DAIDS
Bethesda, MD USA

Manual
DAIDS Good Clinical Laboratory Practice Guidelines

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DAIDS

Good Clinical Laboratory Practice Guidelines

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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Sponsor Statement

The Division of AIDS (DAIDS) in the National Institute of Allergy and Infectious Diseases (NIAID) supports a global research portfolio to advance biological knowledge of HIV/AIDS, its related co-infections, and co-morbidities. With the ultimate goal of creating an "AIDS-Free Generation," DAIDS develops and supports the infrastructure and biomedical research needed to: 1) reduce HIV incidence through the development of an effective vaccine and biomedical prevention strategies that are safe and desirable; 2) develop novel approaches for the treatment and cure of HIV infection; 3) develop interventions to treat and/or prevent HIV co-infections and co-morbidities of greatest significance; and 4) foster partnerships with scientific and community stakeholders to develop and implement effective interventions.

In its clinical trials, DAIDS aims to ensure the safety and optimal management of participants, obtain reliable laboratory-based data critical for the meaningful interpretation of trial findings, ensure the safety of those who perform the laboratory testing, and achieve accurate reconstruction of a trial to allow its submission to a regulatory body such as the Food and Drug Administration (FDA), the European Medicines Agency (EMA), or South African Health Products Regulatory Authority (SAHPRA). To attain these goals, as well as allow data to be pooled and/or comparable regardless of where they are generated, DAIDS has developed the DAIDS Good Clinical Laboratory Practice (GCLP) Guidelines.

These GCLP Guidelines encompass applicable portions of the Code of Federal Regulations (CFR) including 21 CFR part 58 (Good Laboratory Practice [GLP]), 42 CFR part 493 (Clinical Laboratory Improvement Amendments [CLIA] requirements), 21 CFR part 11 (Electronic Records; Electronic Signatures), 29 CFR part 1910.1200 (Occupational Safety and Health Standards - hazard communication), and 49 CFR part 172 (transportation of hazardous materials). The GCLP Guidelines also include guidance from organizations and accrediting bodies, such as the College of American Pathologists (CAP), FDA, American National Standards Institute (ANSI), and Clinical Laboratory Standards Institute (CLSI). CLIA requirements overlap to a large extent with GCLP, therefore, the DAIDS GCLP Guidelines do not apply to laboratories in the United States that are CLIA-compliant. Additionally, based on activities in the laboratory, some GCLP requirements may not apply. The term "must" is used throughout the GCLP Guidelines to signify mandatory policies and practices whereas the term "should" denotes recommended, but not required, guidelines.

The GCLP Guidelines and related documents may be accessed at https://www.niaid.nih.gov/research/daids-clinical-research-laboratory-specimens-management. Within the GCLP Guidelines and reference section, web links are provided to access resources that the laboratory personnel may use. **If used, they should be interpreted to accurately reflect the laboratory's specific processes and/or protocol requirements.**

We thank the laboratory personnel for supporting the DAIDS clinical trials and striving to comply with the DAIDS GCLP. If you have any questions about the content of this document, please contact the DAIDS Clinical Laboratory Oversight Team at NIAIDDCLOT@niaid.nih.gov.

DAIDS Good Clinical Laboratory Practice Guidelines

The development of the GCLP Guidelines was a collaborative effort between DAIDS and PPD. The authors that have contributed to this document are listed below:

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National Institute of Allergy and Infectious Diseases

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1. Organization and Personnel

Laboratory management and personnel share the responsibility for thorough documentation of the structure of the organization, the respective job descriptions and qualifications, and ongoing documentation of an individual's professional experience, training, and skill-assessment. This ensures an employee's ability to adequately and safely perform his/her job. Laboratory management must also ensure that the organization complies with any applicable personnel licensure, certification, or registration requirements for personnel it employs.

The laboratory must employ an adequate number of qualified personnel to perform all the functions associated with the volume and complexity of tasks and testing performed.

Standards for Organization and Personnel

a. Documentation Guidelines

The following documents should be stored in the laboratory or readily available to authorized personnel, as appropriate:

- **Personnel policies** must be available and address such topics as orientation, training, continuing education requirements, performance evaluations, dress code, and security. These policies detail employer and employee responsibilities.
- **Organizational and/or departmental policies** that describe how personnel can communicate issues that may affect study integrity, quality of testing and data, or safety of personnel must be available. The policies must ensure a non-retaliatory environment that encourages communication vital to the integrity of the study and the institution.
- **Job descriptions and job profiles** that define qualifications and delegation of duties for all positions within the laboratory must be available to personnel and other appropriate individuals (as defined below). To be as effective as possible, a job description and job profile need to incorporate standard information (as appropriate) such as:
    - Job qualifications (education, required national, regional, or local license or registration, technical competencies, and needed professional credentials or certifications).
    - Years and types of experience.
    - Reporting structure.
- **Personnel files** must include the following records (in electronic or paper format), as applicable:
    - Dates of employment
    - Experience
    - Education
    - Curriculum Vitae (CV)
    - Applicable licensure/certification (if required)
    - Orientation, training, attendance at job-related workshops

and seminars (refer to the GCLP documents resource link in the reference list for an example of a training attendance log)
    - Safety training
    - Competency assessments
    - Continuing education records
    - Work-related incident and/or accident records

  When paper personnel files are kept, they must be stored in a secure, protected environment such as a locked cabinet or room. When electronic records are kept, the system must include security measures such as user identification and passwords for computer system access, password-protected documents, and computer backup systems. The laboratory must define and establish a process for auditing personnel records, including frequency of, and criteria for, record review.
- **Organizational chart(s) that** represent the formal reporting and communication relationships that exist among personnel and management and between the main laboratory unit and satellite units, as applicable, must be available. These charts provide the current communication structure within the laboratory and help to ensure that the personnel understand communication path options and requirements.

b. Personnel Education and Evaluations

Managerial and technical personnel engaged in the conduct of laboratory testing related to clinical research must have the education, training, and experience commensurate with their assigned functions. All laboratory personnel education and evaluation requirements must comply with applicable local laws and regulations.

c. Job-specific Training, Education, and Assessments

- All personnel must receive direct and detailed training for the duties and tasks that they perform.
- Training must take place at the following times:
    - Before work is performed independently
    - When changes to work processes or procedures occur
    - After repeated performance problems or when competence is in question
- Training records should include the following information:
    - Title of the training event
    - Identity of the trainer(s)
    - Items covered during the training
    - Training dates
    - Name(s) of the person(s) being trained
    - An attestation including the trainee's signature indicating commitment to comply with procedures as trained
- Although there are no specific retraining requirements for personnel returning after an extended absence, the laboratory should determine training or retraining needs individually.

- The laboratory must have a policy that refers to the program and processes used for assessing personnel competence.
- Competency assessments must be conducted and recorded for all tasks at the following times:
    - Upon completion of an employee's initial training
    - For new methods or instruments prior to starting testing and prior to reporting participant results
    - For new and changed processes and procedures
    - When personnel responsibilities change
- Competency assessments should ensure that the personnel maintain their competency to perform test procedures and report results promptly, accurately, and proficiently.
- Competency assessments must compare employee performance against a documented standard and clearly verify competency or lack of competency for each evaluated assigned task.
- Competency records need to identify what was reviewed or observed, when it was reviewed or observed, who conducted the review or observation, and the outcome. Individuals responsible for competency assessments should have the education and experience to evaluate the complexity of the testing being assessed. Laboratory management needs to ensure that personnel do not perform procedures for which they have failed to demonstrate competence. All records created for retraining and reassessments need to include the outcome, be signed by the individual and laboratory management, and be retained in the individual's personnel file.
- Competency assessments for non-waived testing should include at minimum the following elements:
    - Direct observations of routine test performance, including participant preparation (if applicable), specimen handling, processing, and testing
    - Monitoring the recording and reporting of test results
    - Review of intermediate test results or worksheets, quality control records, proficiency testing results, and preventive maintenance records
    - Direct observation of performance of instrument maintenance and function checks
    - Assessment of test performance through testing of previously analyzed specimens, internal blinded testing samples, or external proficiency testing samples

  Competency for non-waived testing must be assessed initially, every six months during the first year of employment, annually thereafter, or more frequently if laboratory management deems necessary.
- Competency for waived testing should be assessed using the following methods:
    - Performance of a test on a blinded specimen (e.g. External Quality Assurance (EQA) sample)

- Observation of routine work at a pre-specified frequency, including adequacy of documentation
- Monitoring of each user's quality control performance
- Use of a written test specific to the test assessed

Competency for waived testing should be assessed according to institution policy at defined intervals, but at least at the time of orientation and annually thereafter.

- Personnel who perform tasks that require interpretation of color (e.g., colorimetric assays) must be tested for color blindness and/or color vision deficiencies. Color discrimination assessments must include colored items pertinent to the job.

d. GCLP Training

CLIA requirements overlap to a large extent with GCLP, therefore the DAIDS GCLP training is not required for clinical laboratory personnel in laboratories in the United States that are CLIA certified. For U.S. specimen processing laboratories and endpoints laboratories, GCLP training is highly recommended. For non-U.S. laboratories that are not covered under CLIA, all clinical laboratory personnel involved in specimen processing and testing must take GCLP training, available on the DAIDS learning portal (https://daidslearningportal.niaid.nih.gov/). GCLP training of study nurses and any other non-lab personnel performing specimen processing and/or testing in the clinic or clinical laboratory is under the purview of laboratory management.

Laboratory management should ensure that training frequency is sufficient to ensure that personnel remain familiar with the GCLP requirements applicable to them.

e. Personnel Identification

If signatures, initials, or codes are used as personnel identifiers on any laboratory documentation, a documented list that links these identifiers to a printed name must be in place. Changes in personnel signatures, initials, codes, and identifiers for new personnel must be updated in a timely manner in the documented list. Personnel identifier documentation must be archived as defined in Section 6, *Records and Reports*.

Refer to the GCLP documents resource link in the reference list for an example of a signature sheet.

