**Procedure: Quality Assurance Policy Version 5**

**Quality Assessment Policy Version 3**

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| **Prepared by Date Adopted Supersedes Procedure #** |
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**PURPOSE**

The laboratory has an ongoing Quality Assessment Program that is designed to monitor, evaluate and improve the quality of laboratory performance and ensures the reliability of test data, and to evaluate the competency of the laboratory staff. The lab will identify and resolve any problems that may affect lab performance and thus patient care.

For the purpose of this document, any work area in which testing of patient samples occurs is subject to the same sets of guidelines and policies as the laboratory. This includes clinic areas and off site locations. Any individual who performs testing on patient samples must adhere to the contents of this policy.

Additional quality assurance procedures may also be listed in Study Specific Procedure manuals.

Manufacturer recommendations must be followed. If the various documentation gives conflicting information, please contact the HPTN or MTN Network Lab for advice. (NetworkLab@HPTN.org or mtnnetworklab@mtnstopshiv.org)

**OBJECTIVES**

1. To ensure that the quality assurance activities are comprehensive and coordinated and that appropriate information is reviewed and reported.

2. To establish, maintain, support, and document an ongoing Quality Assurance

Program that includes effective and systematic mechanisms for monitoring, collecting and evaluating information about important aspects of laboratory performance in

order to identify opportunities for improving patient care.

3. To assist in improving care and identifying problems through the use of ongoing monitors by focusing on identification, assessment, correction, and follow-up of problems that affect laboratory performance.

4. To implement corrective action when problems or improvement opportunities are identified.

5. To follow up on identified problems to assure improvement and resolution in a timely manner with documentation of corrective action.

**QUALITY ASSURANCE MONITORS**

The following Quality Assurance monitors are actively evaluated to maintain an established standard of laboratory performance and compliance. Data from each monitored area is collected, recorded and analyzed. The findings are evaluated to detect trends and overall compliance. When required, appropriate corrective action will be implemented and documented. Monitoring will be continued to assure that the action taken was appropriate and resulted in correction of any problems found. At a minimum, quarterly meetings are held to review the monitored area reports.

**Proficiency Testing**:

Please refer to the Instructions for Handling Proficiency Samples version 2 for specific details.

Proficiency programs are used as an external check on the quality control and quality assurance of a test system. Analytes should be tested a minimum of twice per year, with the recommendation being 3 times per year.

The laboratory will participate in external proficiency panels/surveys, which are blind assessments of the laboratory’s performance. Where possible, the laboratory will participate in a proficiency program for each test performed in the lab/clinic area

1. For testing where no external proficiency program samples are available, other methods of proficiency checks will be used if possible. Proficiency samples are tested in the same manner as any routine specimen submitted to the laboratory.

2. No special assignments will be made for the testing technologist; the routine bench schedule will be followed.

3. The laboratory supervisor or designee will review the final result forms and send to the testing agency in a timely manner.

4. A copy of the final results form will be kept in the External Proficiency Testing file.

5. When the survey results are returned the laboratory supervisor and director will review and sign the results.

6. If there are any noted deficiencies, the deficiencies will be investigated by the laboratory supervisor and director. IF the NL discovers the deficiency, they will send a note to the laboratory and will send a cumulative report from all networks involved in the sites. SMILE will review the proficiency results on a monthly basis and will send a report to the site along with an Investigative Response (IR) form that the site needs to complete.

7. An IR written report of the findings and corrective action will be written. The laboratory supervisor and director will sign this report. The IR should be completed and forwarded to the Network Lab for review and approval.

8. The Network Lab will forward the IR to the appropriate DAIDS contractor.

9. A copy of the response will be filed with the survey results.

All proficiency program reports should be reviewed, signed and dated by the laboratory supervisor and director as soon as possible upon receipt. The signed copy should be filed with the original results. The laboratory supervisor and director must review any deficiencies cited by any proficiency program or accrediting organization in which the laboratory participates.

1. The director, or designee, must submit in writing a plan of corrective action as well as the IR within 30 days of any failures to HPTN or MTN Network Lab. (NetworkLab@hptn.org or mtnnetworklab@mtnstopshiv.org), For IQA or VQA proficiency panels, please submit the IRs and corrective action plan to the appropriate contact person for those agencies as well as the HPTN or MTN Network Lab.

2. The deficiency report will include an explanation of the likely cause(s) of the deficiency along with appropriate corrective action, if indicated.

