A Study to Evaluate the Accuracy, Usability and Readability of the OraQuick® HIV Self-Test Performed by Observed Intended Users in Canada

---

Protocol Number: REACH – HIV – OraQuick – 2.0

Version: 1.0
Version Date: 13 July 2021

PROTOCOL DETAILS

Study Title: A Study to Evaluate the Accuracy, Usability and Readability of the OraQuick® HIV Self-Test Performed by Observed Intended Users in Canada.

Short Study Title: OraQuick HIV Self-Test Study

Other Study Name: OraQuick HIVST Study

Protocol Number: REACH – HIV – OraQuick – 2.0

Version Number: 1.0

Version Date: 13-July-2021

INVESTIGATOR SIGNATURE PAGE

INVESTIGATOR'S AGREEMENT IN ACCORDANCE WITH SUBSECTION 81(k) OF THE *MEDICAL DEVICES REGULATIONS*

Device Name/Nom de l'instrument: OraQuick *ADVANCE*® HIV-1/2 Rapid Antibody Test

Protocol Number/N^{o} du Protocole: **REACH – HIV– OraQuick– 2.0**

I, Sean Rourke, undertake, as outlined in Subsection 81(k) of the *Medical Devices Regulations,* to:

(i) conduct the investigational testing in accordance with the protocol:

A Study to Evaluate the Accuracy, Usability and Readability of the OraQuick® HIV Self- Test Performed by Observed Intended Users in Canada

(ii) inform a patient who is to be diagnosed or treated with the device of the risks and benefits associated with its use and obtain the written consent of the patient,

(iii) not use the device or permit it to be used for any purpose other than the investigational testing specified in the protocol,

(iv) not permit the device to be used by any person other than myself, except under my direction,

(v) in the event of an incident that is related to a failure of the device or a deterioration in its effectiveness, or any inadequacy in its labelling or in its directions for use and has lead to the death or a serious deterioration in the state of health of a patient, user or other person, or could do so were it to recur, report the incident and the circumstances surrounding it to the Site Director and the manufacturer or importer of the device, within 72 hours after its discovery.

Signature

13-July-2021
Date

Table of Contents

1. BACKGROUND 7
1.1. Summary 7
1.2. Device Description 7
1.3. Clinical Studies of Investigational Device 8
1.4. Summary of Known Benefits and Risk of HIV Self-Testing 9
1.5. Study Compliance Statement 10
2. STUDY OBJECTIVES 10
3. STUDY DESIGN 10
3.1. Overall Study Design 10
3.2. Study Population 12
3.3. Study Sites 12
3.4. Study Description 12
3.5. Selection and Withdrawal of Participants 13
4. STUDY PROCEDURES 15
4.1 Recruitment 15
4.2 Informed Consent 15
4.3 Enrollment Questionnaire - Review Eligibility Criteria 16
4.4 Background Data 17
4.5 Medical History/ Oral Health 17
4.6 Concomitant Medications 18
4.7 Dispensing and Return of the OraQuick® HIV Self-Test Device 18
4.8 Participant Self Testing 18
4.9 Observations and Verification of Participant Self-Testing 19
4.10 Observer's Interpretation of Study Participant's Self-Test Result 20
4.11 Interpretation of Results – Mock Devices 21
4.12 Post-Assessment Questions/Label Comprehension 21
4.13 Confirmatory Procedures 22
4.14 Additional Procedures and for Study Participants with Preliminary Positive Self-Test Results 23
4.15 Additional Procedures for Study Participants with Negative Results 23
4.16 Compensation for Study Participants 23
5. QUALITY CONTROL AND ASSURANCE 23
5.1 Training 23
5.2 Trained Researcher/ Observer Responsibilities 23
5.3 Study Monitoring 24
6. DATA ANALYSIS 24
6.1. Data Management Processes 24
6.2. Data Reporting 24
6.3. Primary Analysis 24
6.4. Secondary Analysis 25
6.5. Demographics 25

6.6. Error and Failure Rates 26
6.7. Sample Size 26
7. OBLIGATIONS OF THE INVESTIGATOR 27
7.1 Retention of Records 27
7.2 Device Accountability 27
7.3 Protocol Amendments 27
7.4 Protocol Violations and Deviations 28
7.5 Adverse Events and Adverse Device Events Reporting 28
7.5.1 Adverse Events 28
7.6 Severity of Adverse Events 29
7.7 Relationship of Adverse Events to the Device 29
7.8 Serious Adverse Events (SAE) 30
7.9 Adverse Device Effects (ADE) 31
7.10 Confidentiality of Participant Specimens and Information 31
7.11 Investigator Documentation 31
7.12 Study Termination 32
8. References 33
9. Appendices 35

STUDY PROTOCOL CONTACTS

OraSure Technologies Inc:
Name: Michele Roehler
Title: Director, Clinical Trials
Tel: (484) 353-1658
Fax: (610) 332-3425
Email: mroehler@orasure.com

Principal Investigator:
Name: Dr. Sean Rourke
Title: Scientist, Li Ka Shing Knowledge Institute, St. Michael's Hospital
Professor of Psychiatry, University of Toronto
Director, CIHR Centre for REACH in HIV/AIDS
Director, CIHR CBR Collaborative Centre
Tel: (416) 878-2779
Email: sean.rourke@utoronto.ca

Site Investigators:
Name: Dr. Megan Saunders
Title: Primary Care Physician, Women's Health in Women's Hands
Email: megan@whiwh.com

Name: Dr. Nina Malayil
Title: Medical Director, Hassle Free Clinic
Email: nina@hasslefreeclinic.org

Name: Dr. Réjean Thomas
Title: CEO and Medical Director, Clinique médicale l'Actuel
Email: rejean.thomas@lactuel.ca

Name: Dr. Chris Fraser
Title: Medical Director, Cool Aid Community Health Centre
Email: crrfraser@gmail.com

LIST OF ABBREVIATIONS:

Abbreviation	Description
ACB	African Caribbean and Black
AE	Adverse Event
ART	antiretroviral therapy
CM	Comparator Method
EC	Ethics Committee
GCP	Good Clinical Practice
EIA	Enzyme Immunoassay
HIV	Human Immunodeficiency Virus
HIVST	Human Immunodeficiency Virus Self-Test
ID	Identification
IDU	Injection Drug User
IFU	Instructions for Use
ICH	International Council for Harmonization
MSM	Men who have sex with men
PID	Participant Identification
POC	Point-of-care
RA	Research Assistant
REB	Research Ethics Board
SOP	Standard Operating Procedure
UADE	Unexpected Adverse Device Effect
US	United States
WHO	World Health Organization

1. BACKGROUND

1.1. Summary

Oral fluid based self-testing provides another option to increase the uptake of HIV testing. Studies have shown that interest and acceptability of self-testing with oral fluid is high.[1–3]

Despite significant progress made in improving testing rates over time, concern has been raised that conventional, public, facility-based testing has several weaknesses, including long waiting time, repetitive counselling, the identification of HIV negative people within the testing program without a subsequent effective prevention message, poor quality control on the part of testers in terms of test administration, and the inability to reach key and vulnerable populations.[3,4] Self-Testing for HIV ("HIVST") is an emerging approach with the potential to increase the uptake of HIV testing to be high impact, low cost, and empowering for those who may not otherwise test, notably in key populations and other people at high risk for HIV infection.[5] This technological innovation in the healthcare industry may be considered a disruptive innovation technology, as it brings to the market an innovation that may be affordable, simple, accessible and convenient if successful. There is a growing body of supporting evidence showing the acceptability and usability of HIVST in various key populations and groups[2,5,6] with further plans for evaluations on device performance.