2. Equipment

The laboratory personnel must have regular access to all the equipment required to perform all the analyses within the scope of the laboratory. Standard Operating Procedures (SOPs) and supporting documentation, such as maintenance logs, must exist to demonstrate and provide evidence that all instrumentation and equipment are adequately validated, operated, inspected, cleaned, maintained, tested, and standardized to ensure optimal quality of the data. All preventive maintenance and calibrations must be scheduled and

performed at least as frequently as suggested by the equipment manufacturers to ensure continued accuracy, precision, and extended usable life of the equipment. The performance of all instruments and equipment must be verified prior to initial use, after major maintenance or service, and after relocation to ensure that they run according to expectations.

Standards for Equipment

a. Documentation Guidelines

The laboratory must keep documentation of all scheduled preventive maintenance, unscheduled maintenance, service records, and calibrations for all equipment utilized, as defined by the laboratory or institution. This documentation must be readily accessible. Retain preventive maintenance and service logs as outlined in Section 6, Records and Reports, or until otherwise instructed.

- At a minimum, maintenance and calibration records need to include the following information:
  - Instrument or equipment identification
  - Date maintenance/calibration was performed
  - Maintenance activities performed
  - Results of calibration
  - Acceptability status of calibration (pass/fail)
  - Identity of personnel performing maintenance activity
  - Any necessary maintenance/calibration follow-up actions taken
  - Review and approval
- Laboratory management must review, sign, and date all documentation of equipment maintenance at least monthly.
- All equipment used for DAIDS protocol-related laboratory activities must be listed on an inventory document.

b. General Guidelines

Personnel must conduct all preventive maintenance and schedule service for protocol-related equipment per manufacturer specifications by following these guidelines. The following requirements apply to equipment used for DAIDS protocol-related laboratory activities:

- Personnel must keep equipment clean, avoiding any buildup of dust, dirt, and spills that may adversely affect personnel safety or equipment performance.
- The laboratory must employ and adhere to documented daily, weekly, and/or monthly routine maintenance plans and record completion of these tasks on the appropriate logs in a timely fashion.
- Any equipment that is out of service/not in use for any reason must be clearly identified as such.
- For equipment that has no standard frequency or requirement for maintenance and function checks, each laboratory must establish a schedule and procedure that reasonably reflect the workload

and specifications of its equipment.

c. Temperature Monitoring

- Temperatures must be checked (where applicable) and recorded each day of use for all temperature-dependent equipment and environments using a calibrated thermometer.
- If specific instruments, equipment, kits, or supplies have specified ambient temperature ranges for proper operation, storage, or use, there must be records that the specified ambient temperature is maintained, and corrective action taken when tolerance limits are exceeded.
- Temperatures may be recorded, either manually or using a recording device or system by 1) recording the numerical temperature value; or 2) placing a mark on a graph that corresponds to a numerical temperature. If temperatures are recorded manually, the identity of the individual recording the temperature(s) must be recorded.
- If an automated (including remote) temperature monitoring system is used instead of manual temperature monitoring, laboratory personnel must have ongoing immediate access to the temperature data so that appropriate corrective action can be taken if a temperature is outside of the acceptable range. System records must demonstrate daily functionality of the system.
- If a minimum/maximum thermometer is used to perform continuous monitoring of temperatures between daily temperature readings or following a laboratory downtime (e.g., laboratory closure for weekend or holiday), both the low and high temperatures as well as the actual temperature must be recorded. To ensure correct temperature readings, the minimum/maximum thermometer device must be reset prior to the monitoring period.
- There must be a written policy/procedure in place that explains how temperatures are monitored during the absence of laboratory personnel. This policy must include information concerning corrective actions associated with deviations from the allowable temperature ranges (minimum and maximum, as applicable).
- Monthly supervisor review should be documented for manual and electronic temperature monitoring records.

d. Backup instruments/Correlation Testing

- If a laboratory uses more than one instrument to perform the same test, the primary and backup instruments must be compared to each other to determine the consistency of results.
- For quantitative tests, correlation testing should be performed on a semi-annual basis at minimum, where applicable.
- For qualitative tests, verifying the successful EQA performance or use of participant specimens for the backup lab/instruments should be sufficient.
- Acceptability criteria must be defined for comparability of

instruments and methods, as appropriate, and corrective action recorded when the criteria are not met.
- Statistically defined acceptability limits must be used for quantitative assays.
- Use of study participant samples should be restricted to assays that are required by the applicable clinical trial protocols and may require approval by the applicable Institutional Review Board (IRB) or Independent Ethics Committee (IEC).

e. Service Guidelines

In addition to the above general guidelines, the laboratory must have practices and policies in place for routine equipment and instrumentation, including those described below. Trained laboratory personnel or certified contractors should perform the following services:

Autoclaves

- Verify content processing using heat-sensitive tape with each autoclave batch.
- Verify effective sterilization with an appropriate biological indicator periodically as determined by laboratory management. DAIDS strongly recommends weekly biological indicator testing.
- Perform autoclave maintenance annually, or as per manufacturer, including a pressure check and calibration of temperature device.
- Check autoclave mechanical timing device periodically.
- Maintain records of autoclave operation and maintenance in the equipment log.

Balances

- Check accuracy, as described by the manufacturer, using standard weights of the appropriate American National Standards Institute/American Society for Testing and Materials (ANSI/ASTM) class or equivalent at a predetermined frequency (based on manufacturer suggestions). Document the results with an evaluation of their acceptability.
- Service and calibrate periodically using qualified personnel (per manufacturer's instruction). Maintain records of service and calibrations.
- Place the analytical balance in a location so that vibration does not affect the readings.

Biosafety Cabinets/Laminar Air Flow Hoods

- Verify that air intake grills are not obstructed.
- Certify cabinets/hoods annually using a trained service technician, certified maintenance department, or company.
- Check daily for air flow as instructed by manufacturer and document the results to verify the effectiveness of the personnel and environmental protective functions. For example, a Class 2 biosafety cabinet will likely have an inflow velocity meter. The manufacturer of the cabinet may state that the cabinet must

maintain a minimum of 75 feet per minute (FPM) inflow velocity. The actual airflow obtained on a daily basis must be documented and compared to this limit, with corrective action taken as required.
- Clean the work surfaces after each use with 70% ethanol or other disinfectant as recommended by the manufacturer.
- Clean the Ultraviolet (UV) lamp, if used, weekly with 70% alcohol.
- Use of UV is recommended only when personnel are out of the room.
- Document daily and weekly cleaning.

Centrifuges

- Verify operating speeds annually at a minimum (DAIDS recommends every six months) using a National Institute of Standards and Technology (NIST)-comparable method.
    - The centrifuge must be verified at the same speed(s) at which the laboratory uses the centrifuge for its procedures.

Backup Power Equipment

- The laboratory must have SOPs in place that describe backup power resources; backup power equipment may include generators or uninterruptible power supplies (UPS).
    - This documentation may be included in a business continuity plan SOP.
    - If used to back up specimen storage freezers, UPS units should be capable of supplying power for at least 8 hours.
- The laboratory should retain documentation of how backup power equipment is maintained (this may include logs or SOPs that detail the frequency of maintenance).

Incubators and Water Baths

- Establish tolerance limits for temperatures, carbon dioxide level, and humidity, as applicable.
- Maintain daily (or “date of use”) temperature records.
    - Maintain appropriate documentation of corrective action for out-of-range temperatures.

Microscopes

Ensure that microscopes are clean, adequate (e.g., low, high, dry and oil immersion lenses as appropriate for the intended use), optically aligned, and properly maintained with records of at least annual preventive maintenance. Ensure microscopes used for fluorescence testing are monitored for sufficient light source intensity.

Pipettors

- Check for volumetric accuracy and reproducibility and recalibrate as necessary before placing in service initially and at specific defined intervals. For new pipettors, manufacturer’s certificates may be used.
- DAIDS requires that pipettors be checked for accuracy and reproducibility and recalibrated at least once every six months.

Pipettor malfunction is one of the most common sources of laboratory error. DAIDS strongly recommends that laboratories perform checks for accuracy, reproducibility, and recalibrations four times per year.

Refrigerators and Freezers

- Establish tolerance limits for temperatures and/or for liquid nitrogen level, as appropriate. For example, a given refrigerator's temperature tolerance limits must reflect the most stringent needs of all reagents, supplies, and specimens stored within it. If Reagent A's acceptable storage temperature range is 2-8 ºC, and Reagent B's acceptable storage temperature range is 3-10 ºC, the tolerance limit for the refrigerator must be 3-8 ºC.
- Place liquid nitrogen freezers in facilities that are well ventilated and monitored for oxygen content.
- Maintain daily (at a minimum) levels of liquid nitrogen as appropriate.
- Maintain appropriate documentation of corrective action for out-of-range temperatures and liquid nitrogen levels.

Thermometers

- All non-certified thermometers in use must be checked against an appropriate thermometric standard device (e.g., NIST-certified or equivalent thermometric device) before initial use and periodically, as defined by the laboratory's own policy. For NIST-certified (or equivalent) thermometers, follow manufacturer's recommendations for calibration and expiration date. If digital or other displays of temperatures on equipment are used for daily monitoring, the laboratory must verify that the readout is accurate. The display must be checked initially and periodically, as defined by the laboratory's own policy.

Timers

- Check for accuracy by comparing to a known standard (e.g., NIST-traceable timer) every six months. For NIST-certified (or equivalent) timers, follow manufacturer's recommendations for calibration and expiration date.

3. Testing Facility Operation

A testing facility must have written SOPs to ensure the consistency, quality, and integrity of the data generated by laboratory. Policies provide a statement of intent that an organization will follow a particular course of action, while SOPs detail practical ways in which policies are translated into action. These SOPs should be of uniform format as determined by laboratory management and should include items such as test principles and clinical significance. A document control plan must exist to facilitate the review for accuracy and relevance of all SOPs. Only approved versions of paper-based or electronic documents must be available for use by personnel in all locations where they are needed.

Standards for Testing Facility Operation

The laboratory must write SOPs (including applicable policies and working instructions) in a manner and language that is appropriate to the laboratory personnel conducting the corresponding procedures.

Refer to the GCLP documents resource link in the reference list for an SOP format example.

a. SOP Distribution

The laboratory must distribute all new and revised SOPs to the appropriate laboratory personnel who will be responsible for performing their routine tasks in accordance with the content of those SOPs.

