**Procedure: Quality Control Policy Version 6.0**

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| **Prepared by Date Adopted Supersedes Procedure #** |
| Estelle Piwowar-Manning |  | Version 5.0 |
| Sarah Dawson |  |  |
| Paul Richardson |  |  |

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| **Review Date Revision Date Signature** |
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**PRINCIPLE**

Quality Control is an important part of every laboratory test. Appropriate Quality Control practices will maximize the accuracy of results reported as well as possibly provide early information of potential problems. This procedure is intended to give a summary of the quality control program to be followed in the laboratory. A detailed description of the quality control procedures for individual assays should also be included in the quality control sections of the individual procedures.

The laboratory recognizes that the institution and maintenance of a rigorous quality control program can assure the reliability of patient laboratory data. As the spectrum of the tests offered is broad, so are the quality control procedures and the way in which data from various types of quality control material are handled and presented.

This policy applies to any testing procedure associated with the HPTN. This includes

Laboratories, clinic areas and other off site testing areas.

Additional quality control procedures may also be listed in Study Specific Procedure manuals. Manufacturer recommendations must be followed. If the various documentations gives conflicting information, please contact the HPTN Network Laboratory (networklab@hptn.org) for advice.

**Laboratory Internal Quality Control Requirements:.**

1) Laboratory Internal Quality Control material must be analyzed on a regular basis at least according to manufacturer recommendations.

2) QC Data for protocol related assays for hematology, chemistry, flow cytometry and coagulation must be submitted on a monthly basis to HPTN Network Laboratory, attention Domestic Quality Assurance/Quality Control Coordinator.

3) QC Data must demonstrate acceptable assay performance.

4) The name of the testing technologist is linked to each result and control. The testing technologist must initial/sign their worksheets.

5) The director or supervisor or QA/QC technician/designee reviews patient tests results and quality control results of all patient runs and QC analysis on a daily basis. The initials of the director, supervisor, or QA/QC technician/designee on the worksheets document evidence of this review. Review of QC performed in locations other than the laboratory may be performed on a less frequent basis but must be at least once a month.

6) The compiled summary of quality control material is printed (if automated) and reviewed monthly. Evidence of this review is documented by the initials/signature of the director, supervisor, or QA/QC technician/designee on the quality control records.

7) Review of the QC by the HPTN Network Lab does not replace this review by the Lab

Director.

8) The lot number of reagents and materials used in each assay are recorded directly on the result worksheet or a reagent log, if necessary. This information is retained for a

minimum of five years or two years past the closure of the study or indefinitely, determined by the sponsor.

**PROCEDURE**

**A. Quality Control Program**

The Quality Control Program can be divided into the following main areas of focus:

1. Internal Quality Control (testing of known materials)

2. Parallel Testing – Validation of new controls and reagent lots

3. Blind or Split Sample Testing

4. Proficiency (External) Testing Programs

5. Quality Control Monitoring – Corrective Action Logs

6. Quality Assurance Program Feedback

7. Quality Control through Preventative Maintenance Program

**B. Internal Quality Control (testing of known materials) - Qualitative Test Systems**

1. Quality control of assay reproducibility is achieved by testing materials of known reactivity.

2. Qualitative procedures are checked by positive and negative controls.

3. The frequency of controls is dependent on the manufacturer’s recommendation as well as the lab confidence/experience with each method. As a minimum requirement, manufacturer recommendations have to be followed. New operators may run controls more frequently than the manufacturer’s recommendations. QC must be assayed after maintenance procedures or changes in reagent before patient testing can resume.

4. The number of controls and the frequency of control runs should also be specified in each test procedure.

5. The testing technologist and/or clinic staff is responsible for reviewing and recording the quality control results on the assay worksheet (or equivalent).

6. If the quality control results are within the expected response as stated by the manufacturer and the patient test results appear valid, the testing staff will sign and forward the results to the laboratory supervisor or designee for final review.

7. If the quality control results and patient test results are acceptable, the laboratory supervisor or QA/QC technician/designee will sign and release the test run.