1.2. Device Description

OraQuick® HIV Self-Test

OraSure Technologies, Inc. has developed packaging and labeling for use of a variation of the OraQuick *ADVANCE®* Rapid HIV-1/2 Antibody Test in a self-test environment. This product is known as the OraQuick® HIV Self-Test. It is comprised of the same components as the current OraQuick *ADVANCE®* Rapid HIV 1/2 Antibody Test available in the United States. The test is packaged and labeled for consumer use. The OraQuick® HIV Self-Test is a single-use, qualitative immunoassay to detect antibodies to Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2) in oral fluid.

The OraQuick® HIV Self-Test is a visually read, qualitative, in vitro lateral flow immunoassay for the detection of antibodies to HIV-1 and HIV-2. An oral fluid specimen is collected using the flat pad on the test device, followed by the insertion of the test device into the vial of developer solution.

The OraQuick® HIV Self-Test package includes a specific, step-by-step instructions and a device stand. The actual device and developer vial are not different from the OraQuick *ADVANCE®* Rapid HIV-1/2 Antibody Test (not currently available for commercial use in Canada). The difference is in the packaging and labeling which were specifically designed

for consumer use. This packaging, along with the instructions for reading and interpreting the results and all accompanying materials, will be used in this study.

1.3. Clinical Studies of Investigational Device

The OraQuick® HIV Self-Test packaging is the result of a development effort that incorporated investigator feedback and data collected during clinical investigations of usability, self-test accuracy, and linkage into care which is licensed under the US FDA. See additional information for:

- Approval of OraQuick ADVANCE Rapid HIV-1/2 Antibody Test (June 22, 2004)[7]
- Approval of OraQuick In-Home HIV Test (July 3, 2012)[8]
- Summary of WHO prequalification assessment for OraQuick HIV 1/2 Self-Test (November 2019)[9]

According to a report published by UNITAID in July 2017, an individual's knowledge of their and their partner's HIV status is essential to the HIV response. Despite the many benefits of HIV testing, in 2016, approximately 30 per cent of people with HIV globally, (and up to 14% in Canada), remained unaware of their status. Some of the largest gaps in testing, prevention and treatment coverage are among men who have sex with men, Indigenous communities, people who use drugs, young people and other key populations who are often reluctant or unable to access existing services.[10,11] Recognizing this, the World Health Organization (WHO) recommended that HIVST be offered as an approach to complement existing HIV testing approaches, and subsequently released the guidance document *TSS-1 Human Immunodeficiency Virus (HIV) rapid diagnostic tests for professional use and/or self-testing* in 2016.[12] Since then, HIVST has been scaling up rapidly in global settings.

1.4. Summary of Known Benefits and Risk of HIV Self-Testing

The potential benefits of an HIV Self-Test include immediate and private test results, which may encourage testing of individuals or high-risk groups who may otherwise refrain from testing due to privacy issues and stigma.

While many governments offer free testing for HIV in a clinic setting, the ability to self-test removes the need for time spent visiting a clinic and waiting for results, particularly important where public testing facilities are long distance; many people who make the effort for clinic-based testing often fail to return to receive their test results (both positive and negative). Additionally, private HIV testing can reduce the burden for routine testing for negative or sero-discordant partners, resulting in more people knowing and monitoring their HIV status over time.

Providing individuals with a tool to test themselves could also lead to earlier diagnosis of HIV status, with the potential for earlier medical intervention through both digital health technologies/telephone held lines as well as clinic follow-up for confirmatory testing. With an earlier diagnosis, individuals are empowered to modify their high-risk behaviours, potentially reducing the number of new HIV infections. This empowerment of consumers is not only limited to modification of lifestyle decisions, but also in being proactive in their health-care decisions.

The potential risks of an HIV Self-Test include not understanding the limitations of a screening test, such as use of the test during the window period of seroconversion, or receiving a false positive, false negative, or invalid test result. HIV Self-Tests can be used without a counsellor present, with the potential for adverse outcomes if the user obtains an unexpected result. As far as possible, these risks are identified in the HIV Self-Test instructions for use (IFU; see Appendix A), with instructions on when not to use the test, how to interpret the test result, and what to do next for a positive, negative or invalid result.

Additional risks of HIV Self-Testing include the inability to track individuals for medical follow-up, partner notification, and public health reporting. There is also the potential for coercive testing and testing by unprepared minors. All of these possible risks are being addressed in various forums where experts are developing guidance around HIV Self-Testing.

Participants may experience slight temporary discomfort where the gums are swabbed during the OraQuick® HIV Self-Test.

Although every effort to protect participant privacy and confidentiality will be made, it is possible that participants' involvement in the study could become known to others, and that social harm may result (i.e., because participants could become known as HIV-infected or at "high risk" for HIV infection).

1.5. Study Compliance Statement

This study will be conducted in compliance with The Canadian Medical Research Council Guideline on the "Code of Ethical Conduct for Research Involving Humans" and according to the general requirements of the International Conference on Harmonisation harmonised tripartite guideline E6 (R1): Good Clinical Practice.[13]

2. STUDY OBJECTIVES

The primary objectives of this study will be to:

1) Evaluate the device performance, i.e. sensitivity and specificity, compared to laboratory reference testing
2) To document if intended users (non-professional "lay users"), can successfully perform the steps to use the OraQuick® HIV Self-Test, without product familiarization or demonstration (accuracy/usability)
3) To document if intended users, (non-professional "lay users"), can successfully interpret contrived strong positive, weak positive, negative, and a range of invalid results (test results interpretation) and
4) To document if intended users can understand the key messages in the labeling (label comprehension).