- The laboratory personnel must document that they have reviewed and understood all new and revised SOPs, for example, by signing and dating the SOP after their review. Additionally, electronic means of attestation are acceptable.
- The laboratory must maintain this documentation in a system that readily allows for verification that personnel are knowledgeable of the new or revised SOPs.

b. Document Control Plan

The laboratory must maintain a current document control plan that addresses the following:

- Maintain a master list of SOPs currently used in the laboratory that contains the names of all documents (those in electronic and paper form), the version in use, and the effective dates and locations of controlled copies. Ensure SOPs are procedurally accurate and relevant.
- Keep the authorization process standardized/consistent, limiting approvals to laboratory management.
- Review SOPs every two years and document the review. It is highly recommended that SOPs be reviewed annually.
- Establish a system for tracking all changes made to a currently approved document (along with who made the change and why it was made).
- Maintain the integrity of previous versions of the document; this can be accomplished by recording the date or revision level (number or letter), which identifies the current version of the document.
- Remove retired, superseded, or obsolete printed SOPs from circulation and identify them as retired, superseded, or obsolete.
- Archive retired, superseded, or obsolete SOPs for a period defined by the laboratory or institution. Retention time periods established by the laboratory or institution must meet or exceed the requirements set forth by the sponsor and/or any applicable regulatory bodies such as the U.S. FDA.
- In an electronic document management environment, ensure that

only controlled, approved, and read-only versions are accessible at computer terminals. To reduce the likelihood of unauthorized changes, the documents should be distributed electronically in PDF or "read-only" format. When someone prints a copy of a document, that copy is no longer controlled and should be designated as such.

- Establish a process for identifying when a reference document has been updated, such as watching for updates in resource materials, organizational announcements, and manufacturer communications.

c. SOP Categories

The laboratory must have SOPs for DAIDS protocol-related laboratory activities. General categories of SOPs within the department may include:

- Document Control: describes a plan that ensures relevance of all SOPs, as described earlier in Section 3, *Testing Facility Operation*.
- Organization and Personnel: details procedures that govern communication and administrative components of all personnel in the organization, as described in Section 1, *Organization and Personnel*.
- Personnel Training: explains required training and supporting documentation, as detailed in Section 1, *Organization and Personnel*.
- Equipment Calibration and Maintenance: governs the physical maintenance and calibration of laboratory assets, as described in Section 2, *Equipment*.
- Specimen Management and Chain-of-Custody: features specimen transportation and handling steps required for maintaining specimen integrity, positive identification of specimens, and audit trails from point of collection to delivery of results, as detailed in Section 8, *Specimen Transport and Management*.
- Test Procedures: includes the steps describing the performance of tasks, processes, and assays (safety, diagnostic, and endpoint), as addressed in Section 3, *Testing Facility Operation*.
- Quality Control (QC): expresses the components of establishing, performing, evaluating, troubleshooting, and documenting QC processes, as described in Section 4, *Test and Control*.
- Quality Assurance (QA): explains the systematic approach to ensuring continued improvement of the operations within the laboratory, as detailed in Section 11*, Quality Management*.
- Test Reporting and Record Management: oversees the format, reproduction, and delivery of final information generated by laboratory assays to appropriate individuals; also governs archiving of source documents, as found in Section 6, *Records and Reports*.
- Safety: describes the engineering controls, personal protective equipment (PPE), and processes to reduce risks to personal safety within the laboratory environment, as detailed in Section 9, *Personnel Safety*.
- Laboratory Communications: details steps to take if an individual has concerns regarding how personnel can communicate existing

issues which may affect quality of testing or safety of personnel, as addressed in Section 11*, Quality Management*.

- Operations of Laboratory Information System (LIS): describes procedural stepwise details of routine operation, as defined in Section 10, *Laboratory Information Systems*.
- Facilities: describes procedures of maintaining the facilities for optimal quality of the work and safety of personnel and participants, as addressed in Section 7, *Physical Facilities*.
- Deviations and Corrective Actions: describes how deviations and corrective actions are documented and future occurrence prevented, as addressed in Section 11*, Quality Management*.

4. Test and Control

The management of Quality Control (QC) must include a process of identification and documentation of analytical problems as they occur, with the ultimate goal of evaluating the accuracy and reliability of the analytical testing process. The laboratory must establish and follow written QC procedures for each test system to detect both immediate errors and the changes that happen over time. Frequency of performance, number of samples or specimens to be used, as well as the type of QC materials must be determined by the laboratory. All failed QC results must be investigated and handled according to a documented QC program.

Standards for Test and Quality Control

a. Quality Control Program

The laboratory must have a site-specific, written QC program to define procedures for monitoring analytic performance This program ensures the consistent identification, documentation, and resolution of QC issues. Laboratory management must be actively involved in its design, implementation, and oversight.

b. Evaluation Criteria

Manufacturers' tolerance limits or ranges tend to be set wide to accommodate the various operating systems present in different laboratory settings. The laboratory should establish and document the tolerance limits for acceptance of control results. For example, a laboratory may choose to utilize Westgard multi-rule QC procedures to judge the acceptability of an analytical run. This laboratory should establish the means of new lot numbers of QC materials over a period of 5-21 days, running the new lot in parallel with the current lots in use. Once they have acquired a minimum of 20 replicates of each level of new QC material, the laboratory can then calculate the new mean and use the method's historic coefficient of variation (CV) to calculate the new standard deviation. The laboratory should establish local means and QC ranges based on historical method CVs.

c. Frequency of Quality Control Testing and Types of Control Materials

QC samples must be tested in the same manner as study participant specimens and by the personnel who routinely perform study participant testing. Laboratory management must determine the appropriate number and frequency of QC tests using the following guidelines:

- For quantitative tests, use control materials at more than one level, such as a "high" and "low" control.
  Note: Controls must verify assay performance at result levels where clinical or study decisions are made. For example, medical decisions may be made for study participant glucose levels at 45 mg/dL and 180 mg/dL; two levels of control materials should be representative of these results.
- For qualitative tests, include positive and negative controls with each control run.
- For staining procedures, Gram stains require both Gram-positive and Gram-negative control organisms to be used once per week and with each change of a lot number of any component in the staining procedure. Other stains require daily or day of use QC, using a positive reacting organism and a negative, which could include the participant sample.
- For FDA-approved, CLIA-waived tests, the manufacturer package insert instructions should be followed. In addition, it is recommended that sites conduct external QC weekly during any week in which participant samples are tested.

In addition, daily QC is strongly encouraged in the following situations:

- If results are used for primary endpoint or critical safety determinations
- If there are changes to device reagents, study populations and/or analytes
- When there are new operators performing testing on participant specimens
- For all tests that are not FDA approved, even if they closely resemble a currently CLIA-waived or approved test
- With each new kit lot
- Whenever a new shipment of test kits is received
- If the temperature of the test kit storage area falls outside of the manufacturer's recommended range
- If the temperature of the testing area falls outside of the manufacturer's recommended range

d. Review of Quality Control Data

QC must be run and reviewed for acceptability prior to reporting study participant results and after a change of analytically critical reagents, major preventive maintenance/service, or change of a critical instrument component.

The laboratory personnel performing the testing must determine the appropriate corrective action to take for QC data that falls outside

established tolerance limits, using the QC program as a guide. Corrective action must be documented with the technician's initials and date.

In the event the QC data is determined to be unacceptable, the laboratory must re-evaluate all study participant test results since the last acceptable test run. The laboratory must evaluate study participant results to determine if a significant clinical difference has occurred, in which case, assay or instrument troubleshooting should be conducted and amended results reported as applicable.

e. Quality Control Logs

- QC logs must be present documenting control results assayed with each protocol-related test, as described in each specific protocol-related assay procedure.
    - Control records must be readily available to the personnel performing the test.
    - Results of controls must be recorded or plotted to readily detect a malfunction in the instrument or in the analytic system.
    - Appropriate charts (e.g., Levey-Jennings [L-J] charts or control charts) must be utilized by personnel to document quantitative QC data to allow for determination of acceptability of the QC run and to aid in detection of shifts and trends in the control data.
    - Laboratory personnel performing QC runs, recording of results, and plotting of data on graphs must record their initials, date, and time (as applicable), as testing is performed. For example, if Technologist ABC performs the QC run for HIV viral load on a given morning, Technologist ABC must document their initials, date, and time on all applicable QC records.
    - If QC materials are aliquoted, they must be labeled (applicable to information recorded on paper or electronic log) in such a way that they can be traceable to the material name and lot, preparation date, expiration date and technician.

Refer to the GCLP documents resource link in the reference list for L-J chart and QC log examples.

f. Corrective Action Logs

The laboratory must ensure that a corrective action log, or equivalent electronic record, is present to facilitate documentation and resolution of QC failures.

g. Supervisor Review of Quality Control Documentation

Appropriate laboratory management must regularly review, sign, and date QC records and corrective action logs according to the following

guidelines:

- Laboratory management must review, sign, and date the QC data and the corrective action log at least monthly.
- A listing of all the designee position titles must be included in the current QC plan.

h. Quality Control Record Retention

The following records must be retained by the laboratory in a secured fire-proof (preferred), fire-resistant, or fire-protected (least preferred; e.g., stored in area with operational automatic sprinkler system) storage area/facility for a period of time that has been defined by the laboratory or institution:

- Instrument printouts
- All QC records including worksheets if QC is recorded manually
- Package inserts
- Certificates of Analysis

i. Labeling and Storage of Quality Control Materials and Reagents

All reagents, calibrators, controls, stains, chemicals, and solutions must be properly labeled and stored, as applicable and appropriate, with the following:

- Content and quantity, concentration or titer
- Dated initials of personnel who prepared, filtered, and reconstituted the reagents, and expiration date
- Deteriorated or outdated (expired) kits, reagents, quality controls, and calibrators must not be used. An expiration date must be assigned to QC materials that do not have a manufacturer-provided expiration date or an expiration date that changes upon reconstitution or use.
- Labelling of reagents may be recorded on a log (paper or electronic), rather than on the containers themselves, provided that all containers are identified so they are traceable to the appropriate data in the log.
- If there are multiple components of a reagent kit, the laboratory should use components of reagent kits only within the kit lot unless otherwise specified by the manufacturer.
- Storage requirements:
    - All QC materials, reagents and media currently in use must be prepared and stored as required by the manufacturer. If ambient storage temperature is indicated, there must be documentation that the defined temperature is maintained, and corrective action taken when tolerance limits are exceeded. Temperature logs should be utilized to document the acceptable ambient temperature range, record daily actual temperatures, and allow for documentation of corrective action taken if the acceptable temperature ranges are exceeded. The temperature tolerance limits must reflect the most stringent needs of all reagents, supplies, and

specimens stored at ambient temperature. For example, if Reagent A's acceptable storage temperature range is 20-28 ºC, and Reagent B's acceptable storage temperature range is 23-30 ºC, the tolerance limit for the room must be 23-28 ºC.

j. Inventory Control

The laboratory must have an established documented inventory control system in operation.

