological hazards ("universal precautions").

The clinical performance study outlined in this plan (QVTP-33) shall not begin until the required approval/favourable opinion or waiver from the ethics committee and/or regulatory authority has been obtained, when applicable.

19 Informed Consent Process

Informed consent is documented by means of a written, signed and dated informed consent form. The default personal information collected on the consent form is Name and Date of Birth.

All individuals asked to consider taking part in research must be given information about the research, presented in terms and in a form that they can understand. The participant must sign and date this sheet to show they have read and understood it.

The Designated Individual (DI) or Person Designated (PD), in the DI's absence, will arrange for an informed consent session prior to the donation of any sample. For external volunteers, an online informed consent session or phone call will be held prior to the donation of any sample. Informed consent is recorded on the relevant form and once the DI/PD and the volunteer are happy that informed consent has been given, the sample will be obtained and labelled with the Sample ID assigned to the consent form.

A scanned copy of the signed informed consent form must be added to the secure HTA server and the original hard copy to be stored with the DI. It is the responsibility of the DI/PD to ensure this takes place. Once inputted into the database, only the person's Sample ID must be used in all lab books, data files etc. Personal information on the donor must not be referred to.

A new consent form MUST be completed for each new donation a participant consents to.

20 Adverse Events, Adverse Device Effects and Device Deficiencies

All applicable adverse events shall be reported in an interim or final report of the clinical performance study and reported in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act).