WHO PROTOCOL FOR PERFORMANCE
LABORATORY EVALUATION OF HIV SELF-TESTING SEROLOGY ASSAYS
(CAPILLARY BLOOD)
3. **Introduction**

3.1. **WHO Prequalification of in vitro diagnostics**

The World Health Organization (WHO) Prequalification of In Vitro Diagnostics is coordinated through the Prequalification-Diagnostics Assessment team (PQDx). The aim of the WHO Prequalification of In Vitro Diagnostics Assessment is to promote and facilitate access to safe, appropriate and affordable diagnostics of good quality in an equitable manner. Focus is placed on products for high burden diseases and their suitability for use in resource-limited settings.

The WHO prequalification of in vitro diagnostics process includes three main components:

- Review of an pre-submission form and product dossier;
- Performance evaluation of the product;
- Inspection of the manufacturing site(s).

Performance evaluation will be conducted by two different mechanisms as described at: [http://www.who.int/diagnostics_laboratory/evaluations/alternative/en/](http://www.who.int/diagnostics_laboratory/evaluations/alternative/en/). Performance evaluation in List 1 laboratories will be coordinated and paid for by WHO. Performance evaluation in List 2 laboratories will be coordinated and paid for by the manufacturer.

This protocol provides the details of the procedure for evaluation of HIV self-testing serology assays using capillary blood submitted for Performance evaluation as part of the WHO Prequalification of In-vitro Diagnostic assays on behalf of World Health Organization at the WHO Prequalification Evaluating Laboratory.

This protocol shall not replace more extensive IVD manufacturer’s protocols required for validation and verification studies of their products

3.2. **WHO Performance laboratory evaluation of rapid diagnostic tests (RDTs) for HIV-1/2 antibodies using capillary blood.**

The performance evaluation determines the accuracy of HBsAg assays in comparison with established performance criteria. These characteristics include: sensitivity, specificity, negative and positive predictive values as well as the accuracy. In addition, a number of operational characteristics are assessed including the suitability for use in laboratories and/or testing settings with limited infrastructure.

Rapid diagnostic tests for the detection of HIV-1/2 antibodies using capillary blood are covered in this protocol.

All assays submitted for performance evaluation are assessed at a WHO Prequalification Evaluating Laboratory which has been assessed and listed using the WHO Alternative Performance evaluation Mechanism upon the instruction of WHO/PQDx (List 1 laboratories) or a manufacturer (List 2 Laboratories) who has submitted an IVD for WHO assessment.

The HIV specimen reference panel shall comprise a minimum of 400 anti-HIV positive and 600 anti-HIV negative capillary blood specimens plus several well-characterized commercial seroconversion panels and performance panels, a lot-to-lot variation panel, WHO international biological reference preparations.
4. Study objectives

4.1. Overall objectives
The overall objectives are:
1. To evaluate and compare the accuracy of currently available HIV rapid diagnostic tests (RDTs) for detection of HIV-1/2 antibodies using capillary blood against a reference testing result.

4.2. Specific objectives
The specific objectives of the performance evaluation are:
1. To determine the sensitivity and specificity of currently available HIV RDTs for the detection of HIV-1/2 antibodies in capillary blood samples as compared to a reference testing result of using (one antibody detection enzyme immunoassay (EIA), one antibody/antigen EIA and/or one HIV nucleic acid testing (NAT), performed on a matched plasma specimen.
2. To evaluate the operational characteristics of the HIV RDTs, e.g. ease of performance, inter-reader variability, reaction endpoint stability, rate of invalid runs/devices, suitability for use in extreme climates (high/low temperatures, high humidity), and suitability for use in countries with limited infrastructure (no/limited electricity, no/limited clean water, and inadequate means of biosafety disposal).

5. Study Design

5.1. Reference laboratory
The WHO Prequalification Evaluating Laboratory shall be one that has undergone assessment using the WHO Alternative Laboratory Evaluation Mechanism which include submission of an EoI, Stage 1 audit (Assessment of EoI and specific quality management system (QMS) documentation), Stage 2 audit which include On-site audit of the laboratory to assess compliance with WHO requirements and lastly listed as WHO Prequalification Evaluating Laboratories. http://www.who.int/diagnostics_laboratory/evaluations/alternative/en/.

The laboratory shall hold the following certification for quality management within the laboratory: ISO17025 (General requirements for the competence of testing and calibration laboratories), ISO15189 (Medical laboratories: Particular requirements for quality and competence) or equivalent.