- There must be evidence of a system which highlights the need to place supply orders, receives and tracks orders, and defines alternate plans for delayed deliveries of supplies and recovery procedures for "out-of-stock" conditions (a system that details steps to ensure minimal lapse in ability to perform testing).
- The laboratory storage area must be sufficient to maintain an appropriate amount of "working" supplies and reagents. Appropriate levels of working supplies and reagents is defined as an amount that is adequate to handle current workload demands until new orders can be placed and received for use.
- All storage areas must be temperature controlled, well organized, free of clutter, and allow for ease in determining supply levels.
- If reagents and supplies are stored in a centralized area outside of the laboratory, they must be stored and handled in accordance with the manufacturer's instructions, and temperatures should be checked and recorded daily using a calibrated thermometer.

k. Parallel Testing, Lot Release, and Reagent Equivalency

The goal of parallel testing, lot release, and reagent equivalency of reagents is to provide an approach for lot verification and release for use. These processes are used to demonstrate equivalency of testing materials with prior or in-use lots, to ensure quality is maintained throughout the distribution process.

For each new lot of reagents, the laboratory must document that samples are tested in parallel with each current lot and that comparable results are obtained before or concurrently with their use as applicable.

- For *qualitative* non-waived tests, the minimum cross-checking includes retesting at least one positive and one negative sample. A weakly positive sample is recommended in systems where participant test results are reported in that fashion.
  Examples of suitable reference materials for qualitative tests include:
  - Positive and negative samples tested on a previous lot.
  - Previously tested proficiency testing materials.
  - External QC materials tested on the previous lot.
  - Control strains of organisms or previously identified organisms for microbiology reagents used to detect or evaluate cultured microorganisms.

  If none of the above options are available, control material provided

by the assay manufacturer with the new test kit may be used.

- For *quantitative* non-waived tests, participant specimens should be used to compare a new lot against the previous lot, when possible. Manufactured materials, such as EQA or QC materials, may be affected by matrix interference between different reagent lots, even if results show no change following a reagent lot change. The use of participant samples confirms the absence of matrix interference. QC materials must also be run when comparing old and new lots. The following materials may be used:
  - Participant samples tested on a previous lot
  - Reference materials or QC products provided by manufacturer with method specific and reagent lot specific target values
  - EQA materials with peer group established means
  - QC materials with peer group established means based on interlaboratory comparison that is method specific and includes data from at least 10 laboratories
  - Third-party general-purpose reference materials if the material is affirmed in the package insert or by the method manufacturer to be interchangeable with participant specimens for the method

  QC material for the current lot may be used to check a new shipment of the same reagent lot, as there should be no change in potential matrix interactions between the QC material and different shipments of the same lot number of reagents.

I. Water Quality Testing

If specific water types are required per manufacturer for certain testing procedures, the laboratory must have a documented policy that defines the standards and frequency of water testing. Each water type has different specifications for maximum microbial content, electric resistivity, and total organic carbon.

- The quality of water from the laboratory's purification system should be checked at least monthly for parameters such as electric conductivity/resistivity, pH, temperature, etc. Where applicable, microbiological analysis should be performed periodically. The frequency and extent of checking may vary, according to the source water and specific laboratory needs.
- The laboratory must ensure that records of water quality testing are complete and/or indicate that the required standards for water quality (e.g., pH, resistivity, and where applicable, microbial content) are consistently met.
- The laboratory must document evidence of corrective action taken when water testing does not meet defined tolerance limits.
- When decontaminating the clinical analyzer water reservoirs and water storage containers, manufacturer's recommendations should be followed to avoid problems linked to poor water quality and due to contaminants.

- Certificates of Analysis must be maintained to attest that commercially bottled purified water meets the required specifications for its intended use.

m. QC of Media

Performance of complete quality control by the user should include visual and contamination checks, to verify acceptable growth and/or inhibitory properties with appropriate bacterial or fungal control organisms. Laboratories are strongly encouraged, regardless of media exempt status, to confirm the ability to support growth for all media used for the recovery of microbiological organisms. To monitor the performance of in-vitro susceptibility tests, it is necessary to know the acceptable variability in expected results using appropriate QC strains. Document all media QC activities and corrective action. Identify and/or correct the cause of any media failure.

5. Test Method Validation and Verification

Analytical verification is the process by which a laboratory determines that an unmodified FDA-cleared/approved test performs according to the specifications set forth by the manufacturer.

Analytical validation is the process used to confirm with objective evidence that a laboratory-developed or modified FDA-cleared/approved test method or instrument system delivers reliable results for the intended application.

Qualification (using a standardized SOP) is a process by which experiments are conducted to identify how the assay performs with regard to each of the qualification/validation parameters. The qualification experiments provide the knowledge needed to set acceptance criteria for each parameter to be applied during formal validation experiments.

Laboratories must perform qualification, analytical validation, or verification of each non-waived test, method, or instrument system before testing participant samples, regardless of when it was first introduced by the laboratory, including instruments of the same make and model and temporary replacement (loaner) instruments. The method performance specifications (i.e., the applicable analytic performance characteristics of the test, such as accuracy, precision, etc.) must be validated or verified in the location in which participant testing will be performed.

For tests that are used for diagnosis, eligibility, safety, clinical management decisions, and for most primary study endpoints and products on a regulatory approval track, DAIDS requires laboratories to perform qualification, verification, or validation, as appropriate. Additionally, this requirement applies when placing a new method or instrument into routine use, when conditions for which the method has been validated change (if the change is outside the original scope of the method), after major maintenance or service of equipment used, or after relocation of equipment.

Methods that are defined as **waived** by CLIA do not require method validation.

Not all method performance specifications apply to qualitative tests. For qualitative tests, the laboratory must verify or establish the method performance specifications that are applicable and clinically relevant.

- For **unmodified FDA-approved** testing systems, the following experiments must be performed:
    - Reportable range of test results
    - Linearity (should be verified concurrently with reportable range)
    - Precision
    - Accuracy
    - Verification that the manufacturer's or other adopted reference ranges (normal values) are appropriate for the laboratory's study participant population

  Analytical sensitivity and analytical specificity (interfering substance) data provided by the manufacturer can be used and do not need to be verified.

- For **modified FDA-approved**, and/or **non-FDA-approved** testing systems, the following experiments must be performed:
    - Reportable range of test results
    - Analytical sensitivity
    - Analytical specificity
    - Precision
    - Accuracy
    - Establishment of reference ranges that are appropriate for the laboratory's study participant population, if applicable

  Should the results of validation experiments not meet the manufacturer’s specifications, laboratory management must work with the manufacturer to determine the source(s) of disparate results. A corrective course of action must then be taken to resolve the issue(s) that may include on-site repairs, upgrades, or method replacement.

  A written summary of the validation, including assessment of each component of the validation with acceptability criteria, must be available with signed approval by laboratory management.

  Standards for Performance Specifications

  Verification and documentation of normal responses for each test system, including reportable range and normal range(s), must be performed to determine the usable and reliable range of results produced by that system.

  Reportable Range: useful analytical range of a laboratory method (i.e., the lowest and highest test results that are reliable and can be

reported).

Analytical Measurement Range (*AMR):* the lowest and highest test results that may be reliably reported by an assay without additional steps beyond the routine procedure, such as dilutions or concentrations.

Clinically Reportable Range (*CRR)*: the range of analyte values that a method can measure with additional pretreatment of the original specimen and which thereby extends the reportable range of an assay/methodology.

Verification and documentation of both the AMR and the CRR must be performed when establishing the reportable range.

The following guidelines must be used when selecting materials for AMR validation and when performing the validation experiment:

- If using purchased materials for AMR validation experiments, the matrix of these materials should not interfere with or otherwise bias results of the method.
- The validation materials must have analyte values which span the range of the AMR (i.e. near the low, mid-point, and high values of the stated AMR).
- Each laboratory must define limits for accepting or rejecting validation tests of the AMR.

  Note: Often, the manufacturer will specify the AMR and procedures in the format of "if result is greater (or less) than X, dilute (or concentrate) specimen". If unable to discern the manufacturer's claims for AMR from published information, contact the manufacturer.

The CRR takes into consideration the need for dilutions or changes in concentrations, combined with clinical decisions made by a medical director or principal investigator, as to the clinical significance of results obtained by such dilutions or concentrations.

- The following guidelines and considerations must be used when performing the CRR validation experiment:
  - The CRR must be determined during initial verification of a method and not revised/updated until the method changes.
  - Values lower than the CRR must be reported as "less than" the limit.
  - The upper limit of the CRR will usually not be indicated unless there is a method or analyte limitation of a dilution protocol. Otherwise, it will be considered to be good clinical laboratory practice to dilute until a value in the AMR is achieved.
  - The diluent must be specified for each analyte that can be

successfully diluted to bring its quantity into the AMR.
        - The lower limit of the CRR will often be represented by the lower limit of the AMR as described previously. For example, an assay for quantitative human chorionic gonadotropin (hCG) demonstrates a lower AMR limit of 3 mIU/mL; the medical director for the laboratory decides that the lower limit of 3 mIU/mL is acceptable for diagnostic and prognostic causes and does not need to be extended to a lower value. In this case, the medical director has effectively set the lower limit of CRR equal to the lower AMR of 3 mIU/mL.
    - The laboratory may perform verification of reportable range by using the following materials and methods:
        - The laboratory may assay low and high calibration or control materials.
        - The laboratory may evaluate known samples of abnormal high and abnormal low values.