3. STUDY DESIGN

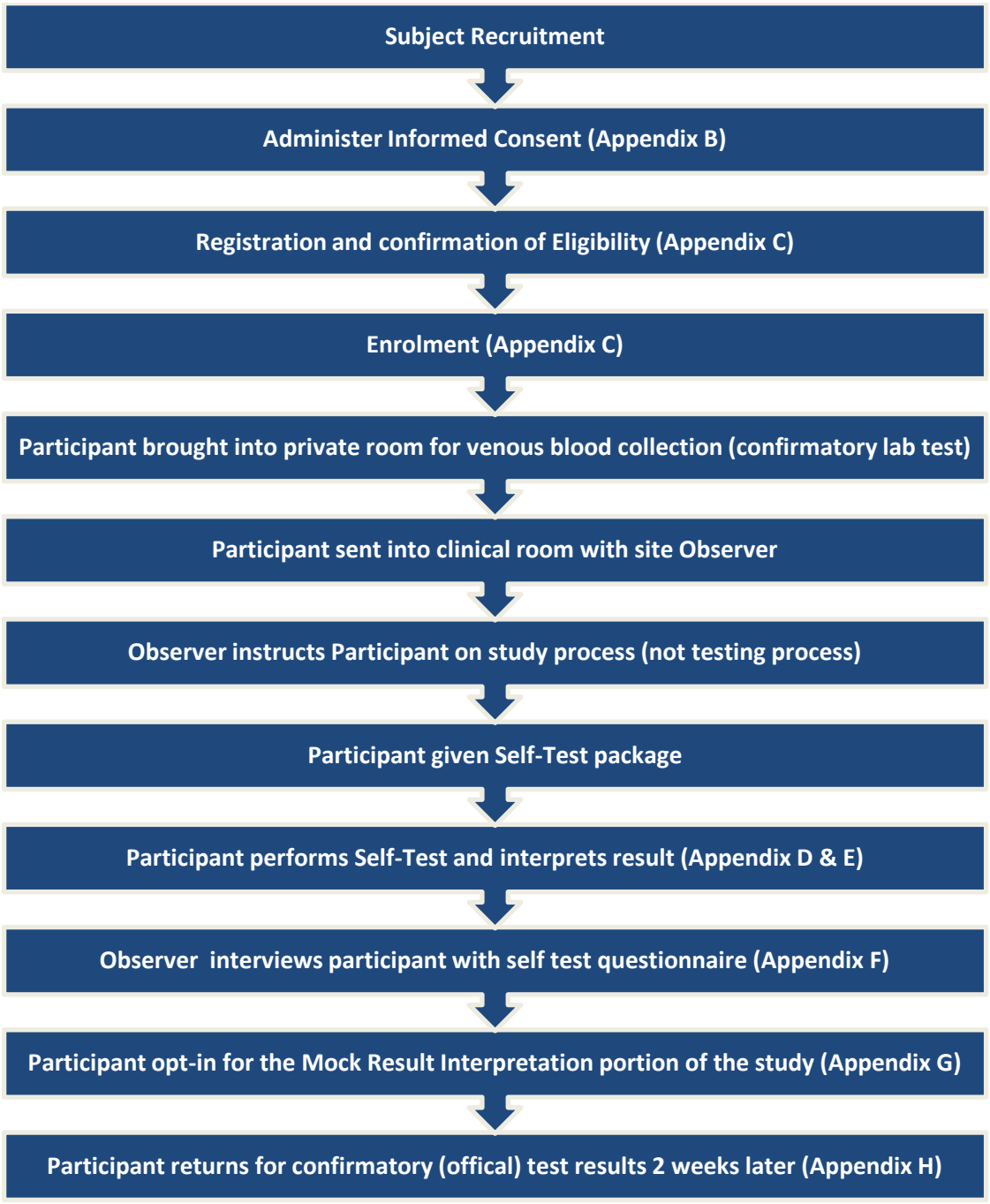
3.1. Overall Study Design

This is a cross-sectional study that employs both observational and interview-based methods.

A minimum of 900 lay participants (non-healthcare professional and inexperienced in HIV self-testing) will read the instructions for use (IFU) and conduct the OraQuick® HIV Self-Test. They will not be provided any training prior to use of the test. A trained healthcare provider or researcher (trained Observer) will watch, and document use of the test and independently read the participants self-test result. The participants will then complete a questionnaire to share their opinion on usability and label comprehension of this test. A minimum of 400 participants will also be provided five mock devices with different results and asked to interpret those results i.e. strong positive; weak positive, negative, invalid with no control and no test line, and invalid with no control and a positive test line.[14]

All participants will also have a venous blood sample collected for testing of plasma at a central laboratory with a 4th generation HIV enzyme immunoassay (EIA) that will serve as the Comparator Method (CM). All self-tests will be confirmed using a Canadian standard HIV testing algorithm. The sensitivity and specificity of the self-test result will be calculated relative to the "clinical truth" of the participants' HIV status determined by the confirmatory test process, where applicable. Participants will be instructed to return to the clinic for a follow-up visit, two (2) weeks after self-testing to obtain their laboratory test results which will be their official result.

Flowchart representation of the overall process from recruitment through Confirmatory testing:



3.2. Study Population

In this study, eligible participants will be those eighteen (18) years or older, of any race or gender. The population will be comprised of a minimum of 900 participants with unknown HIV status (never tested or last known HIV negative test must be a minimum of 3 months prior), including 400 participants at risk for HIV infection e.g. injection drug users (IDU), men who have sex with men (MSM), etc. These participants will be recruited from geographically distinct study sites to represent an ethnic, genetic and HIV risk diverse population across Canada.[14]

3.3. Study Sites

The study will be in up to seven (7) sites across Canada, along with regions utilizing their provincial laboratories, where available. These sites will include clinics that provide services to individuals from high-risk populations such as IDUs, MSM, and members of the African, Caribbean and Black (ACB) and Indigenous communities. This will ensure that we reach our quota of high-risk persons.[14] All study procedures will be conducted under the supervision of the local site principal investigator or his/her designee.

Note: The study sites will follow all appropriate safety requirements that are in place during entire study conduct, to ensure the safety of all participants and the healthcare providers. This will include the use of any appropriate personal protective equipment (PPE), as recommended by each provincial jurisdiction.

3.4. Study Description

Usability

The self-test portion of the study will be performed on consenting persons (referred to as participants) and will include recruitment of participants who have consented to be tested for HIV as per the test procedures outlined.

The participant will be evaluated for the self-test process success or difficulty by a silent, non-interacting trained healthcare professional / researcher (Observer) in the same room. Overall processes include self-test Usability (observation to determine if participants perform all critical steps correctly), Results Interpretation (confirmation by observer to determine if participant interprets test results correctly), and Label Comprehension (questionnaire to determine that the participant is aware of test limitations and what to do following the test result). Successful completion of these tasks will be evaluated as a percentage of the overall process, with all critical errors identified.
Each participant will obtain an oral fluid specimen and perform the test, including result interpretation, according to only those materials provided with the OraQuick® HIV Self-Test (e.g. instructions for use).

Each self-test will be observed by trained healthcare professional/ researcher (referred to as Observers). The Observer does not tutor or interact with the participant conducting the self-test but notes errors and other observations about the participant.

The Observer also interprets the test result, immediately after the participant and within the validated reading time stated in the instructions for use and records the result separately.

All participants will have a venous blood sample taken (typically from the forearm; up to 7mls or about 1.5 tablespoons) and sent to a local provincial laboratory for HIV EIA testing. The laboratory portion of the study will conduct Comparator Method ("CM") testing on plasma from venous blood samples collected from study participants with Health Canada licensed HIV-1/HIV-2 combination antigen/antibody test that is in routine use in the participating local laboratories. Results of all laboratory testing will be shared with the intended use sites since the lab test will serve as the standard of care test.

Sites will be using their local lab or arrange to have samples sent to a lab that uses the same comparator assay.

Results from the lay user OraQuick® HIV Self-Test will be compared to the laboratory HIV EIA testing.

Subsequent care decisions will be based solely on the results of the study site's standard of care test, not on the OraQuick® HIV Self-Test result.

Readability

Participants will also be provided five (5) mock devices with different results and asked to interpret those results. These responses will document whether intended users, (non-professional and inexperienced in HIV self-testing), can successfully interpret contrived strong positive, weak positive, negative and a range of invalid results.

The participants will then complete a questionnaire (see Appendix G) to share their opinion on usability of this test.

3.5. Selection and Withdrawal of Participants

3.5.1. Inclusion/Exclusion Criteria

Participant's eligibility to enroll will be based upon inclusion and exclusion criteria and the signing of informed consent. The requirements for inclusion/exclusion are as follows:

Inclusion Criteria
Participants considered eligible for inclusion are those who:

1. Are 18 years of age and older
2. Are able to speak / read / write English or French
3. Have presented for voluntary testing for HIV infection in the clinic or community based setting
4. Are willing to participate in the study site's standard of care HIV counselling and testing program and receive the study site's standard of care test results
5. Are willing to be a participant in the study
6. Are able to provide informed consent i.e. understands and signs the informed consent form

7. Are able to complete the required testing on the allocated testing day
8. Are willing to provide the necessary oral fluid and venipuncture blood for use in the study protocol testing methods.
9. Are of unknown HIV status (last HIV negative test must be a minimum of 3 months prior)

Exclusion Criteria

Participants considered ineligible for participation in the study are those who meet **any** of the following exclusion criteria:

1. Do not meet all the inclusion criteria
2. Are known HIV positive
3. Are on antiretroviral therapy (ART) or anti-HIV medications for the treatment of HIV, either as pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP) or experimental vaccine
4. Have any experience or have ever conducted a rapid diagnostic self-test for HIV or any other infectious disease
5. Are currently participating in a concurrent trial of HIV self-tests
6. Are investigator site employees or immediate family members of sponsor or investigator site employee
7. Are a practicing medical healthcare professional (doctor, nurse or HIV counsellor that performs HIV testing with Rapid Tests)
8. Any condition which, in the opinion of the Observer, would make the participant unsuitable or unsafe for enrolment or could interfere with the completion of the assessment and questionnaire etc. or bias the outcome, e.g. being unable to see / read by forgetting to bring reading glasses, being intoxicated, acute sickness, visibly distressed.