8. All results (quality control and patient) must be reviewed, evaluated and signed by the laboratory supervisor or QA/QC technician/designee before the patient test results can be released.

9. In the event that the lab supervisor or QA/QC technician/designee is unavailable and result release will be delayed, peer review is allowed for release of results. Peer result review must be documented by signature. The laboratory supervisor or QA/QC technician/designee review must be documented as soon as possible.

10. If the quality control results are not as expected as stated by the manufacturer or a potential problem is noted, the testing technologist and/or clinic staff will review the results with the laboratory supervisor or QA/QC technician/designee.

11. All quality control results must be documented including any out-of-range results.

12. Out-of-range results and follow-up action will be documented on the appropriate

Corrective Action Log.

13. When a control does not give results as expected or potential problems are noted, the laboratory supervisor or director will make the final decision on the disposition of the run.

14. If the run is considered invalid based on review of the quality control results, all tests must be repeated. The laboratory supervisor or QA/QC technician/designee will review and sign off the corrective action logs once per month. If potential problems exist, the quality control results will be reviewed more frequently.

15. The laboratory supervisor may increase the number of controls, the frequency of controls or request outside testing. There must be sufficient documentary evidence that the laboratory of choice for outside testing can consistently and reliably produce patient results that are not considered to be significantly different. Outside testing laboratories need to be pre-approved by the Network, mentioned in back-up plans and participate in the appropriate proficiency testing. The Laboratory Director or designee is ultimately responsible for making this decision.

16. QC material must be handled exactly as stated in the manufacturer documentation.

17. Any in clinic testing needs to be reviewed by the appropriate laboratory supervisor or designee on a monthly basis. Any problems noted with the in-clinic testing must be brought to the attention of the laboratory supervisor or director as soon as possible.

**C. Internal Quality Control (testing of known materials) - Quantitative Test Systems**

1. Quantitative procedures are checked by a low to high range of two to three controls depending on the procedure.

2. The frequency of controls is dependent on the manufacturer’s recommendation as well as the lab confidence/experience with each method. As a minimum requirement, manufacturer recommendations have to be followed. All levels of the QC material must be analyzed each time QC is performed. QC must be assayed after maintenance procedures or changes in reagent before patient testing can resume

3. The number of controls and the frequency of control runs should be specified in each test procedure.

4. For commercial quality control material, the manufacturer’s ranges can be used until sufficient data has been gathered to enable the establishment of a laboratory or analyzer specific QC range. The mean of the results obtained must lie within the manufacturer recommended ranges unless otherwise stated by the manufacturer. Sufficient data would normally be 20 data points. For hematology systems this may be considered too many, please consult HPTN Network Lab for guidance.

5. The testing technologist is responsible for reviewing and recording the quality control results on appropriate quality control logs. This would normally be control logs and Levy-Jennings charts. The exception to this requirement is if the analyzer or LIS system keeps track of the quality control. If this is the case, the technologist must sign off on a log sheet indicating the QC was run and within range.

6. If the test system has an automated quality control record function, the control logs and

Levy-Jennings charts must be checked each time the controls are run.

7. Patient samples should not be reported before the controls are reviewed and found to be acceptable.

8. If the quality control results are within the established guidelines and no shifts, trends or potential problems are noted on the Levy-Jennings charts, the testing technologist will forward the patient results to the laboratory supervisor or designee for final review.

9. If the quality control results and patient test results are acceptable the laboratory supervisor will sign and release the test run. Generally patient results are considered acceptable if all quality control material fall within the established QC ranges. Lab should have guidance such as a QC Acceptability Policy that describes in detail the criteria for QC acceptability and rejection.

10. All results (quality control and patient) must be reviewed, evaluated and signed by the laboratory supervisor or QA/QC technician/designee before the patient test results can be released.

11. In the event that the lab supervisor or QA/QC technician/designee is unavailable and result release will be delayed, peer review is allowed for release of results. Peer result review must be documented by signature. The laboratory supervisor or QA/QC technician/designee review must be documented as soon as possible thereafter.

12. If the quality control results are not within the expected ranges and guidelines, the testing technologist will review the results with the laboratory supervisor or QA/QC technician/designee.