Refer to the GCLP documents resource link in the reference list for an example of reportable range experiment results.

Analytical Sensitivity: estimate of the lowest concentration of an analyte that can be measured.

The analytical sensitivity (lower detection limit) estimates the lowest concentration of an analyte that is reliable and reproducible. The analytical sensitivity of each assay must be verified or established and documented according to the following guidelines:

- For FDA-cleared/approved tests, documentation may consist of data from manufacturers or the published literature.
- If non-FDA-approved methods are utilized, the laboratory must establish and document analytical sensitivities.
- Analytical sensitivity may be verified by the laboratory by preparing dilutions of controls, standards, or specimens and determining the lowest concentration that can be determined reliably. Analytical sensitivity values that are smaller than the applicable standard deviation of the method are typically unreliable indicators of the method's lower detection.

Refer to the GCLP documents resource link in the reference list for an example of analytical sensitivity experiment results.

Precision: measurement of the scatter or random error between repeated measurements.

Precision of each test must be established by performing repeat measurement of samples at varying concentrations or activities (such as one would measure with enzymatic reactions) by using the following guidelines:

- The laboratory must verify the precision of each test by assessing

day-to-day, run-to-run, and within-run variation.

- Precision verification may be accomplished by one or a combination of the following methods:
    - The laboratory may repeat testing of known study participant samples over a period of time.
      Note: Use of study participants for internal QA practices, such as method validation, may require approval by the applicable IRB or IEC.
    - The laboratory may test QC materials in duplicate and over time.
    - The laboratory may repeat testing of calibration materials over time.
- Precision validation for qualitative tests:
    - Validation of a test's precision should be performed if the manufacturer's package insert mentions precision testing AND if value will be gained with such testing.

Refer to the GCLP documents resource link in the reference list for an example of precision experiment results.

Analytical Specificity (Analytical Interferences): The analytical specificity experiment is performed to estimate the systematic error caused by non-analyte materials (such as hemolysis, icterus, lipemia, or medications) that may be present in the specimen being analyzed.

Analytical interferences for each test must be verified or established and documented according to the following guidelines:

- For FDA-cleared/approved tests, the laboratory's documentation may consist of data from manufacturers or the published literature.
- If non-FDA-approved methods are utilized, the laboratory must establish and document interfering substances.

Refer to the GCLP documents resource link in the reference list for an example of analytical specificity experiment results.

Accuracy: measure of how close a measured value is to the true value.

Where current technology permits (i.e., comparative or reference methods exist), the laboratory must establish accuracy of the test system.

- The laboratory may use reference materials with known concentrations or activities (such as one would measure with enzymatic reactions).
- The laboratory may compare results of tests performed by the laboratory against the results of a reference method or compare split-sample results with the results obtained from a method which is shown to provide clinically valid results.
  Note: For qualitative methods, the laboratory must verify that a method will identify the presence or absence of the analyte.

Refer to the GCLP documents resource link in the reference list for an example of accuracy experiment results.

Reference (Normal) Ranges: specified interval bound by two limiting values that contains 95% of the values found in healthy individuals.

If the test system to be verified is an unmodified, FDA-approved method, the manufacturer's reference range should be verified. If the test is modified, or not FDA- approved, the reference range must be established, as applicable. It is noted that not all laboratory tests, including specialized tests, have defined reference ranges.

- The reference range must be established or verified for each analyte and specimen source/type (e.g., blood, urine, cerebrospinal fluid), when appropriate.
- The laboratory may use the manufacturer's reference range when appropriate specimens are difficult to obtain (e.g., 24-hour urine specimens, 72-hour stool specimens, urine toxicology specimens), provided the range is appropriate for the laboratory's study participant population.
- In cases where the appropriate specimens are difficult to obtain, and the manufacturer has not provided reference ranges appropriate for the laboratory's study participant population, the laboratory may use current published reference range(s).
- An appropriate number of specimens should be evaluated to verify the manufacturer's claims for normal values or, as applicable, the published reference ranges. Typically, the minimum number of specimens required to verify the manufacturer's or published ranges is 20 specimens. These specimens should be fresh and appropriately collected and predetermined as "normal" by established inclusion/exclusion criteria (e.g., HIV-negative, HBsAg-negative). The specimens should be representative of the population (age, gender, etc.).
- An appropriate number of specimens should be evaluated to establish reference ranges. Typically, the optimal number of specimens required to establish reference ranges is 120 specimens per demographic group, if applicable.
- Reference ranges must be evaluated at the following times:
    - Upon introduction of a new analyte to the test offerings by a laboratory (e.g., a laboratory that uses a FACSCalibur to perform CD4 testing plans to also add CD8 testing to their test menu)
    - With a change of analytic methodology (e.g., replacing CD4 testing performed on the FACSCount with testing performed using the FACSCalibur)
    - With a change in study participant population (e.g., a method typically used for determining test results for adults is to be used for a primarily pediatric population)

Refer to the GCLP documents resource link in the reference list for an example of how to determine reference ranges.

Correction Factors: If the laboratory has determined the need for correction factors based on the validation exercises, then they must be incorporated into the relevant test procedure and reflected in the appropriate SOPs.

Correction factors represent adjustments made to compensate for constant and proportional error (or bias) and are often written in a linear regression equation format. For example, two similar assays, “A” and “B”, are used interchangeably within a laboratory to perform quantitative human chorionic gonadotropin (hCG). Assay B has been found to have a proportional bias of 2% and a constant bias of 3 mIU/mL when compared with Assay A. In order to ensure interchangeability of results obtained from either assay, the laboratory applies the equation, “A = 1.02 (B) + 3” to any raw result that is produced by Assay B before reporting the final, calculated result.

For tests taken out of production for a period of time (e.g., seasonal testing for influenza), the laboratory should meet the following requirements prior to resuming testing:

- Perform EQA or alternative assessment within 30 days prior to restarting testing.
- Verify method performance specifications as applicable, within 30 days prior to restarting testing.
- Assess competency for analysts within 12 months prior to restarting testing.

A test is considered to be taken out of production when: (1) testing is not offered; and (2) EQA or alternative assessment, as applicable, is suspended.

6. Records and Reports

All additional information and documentation generated by the laboratory, such as specimen tracking, chain-of-custody, availability of normal ranges on the reports, and identity of performing laboratories are crucial to troubleshooting and attest to credibility of test results. These documents are also necessary in full study reconstruction and other similar auditing purposes. For these reasons, laboratories involved in specimen testing that supports a clinical trial should maintain all applicable records and reports following the standards below.

There are regulations, such as 21 Code of Federal Regulations (CFR) 312.62 and International Conference on Harmonisation Good Clinical Practice (ICH GCP) 4.9.5, which address record retention periods. DAIDS Policy on Storage and Retention of Clinical Research Records, (https://www.niaid.nih.gov/sites/default/files/Record_Retention_policyVersion2%20Final. pdf) states that clinical trial records belong to the institution that

conducts the DAIDS-sponsored and/or funded trial.

Standards for Records and Reports

a. Record and Report Tracking

The laboratory must maintain a system for providing and maintaining clinical trial data records and reports. These records and reports may include the following:

- Specimen tracking forms/laboratory requisitions
- Chain-of-custody documents
- Laboratory test reports
- EQA and QC data (including all records pertaining to corrective action and preventive action)
- Equipment service and maintenance logs (all records pertaining to the maintenance, repair, temperature monitoring, validation, and any other pertinent documentation related to the performance of the instrumentation)
- Analyte test results with reference ranges (as applicable)
- Raw data and source documentation (laboratory worksheets, records, memoranda, notes, or exact copies thereof) that are the result of original observations and activities of a non-clinical laboratory study and are necessary for the reconstruction and evaluation of the report of that study
- Other operational documentation (all policies and procedures pertinent to the conduct of the study, including but not limited to standard operating procedures, safety policies, safety incident reports, protocols/manuals, Laboratory Information System (LIS), tools to facilitate quality, management and transmission of endpoint assay data to data management centers, and specimen management documentation)

b. Data Integrity

Adequate procedures and manual or electronic systems must be in place to ensure assay results and other study participant-specific data (e.g., participant identifiers) are accurately and reliably sent from the point of data entry (whether entered via an analyzer interface or manually) to the final report destination in an accurate and timely manner, or according to specifications detailed within specific protocols and/or the study/analytical plan. These data include the following:

- Results reported from calculated data
- Results and study participant-specific data (e.g., participant identifier) electronically reported to the data management center, or via interfaced systems
- Manually transcribed or electronically transmitted results and study participant-specific information reported directly (or upon receipt) from outside referral laboratories, satellite, or point-of-care testing locations
- Test report information maintained as part of the study participant's chart or medical record. The laboratory must ensure that internal

and external storage and transfer of data maintain participant confidentiality and security. Written procedures must address participant confidentially during transfer of data to external referral laboratories or other service providers.

Verification must be performed prior to implementation of an interface (i.e., pre go-live) and whenever any change is made to an existing interface that could affect the accuracy of transmission of participant results. In addition, it must be reverified at least every two years. This includes evaluation of data transmitted from the LIS to other computer systems and their output devices.

Calculated values reported with participant results should be reviewed every two years or when a system change is made that may affect the calculations. This requirement applies only to calculations based on formulas modifiable by the user.