3. These deficiency reports will be filed in the proficiency test result manual with the original report.

**Specimen Management:**

Specimens sent to the lab are monitored to determine the effectiveness of the collection procedures as well as the integrity of the specimens received. The following areas will be monitored, recorded and investigated in a timely manner:

1. Lost specimens (at point of collection to lab or within the lab).

2. Rejected specimens (unsuitable specimens).

3. Missed Testing – test missed by lab.

4. Specimen integrity – specimen too old to test or stored at wrong temperature

**Reporting of Results:**

Results released to the clinician or study personnel are monitored to determine the effectiveness of the laboratory review and reporting system. The following areas are used to monitor the accuracy of released results.

1. A portion of the results (not less than 5%) released from the laboratory are to be monitored by comparing the final report result to the result on the worksheet. This review is to be documented along with any discrepancies detected and the corrective action taken.

2. The number of modified or amended results is to be documented along with the reason for the change and any corrective action taken.

3. The laboratory must have a policy in place to deal with the reporting of amended results.

**Technical Delays**:

Technical delays are monitored to help evaluate the overall effectiveness of the laboratory. Any time delay in reporting of patient test results due to a technical problem in the lab needs to be documented. This includes such parameters as scheduled and unscheduled instrument down times, acute or chronic staff shortages, contaminated cultures, failed reagents, failed quality control, and supply back orders. Clinic staff need

to be notified when the downtime causes delays in resulting of routine reports if the delay is to exceed the established turn round time. If the delay will adversely affect the study, the laboratory should discuss the issue with the clinic staff and the HPTN or MTN Network Laboratory to determine if the back-up plan needs to be implemented.

Turn around time (TAT) is a time measurement between 2 specified processes such as sample receipt and result release. It can be affected by items such as specimen transport difficulties or the above mentioned technical problems in the laboratory. Maximum acceptable turn round times must be available to the laboratories clients. The Laboratory Director mandates the TAT for each test. Monitoring of pre-analytical, analytical and post-analytical processes help to identify potential problematic areas within the laboratory. TAT should be reported on a periodic basis (suggest monthly)

**Complaints**:

Complaints received by the laboratory are monitored for response, corrective action and follow-up. The supervisor or designee will respond to any written or significant oral complaint concerning the quality of service or results. Patient care/well being as well as clinical study support are taken into consideration in designing and responding to the corrective action. The timeline for responding to complaints needs to be defined by the laboratory. Responses to complaints will be forwarded to the director for review and any additional recommendations of appropriate action

**Performance Improvement Monitoring/ QIP – Quality Improvement Program**

The laboratory will identify potential problems or areas of improvement within the laboratory. These areas will be monitored for frequency, possible causes, corrective action and improvement. The information will be documented by the laboratory supervisor or designee and reviewed by the laboratory director.

**TRAINING**

**New Employee**: Lab specific job descriptions entailing the duties of each employee are kept on hand in the individual personnel files. Each employee must read and sign off on their particular job description. A checklist for the training of new personnel has been established for the assays in the laboratory. Personnel sign each section on the checklist as well as their trainers. These records are kept in the personnel file and should be available for inspection.

**New Procedures/New Equipment**:

Each employee must be trained on new procedures or new equipment. The training must be documented and signed by the employee and the trainer. These records are kept in the employee’s personnel file and should be available for inspection.

**CONTINUING EDUCATION:**

Continuing education provides personnel an opportunity to review and expand their knowledge of laboratory procedures and policies, and any other subjects pertinent to successful laboratory operations.

1. Each technical employee is required to fulfill a minimum of 10 hours per year.

2. Continuing education may be earned through reading, videos, cassette tapes, departmental lectures, teleconferences, training seminars, workshops, tech sample reviews or safety training (fire safety, universal precautions, blood borne pathogens).

3. Dangerous Goods Shipping certification is required every 24 months.

4. Each employee should keep a record of his or her continuing education. Any supporting documents should be given to the supervisor to maintain in the personnel file. (Refer to appendix for CE Record form.)

**QUALITY CONTROL:**

Each procedure outlines the required control materials and analysis frequency for the

tests performed in the laboratory or other testing location. It is the responsibility of every technologist to ensure that the required controls have been performed and satisfactory performance has been obtained prior to the release of any patient results.

Please refer to the Quality Control Policy for further information.

 **NEW REAGENT LOT VALIDATION.**

Reagent kits and controls the lab uses have a limited shelf life. It is important to ensure that test kits and reagents are not used beyond their expiration date. New lot check in of reagents is done in order to validate the lot to lot variability.