13. All quality control result including any out of range results must be documented.

14. Any shifts or trends must be reported to the laboratory supervisor and/or local QA/QC

technician. Any shifts or trends must be examined.

15. Out-of-range results and follow-up action will be documented on the appropriate

Corrective Action Log.

16. When a control result falls outside the established range or potential problems are noted, the laboratory supervisor or director will make the final decision on the disposition of the run.

a. Results may be considered acceptable after review.

b. The review and consideration will be documented on the assay sheet and the corrective action log.

17. If the run is considered invalid based on review of the quality control results, all patient analysis must be repeated

18. The laboratory supervisor or QA/QC technician/designee will review and sign off the quality control data and corrective action logs once per month. If potential problems exist, the quality control results will be reviewed more frequently.

19. The Laboratory supervisor, manager or director may increase the number of controls, the frequency of controls or request outside testing to resolve potential problems.

20. QC material must be handled exactly as stated in the manufacturer documentation.

21. All safety laboratory related QC Data must be submitted on a monthly basis to HPTN Network Laboratory, attention Domestic Quality Assurance/Quality Control Coordinator. (email: networklab@hptn.org )

22. QC Data must demonstrate assay performance which is comparable to the performance specifications published by the manufacturer.

**D. Parallel Testing – Validation of new controls**

Whenever possible, new lots of control material must be assayed in parallel alongside the current in use lot. This is to enable the calculation of laboratory QC ranges and to demonstrate that the QC material is performing as expected. (see HPTN Quality Assessment Policy Version 3 for specifics)

**1. Controls for Quantitative Assays**:

a. In order to validate new controls, the new lot of controls will be run in parallel with the old lot of controls 2-3 times a day for 5-10 days, to give a minimum of 20 values to enable the calculation of laboratory specific QC ranges. The mean and QC ranges for the new lot of controls will be reviewed and signed off by the laboratory supervisor or director before being put into use.

b. For hematology the new lot of controls should be run in parallel with the old lot of controls to give a minimum of 10 values over a period 5 days if possible. The mean and ranges for the new lot of controls will be reviewed and signed off by the laboratory supervisor or director before being put into use. The use of historic precision data for the calculation of QC ranges is acceptable practice. Please contact the HPTN or MTN Network Lab for clarification if needed. (email: networklab@hptn.org or mtnnetworklab@mtnstopshiv.org)

**2. Controls for Qualitative Assays**:

Each new lot of QC for qualitative assays must be run and give an expected response. The lot of controls will be reviewed and signed off by the laboratory supervisor or director before being put into use.

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

1. Gram Stain

a) Gram stain reagent and procedure will be quality controlled each day of use by including a control slide containing gram positive and negative organisms such as E. coli and Staphylococcus aureus or equivalents.

b) These control slides may be made in-house from known cultures. c) Acceptance criteria for the gram stain slides will be defined.

d) The slide control results will be documented on a gram stain quality control log. e) The control log will be initialed and dated by the technologist performing the

quality control.

f) The control log will be reviewed and signed at least once per month by the laboratory supervisor or designee.

g) If the control slide stain is not acceptable, check both the staining technique and the stain.

h) Document any problems and corrective action on the gram stain corrective action log.

2. Differential and/or Malaria Stain

a) The differential stain will be checked each day of staining.

b) The first slide read after staining will be reviewed for correct color formation for the WBC’s and RBC’s along with excessive background debris.

c) Acceptance criteria for the differential stain will be defined and documented on the control log.

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

e) The control log will be reviewed and signed at least once per month by the laboratory supervisor or designee.

f) If the control slide stain is not acceptable, check both the staining technique and the stain.

g) Document any problems and corrective action on the gram stain corrective action log.

**F. Proficiency (External) testing Programs And Blinded/Split Samples**

See HPTN Quality Assessment Policy Version 3 for information

**G. Built in / procedural controls**

Many test systems such as Rapid HIV tests or Pregnancy Tests contain a built in procedural Control Test line. These built in controls indicate whether sample has reached the desired portion of the test strip / reaction chamber. The response obtained from the control portion must as expected for each test strip before patient results can be reported. Please refer to manufacturer kit instructions for specific details.