Errors can be inadvertently introduced into established computer programs. Calculations involving reportable participant results must be rechecked to ensure accuracy and records retained. This requirement applies to laboratory information systems, middleware, and analyzers. More frequent checks may be required for certain specific calculations (e.g., International Normalized Ratio [INR]).

c. Report Format

The laboratory's test report must indicate the following items:

- Either the study participant's name and/or unique study participant identifier
- Date of specimen collection, and if appropriate, time of collection
- Specimen source (e.g., blood, cerebrospinal fluid, urine)
- The date and time of specimen receipt into the laboratory
- Any information regarding the condition and disposition of specimens that do not meet the laboratory's criteria for acceptability
- The name of the test performed
- The name and address of the laboratory location where the assay was performed
- Identification of the personnel who performed the test(s)
- The assay result and, if applicable, the units of measurement or interpretation or both
- Reference ranges along with age and gender of study participants, if these affect the reference range
- The assay report date
- Time of report release, if applicable (if not on the report, this information should be readily accessible)
- Name of the physician of record, or legally authorized person ordering the test(s), as appropriate

Laboratory management should review and approve the content and format of paper and electronic reports at least every two years. Reports for clinically relevant laboratory-developed tests (LDTs), including those performed using class I analyte-specific reagents (ASRs), should contain

the following (if applicable):

- A statement that the assay was developed by the laboratory
- A brief description of the method and performance characteristics needed for clinical use, unless the information is readily available to the clinician in an equivalent format (e.g., test catalog)
- The following disclaimer statement: "This test was developed, and its performance characteristics determined by, <insert laboratory/company name>. It has not been cleared or approved by the U.S. Food and Drug Administration." Laboratories not subject to U.S. regulations must include an equivalent statement.

d. Pertinent Reference Ranges

Pertinent reference ranges (relevant or applicable to the local or study population, as defined in Section 5, *Test Method Validation and Verification*), as determined by the laboratory performing the tests, must be available to the authorized person who ordered the tests and, if applicable, the individual responsible for using the test results.

e. Laboratory Assays and Performance Specifications

The laboratory must, upon request, make available a list of test assays employed by the laboratory and, as applicable, the performance specifications established or verified. This list may also contain expected time-to-result (turnaround time, or TAT) for each assay.

The laboratory should also maintain a list of laboratory-developed tests (LDTs) and modified FDA-cleared/approved tests implemented by the laboratory.

Refer to the GCLP documents resource link in the reference list for a laboratory test method list example.

f. Assay Results

- Results and reports should be delivered effectively, efficiently, and securely. The laboratory needs to identify the communication pathway used for each report type. The laboratory should have a policy regarding the timely communication, and documentation thereof, of diagnoses of infectious diseases of particular significance (e.g., HIV and TB).
- Information that may affect the interpretation of assay results (e.g., test interferences) must be provided upon request.
- Assay results must be released only to authorized persons and, if applicable, the individual responsible for requesting the test(s).
- Alert and critical values:
    - Laboratory management must define alert or critical values in consultation with clinicians served.
      Note: Alert or critical values represent those results that require prompt, rapid clinical attention to avert significant study participant morbidity or mortality.
    - Complete procedures must be in place for immediate

notification of key study personnel/responsible clinic personnel when assay results fall within established alert or critical ranges.
    - Communication logs must be maintained that show prompt notification of the appropriate clinical personnel after obtaining test results that fall within a critical range. Documentation on these logs must include:
        - The date and time of notification.
        - The name of the responsible laboratory individual performing the notification.
        - The name and credentials of the person notified at the clinic and the test results given.
        - Any problems encountered in accomplishing this task.
    - When critical results are communicated verbally, “read-back” of the results is requested and recorded.
    - Transmission of critical results by electronic means (e.g., FAX or computer) is acceptable. If critical results are transmitted electronically, the laboratory must confirm receipt of the result by the intended recipient (e.g., by a phone call); however, no read-back is necessary.
- When the laboratory cannot report study participant test results within the time frames established by the laboratory or institution, the laboratory must notify the appropriate individual(s) of the delayed testing.
- If a laboratory refers study participant specimens for testing to another laboratory:
    - The referring laboratory must not revise results or information directly related to the interpretation of results provided by the testing laboratory.
    - The referring laboratory may permit each testing laboratory to send the test result directly to the authorized person who initially requested the test.
    - The referring laboratory must retain, or be able to produce an exact duplicate of, each testing laboratory's report for the period of time defined by the laboratory or institution.
    - The authorized person who orders a test must be notified by the referring laboratory of the name and address of each laboratory location where the test was performed.
- All test reports and records must be maintained by the laboratory in a manner that permits ready identification and timely accessibility.

g. Result Modification Log and Errors in Test Results

The laboratory must follow a written policy/procedure for the detection, management, and correction of significant clerical and analytical errors and unusual laboratory results, in a timely manner, including quality control data and intermediate test results or worksheets.

Clinical or trial decisions or actions are often based on the results obtained by laboratory testing. If an erroneous result is reported and then corrected,

it is important to replicate all of the previous information (test results, interpretations, reference ranges) for comparison with the revised information, and to clearly indicate that the result has been corrected.

- A log, or other appropriate record, must be kept for result modifications.
  Note: Result modification is defined as reports that contain any changes to study participant results, accompanying reference ranges and interpretations, or study participant identifiers, but not minor typographical errors that are not of any clinical consequence.
- The laboratory must ensure that all forms of study participant reports (paper, computer displays, etc.) that display revised results clearly indicate that the new result is a change from a previously reported result.
- The laboratory must have a system that will always provide identification of the personnel performing and completing the test result modification, along with the date and time and reason for change, without obscuring the previous entry.
  - When there are multiple sequential corrections of a single test result, all corrections must be referenced in sequential order on subsequent reports.
  - All corrections must be referenced in the study participant report.
  - Laboratory management must review, sign, and date the Result Modifications/Corrective Action Logs at least monthly. *Note:* A laboratory may perform more frequent review at intervals that it determines appropriate.
- When errors in the reported study participant test results are detected, the laboratory must do the following:
  - Promptly notify the appropriate clinician and/or clinic personnel member.
  - Promptly issue corrected reports to the authorized person ordering the test and, if applicable, the individual using the test results.
  - Maintain copies of the original report as well as the corrected report.

h. Archiving and Retention of Reports or Records

The laboratory may archive test reports or records, but these documents must remain readily available (able to be produced for review within 24 hours) for the duration defined by DAIDS Policy on Storage and Retention of Clinical Research Records (https://www.niaid.nih.gov/sites/default/files/Record_Retention_policyVersion2%20Final. pdf). These documents may be archived either on- or off-site, at the laboratory's discretion. A commercial archiving service may be contracted if needed.

- These records must be safely and securely kept for confidentiality purposes, and to ensure the ability to fully reconstruct the study if necessary.
- Access to archived records must be limited to authorized personnel.

- The use of correction fluids, tapes, or other methods of obliterating results must be prohibited for all research-related and clinical laboratory documents.
- Proper error correction techniques (e.g., single line through error, signature, and date) must be utilized at all times by the laboratory.
- Storage conditions must ensure document preservation for the specified retention time to maintain data and information integrity; the laboratory must implement appropriate solutions to mitigate the risk of physical damage. Sole copies of research documents, defined as documents not having any backup copy, must be stored by the laboratory in such a manner to protect them from damage due to the elements (fire, water, wind, humidity, etc.).
- Electronic storage devices need to be protected from degradation, erasure, deletion, or corruption.
- Records may be retained either as original records or as certified true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records.
- To determine how long to retain laboratory records, refer to DAIDS Policy on Storage and Retention of Clinical Research Records https://www.niaid.nih.gov/sites/default/files/Record_Retention_policyVersion2%20Final. pdf). Record retention is governed by multiple authorities, both in the U.S. and non-U.S. settings. Local IRB/IEC policies, regulations, and laws are to be followed if more stringent retention guidelines apply.

7. Physical Facilities

The laboratory facility must be designed in such a manner that the safety of the personnel, participant laboratory-related services, and the quality of the work are not compromised. Proper space for instrument placement, lighting, ventilation, temperature control, and operation must be available. Working environments should include adequate water taps, sinks, drains, electrical outlets, gas, and suction, when applicable. Specimen movement and workflow through the laboratory should be such that opportunities for specimen loss, specimen mix-up, and exposure of laboratory personnel to biohazards are minimized.

Standards for Physical Facilities

a. General Space

- Laboratory work areas must have sufficient space so that there is no hindrance to the laboratory work, as per laboratory management.
- Laboratory walkways should be unobstructed.
- Reasonable accommodation must be made for disabled persons.
- The laboratory must have a written policy for restricting access to the laboratory to authorized individuals. This may be accomplished through the use of access codes (security codes, user codes),

locks, or other processes (e.g., policies and procedures) that limit access to authorized personnel.
- Access authorization should be maintained and current (e.g., inactivated when employment of an authorized individual ends). The written policy should include:
    - A list of those authorized to enter the laboratory on a routine basis.
    - How non-laboratory personnel (e.g., visitors, vendors, contractors) can obtain access on a temporary basis.

b. Temperature and Humidity Controls

- Laboratory room (ambient) temperature must be controlled (where applicable) so that equipment and testing are maintained within the tolerance limits set forth by the manufacturer.
- In some climatic regions, humidity may need to be controlled within the tolerance range specified by the manufacturer for optimal equipment and assay performance. If necessary, an additional air-cooling system, humidifier, or dehumidifier may be used to control the humidity.

c. Liquid Nitrogen Environmental Monitoring

In areas where liquid nitrogen is used, there should be oxygen sensors with a low oxygen alarm mounted in an appropriate location and sufficient airflow to prevent asphyxiation.

d. Cleanliness of Facilities

All floors, walls, ceilings, bench tops, cupboards, drawers, and sinks of the laboratory must be clean and well maintained.

e. Archiving and Storage Spaces

- Space must be allocated to the archiving of data in a secured fire-proof (preferred), fire-resistant, or fire-protected (least preferred; e.g., stored in area with operational automatic sprinkler system) environment which is accessible only to authorized personnel. These documents may be archived either on- or off-site, based on the laboratory's discretion.
- Laboratory storage areas must be allocated to adequately preserve the identity, purity, and stability of laboratory reagents, control materials, calibrators, and other laboratory materials.

f. Molecular Amplification Work Areas

Molecular amplification procedures within the laboratory that are not contained in closed systems must have a unidirectional workflow. This must include separate areas for specimen preparation, amplification, detection, and, as applicable, reagent preparation.

g. Emergency Power

Emergency power must be adequate for refrigerators, freezers, incubators, etc., to ensure preservation of participant specimens.

Depending on the type of testing performed in the laboratory, emergency power may also be required for the preservation of reagents, the operation of laboratory instruments, and the functioning of the data processing system.