3.5.2. Withdrawal of Participants

Participants may withdraw from study participation at any time. The Observer will attempt to acquire all study related information and document the reason for withdrawal. Information and data collected up to the time of participant's withdrawal from the study may be used without identifying any personal information, consistent with the informed consent signed for enrollment, unless the participant provides a written request to limit the use and sharing of their study data.

Investigator(s) may separately determine if participation by any subject in this study should be limited or be withdrawn. The investigator may close the study prematurely for any reasons including administrative decisions.

4. STUDY PROCEDURES

4.1 Recruitment

Participants will be recruited from up to seven (7) geographically distinct Canadian sites. Prospective participants will be representative of the Canadian HIV testing population, including a minimum of 400 participants at risk for HIV infection (e.g. IDU, MSM, etc.).

Recruitment of participants will be done through i) clinic and community-based recruitment - after strategic planning and relevant research, the co-investigators will identify active HIV testing clinics and institutions that have an appropriate participant base, ii) word-of-mouth recruitment - participants will be encouraged to tell others about the study and iii) various media channels.

Once participants have been identified through recruitment, they will be approached, informed about the study and the role they will play in the study procedure. These participants must consent to be tested for HIV as per the study site's standard of care procedures before enrolling in the study. These sites will direct all investigative and administrative functions for the study. The participating sites must have the ability to comply with all local government requirements for HIV testing and reporting.

It is anticipated that the target population for this study will include a mix of high-risk and low-risk populations. The total study population will include a minimum of 900 participants whose HIV status is unknown. All 900 participants will be assessed for usability and label comprehension and 400 from the 900 participants enrolled will be asked to participate in a results interpretation study using pre-made devices that will mimic the different test results that might be observed.

Study numbers for each of the study objectives were not computed. They were determined to meet compliance requirements from the Health Canada Guidance Document: Guidance for Manufacturers pf Human Immunodeficiency Virus (HIV) Rapid Diagnostic Tests (RDTs) for use at the point of Care of for Self-Testing.[14]

4.2 Informed Consent

Informed Consent will be obtained from individuals before they are allowed to participate in the trial. The Informed Consent form will be reviewed and approved by a Research Ethics Board (REB) or Ethics Committee (EC). The principal investigator or his/her designated staff will provide the Informed Consent for participation in this study to the participant, explain the nature of the study and sample collection procedures, and answer any questions that might arise. The Informed Consent will contain general information about the study (see Appendix B).

Participants will be consented prior to conducting any study-related procedures. Participants will be encouraged to ask questions to ensure the entire process is clearly understood. Study participants will be instructed that they may reject the specimen collection procedure and withdraw from the study at any time. Participants must agree to and submit their Informed Consent form prior to formal enrolment into the study. The informed consent will be offered after verbal explanation of the study procedures in English/French. The Informed Consent will have the appropriate signature lines that need to be filled out to complete the Informed Consent process, facilitating enrollment.

4.3 Enrollment Questionnaire - Review Eligibility Criteria

Participants providing informed consent and meeting inclusion criteria may be eligible to participate in the study. Participants will be administered an Enrolment Questionnaire to ascertain successful qualification for enrolment (Appendix C). The questionnaire clearly outlines the inclusion and exclusion criteria. If participants satisfy all the inclusion criteria and none of the exclusion criteria, eligibility for enrolment can be confirmed. All participants evaluated for participation in this study will be assigned a unique participant identification number (PID number). Enrolment questionnaires will capture information such as PID Number, Age, Nationality and Employment status. Participants that do not satisfy inclusion/exclusion criteria are documented and reported as exclusions. In addition, the reason for the enrolment failure will also be recorded.

The PID number will also be considered the Participant Number, following the format below:

- AA = Study name
- BB = Province of Investigational Site; example ON for Ontario, QC for Quebec.
- CC = Investigational site number identifier
- DDD = Sequential sample identifier, starting at 001 for all participants
  For example, Self-Test-Ontario-Site#1-Participant#1: ST-ON-01-001:

Multiple copies of pre-printed labels with the PID Number will be provided to the study site facility. These labels will be placed on the forms and whole blood samples.

The enrollment questionnaire will gather the following demographic information:

- Age
- Ethnicity
- Gender
- Experience with HIV testing
- HIV Status/Risk
- Language capabilities
- Visual Status (glasses/contacts)

4.4 Background Data

For all study participants meeting inclusion/exclusion criteria, background data to be collected will include:

- Experience with HIV testing
- Date of last HIV test (approx.)
- Highest education level achieved (None, Primary, Secondary /High School, College/University or Higher)
- Language capabilities
- Employment status (employed/unemployed)
- Visual status (use of reading glasses)
- Reading/writing impairment

4.5 Medical History/ Oral Health

For all study participants meeting inclusion / exclusion criteria, their self-reported medical history will be obtained and documented. In addition to any self-reported medical conditions, specific medical conditions will be queried, in particular the study participant's HIV status. Data to be documented will include:

Medical History - Participants may choose to report their medical history; this will be documented and archived for statistical review. Information may include:

- Self-reported HIV status.
  - Unknown, never tested
  - Unknown, previously tested negative at least three (3) months prior. The date and location of testing along with the type of test is to be recorded, if known.
  - HIV positive. (If yes, the exclusion criterion will be applied)
- Self-reported medical conditions (e.g. diabetes, hypertension, sexually transmitted infections, etc.).
  - Self-reported Ocular health / visual impairment
    - Requirement for, and current use of, glasses or contacts
    - Any condition that specifically affects vision (besides the need of glasses or contacts, (e.g. macular degeneration, etc.)
    - Any other medical condition that the participant has experienced or currently reports, and the date of diagnosis. Study participants' self-report will serve as the source of these data and verification in medical records is not required.
- Self-reported risk category:
  - Unprotected sex with men
  - Unprotected sex with women
  - Multiple sexual partners
  - Injection drug user

  - Born to an HIV positive mother
  - Sexual partner is HIV positive
  - Sexual partner is a bisexual male
  - Other
- Self-reported pregnancy, if applicable.

Oral Health

- Responses to specific oral health questions - Specific presence or absence of oral health conditions
  - Cavities and/or fillings
  - Braces
  - Periodontal disease and/or bleeding gums
  - Oral fixtures; full or partial dentures
  - Specific last use of oral products, food and drink
    - Last food and/or beverage consumption
    - Tooth paste
    - Mouthwash or oral rinse
    - Smoking or smokeless tobacco

4.6 Concomitant Medications

For all study participants meeting inclusion / exclusion criteria, their self-reported current concomitant medications will be obtained and documented. Data documented throughout the study will include:

- General concomitant medications, and herbal or dietary supplements.
- Any medication to treat or prevent HIV (ARV and/or PrEP).

4.7 Dispensing and Return of the OraQuick® HIV Self-Test Device

One OraQuick® Rapid HIV Self-Test will be provided to each participant who qualifies for self-testing. At the conclusion of all testing, the used devices will be collected by the study staff and discarded in accordance with local requirements at the site.

4.8 Participant Self Testing

Study participants will be instructed to perform the self-testing using the OraQuick® Rapid HIV Self-Test. The self-testing is to be completed under the direct observation of the study staff. The study staff will verbally instruct the participant as follows:

"This is the part of the study in which you will be asked to use the study product. With this product and the instructions provided, you can perform the test yourself. Although I will be in the room observing you, I will not be able to answer any questions or talk to you while you are using the product, but I will be looking to see how you use it. When you are finished, I would like you to tell me what you think the

test result is. I will also ask you questions about your experience and what you observed during the test."