The person(s) listed in the EoI letter to WHO will act as the Principal Investigator (PI) for the work performed by the WHO Prequalification Evaluating Laboratory.

5.2. Training, performance evaluation and supervision
The following issues are key to minimizing error and maximizing the value of this evaluation:
- The PI will be responsible for training the laboratory technicians on the evaluation protocol and on the performance of each assay undergoing evaluation after demonstration by the manufacturer;
- Only those personnel who have received specific training for this evaluation will be involved in the evaluation;
- Accurate record keeping is crucial to the success of the evaluation and the PI will be responsible for ensuring that all data collected during the evaluation are recorded on the agreed data collection sheets, and are accurate and up to date;
It is important to plan work in advance and follow standard operating procedures as prepared and controlled by WHO Prequalification Evaluating Laboratory;

To reduce the risk of adding an incorrect specimen to a test device/well, before starting the test run, the operator will prepare worksheets and label all tubes, dilution vessels, test devices or plates with the specimen’s unique number;

Because objective, machine-generated, permanent results for simple/rapid diagnostic tests are not feasible, it is essential that the PI emphasizes to the operator performing the tests the need for accurate recording of results and recordkeeping;

To minimize the risk of error, it is recommended that the results are read and recorded independently by two trained staff members. If the two readers disagree, a third reader will act as tie-breaker reader. A consensus result will be recorded as the interpretation that occurs two out of three times.

To allow immediate correction of erroneous recording of results (rather than differences in visual interpretation), the PI or designee should assess the results as soon as possible to allow her to return to the original test device to investigate apparently discordant readings;

At least one representative result from both HIV positive and negative specimens will also be recorded by taking electronic images. Unexpected test results will also be digitally recorded as well an image of the instructions for use.

5.3. Safety

HIV, Hepatitis B and Hepatitis C and other blood borne pathogens are transmissible by blood and body fluids. Therefore, all types of specimens (including venous and capillary whole blood, serum/plasma, etc.) must be handled as potentially infectious. Appropriate precautions to minimize infectious hazards must be taken at all stages from the collection of specimens to the disposal of used materials from the laboratory. The WHO Guidelines on HIV Safety Precautions, and Guidelines for the Safe Transport of Specimens (WHO/EMC/97.3) and the NHLQA&TC guidelines on laboratory safety should be carefully followed by the laboratory staff.

5.4. Storage of assays

All reagents must be stored as indicated in the instructions for use. Some assays may not need refrigeration. If refrigerated storage space is inadequate to store the entire test kit, they may be divided so that labile reagents can be refrigerated separately from the non-labile supplies. Calibrated thermometers are placed at each location where reagents and specimens are stored, i.e. ambient, refrigerator and freezer. Temperatures are recorded daily on the WHO Prequalification Evaluating Laboratory temperature logs. The lot numbers of the test kits received/used and their expiry dates are recorded on the individual run worksheets.

Two separate production lots (with different lot numbers and different expiry dates) will be requested for evaluation, according to the following definition of a lot: “The amount of material that is uniform in its properties and has been produced in one process or series of processes. The material can be either starting material, intermediate material or finished product.” Furthermore, lots must be sourced from a representative production run and not produced especially for the purpose of this evaluation. WHO will verify this information before the product assessment has been finalized.
6. Specimens

6.1. Capillary blood specimen collection and testing

6.1.1. Ethical consideration

The study participants will include patients attending HIV care and treatment Centre and donors at blood donation centre. The participants will be asked to provide written informed consent before collection of the blood specimen. The specimens will include capillary whole blood collected directly into the device and matched left over plasma specimens collected for clinical care. The collected plasma specimens will only be used to evaluate new assays after the clinical testing results have been obtained and used for patient care where relevant. All the individual identifiers will be removed and replaced by WHO identification numbers. None of the results generated from assays being assessed will be used for determining the HIV serostatus of the individual. After the study, the remaining specimens will be retained at the testing laboratory according to the national regulations for bio-banking.