8. Specimen Transport and Management

Standards for Specimen Transport and Management

The accuracy of all laboratory test results depends on the quality of the specimen submitted. The laboratory can ensure specimen integrity when appropriate specimen management and transportation procedures are followed. The establishment of a sound specimen chain-of-custody is paramount in ensuring that the aforementioned procedures are carried out properly.

a. Standard Operating Procedure

The laboratory must have a documented procedure describing methods for the following tasks associated with specimens:

- Specimen collection
- Tracking
- Labeling
- Preservation
- Conditions for transportation
- Storage
- Specimen destruction

b. Specimen Labeling

The laboratory must have documented standard labeling practices in place and demonstrate evidence of adherence.

- All specimen containers must be properly identified with the unique participant identifiers.

c. Laboratory Testing Request Form (Requisition)

A properly completed request form/log or equivalent must accompany each study participant sample to the laboratory; this documentation serves as the integral link between a specimen, the study participant from which it was collected, and the testing requested.

- The request form must document unique study participant identifiers, specimen collection date and time, study participant demographics, specimen type, and the collector's (phlebotomist's) identity.
- Any discrepant or missing information must be verified promptly, before specimens are processed or stored by laboratory personnel.

d. Specimen Acceptance/Rejection Criteria

The laboratory must have in place documented instructions for receipt and inspection of samples (including rejection criteria) and demonstrate evidence of adherence in order to ensure positive study

participant/specimen identification, adequacy, and integrity of the specimen.

- The specimen inspection process must involve verification of the specimen container label information with the request form or log sheet.
- Specimen evaluation must also involve checking for the volume and quality of the samples (as influenced by such factors as hemolysis, lipemia, and icterus).

e. Audit Trails and Chain-of-Custody

The laboratory must maintain a complete audit trail for every specimen from collection to disposal or storage. Audit trails must verify the date and time (if applicable) an activity was performed and the personnel responsible for that activity. Procedures must be available to document the chain-of-custody for all specimens. Chain-of-custody forms and/or internal laboratory tracking documents must be maintained and should include the following information:

- Collection site, date, and time of specimen collection and shipping
- Name, date, and signature of phlebotomist or person who collected the specimen from the trial volunteer
- Name, date, time, and signature of person transporting the specimen
- Type of sample
- Types of testing requested by clinician or as per study visit requirements, as defined by the protocol and study/analytical plan
- Project and collection site names
- Identity of the receiver and inspector of the specimens (upon arrival at the testing or storage facility)
- Date and time of sample receipt
- Observed sample condition and documentation of other factors that may affect specimen integrity noted at time of receipt
- Sample and/or cooler temperatures at time of receipt

f. Specimen Transportation and Shipment

- Transportation of samples must be monitored to maintain specimen integrity. This ensures that they were shipped:
    - Within the timeframe appropriate for the nature of the requested specimen and test to be performed.
    - Within the temperature interval specified.
    - In the designated preservatives (e.g., anticoagulants).
    - In a manner that ensures safety for the laboratory, carrier, and public.
- A shipping procedure must be documented that addresses safety and logistical issues when transporting samples. This procedure must be readily available and detail the following items:
    - Proper organization, labeling (e.g., biohazard), packaging, shipping, and handling of specimens to ensure specimen integrity, while maintaining timely and safe shipment of

specimens
        - Shipment preparation processes that conform to all federal and local transportation of dangerous goods regulations (e.g., International Air Transport Association [IATA])
    - Laboratory personnel who ship specimens must be trained and certified in hazardous materials/dangerous goods transportation safety regulations.
        - The regulation training must be renewed every two years or more frequently if required by national, state, provincial, or local laws and regulations.
        - The regulation training course must include the shipment of infectious substances, dry ice, and liquid nitrogen, as applicable.
        - Certification of regulation training must be on file and readily available.

g. Specimen Preparation, Analysis, and Retention

- Documented protocol-specific procedures for specimen preparation and analysis must be available and must address (if applicable) the following:
    - Any specimens which must be retained for potential reanalysis, including retention time and storage conditions appropriate for the type of specimen and test
        Example: EDTA specimens might be stored up to seven days at 4 °C for CBC testing; however, if the EDTA was for CD4/CD8 testing, the specimen should be kept at room temperature and only for 24 hours.
- Twenty-four-hour monitoring of storage conditions (using personnel and/or electronic monitoring with alert systems) and SOPs for response to alerts must be in place to ensure that the integrity of samples is maintained.
- A documented disaster recovery procedure must be available to ensure the continued integrity of specimens.

9. Personnel Safety

Safety of laboratory personnel must be a top priority for any laboratory facility. Engineering controls (e.g., shields and biosafety hoods), personal protective equipment (PPE) (e.g., gloves, laboratory coats), and adequate training on the use of these tools are paramount in ensuring a safe working environment for all laboratory personnel. The laboratory safety program and training should address topics such as blood-borne pathogens, chemical hygiene, and fire safety, especially as these topics relate to site-specific characteristics such as testing of blood products or potential exposure to a specific pathogen. The laboratory safety program and training should also address availability of prophylaxis measures, such as Hepatitis B vaccinations and post-pathogen exposure options.

Standards for Personnel Safety

a. Safety Equipment

- The following safety equipment should be in the laboratory, where applicable and per local institutional safety regulations, to ensure the continued safety of laboratory personnel and any authorized individual who may enter the laboratory:
    - Eyewash facility that may be plumbed or self-contained
    - Emergency shower/drench hose
    - Fire extinguishers
    - Sharps containers
    - Spill kit
    - An automatic fire detection (e.g., smoke detectors) or alarm system
    - A fire alarm station in or near the laboratory
    - A sink that can be utilized for hand washing
    - A basic first aid kit that is restocked periodically and is accessible

- The laboratory should test and/or inspect safety equipment on a laboratory-defined schedule. A recommended schedule is described below:
    - Plumbed eyewashes (attached to sinks or installed as "stand-alone" stations) should be flushed weekly.
    - Self-contained eyewash units should be visually examined weekly.
    - Sealed portable eyewash bottles should be inspected monthly for signs of contamination and replaced prior to expiration or as required by the manufacturer.
    - Refillable portable eyewash bottles should be cleaned and refilled weekly or as required by the manufacturer.
    - Emergency showers/drench hoses should be flushed weekly (preferred) but no less often than once per month, if applicable.
    - Fire extinguishers should be inspected monthly to ensure proper charge and recharged as required by local standards or the manufacturer's requirements, if applicable. In addition, laboratories should make sure that access to fire extinguishers is not blocked, extinguishers are not damaged, seals are in place, nameplates are readable, and dates of inspection are documented.
    - Sharps containers should be inspected daily and replaced when three-fourths full.
    - Smoke detector inspections should follow manufacturer's guidelines.

b. Documentation

- The laboratory must document the testing and/or inspection of safety equipment (the laboratory may forego the documentation of the sharps container inspection and replacement).
- Documents recording the testing and/or inspection of safety equipment must be signed and dated by the personnel performing

the task. Records of inspection must be readily available.

c. Evacuation Policy/Plan

The laboratory must have a comprehensive, documented, and workable evacuation plan that is available to all laboratory personnel and visitors. Laboratory personnel must be appropriately trained in the evacuation plan/policy. Evacuation routes must be clearly marked and emergency lighting adequate for safe evacuation of the laboratory. DAIDS strongly recommends annual fire drills. All personnel should participate at least once a year.

d. Personal Protective Equipment (PPE)

- The laboratory employer must assess the workplace to determine if hazards are present or are likely to be present which necessitate the use of PPE. PPE must be provided to all laboratory personnel and maintained in a sanitary and reliable condition. PPE includes but is not limited to:
  - Gloves (both latex and non-latex).
  - Gowns or laboratory coats (must be fluid resistant).
  - Eye protection (goggles, face shield, engineering controls such as laminar flow hoods and splash shields).
  - Masks (required when using goggles).
- All laboratory personnel must use PPE if there is a potential for exposure to blood or other potentially infectious material through any route (e.g., skin, eyes, other mucous membranes).
- Personnel must use the proper personal protective devices when handling corrosive, flammable, biohazardous, and carcinogenic substances.
- PPE must be made available to laboratory visitors, as applicable.

***e.* Personnel Responsibility**

Personal electronic devices should not be used in the technical work area in the following circumstances:

- When working with hazardous materials
- When wearing gloves or other PPE
- While performing work on laboratory specimens, data, or any process that may affect testing outcomes
- When in an area in which they might distract or interrupt others
- When in an area in which accidental release of protected health information could occur
- If they cannot be worn without hanging wires or other dangling accessories that may pose a safety hazard
- If they interfere with the personnel's ability to detect potential hazards, such as hearing an alarm or an approaching obstacle

f. Safety Data Sheets (SDS) or Material Safety Data Sheet (MSDS)

To ensure proper handling and storage, the laboratory must have SDS or equivalent in the workplace for each hazardous chemical that they use

(SDS are only required for hazardous chemicals, which are defined by the Occupational Safety and Health Administration (OSHA) as chemicals that are health hazards or physical hazards).

- SDS must include information about chemicals that are used for testing (e.g., Ficoll-Hypaque) and general use (bleach, disinfectants, etc.).
- The laboratory must maintain each SDS in the language understood by personnel.
- Laboratory personnel must be trained on reading the SDS. There is no standard format or order of information presented within SDS; this training is necessary to ensure they can identify and locate the different types of information contained within an SDS, such as hazard identification, first aid measures, handling, and storage.
- SDS must be readily available to personnel during each work shift and to personnel when they are in their work area(s).
- SDS may be maintained electronically as long as no barriers to immediate employee access in each workplace are created by such options.
- It is recommended that an index of printed SDS be maintained and that all SDS should be updated periodically, within a two-year period, to ensure personnel is equipped with the most current hazard and first aid information.

g. Gas Cylinder Storage

Compressed gas cylinders must be secured to prevent accidental falling and damage to the valve or regulator. Flammable gas cylinders, if inside a health care facility, must be stored properly. Proper storage practices include:

- Use of separate, ventilated rooms or enclosures.
- Positioning cylinders well away from open flame or other heat sources.
- Prohibiting storage of cylinders in corridors and within exhaust canopies.

h. Safety Policies

Safety policies, defined according to regulatory organizations such as OSHA or the International Organization for Standardization (ISO) and compliant with all applicable safety codes and regulations, must be present in the laboratory. The following safety policies must be in place to ensure the continued safety of laboratory personnel and any authorized individual who may enter the laboratory:

- *Standard Precautions/Universal Precautions Policy:* This policy, or group of policies, defines all human biological specimens as potentially infectious and addresses topics of consideration when dealing with potentially infectious specimens, such as hand hygiene, PPE, working with open lesions, handling contaminated needles and other sharp objects, autoclaving, and disposal of materials.