1. **HIV EIA Assay**: In order to validate the lot to lot variability with the HIV EIA assay, a minimum of 3 patient samples (negative, low positive and high positive) identified by the lab supervisor are run using the new reagent/kit lot and the in use lot. The patient results should be reproducible between the two lots. The laboratory

supervisor or director will sign off on the validity check. The patient samples will be marked validation samples and filled with the other HIV EIA runs.

2. **HIV RNA PCR, Quantitative Assay**: In order to validate the lot to lot variability, three (3) patient samples (not detected, a mid range viral load and a high viral load) are assayed on the old and the new lot number. The laboratory supervisor or director will sign off on the validity check. These results will be recorded in chart form and filed with the quality control records for this assay by the laboratory supervisor. As the laboratory is starting to perform the assay, lot to lot variation should be less than

0.5 log with any variation greater than 0.3 log difference being investigated and documented. After the lab is established this difference may be tighten but the ultimate decision is made by the laboratory director. Please note: commercial standards or those provided through the Virology Quality Assurance (VQA) can be utilized in place of patient samples.

3. **PCR (HIV, GC, Chlamydia) Qualitative Assay**: In order to validate the lot to lot variability, a minimum of 3 patient samples (negative, low positive and high positive) are run using the in use lot and new lot of reagent/kit. The patient results should be reproducible between the two lots. The laboratory supervisor or director will sign off on the validity check. The patient samples will be marked validation samples and filled with the other PCR runs.

4. **SDA (GC, Chlamydia) Qualitative Assay:** In order to validate the lot to lot variability, the positive and negative control samples from the old lot are assayed on the new lot/kit. The laboratory supervisor or director will sign off on the validity check.

5. **Other ELISA Quantitative assays Assay**: In order to validate the lot to lot variability with the p24 media assay, a known positive supernatant from a previous run is assayed. The laboratory supervisor or director will sign off on the validity check. The patient samples will be marked validation samples and filled with the other P24 runs

6. **CD4/CD8 Assay**: In order to validate the lot to lot variability of reagents, a minimum of 2 patients (one with CD4/8 ratio <1.0 and one with CD4/8 ratio >1.0) are run using both the in use and new lots of reagents. The patient results should be reproducible (based on manufacturers guidelines for sample to sample, lot to lot variation) between the two lots. Typically the results should be within 15% of each other. The laboratory supervisor or director should sign off on the validity check. The patient samples will be marked validation samples and filled with the other CD4/8 runs. It is also

important to check expiration dates and perform lot testing on primary and secondary antibodies used for this purpose.

**7. Chemistry, Hematology and Coagulation – New Reagent Lot Check In:**

New lot numbers of reagent must be validated before being introduced into routine use. 10 patient samples must be assayed using the old reagent are re assayed using the new reagent. QC should be acceptable for old and new lots. Samples should be assayed by both lots within a time period in which there has been no loss of integrity to the sample or analyte. Results should be compared to the old lot. Acceptability criteria should be set by the Lab Director.

**8. Internal Quality Control (testing of known materials) - Other Test Systems**

a.. Culture Media

1) All culture media will be checked for expiration dates before being put into use.

2) A culture media control log will be used to document the lot number and quality control results.

3) Any media that appears cloudy, has a color change or shows contamination will be discarded.

4) Appropriate control organisms will be used to check selective media.

5) The control log will be initialed and dated by the technologist performing the quality control.

6) The control log will be reviewed and signed at least once per month by the laboratory supervisor or QA/QC technician/designee.

7) Media that fails the quality control check will be documented and discarded.

b. Animal Sera

1) All animal sera will be checked for cytotoxicity before use.

2) An animal sera control log will be used to document the lot number, expiration date and quality control results.

3) Acceptance criteria for cytotoxicity will be defined.

4) The control log will be initialed and dated by the technologist performing the quality control.

5) The control log will be reviewed and signed at least once per month by the laboratory supervisor or QA/QC technician/designee.

6) Animal sera that fails the cytotoxicity check will be documented and discarded.

**VALIDATION STUDIES:**

Any time an instrument or methodology is changed within the laboratory, validation studies must be performed.

Please Refer to HPTN Quantitative and Qualitative Assay Validation Policies for details.

**MAINTENANCE OF REFERENCE RANGES**

Reference ranges are adopted/established for the study population during the initial assay validation period.

The population demographics are likely to change over time so it is recommended that reference ranges are reviewed on a regular basis to ensure that they remain valid for the study population.