The participant will then be permitted to perform the self-test. Their test result and any additional comments will be record in Appendix D - Participant's OraQuick® HIV Self-Test Result Record Form. After the result interpretation portion, the Observer will ask the participant questions about the test procedure and complete Appendix F - Self-Test Questionnaire with the participant's responses.

4.9 Observations and Verification of Participant Self-Testing

The self-testing site must minimally provide for the following:

- Privacy from other study participants, or study staff other than the staff performing observations
- Seating
- Counter, desk, or other space to place the test kit
- Adequate lighting, with the ability for the participant to control lighting
- An obvious manner to measure time (wall clock, desk clock)

Dependent upon the study sites' physical layout, the research staff observing the study participant may or may not be visible to the participant. In any case, the staff is **not** to interact with the participant during testing, unless intervention is required for a study participants' wellbeing or privacy. During the study participant self-testing, the study staff will collect the following observational data for correct performance of the test. These ratings will be collected as the Observational Ratings of Self-Test Performance. Data that will be collected are described in Appendix E - Observer's data collection form.

Observational Ratings of Study Participant-Self Test Performance include:

- Did the study participant read the instructions for use?
- Was the study participant able to find the test tube packet?
- Did the study participant remove the test tube from the packet?
- Did the study participant remove the cap from the test tube?
- Did the study participant place the test tube in the holder?
- Did the study participant have any difficulty with the test tube?
- Was the study participant able to find the test stick packet?
- Did the study participant remove the test stick from the packet?
- Did the study participant touch the flat pad?
- Did the study participant collect the sample correctly (1x upper and lower swab)?
- Did the study participant place the test stick in the test tube correctly?

Observers will also record the following:

- IFU language instruction the study participant used (French or English)
- Time study participant starts the test (places the device in the test stand after collecting oral fluid).
- Time of study participant reads the test.
- Study participant's apparent level of distress:
  - Calm
  - Appears anxious
  - Verbally communicates distress
  - Staff intervention required

After the study participant has completed the self-testing they will be requested to provide their result to the staff. The Observer will question the study participant, as follows:

"According to the product instructions, can you please tell me what you think the result of your test is?"
Any ambiguous verbal answer by the participant will have one attempt made to clarify it.

The study participant's response will be interpreted by a check box with five possible selections:

- Do not have HIV / negative
- May have HIV / preliminary positive
- Test not working / invalid
- Not sure / don't know
- Refused or ambiguous answer

If the test could not be completed, this will also be documented.
The Observer will also review the study participant's interpretation of their test.

4.10 Observer's Interpretation of Study Participant's Self-Test Result

Following the completion of the study participant's self-testing interpretation, the Observer will make their own interpretation of the study participant's test result. This should be the site staff who observed the study participant's self-test. Data to be collected will be:

- The Observer's interpretation of the study participant's self-test result.

The Observer's interpretation of the study participant's self-test is intended to allow for review of the data regarding study participants' potential failure to obtain a result versus incorrect interpretation of the result they do obtain.

In the case of a truly invalid test by the study participant, the test will not be repeated.

4.11 Interpretation of Results – Mock Devices

At the end of the self-testing process, the Observer may ask subjects to participate in a 'Mock Result Interpretation' study that will involve interpreting a separate set of OraQuick® HIV Self-Test results prepared by the manufacturer. Participation is voluntary and up to 400 participants recruited from the 900 participants who consented for the device accuracy study will conduct this Mock Result Interpretation. If participant agrees to participate, they will be presented with five (5) OraQuick® HIV Self-Test mock result types and asked to interpret the results using the Self-Test instructions for use (IFU) as a guide. The five (5) mock devices will be the following:

1. Strong Positive
2. Weak Positive
3. Negative
4. Invalid (no control line present, test line present)
5. Invalid (no control line or test line present)

Mock devices will be presented in a randomized order to control bias.

Although the self-test study participants will be interpreting the results of their own OraQuick® HIV Self-Test, the purpose of this sub-study is to document if intended users, (non-professional and inexperienced in HIV self-testing), can successfully interpret contrived/mock strong positive, weak positive, negative and invalid results. Results of this interpretation will be recorded by the Observer on Appendix G - Participant's Mock OraQuick® HIV Self-Test Result Interpretation Record Form.

4.12 Post-Assessment Questions/Label Comprehension

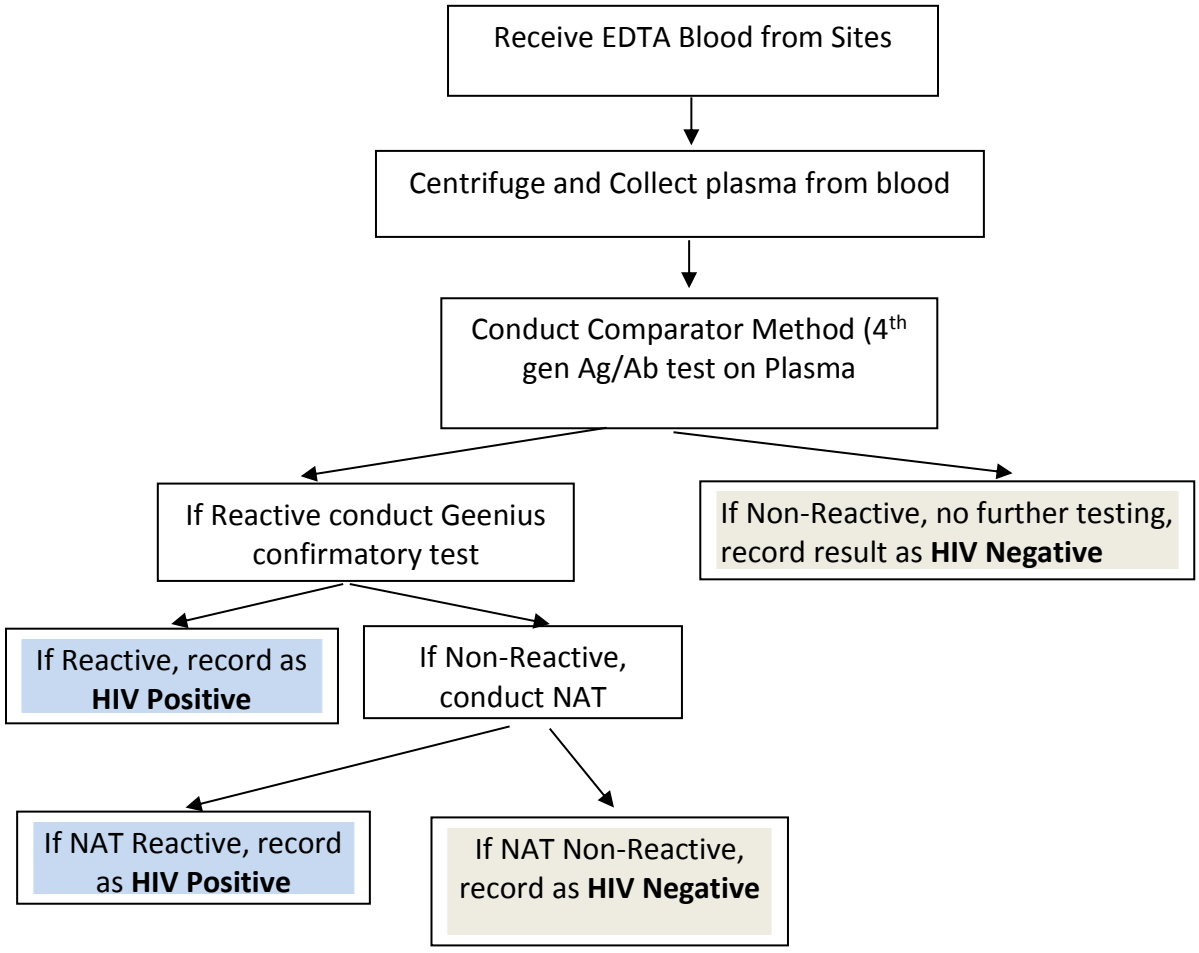
Participants will answer a series of questions after they complete the OraQuick® HIV Self-Test assessment and Interpretation of Results – Mock Devices. Questions related to warnings and precautions and the key following information is included in the post-questionnaire:

- What would you do next if your test results were negative?
- What would you do next if your test results were positive?
- What would you do if your test results were invalid?
- Did you use the Instruction sheet to help you complete the test? If No, please explain
- Was the device easy to use? If No, please explain
- Are you confident you could perform this test on your own? If No, please explain
- Would you use this test again if it were available to you? Would you recommend this test to others?
- How long after ingesting food or drink should you wait to test?