6.2. Composition of the HIV capillary blood specimen testing panel

The overall panel will consist of minimum of 400 anti-HIV positive specimens and 600 anti-HIV negative specimens

Table 1 - WHO HIV Capillary blood Specimen Evaluation Panel

<table>
<thead>
<tr>
<th>HIV positive specimens (HIV clinic)</th>
<th>HIV negative specimens (Blood Centre)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>400</td>
<td>600</td>
<td>1000</td>
</tr>
</tbody>
</table>

The corresponding plasma specimens shall be characterized using a standardized combination of assays i.e. a testing algorithm. These results are used to determine the HIV status of each specimen for the purpose of the performance evaluation see Figure 1. Use of any other combination of assays for characterization of the HBsAg specimen evaluation panel shall be communicated, discussed and agreed with WHO beforehand.

Each plasma specimen will be tested on VIDAS HIV Duo Quick (bioMérieux): a CIFA for detection of HIV-1/2 antibodies and HIV-1 p24 antigen, Genscreen HIV Ag/Ab Ultra (Bio-Rad Laboratories); an EIA for detection of HIV-1/2 antibodies and HIV-1 p24 antigen in parallel. In addition, all specimens will be tested and on Genscreen HIV 1/2 v2: an EIA for detection of HIV-1/2 antibodies. All specimens will be further characterized on INNO-LIA™ HIV I/II Score (Fujirebio)) line immunoassay.

Specimens that are negative by line immunoassay are further tested on Innotest® HIV Antigen mAb (Fujirebio) EIA and if found non-reactive then are assigned anti-HIV negative. If found to be neutralisable for HIV-1 antigen, the specimen is considered HIV-1 antigen positive and anti-HIV negative and is retained for the evaluation of 4th generation assay but not for 3rd generation assays.

Specimens that are indeterminate by line immunoassay are further tested on Innotest® HIV Antigen mAb (Fujirebio) EIA and if found non-reactive then are excluded from the panel. Specimens that are reactive for
antigen (and neutralisable) are assigned as HIV-1 antigen positive and anti-HIV inconclusive. These specimens are retained for the evaluation of 4th generation assay but not for 3rd generation assays.

Specimens that are positive by line immunoassay are assigned as anti-HIV-1 positive or anti-HIV-2 positive. Those specimens that cannot be discriminated (i.e. anti-HIV positive) are further tested on the NEW LAV II Blot (BioRad Laboratories). Specimens that are indeterminate or negative by the NEW LAV II Blot are assigned as anti-HIV-1 positive. Specimens that are positive by the NEW LAV II Blot are assigned as anti-HIV positive.
Figure 1 - Testing algorithm for characterization of the WHO HIV specimen reference panel (serum/plasma specimens)

EIA 1 Vironostika® HIV Ag/Ab (bioMérieux)
EIA 2 Enzygnost® Anti-HIV 1/2 (Siemens Healthcare Diagnostics) **in parallel**

- **+ +**
  - Positive
    - Anti-HIV-1 Positive
    - Anti-HIV Positive
    - New LAV II Blot (BioRad Laboratories)

- **+ -**
  - Indeterminate
    - INNOTEST® HIV Antigen mAb (Fujirebio)
      - Neutralisable Ag
      - Non neutralisable Ag
        - HIV Antigen Positive/ Anti-HIV Inconclusive
          - Excluded from the analysis if evaluation of 3rd gen assay but included if evaluation of 4th gen assay but considered as a ‘true’ positive specimen

- **- -**
  - Negative
    - INNOTEST® HIV Antigen mAb (Fujirebio)
      - Neutralisable Ag
      - Non neutralisable Ag
        - Anti-HIV Negative
          - Excluded from the analysis if evaluation of 3rd gen assay but included if evaluation of 4th gen assay but considered as a ‘true’ positive specimen

INNO-LIA™ HIV I/II Score line immunoassay (Fujirebio)
6.3. Lot-to-lot variation panel
Lot-to-lot variation is assessed by testing the same ten dilution series (comprised of 2-fold dilutions of 10 stock HIV positive specimens in commercially available normal human serum) on two separate production lots of the assay under evaluation in the same testing session.

6.4. HIV seroconversion panels
A seroconversion panel is a series of specimens, sequentially collected over a period of time, from an individual developing antibody in response to acute infection. The following commercial seroconversion panels: PRB914, PRB925, PRB926, PRB930, PRB955, PRB965, PRB968, PRB969 [sourced from SeraCare Life Sciences Inc] are tested using the assay under evaluation in singular on one lot. These panels consist of a total of 52 specimens collected from eight individuals during seroconversion.