These built in control lines only indicate that the sample flow has been achieved as desired.

A positive control line does not indicate that assay has performed as expected with the patient sample.

Quality Control specimens must be assayed for all test systems on a regular basis for all

DAIDS related procedures (including FDA Waived test kits).

**H. Quality Control Monitoring – Corrective Action Logs**

1. Corrective Action Logs are maintained for each test and instrument.

2. The corrective action logs are used to document quality control results that fall outside the established ranges, inconsistency in results or problems with test system (reagents, controls, instrument or equipment).

3. The testing technologist is responsible for documenting any problems and corrective action taken on the appropriate corrective action log

4. The logs provide valuable information for troubleshooting test method or instrument problems.

5. The laboratory supervisor or QA/QC technician/designee is to be notified immediately of any problems and will review the corrective action.

6. The corrective action logs will be reviewed and signed off once per month by the laboratory supervisor or QA/QC technician/designee.

7. Corrective action logs should also indicate the status of patient results. ie. whether patient results were reported or not.

**I. Quality Assessment**

See HPTN Quality Assessment Policy Version 3 for information

**J. Preventative Maintenance**

See HPTN Quality Assessment Policy Version 3 for information

**APPENDICES**

1.Quality Control Testing Summary

2.Corrective Action Log

Quality Control Policy version 6

**QUALITY CONTROL TESTING SUMMARY**

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| --- | --- | --- | --- | --- |
| Test | Quality Control | Proficiency Program(check with appropriateDAIDS contractor) | ParallelTesting/New reagent lot Verification | Comments |
| Material | Frequency | CAP | UKNEQAS |
| CBC | Low, Normal, High | Daily | X |  | Overlap Controls | Calibrate per manufactures instructions or every 6 mos |
| Differential - Manual | Stain Check | Daily | X |  |  |  |
| ESR | Low/High | Daily | X |  |  |  |
| Malaria Smear –Giemsa/WrightGiemsa | Stain Check | Daily | X |  |  |  |
| CD4/CD8 | Manufactures Controls | Daily | x | X | Reagents |  |
| Coagulation | Manufacturer controls(normal and abnormal) | Every 8 hours |  |  | Overlap Controlsand Reagents | QC required with every reagent change |
| Chemistry | Minimum 2 levels | Daily | X |  | Overlap Controlsand Reagents | Calibrate per manufacturers instructions or every 6 mos |
| HIV-1/2 EIA | Kit controls plus external lowlevel positive control | Run | X |  | Reagents | Known Neg and positive patients (minimum 1 each)withevery new lot |
| HIV-1/2 Rapid | Commerical or In-House | weekly | X |  | New kit, new user |  |
| HIV-1 Western Blot | Kit: Neg/WeakPos/StrongPos | Run | X |  |  |  |
| Urinalysis | Commerical,Normal/Abn | Weekly | X |  |  | New lots need QCed in lab prior to distribution to clinic.Weekly in the lab, clinic per use |
| Urine Pregnancy | Commerical, Neg/Pos | weekly | X |  | New lot and newdelivery |  |
| RPR | Neg/Weak/Pos | Run | x |  |  |  |
| HIV RNA PCR QT | Kit Controls, Neg/L-H Pos | Run | X |  | Reagents | Recommendation : VQA log controls |
| GC,Chl PCR QL | Kit Controls, Neg/Pos | Run | X |  | Reagents | Run controls and 1 pos and 1 neg |
| Gram Stain | Controls(E.coli and Staphaureus) Stain Check | Daily | x |  |  |  |
| Media (cell prep) | Media Check | Per Lot |  |  |  |  |
| Storage-Pla,Ser | Self Audit | Weekly |  |  |  |  |

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Quality Control Policy version 6

**CORRECTIVE ACTION LOG**

CORRECTIVE ACTION/REMARKS LOG for INSTRUMENT/TEST SYSTEM

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Date | Problem/Comments | Initials | Corrective Action/Comments | Initials | Date |
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