4.13 Confirmatory Procedures

All self-test results will be confirmed using a HIV-1/HIV-2 Antigen/Antibody Combo Test (Comparator Method "CM") performed on venous blood plasma at the central laboratory. A venous whole blood specimen will be collected from all study participants and sent to a central laboratory within 72 hours to establish the CM and any further confirmatory results for all participants. An appointment will be scheduled with the participants to return to the study site to collect their standard-of-care testing result. The Laboratory Confirmatory testing decision tree is presented below.

Laboratory Testing Procedure for HIV EDTA Blood and Plasma



For venous blood collection, the study site personnel will follow standard phlebotomy procedures. A maximum of 7 mL of whole blood will be collected by the study site personnel using a lavender top (EDTA) blood collection tube for HIV confirmatory testing done at the laboratory from study participants.
All clinical laboratory testing will be performed using a 4th generation HIV-1/HIV-2 Antigen/Antibody Combo Test.

4.14 Additional Procedures and for Study Participants with Preliminary Positive Self-Test Results

Any study participant who has a preliminary positive OraQuick® HIV Self-Test result, as determined by the trained Observer's interpretation of the study participant's self-test will be counseled by the appropriate study staff regarding the meaning of their result consistent with current guidelines and local standard operating procedures (SOPs) for HIV counseling knowing that this test is investigational and that their laboratory results will be the official reportable results.

4.15 Additional Procedures for Study Participants with Negative Results

Any study participant who has a negative OraQuick® HIV Self-Test result, as determined by the trained Observer's interpretation of the study participant's self-test will be counseled by the appropriate study staff regarding the meaning of their result consistent with current guidelines knowing that this test is investigational and that their laboratory results will be the official reportable results.

4.16 Compensation for Study Participants

Participants will be compensated for their time and effort in this study. The compensation amount will be up to $75 in total. On the 1st visit to the clinic and upon completion of the main study procedures (Appendix H), the participant will receive $50 and if they return in two weeks for their laboratory test result, they will receive the remaining $25.

5. QUALITY CONTROL AND ASSURANCE

Quality Control on the study will be done following the Standard Operating Procedures developed for the study and those generic to the organization. The Research Manager assumes overall responsibility for ensuring all procedures are adhered to and quality controlled.

5.1 Training

Prior to the study, the Principal Investigator will ensure that all study staff are trained on the protocol and all study procedures.

5.2 Trained Researcher/ Observer Responsibilities

The site will provide a minimum of two (2) trained Observers responsible for enrolling eligible participants, collecting samples, and running, interpreting, and documenting the results of the OraQuick® HIV Self-Tests. Prior to the beginning

of the study, all trained observers will receive appropriate training that covers study procedures, as well as, instructions for performing the test.

5.3 Study Monitoring

The study will be monitored by the Research Manager or designate to ensure compliance with local laws and regulations and to ensure data quality. This person has the obligation to follow the study closely and in doing so, will routinely visit the site(s) at periodic intervals, to assess study status and review study procedures and applicable documents. Site visits can be in person or virtual, depending on any pandemic-related restrictions in place during the study period. They will also maintain necessary telephone and email contact. The monitor will maintain current personal knowledge of the study through observation, review of study records and source documentation, and discussion of the conduct of the study with the Principal Investigator and study staff.

6. DATA ANALYSIS

6.1. Data Management Processes

All participant data will be collected using tablets on the survey software tool Qualtrics. All tablets are password-protected. Qualtrics software stores participant data on local, secure servers in Toronto. Only the St. Michael's Hospital Research staff will be able to access the data from the Qualtrics servers. This data will be password-protected. Data will then be downloaded and saved to secure encrypted servers at St. Michael's Hospital for further analysis. Data monitoring will be performed daily by the St. Michael's Hospital Research staff. All data will be stored on secure servers at St. Michael's Hospital until the data analysis stage of the project. All study data will be tabulated using appropriate software and methods. Data will be archived by the study Sponsor and maintained for 7 years after the end of the study.

6.2. Data Reporting

Data analysis and reporting will be performed by the Research Manager and study consultants. A research report will describe the study area, the study population, the execution of the research, and present the study results. The report will present both qualitative and quantitative discussions of the outcomes of the study.

6.3. Primary Analysis

The primary analyses will be sensitivity and specificity of study participants' self-interpreted self-test results with the OraQuick® HIV Self-Test versus the HIV status as determined by the 4th generation EIA and confirmatory testing if necessary. The 95% confidence interval will also be determined by the Wilson Score Method.

- Sensitivity = [TP / (TP + FN)] x 100, where
  - TP (true positive) is positive OraQuick® HIV Self-Test in agreement with HIV positive status and
  - FN (false negative) is negative OraQuick® HIV Self-Test discordant with HIV positive status.
- Specificity = [TN / (TN + FP)] x100, where
  - TN (true negative) is negative OraQuick® HIV Self-Test in agreement with HIV negative status , and
  - FP (false positive) is positive OraQuick® HIV Self-Test discordant with HIV negative status.

Invalid and unknown/unsure results and participants with inclusion/exclusion violations will be excluded from the sensitivity and specificity analysis. All excluded participant results will be documented with the reason why.

6.4. Secondary Analysis

Secondary efficacy analysis may be performed for the following sub-groups listed below. If conducted, it will include descriptive statistics of the sensitivity and specificity analyses among various subgroups for each specificity and sensitivity for the following factors:

- Age.
- Language capabilities (self-reported).
- Educational level.
- Literacy level
- Risk Factors
- Risk Populations

Additional secondary efficacy analyses will include the descriptive statistics of the following:

- Observational Ratings of Study Participant Self-Test Performance
- Trained User's (Observer) Interpretation of Study Participants Self-Test Result
- Participant Mock Study Results

6.5. Demographics

The following will be summarized with descriptive statistics:

- Demographic Data
- Background Data
- Medical History

6.6. Error and Failure Rates

Specific critical and non-critical steps are identified from the OraQuick® HIV Self-Test Instructions for Use.

Critical errors occur when participants perform operational errors during the assay which could potentially invalidate the results, such as specimen collection errors or terminating the process before completion.

Non-critical errors occur when participants perform errors that may deviate from the Instructions for Use but do not invalidate results. The successful completion of tasks will be evaluated as a percentage of the overall process, with all critical errors identified.