One method of accomplishing this would be to analyze specimens from 20, healthy, non diseased individuals from each subgroup. If 2 or fewer results fall outside of the established reference range, it is still considered to be valid.

If however more than 2 results fall outside of the reference range, a more extensive study may be required.

It may be difficult to obtain 20 normal individuals for some study groups, eg. Pediatric patients. In this situation the Laboratory Director would have to use an alternate strategy, but should still sign a dated copy of the ranges to indicate that the ranges are still valid.

Annual review/signature is recommended.

**METHOD COMPARISON**

Performed semi-annually between similar instruments or methods. Run a minimum of 10 samples and perform comparison.

There must be a back up method available for protocol related safety and end point assays. This can be performed in-house or at a back up lab. Primary methodology and back up methodology must be compared during initial validation and semi annually thereafter.

The lab director sets the acceptable limits of the method comparison.

**CARRYOVER**

Sample carryover may cause one high patient sample to affect the sample that follows it. Most of today’s diagnostic analyzers take every possible precaution to avoid sample carryover. In spite of these efforts a sample having a high result may affect one or more samples that follow it. The lab must show that their instruments or test system does not have any unacceptable carryover.

Follow manufacturer instructions for assessing carryover and acceptability limits. Carryover studies must be performed during assay validation, at least annually thereafter,

and when carryover is suspected.

**PROCEDURE REVIEW:**

All procedures used in the lab must be documented and reviewed.

1. All laboratory procedures are reviewed on an annual or more frequently if needed basis.

2. Procedure reviews are done by the supervisor and director on an annual basis. Any changes that occur at that time need to be communicated with the staff. Note: It is best to have the annual time point review the same for all procedures.

3. Each procedure is preceded by the documentation of review (also known as a signature page).

4. Modifications of a procedure can occur at any time due to newly published guidelines, revised package inserts, changes in central policy, etc. All revisions should be documented in ink on the original copy along with initials of the supervisor or designee and the date of change. This superceded/obsolete copy must be kept for

at least 5 years.

5. The revised procedure should include the revision number and effective date to help identify it as the current procedure.

6. All changes must be documented and communicated to the technical staff.

7. Appropriate version control must be maintained.

8. Any copies of procedures must be removed from the technical work areas and replaced with the updated version.

9. Documentation for all HPTN and / or MTN protocol related procedures must be approved by the HPTN or MTN Network Laboratory prior to study activation.

**COMPETENCY:**

New employees are checked for competency twice during their first year of employment in the laboratory. The first competency check should be completed before any patient results are reported by the new employee. Existing employees are checked annually and periodically as needed. Competency may be checked by:

1. Direct observation (use SOP or a check list to insure no steps are omitted)

2. Quality control result review

3. Repeat and split sample testing

4. Unusual patient or unusual control result review

5. Proficiency testing review

6. Blind specimen analysis.

7.Oral examinations

If an employee fails his/her competency checks, they must complete a retraining procedure and pass a further competency evaluation before they can test patient samples

**Blind or Split Sample Testing (Internal Proficiency Testing)**

1. As part of the laboratory’s internal proficiency testing program, personnel proficiency testing is done periodically during the year. Coded samples, blind samples or split samples may be given to the technologists and or clinic staff to assess the reproducibility of the assays as well as the technologist to technologist variability and accuracy.

2. The laboratory supervisor or designee (such as the QA/QC technologist) will be responsible for assigning the samples, documenting the results and reviewing the results.

3. The acceptable range of reproducibility will be determined by test and documented on the result form.

4. The documentation will include the results by technologist and whether the results compared acceptability for accuracy and reproducibility.

5. The laboratory supervisor and or director will sign off the results.

6. The results will be filed as Internal Proficiency Testing records.

**STORAGE OF LABORATORY RECORDS:**

All laboratory records inclusive of requisitions, patient results, QC logs, maintenance logs, QA logs are retained for a minimum of five years or two years after study completion.

1.Records are to be stored in an orderly manner that allows retrieval within 24 hours.

2.Records may be stored off site and on site in locked and secure storage.

**RESULT MODIFICATION / AMMENDMENT**;

In the event of incorrect verification of data, the incorrect result needs to be modified and the correct result entered. Discrepancies are to be resolved immediately

1. All modified results must be brought to the attention of the ordering physician/clinic in a timely manner, and documented.