6.5. HIV performance panels
One anti-HIV mixed titer performance panel containing 25 members, PRB205 [sourced from SeraCare, Life Sciences Inc] and, if evaluating a 4th generation antigen/antibody detection assay, one HIV-1 p24 antigen performance panel containing 25 members, PRA204 [sourced from SeraCare Life Sciences Inc] are tested using the assay under evaluation in singular on one lot.

6.6. WHO international reference preparations
The WHO international biological reference preparation panel with the catalogue number 02/210 (Anti-HIV antibodies [HIV-1 subtypes A, B, C, CRF01_AE, group O and HIV-2]) is tested using the assay under evaluation in singular on one lot. If evaluating a 4th generation antigen/antibody detection assay, the WHO international biological standard with the catalogue number 90/636 (HIV-1 p24 Antigen) is tested in 2-fold dilutions in singular on one production lot.

6.7. External quality control specimen
See section 9 for further details.

7. Laboratory testing

7.1. Sequence of testing
Each product under evaluation is used strictly in accordance with the instructions for use (IFU) issued by the manufacturer. The WHO Prequalification Evaluating Laboratory will send a hard or electronic copy of the IFU to WHO/PQDx upon delivery of the test kits and prior to the commencement of the laboratory evaluation. The IFU must be reviewed against the IFU submitted to WHO/PQT as part of the dossier assessment for the prequalification assessment. If the IFU has been updated since dossier submission, a letter from the manufacturer detailing changes made must be sent to WHO/PQDx prior to the laboratory evaluation commencing.

The specimen reference panel is run in order that approximately one half of the specimen panel will be run with the one lot and the other half of the panel with the other lot. The specimens of the WHO HIV specimen reference panel should initially be tested in singular and in a blinded manner.

Lot-to-lot variation is assessed by testing the same set of dilution series (comprised 2-fold dilutions of 10 stock HIV positive specimens) on two separate production lots of the assay under evaluation.
The seroconversion panels, performance panels [PRB205 for both 3rd and 4th generation assays, PRA204 for 4th generation assays only], WHO international biological reference preparation panel [WHO p24 antigen standard for 4th generation assays only] and culture supernatant panel [for 4th generation assays only] are then tested in singular on a single lot.

For the purpose of evaluating the rapid diagnostic tests, a ‘test run’ is defined as a consecutive run of simple/rapid tests of the same production lot performed during the same ‘session’. A ‘testing session’ might be considered to be a morning or afternoon.

7.2. Recording test results

All test results are recorded on standardized test result worksheets and then entered in a Microsoft Excel spreadsheet for further data analysis. For subjectively read assays such as RDTs or line immunoassay, the intensity of band/line/spot is additionally entered into the data collection sheet. The intensity rating system reads as described in Table 2.

Table 2 - Results legend for data collection sheets for subjectively read assays

<table>
<thead>
<tr>
<th>Scoring index</th>
<th>Intensity reading scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Negative</td>
</tr>
<tr>
<td>1</td>
<td>Uncertain Reactivity, Indeterminate</td>
</tr>
<tr>
<td>2</td>
<td>Very Weak, but Definitely Reactive</td>
</tr>
<tr>
<td>3</td>
<td>Medium to Strong Reactivity</td>
</tr>
<tr>
<td>7</td>
<td>Debris</td>
</tr>
</tbody>
</table>

Visual interpretation of results of subjectively read assays is made independently by two readers (without the knowledge of the other set of results) and entered onto the data collection sheets. These results are compared by the operator carrying out the assay so that any mistakes may be identified and rectified immediately. Should recording errors be identified, both the original and corrected result are recorded and initialed by the reader. When the three readers interpret the results differently from each other, the consensus is recorded as that interpretation which occurs two out of three times. In cases where all three interpretations are different, the result is recorded as indeterminate.

A technician’s appraisal is made of each assay under evaluation and is completed by the operator performing the testing. It includes questions about the ease of the procedure, reading of results, clarity of IFU, as well as room to record any specific difficulties encountered during the evaluation.

8. Quality control and interpretation of test results

8.1. Test kit controls

Manufacturer-supplied positive and negative test kit controls will be run as indicated in the IFU for all test formats included in each test run for EIAs and at the commencement of each testing session for rapid diagnostic tests and other formats. Where positive and negative test kit controls are not supplied by the
manufacturer, as will be the case for many rapid diagnostic tests, the external quality control specimen will act at the control specimen, see section 9.3 for more details.