Errors are defined in the table below:

Task	**Category (critical / non-critical)**
Reads the instructions for use	Critical
Able to find the test tube packet	Non-Critical
Remove the test tube from the packet	Critical
Remove the cap from the test tube	Critical
Placed the test tub in the test stand (holder)	Critical
Able to find the test stick packet	Non-Critical
Remove the test stick from the packet	Critical
Touching the flat pad	Critical
Correctly collected the oral fluid sample	Critical
Placing the device in the test tube (developer vial)	Critical
Read the results within the 20-40 minute window	Critical

6.7. Sample Size

Sample size for this study was based on the Health Canada Guidance Document: Guidance for Manufacturers of Human Immunodeficiency Virus (HIV) Rapid Diagnostic Tests (RDTs) for use at the Point of Care or for Self-Testing.[14] The sample size requirements for a near-patient study with untrained self-testers is a minimum of 900 laypersons with unknown HIV status, including 400 persons at risk for HIV infection (e.g. IDU, MSM, etc.). To assess the ability of untrained self-testers to correctly interpret a variety of pre-made mock (contrived) devices test results, a minimum of 400 persons are required. A minimum of 200 self-testers are required to assess for label comprehension.[14]

It should be noted that the OraQuick ADVANCE® HIV-1/2 Rapid Antigen Test is not intended for use by individuals that are known to be HIV positive.

7. OBLIGATIONS OF THE INVESTIGATOR

7.1 Retention of Records

Data collected throughout the duration of the study will be stored for 7 years on secure servers at St. Michael's Hospital. After this time period, all data will be destroyed by the SMH Study Team. This storage strategy is compliant with St. Michael's Hospital Data Security to store/encrypt all data. Electronic data will be securely and confidentially stored and will not contain any identifying information. Other sites that obtained data though data transfer will also destroy any data after 7 years of study completion.

If an investigator moves, withdraws from an investigation, or retires, the responsibility for maintaining the records may be transferred to another person, who is willing to accept the responsibility.

7.2 Device Accountability

The principal investigator or his/her designees will maintain accurate records of all investigational assays/devices used in each study performed under this protocol. Damaged, dropped, or otherwise destroyed devices will be noted and documented on the device accountability form.

7.3 Protocol Amendments

Amendments to the protocol must be submitted in writing to the REB for approval before participants are enrolled into an amended protocol, except where it is necessary to eliminate an immediate hazard to participants or where the changes involve only logistical or administrative aspects of the clinical study. This should be fully documented. Protocol amendments must be prepared by the Principal Investigator responsible for the study and reviewed and approved according to local authorities and REB/EC. With the exception of administrative changes, any modifications or additions to this study protocol require a justified, written protocol amendment that must be approved by the Principal Investigator, local authorities, and REB/EC. Amendments potentially affecting the safety of study participants, the scope of the investigation or the scientific quality of the study, require approval. A copy of the written approval must be maintained by the Principal Investigator.

Examples of amendments requiring such approval are:

- A significant change in the study design
- An addition or deletion of a test procedure for safety monitoring

These requirements for approval should in no way prevent any immediate action from being taken by the investigator or the sponsor in the interests of preserving the safety of all study participants included in the trial. If an immediate change to the protocol is deemed necessary by the investigator and is implemented by

him/her for safety reasons, the study Principal Investigator should be notified and the REB/EC should be informed within ten (10) working days.

7.4 Protocol Violations and Deviations

The Principal Investigator or designate must document and explain in the participant's source documentation any deviation from the approved protocol. The principal investigator or designee may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial participants without prior REB approval. As soon as possible after such an occurrence, the implemented deviation or change, the reasons for it, and any proposed protocol amendments should be submitted to the REB for review and approval and to the regulatory authorities, if required.

A deviation from the protocol is an unintended or unanticipated departure from the procedures or processes approved by the REB and agreed to by the principal investigator or designee. Deviations usually have an impact on individual participants or a small group of participants and do not involve inclusion, exclusion or primary endpoint criteria.

A protocol violation occurs when there is non-adherence to the protocol that results in a significant, additional risk to the participant, when the participant or principal investigator or designee has failed to adhere to significant protocol requirements (inclusion and exclusion criteria) and the participant was enrolled without prior approval, or when there is non-adherence to regulations or some ICH GCP guidelines.

Protocol violations and deviations will be documented by the Research Manager or designate throughout the course of monitoring visits. Principal investigators or designees will then be notified in writing of violations and deviations. The REB should be notified of all protocol violations and deviations in a timely manner.

7.5 Adverse Events and Adverse Device Events Reporting

7.6 7.5.1 Adverse Events

Adverse events shall be reported as per section 59 and section 62 of the Medical Device Regulations. Any Serious Adverse Event or Adverse Device Event which may occur in a Participant from this population will be reported to the Principal Investigator.

Assessment of adverse events (AE) will be carried out during all parts of the study. An AE is defined as any untoward medical occurrence in a Participant using the device under this protocol, which does not necessarily have a causal relationship with this use. An AE, therefore, can be any

unfavorable and unintended sign, symptom, or medical condition temporarily associated with the use of the study product, even if the event is not considered to be related to the study product.

Adverse events will be collected from the time the informed consent signed until the completion of all study procedures during an individual study visit. Information about all AEs, whether volunteered by the Participant, discovered by investigator questioning, or detected through physical examination, or other means, will be collected and recorded on the Adverse Event CRF (Appendix J) and followed as appropriate.

As much as possible, each AE will also be described by:

1. Its duration (start and end dates)
2. The severity grade (mild, moderate, severe)
3. Its relationship to the study product (definite, probably, possibly, unrelated)
4. The action(s) taken and
5. Any relevant outcome.

7.7 Severity of Adverse Events

The investigator is to classify the severity of an AE according to the following definitions:

- Mild: The Participant is aware of signs or symptoms, which are easily tolerated.
- Moderate: The signs and symptoms are sufficient to restrict, but not prevent, usual activity.
- Severe: The Participant is unable to perform usual activity.

The maximum intensity of an AE (mild, moderate, or severe) will be assessed at each visit taking into account the possible range of intensity of the symptom(s).

7.8 Relationship of Adverse Events to the Device

The investigator is to classify the relationship of an AE to the investigational product according to the definitions outlined below.

Association	Definition
None (unrelated)	(1) The existence of a clear alternative explanation or (2) non-plausibility.
Possible	A clinical event with a reasonable time sequence to product use, but which could also be explained by concurrent disease or other agents.
Probable	A clinical event with a reasonable time sequence to product use, unlikely to be attributed to concurrent disease or other agents, and which follows a clinically reasonable response on withdrawal.
Definite	The properties of the study device and the course of the AE after treatment indicated involvement of the study product in the occurrence/worsening of the AE and no indication of other causes existed.

7.9 Serious Adverse Events (SAE)

The ICH Guideline E2A, entitled "Clinical Safety Data Management: Definitions and Standards for Expedited Reporting" defines a **serious adverse event (SAE)/experience** or reaction as being any untoward medical occurrence which:

- Is fatal or life-threatening
- Requires or prolongs hospitalization
- Results in persistent or significant disability/incapacity
- Is medically significant, may jeopardize the participant, and may require medical or surgical intervention to prevent one of the outcomes listed above or
- Is a congenital anomaly/birth defect.

Events **not** considered to be serious adverse events are hospitalizations for the:

- Routine treatment or monitoring of the studied indication, not associated with any deterioration in condition
- Treatment, which was elective or pre-planned, for a pre-existing condition that did not worsen and/or
- Treatment on an emergency, on a participant-by-participant basis for an event not fulfilling any of the definitions of serious given above and not resulting in hospital admission.

To ensure participant safety each SAE must also be reported to the sponsor or its designee and to the responsible REB within 72 hours of learning of the occurrence.

7.10 Adverse Device Effects (ADE)

An Adverse Device Effect (ADE) is any AE that occurs to the participant as a result of using the device (i.e., is Possible, Probable or Definite in relationship).

Unanticipated Adverse Device Effects (UADEs)

An Unanticipated Adverse Device Effect is any adverse events that the principal investigator determines to be attributable to an investigational specimen collection device that is serious or not previously identified in nature, severity of degree of incidence in the current protocol or investigator brochure.

For all ADEs (AEs related to the use of the device) that are unexpected, unanticipated AND serious, the investigator should notify the responsible REB/EC and the manufacturer within 72 hours or learning of the occurrence.