2. The modified report must include the initials of the lab supervisor as well as a brief explanation if appropriate

3. Modified (amended) reports will be documented under the quality assurance monitoring.

**RESULT REPORTING CHANGE:**

Changes in test methodology and /or reference ranges must be communicated to the ordering staff by a lab note or department memo. These changes should be communicated to the HPTN or MTN NL before implementation. These changes must also be communicated to the FHI CRM and SDMC POC associated with the study as changes may have an effect on data analysis or safety reporting requirements.

Changes in methodology and / or reference ranges for HPTNor MTN protocol assays must be approved by the HPTN or MTN Network Laboratory.

**MAINTENANCE OF EQUIPMENT**;

A separate manual for equipment maintenance is kept in the laboratory. Each instrument in use has a separate procedure for maintenance and the time frame for the performance of the maintenance

Maintenance of equipment should follow manufacturer recommendations at a minimum.

1. Maintenance log sheets are kept on a daily, monthly, quarterly, semi-annually, and annually basis.

2. These records are reviewed and signed by the laboratory supervisor or director.

3. These records are retained for a minimum of five years.

4. Any preventive maintenance, repairs, or part replacement records is kept for the lifespan of the equipment or 5 years (whichever is greater).

**Instrument Maintenance**

1. All instruments used in the lab follow a preventative maintenance program which must follow the manufacturer’s recommendations.

2. Documentation of the instrument maintenance, calibration, service and corrective action logs is generally found in the bench workbook for each area.

3. The area technologist maintains these records.

4. These records are reviewed and signed monthly by the laboratory supervisor or designee.

**Equipment Maintenance**

1. Routine maintenance on laboratory equipment is performed according to the manufacturer’s recommendations.

2. The technologist performing the maintenance documents the maintenance and results.

3. The laboratory supervisor reviews and signs off the maintenance records monthly.

4. Documentation of the equipment maintenance is generally found in the laboratory

Maintenance Manual.

5. Preventative maintenance, monitoring or calibration generally covers the following equipment:

a. Precision pipette calibration

b. Centrifuge calibration (rpm, timer and temperature if applicable)

c. Thermometers d. Timers

e. Plate washers f. Plate readers

g. Thermocyclers h. Incubators

i. Biological/Fume Hoods

**Temperature Monitoring** (include a chart to monitor room temperature for labs)

1. All temperature sensitive equipment such as freezers, refrigerators, water baths and incubators must be monitored on a regular basis. ie. at least each working day.

2. Thermometers used must be compared to a NIST (or equivalent) traceable thermometer at least annually. This comparison must be documented and accepted y the lab director.

3. All test work areas and reagent storage areas must be monitored on a regular basis. ie. at least each working day. (ie room temperature monitoring where equipment and testing is done as well as where room temperature reagents are stored).

4. Temperature charts must include the name of the equipment (if applicable), the location, the acceptable temperature range, serial number of the thermometer used, space to record the actual temperature, date and time, and the initials of the person recording the temperature.

5. Maximum/minimum thermometers may also be used when staff are not available for weekends and holidays. In this case, the lowest and highest temperature over the period of time should also be documented.

6. The temperature chart may include a comments/corrective action section or corrective action may be recorded on another form.

7. The charts must be reviewed on a monthly basis by the laboratory supervisor.

**Reagent Water**

The following procedures and specifications are for the testing of water which has been purified for clinical laboratory use. There are three grades of water recognized along with the minimum specifications for bacterial count for each.

Type I Used for the preparations of solutions, reagents (EIA testing) requiring minimum interference and maximum precision and accuracy (10cfu/ml)

Type II Used for general laboratory testing other than described above

Type III Used for glassware washing, but not final rinsing and for feedwater for production of higher-grade water

The preferred water is Type I, distilled, deionized water. If this is not available, distilled water can be used and sterilized if necessary.

If the laboratory has a water purification system, the quality of the water must be checked on a regular basis. ie. at least each working day. This must be documented on a chart which may include a comments/corrective action section or corrective action may be recorded on another form.

The charts must be reviewed on a monthly basis by the laboratory supervisor.

**APPENDICES**

!.Corrective Action Log

2.Continuing Education Record form

**JHU HPTN CENTRAL LABORATORY QA POLICY**

**CORRECTIVE ACTION/REMARKS LOG for INSTRUMENT/TEST SYSTEM**

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| Date | Problem/Comments | Initials | Corrective Action/Comments | Initials | Date |
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Reviewed by:

Date:

JHU HPTN CENTRAL LABORATORY

**CONTINUING EDUCATION RECORD for**

Employee name

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| **Date (s)** | **Activity Discription** | **Hours** | **Supervisors****Initials** |
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