8.2. Internal control lines for rapid diagnostic tests
Generally, RDTs contain a control band, line or spot to determine that the test device is operating correctly. Most control bands/lines/spots will become visible with the addition of reagent (i.e. buffer) only. However, some RDTs will contain a control band/line/spot that becomes visible with addition of specimen (i.e. presence of IgG). It is imperative that the exact nature of the control band/line/spot is ascertained and recorded in the report. An experiment is performed to verify this point, if not explicitly mentioned in the IFU.

8.3. External quality control specimen
The WHO prequalification evaluating laboratory supplies an external quality control (QC) specimen which is tested in singular at the beginning of each test session for rapid diagnostic tests and other formats and in triplicate for each test run for EIAs. See definition of testing session in section 5.1. The QC specimen represents a weakly reactive HIV positive specimen, and thus may be different for different assays and different assay formats. The QC specimen are made by the WHO Prequalification Evaluating Laboratory or acquired commercially, depending on the assay under evaluation.

8.4. Proficiency panels
For assays under evaluation that have already been evaluated on the WHO specimen reference panel for serum/plasma, proficiency will have already been established. For other assays, a proficiency panel (serum/plasma) must be run successfully for each assay by each operator before the evaluation commences.

8.5. Limits of acceptability
All results on test kits controls and QC specimens are entered on the data collection sheets. Should the test kit controls or the QC specimen not give results within the expected ranges, evaluation testing on that assay is suspended until the cause has been identified and a satisfactory solution identified. Such problems must be communicated immediately to WHO and recorded on the data sheets. The PI is responsible for carefully checking all data entry forms for legibility, accuracy and completeness.

8.6. Interpretation of results
The interpretation of results for each assay under evaluation is made strictly according to the manufacturers’ instructions in the IFU. Invalid test results are recorded on the data collection sheets including where the control line does not appear or in any other way the test result is invalid as defined by the IFU. For test results that are indeterminate according to the IFU, the results are recorded on data collection sheets.

9. Analysis of data

9.1. Invalid test devices
The number of invalid devices is recorded as the number of invalid test results as a percentage of the total number of devices used for the evaluation.
Invalid results may mean invalid test results as defined by the instructions for use such as where the control line/band/spot does not appear or invalid due to obviously defective test device or defective transfer pipette. Specimens that do not flow along or through the membrane will also be noted.

9.2. Inter-reader variability

The inter-reader variability is calculated when assay readings must be performed without any objective reading instruments i.e. RDTs. Two persons independently interpret each test result. The inter-reader variability is expressed as the percentage of specimens for which initial test results are differently interpreted (i.e. reactive or non-reactive or indeterminate) by the independent readers.

9.3. Performance characteristics from HIV specimen testing panel

The following strategies are used to calculate the performance characteristics for each assay under evaluation and are closely linked to the reference testing results gained during specimen panel characterization.

Table 3 - 2 x 2 table for calculation of performance characteristics

<table>
<thead>
<tr>
<th>Results of assay under evaluation</th>
<th>Reference testing results</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reactive</td>
<td>Non-reactive</td>
<td>Total</td>
</tr>
<tr>
<td>Reactive</td>
<td>a (true positives)</td>
<td>b (false positives)</td>
<td>a + b</td>
</tr>
<tr>
<td>Non-reactive</td>
<td>c (false negatives)</td>
<td>d (true negatives)</td>
<td>c + d</td>
</tr>
<tr>
<td>Total</td>
<td>a + c</td>
<td>b + d</td>
<td>a+b+c+d</td>
</tr>
</tbody>
</table>

9.3.1. Sensitivity

Sensitivity is the ability of the assay under evaluation to detect correctly specimens that contain HIV-1/2 antibodies (reference results positive).

Thus sensitivity is the number of true positive specimens identified by the assay under evaluation as positive (a), divided by the number of specimens identified by the reference assays as positive (a+c), expressed as a percentage.

Sensitivity = \( \frac{a}{a + c} \)

9.3.2. Specificity

Specificity is the ability of the assay under evaluation to detect correctly specimens that do not contain HIV-1/2 antibodies (reference results negative). Thus specificity is the number of true negative specimens identified by the assay under evaluation as negative (d), divided by the number of specimens identified by the reference assays as negative (b+d), expressed as a percentage.