7.11 Confidentiality of Participant Specimens and Information

Participant confidentiality will be carefully maintained. All documents, reports, and other records will be identified in a manner designed to maintain participant confidentiality. Participants will only be identified in the study by their PID number. Testing records and laboratory specimens will be coded to protect the participants' confidentiality. All records will be kept in a secure storage area with limited access. Clinical information will not be released without the written permission of the participant, except as necessary for monitoring and auditing by the regulatory authorities or the Research Manager. The Principal Investigator and all employees involved with this study may not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished confidential information disclosed to those individuals for the purpose of the study. All computers will be password-protected and records can only be accessed by permitted study staff. Compliance with Federal and Provincial Data Protection regulations, including the Personal Information Protection and Electronic Documents Act (PIPEDA 2000) will be ensured throughout the study conduct.

7.12 Investigator Documentation

Prior to beginning the study, the Investigators will be asked to comply with ICH E6 (R1) 8.2 by providing the following essential documents, including but not limited to:

- An original investigator-signed investigator agreement page of the protocol
- An REB-approved Consent Form, samples of any site advertisements for recruitment for this study, and any other

written information regarding this study that is to be provided to the participants

- REB approval for the study site jurisdiction if required above a central REB approval
- Curriculum vitae for the principal investigator and each investigator. They will be signed and dated by each investigator at study start-up, indicating that they are accurate and current.
- Principal investigators or designee and institutions involved in the study will permit study-related monitoring, audits, review, and regulatory inspections by providing direct access to all study records.

7.13 Study Termination

Although REACH 3.0 has every intention of completing the study, it reserves the right to discontinue the study at any time for clinical or administrative reasons. The end of the study is defined as the date on which the last participant completes their last visit to the study site.

8. References

1. Kurth AE, Cleland CM, Chhun N, Sidle JE, Were E, Naanyu V, et al. Accuracy and Acceptability of Oral Fluid HIV Self-Testing in a General Adult Population in Kenya. AIDS Behav [Internet]. 2016 Apr 1 [cited 2021 Mar 12];20(4):870–9. Available from: https://pubmed.ncbi.nlm.nih.gov/26438487/
2. Choko AT, MacPherson P, Webb EL, Willey BA, Feasy H, Sambakunsi R, et al. Uptake, Accuracy, Safety, and Linkage into Care over Two Years of Promoting Annual Self-Testing for HIV in Blantyre, Malawi: A Community-Based Prospective Study. Bangsberg DR, editor. PLOS Med [Internet]. 2015 Sep 8 [cited 2021 Mar 12];12(9):e1001873. Available from: https://dx.plos.org/10.1371/journal.pmed.1001873
3. Pant Pai N, Sharma J, Shivkumar S, Pillay S, Vadnais C, Joseph L, et al. Supervised and Unsupervised Self-Testing for HIV in High- and Low-Risk Populations: A Systematic Review. Weiser SD, editor. PLoS Med [Internet]. 2013 Apr 2 [cited 2021 Mar 12];10(4):e1001414. Available from: https://dx.plos.org/10.1371/journal.pmed.1001414
4. Miller CM, Ketlhapile M, Rybasack-Smith H, Rosen S. Why are antiretroviral treatment patients lost to follow-up? A qualitative study from South Africa. Trop Med Int Heal [Internet]. 2010 Jun [cited 2021 Mar 12];15(SUPPL. 1):48–54. Available from: https://pubmed.ncbi.nlm.nih.gov/20586960/
5. Johnson C, Baggaley R, Forsythe S, Van Rooyen H, Ford N, Napierala Mavedzenge S, et al. Realizing the potential for HIV self-testing [Internet]. Vol. 18, AIDS and Behavior. Springer New York LLC; 2014 [cited 2021 Mar 12]. Available from: https://pubmed.ncbi.nlm.nih.gov/24986599/
6. Kalibala S, Tun W, Cherutich P, Nganga A, Oweya E, Oluoch P. Factors associated with acceptability of HIV self-testing among health care workers in Kenya. AIDS Behav [Internet]. 2014 Jun 29 [cited 2021 Mar 12];18(SUPPL. 4):405–14. Available from: https://link.springer.com/article/10.1007/s10461-014-0830-z
7. US Food and Drug Administration. FDA - OraQuick ADVANCE Rapid HIV-1/2 Antibody Test [Internet]. US FDA. 2020 [cited 2021 Apr 1]. Available from: https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/oraquick-advance-rapid-hiv-12-antibody-test
8. US Food and Drug Administration. FDA - OraQuick In-Home HIV Test [Internet]. US FDA. 2020 [cited 2021 Apr 1]. Available from: https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/oraquick-home-hiv-test
9. World Health Organization. WHO Prequalification of In Vitro Diagnostics Public Report: OraQuick HIV Self-Test (WHO ref. num: PQDx 0159-055-01; OraSure Technologies, Inc.) [Internet]. Geneva; 2019 Nov [cited 2021 Apr 1]. Available from: https://apps.who.int/iris/bitstream/handle/10665/251857/9789241511742-
10. Gauss E. Unitaid and HIV/AIDS [Internet]. 2017 Jul [cited 2021 Apr 1]. Available from: www.unitaid.org
11. Unitaid. Marketplace and technology landscape: HIV rapid diagnostic tests for self-testing, 3rd Edition. Geneva; 2017.
12. World Health Organization. Technical Specifications Series for submission to WHO Prequalification - Diagnostic Assessment Human: TSS-1: Immunodeficiency Virus (HIV)

rapid diagnostic tests for professional use and/or self-testing [Internet]. Geneva; 2016 [cited 2021 Apr 1]. Available from: https://apps.who.int/iris/bitstream/handle/10665/251857/9789241511742-eng.pdf;sequence=1

13. International Council for Harmonisation of Technical Requirements. ICH Efficacy Guidelines [Internet]. ICH. [cited 2021 Apr 1]. Available from: https://www.ich.org/page/efficacy-guidelines
14. Health Canada: Therapeutic Products Directorate - Health Products and Food Branch. Guidance Document: Guidance for Manufacturers of Human Immunodeficiency Virus (HIV) Rapid Diagnostic Tests (RDTs) for use at the Point of Care or for Self-Testing [Internet]. Ottawa; 2017 Nov [cited 2021 Mar 15]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/guidance-documents/human-immunodeficiency-virus-rapid-diagnostic-tests-home-use.html#table1

9. Appendices

1) Appendix A: OraQuick HIV Self-Test Instructions for Use (IFU)
2) Appendix B: Informed Consent Template
3) Appendix C: Enrolment Questionnaire
4) Appendix D: Participant's OraQuick® HIV Self-Test Result Record Form
5) Appendix E: Observer's Data Collection Form
6) Appendix F: Self-Test Questionnaire with the Participant's Responses
7) Appendix G: Participant's Mock OraQuick® HIV Self-Test Result Interpretation Record Form
8) Appendix H: Visit 1 Completion Form
9) Appendix I: Participant's Confirmatory Test Results Record Form (Visit 2 Completion)
10) Appendix J: Adverse Event Reporting Form

Appendix A: OraQuick HIV Self-Test Instructions for Use (IFU)

Appendix B: Informed Consent Template

Appendix C: Enrolment Questionnaire

Appendix D: Participant's OraQuick® HIV Self-Test Result Record Form

Appendix E: Observer's Data Collection Form

Appendix F: Self-Test Questionnaire with the participant's responses

Appendix G: Participant's Mock OraQuick® HIV Self-Test Result Interpretation Record Form

Appendix H: Visit 1 Completion Form

Appendix I: Participant's Confirmatory Test Results Record Form (Visit 2 Completion)

Appendix J: Adverse Event Reporting Form