Specificity = \( \frac{d}{b + d} \)
9.3.3. Confidence intervals

The 95% confidence intervals are calculated for both sensitivity and specificity in order to assess the level of uncertainty introduced by sample size, etc. Exact 95% confidence intervals for binomial proportions were calculated from the F-distribution. [Armitage, 2002; Kirkwood, 2003]

9.3.4. Positive predictive value (PPV)

The probability that when the test is reactive that the specimen does contain HIV-1/2 antibodies. PPVs were calculated using the formula.

$$PPV = \frac{(prevalence)(sensitivity)}{(prevalence)(sensitivity)+(1-prevalence)(1-sensitivity)}$$

9.3.5. Negative predictive value (NPV)

The probability that when the test is negative that a specimen does not contain HIV-1/2 antibodies. NPVs were calculated using the formula.

$$NPV = \frac{(1-prevalence)(specificity)}{(1-prevalence)(specificity)+(prevalence)(1-sensitivity)}$$

The probability that a test result will accurately determine the true infection status of a person being tested varies with the prevalence of HIV infection in the population from which the person comes. In general, the higher the prevalence of HIV infection in the population, the greater the probability that a person testing positive is truly infected (i.e., the greater the positive predictive value [PPV]). Thus, with increasing prevalence, the proportion of individuals testing false-positive decreases; conversely, the likelihood that a person whose test result is negative is truly uninfected (i.e., the negative predictive value [NPV]), decreases as prevalence increases. Therefore, as prevalence increases, so does the proportion of individuals testing false-negative.

The PPV and NPV are calculated at a prevalence of 0.1%, 1% and 5%.

9.4. Indeterminate results

Specimens which are found to be indeterminate (grey zone) by the criteria stated in the IFU will be recorded as such, and excluded from the denominator and numerator for the sensitivity and specificity estimates.

9.5. Discrepant results

Due to the nature of the prospective sampling for this study, it will not be possible to collect additional specimens from those individuals with specimens giving results discrepant from the expected reference results.

9.6. Technician’s appraisal

The technical aspects of the assay under evaluation are assessed by the technician who performed the testing. These assessments, along with other selected assay characteristics, contribute to an overall appraisal of each assay’s suitability for use in small laboratories. To enable comparison between assays, a scoring system is used to rate specified operational characteristics.
9.7. Report preparation

WHO prequalification evaluating laboratory and sent to WHO for List 1 laboratories. In case of list two laboratories the data and the report will be sent simultaneously to WHO and the Manufacturer in a timely manner. WHO verifies the draft report from List one laboratories and sends to the authorized contact designated by the manufacturer for comment. The company has one month right of reply. The final report is prepared after one month has elapsed. The WHO scientist ensures that the comments of the authorized contact are reviewed and any outstanding issues are resolved before final publication. The final report is prepared and disseminated by WHO. A copy of the final report is sent to the authorized contact designated by the manufacturer and to WHO prequalification evaluating laboratory.

10. Materials and supplies

10.1. Data collection sheets

All data will be reported to WHO/PQ-diagnostics on the following forms:

A. Data collection Microsoft Excel spreadsheet for the RDTs
   - Anti-HIV-1/2 Capillary blood
B. Technician’s appraisal worksheet

10.2. Supplies

The manufacturers of products will provide the products and any equipment necessary for the evaluation free of charge.

11. Roles and responsibilities

11.1. Responsibilities of the WHO Prequalification Evaluating Laboratory

- Act as repository for the matched plasma specimens;
- Conducting the laboratory evaluation in accordance with internationally recognized best practice;
- Preparation of QC specimens and proficiency panels;
- Preparation of draft report on laboratory evaluation;
- Advising WHO on operational characteristics of assays evaluated.

All source data, data analysis records and all correspondence are retained and archived for a period of at least ten years.

11.2. Responsibilities of WHO

i. Technical advice to the PI;
ii. Technical and administrative management of the laboratory evaluation;
iii. Verification of the draft report, seeking of comments from manufacturer;
iv. Preparation and dissemination of the final report;
v. Formal contacts with authorized contacts of the manufacturers.

Any publication by WHO of the results of these evaluations and the WHO recommendations derived therefrom will, however, be accompanied by the following disclaimer:
The mention of specific companies or of certain manufacturers’ products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

WHO and the WHO Prequalification Evaluating Laboratory, do not warrant or represent that the evaluations conducted with the HIV test kits referred to in this document are accurate, complete and/or error-free. WHO and the WHO Prequalification Evaluating Laboratory disclaim all responsibility for any use made of the data contained herein, and shall not be liable for any damages incurred as a result of its use. This document must not be used in conjunction with commercial or promotional purposes.

12. References


World Health Organization Guidelines on HIV Safety Precautions, and Guidelines for the Safe Transport of Specimens (WHO/EMC/97.3)

International Standards

EN 13612:2002 Performance evaluation of in vitro diagnostic medical devices
ISO 17025 (General requirements for the competence of testing and calibration laboratories)
ISO15189 (Medical laboratories — Particular requirements for quality and competence)
13. Informed Consent Form

Informed Consent for Collection of Capillary and Venous Blood specimen for in an evaluation of simple rapid assays for HIV self-testing

[Name of Principle Investigator]: <Insert name>
[Name of Organization]: <Insert name>
[Name of Sponsor]  <Insert name>

This Informed Consent Form has two parts:
1. Information Sheet (to share information about the evaluation with you)
2. Certificate of Consent (for signatures if you agree to take part)

You will be given a copy of the full Informed Consent Form

PART I: Information Sheet
Introduction
I am ........, working for [Name of the hospital]. We are doing an evaluation of simple rapid tests for HIV self-testing using both capillary and venous blood specimens. I am going to give you information and invite you to participate in this evaluation. You do not have to decide today whether or not you are willing to participate in the evaluation. Before you decide, you can talk to anyone you feel comfortable with about the evaluation. There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask me, the study staff.

Purpose of the evaluation
HIV is one of the most common diseases in this region. Despite recent achievements in scaling-up HIV testing services, major gaps in testing coverage still persist. HIV self-testing (HIVST) has the potential to increase access to HIV services, but the performance of simple rapid test using capillary blood specimens has to be verified before being prequalified by WHO. We aim to evaluate the performance of several simple rapid tests using capillary blood.

Type of Evaluation
This evaluation process will involve comparing the results of HIV testing in capillary blood compared to results obtained using venous blood tested in more established and accurate test methods.

Participant selection
We are inviting all patients attending this clinic or blood bank to participate in the evaluation to assess the performance of several rapid tests. Your participation in this evaluation is entirely voluntary. It is your choice whether to give a blood sample or not. Whether you choose to participate or not, all the medical services you receive at this clinic/donation room will continue and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

Procedures and Protocol
About three table spoons of blood will be collected from the arm using a syringe. In addition we will take a drop of blood from your finger tip and put it on the test device. We will take your blood only once.
Risks
We do not expect that any harm will happen to you because of joining this study. Sometimes, you may feel some little pain and a small bruise may occur due to the finger prick.

Benefits
If you participate in this evaluation, you will not have immediate individual benefits but your participation is likely to help WHO to identify suitable simple rapid assays which can be used for HIV self-testing in order to expand HIV testing opportunities all over the world.

Reimbursements
You will not be given any money or gifts to take part in this evaluation.

Confidentiality
The information that will be collected from this evaluation will be kept confidential. Information about you that will be collected during the evaluation will be put away and no-one but the evaluation team will be able to see it. Any information about you will have a number on it instead of your name. Only the evaluators will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name] who will have access to the information, such as evaluation sponsors, etc.)

Right to Refuse
You do not have to take part in this evaluation if you do not wish to do so and refusing to participate will not affect your treatment at this clinic or blood centre in any way. You will still have all the benefits that you would otherwise have at this clinic/blood donation centre.

Who to Contact
If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: [<Insert name>]

This proposal has been reviewed and approved by the <Insert name>, which is a committee whose task it is to make sure that evaluation participants are protected from harm. If you wish to find about more about the IRB, contact <Insert name>

You can ask me any more questions about any part of the evaluation study, if you wish to. Do you have any questions?

PART II: Certificate of Consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this evaluation.

Name of Participant__________________
Signature of Participant ___________________
Date ___________________________ (Day/month/year)

If illiterate
I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness____________________ AND Thumb print of participant 
Signature of witness __________________________
Date ______________________ (Day/month/year)

Statement by the evaluation team leader/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:
1. We will collect few mls of blood using venepuncture 
2. We will also collect capillary blood using the finger tip 

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily. A copy of this ICF has been provided to the participant.

Name of Evaluation team lead/person taking the consent________________________
Signature of Evaluator /person taking the consent________________________
Date ___________________________ (Day/month/year)