- *Viral Exposure Policy*: There must be a policy for follow-up after possible and known percutaneous, mucous membrane, or abraded skin exposure to HIV, Hepatitis B Virus (HBV), or Hepatitis C Virus (HCV) that includes the following elements:
    - HIV, HBV, and HCV testing of the source participant after consent is obtained
    - Appropriate clinical and serologic evaluation of potentially exposed personnel
    - Consideration of appropriate prophylaxis for personnel acutely exposed to HIV, HBV, or HCV, based upon medical indications, the serologic status, and the individual's informed consent
    - Reporting of the exposure as required by law
- *Chemical Hygiene/Hazard Communication Policy:* This policy or group of policies addresses aspects of safe chemical handling. Chemical hygiene policies typically address storage, utilization, and disposal of chemicals, with the goal of minimizing exposures and risks associated with those chemicals. Hazard communication policies typically provide information about the identities and hazards of chemicals, required appropriate labeling, SDS, exposure first aid, etc.
- *Waste Management Policy:* This policy details appropriate measures to take when disposing of waste materials to ensure continued human and environmental health in compliance with national and local authorities.
- *General Safety Policies:* These policies address less specific topics as they relate to laboratory safety, such as fire safety.
- *Safety Equipment Policies:* These policies typically detail all available safety equipment, their purposes, and proper utilization.
- *Emergency Preparedness Policy*: There must be written policies and procedures defining the role and responsibilities of the laboratory in emergency preparedness for harmful or destructive events or disasters. The specific elements to be included in the emergency preparedness plan must be based on a risk assessment using an "all-hazards" approach to evaluate the types of hazards most likely to occur that would potentially disrupt services. Written policies and procedures must be developed to support the execution of the laboratory's emergency response plan and the path of workflow, including a communication plan.

  *Note***:** Laboratories located within a healthcare facility or integrated health system may participate in development of a facility or system-wide emergency preparedness plan rather than an individual laboratory plan but must ensure that policies and procedures for the plan are clearly defined and address the relevant site-specific risks. Examples of events that may be addressed in the emergency preparedness plan include situations such as unexpected system failures (e.g., heating, ventilation, and air conditioning (HVAC), water, communication, computer system),

power failures, natural disasters (e.g., tornado, hurricane, earthquake, fire, flood), emerging public health threats, cyber-attacks, terrorist events, or workplace violence.

- *UV Light Exposure Policy*: There should be written policies and procedures to prevent or reduce ultraviolet light exposure from instrument sources. UV light may cause corneal or skin burns from direct or deflected light sources. Wherever UV light sources are used, suitable and adequate personal protective equipment must be provided, and appropriate approved signage displayed. Laboratories may obtain information on safety from manufacturers of devices that emit UV light.
- *Mercury Safety Policy*: A mercury safety policy and SDS are required in laboratories where mercury-filled thermometers are used.
- *Latex Allergy Program*: The institution or laboratory should have a written program to protect personnel and participants from allergic reactions from exposures to natural rubber latex in gloves and other products. For laboratories that are part of healthcare systems, it may be appropriate to reference institutional or healthcare system-wide policies.

i. Safe Work Practices Review

There must be records of periodic review (at least annually) of safe work practices to reduce hazards. If a problem is identified during the review, the laboratory must investigate the cause and consider if modifications are needed to the safety policies and procedures to prevent reoccurrence of the problem or mitigate potential risk.

j. Safety Training

All laboratory personnel must receive safety training. At a minimum, the safety training must include:

- Blood-borne pathogens (includes information on standard precautions, risks and types of infectious diseases contracted through exposure, proper safeguards, and methods of handling potential contaminants).
- PPE; all laboratory personnel must be trained on the proper use of PPE prior to starting work in the laboratory (i.e., at employment), and periodically thereafter. Such training must include/describe:
    - When PPE is necessary.
    - What PPE is necessary.
    - How to properly wear PPE.
    - The limitations of PPE.
    - The proper care, maintenance, useful life, and disposal of PPE.
- Chemical hygiene/hazard communication (how to properly handle chemicals and what to do to avoid exposure and in the event of an exposure).
- Use of safety equipment in the laboratory (eyewash, emergency

shower, fire extinguisher, etc.).
- Use of cryogenic chemicals (dry ice and liquid nitrogen), if handled by laboratory for shipping, receiving and/or storage of specimens, supplies, and reagents.
- Transportation of potentially infectious material (IATA-proper packaging and labeling of shipped materials).
- Waste management/biohazard containment (appropriate disposal of biohazards).
- General safety/local laws related to safety.
- Accident reporting.
- Emergency preparedness and management.
- Fire safety (locations of emergency exits, evacuation routes, fire alarm pull stations, and fire extinguishers; location outside of the facility where personnel should report in the event of an emergency evacuation; procedure for notifying appropriate authorities in a fire event).
- Decontamination procedures (location of materials for decontamination, decontamination and spill cleanup procedure, whom to notify in event of a spill).

Documentation of completion of safety training must be maintained. Safety training records should include the title of the training, a brief description of the topics covered, identity of the trainer(s), names of the person(s) being trained, and the date of the training.

Safety training, at a minimum addressing the above topics, must be completed before any employee begins working in the laboratory and on a regular basis thereafter (to be determined by laboratory management).

k. Safety Incident Reporting

- Safety-related incidents must be documented and submitted to laboratory management. Examples of safety-related incidents include, but are not limited to:
    - Injuries (needlestick, sharps injury, falls, burns, etc.).
    - Chemical exposure.
    - Malfunctioning equipment posing a safety risk (e.g., potential for electrical shock).
    - General accidents.
- Submitted safety incident reports must be reviewed and signed by laboratory management on a regular basis, but this review must not exceed one month from time of submission. Timeliness of incident reports will allow for rapid correction of a problem to prevent recurrence.
    - Safety reports must be incorporated into the quality management (QM) program. This would allow the laboratory to note trends and correct problems to prevent recurrence.
    - To maintain employee confidentiality, all personal identifiers must be removed from safety reports prior to submission to the QM team.

10. Laboratory Information Systems

Clinical laboratories perform laboratory tests as requested by physicians or as directed by clinical trial protocols. These laboratories must often generate data (often in the form of a report) on the appropriate study participant and deliver or transmit the report to a predetermined location or individual, such as a principal investigator, within a clinically useful period of time.

A computer alone does not constitute a Laboratory Information System (LIS). An LIS consists of computer hardware, software, and data; it performs or assists with functions such as test ordering, delivery of necessary specimens to the laboratory, clerical duties of specimen receipt, as well as unique identifier generation, aliquoting, worksheet generation, order information transmission to analyzers, translation of instrument output into usable results, storage of data, transfer of data via secure files to a data center, report generation, and QC functions. Reports generated by the LIS must be concise, readable, standardized in format, and chronological.

Standards for Laboratory Information Systems

a. Laboratory Information System Validation

The laboratory must maintain documented validation data for the LIS. All steps and results of validation must be available for review:

- Installation of new computer programs
- Any changes or modifications to the system
  Note: laboratory management must approve all changes before they are released for use.
- Testing of all possible anticipated permutations of processes (e.g., entry of normal, abnormal low, abnormal high, critical, and absurd results)
- Testing and validation of all calculations that are performed by an LIS
- Validation of all data transmitted from the LIS to other computer systems and their output devices
- Verification of reference ranges and comments as well as actual testing results
- Validation of the emergency preparedness system

b. Generation of Reports

- The LIS must be capable of generating accurate and complete copies of study participant results.
- The laboratory must be capable of reprinting a complete copy of archived study participant test results.
  - Results must include original reference ranges and interpretive comments.
  - Results must include any flags or footnotes that were present in the original report.
  - Results must include the date of the original report.
- Stored study participant result data and archival information must

be readily retrievable within a time frame consistent with study/trial needs (e.g., within 24 hours).

c. Audit Trails

- Computer time-stamped audit trails must be used by the LIS.
- The laboratory must ensure that when individual tests from a single test order (e.g., multiple tests with same accession number) are performed by separate individuals and the test results are entered into the LIS, the system must provide an audit trail to document each person involved (including sequential corrections made to a single test result).
- If auto-verification is used, then the audit trail must reflect that the result was verified automatically at a given time and date.
- When multiple identical analyzers are used, they are uniquely identified such that a test result may be appropriately traced back to the instrument used to perform the test.

d. Access and Security

- The laboratory must ensure that LIS access is limited to authorized individuals.
- Documentation must be maintained indicating that all users of the computer system receive adequate training both initially and after system modification.
- The laboratory's LIS policies must define users who may only access study participant data and users who are authorized to enter study participant results or modify results.
- The laboratory must establish user codes to permit only specifically authorized individuals to access study participant data or alter programs.
    - A user code is typically assigned to each employee upon employment or at the point of completion of training.
    - All personnel who will use the system must have a user code that is linked to an appropriate level of access, as determined by his/her job requirements.
    - The system typically maintains active personnel access codes as a database from which hard-copy reports may be created.
    - User codes must not be shared.
    - User access codes must be inactivated upon termination of an employee. The user code, once inactivated, must not be used for another employee.
- The security of the system must be sufficient to prevent unauthorized personnel from installing software. Unauthorized installation of software may expose the system to a security breach, virus, worm, or spyware.
- Access control policies should include physical entry to data center(s) housing the LIS, logging into server operating system(s) hosting the LIS, as well as software system(s) that comprise the

LIS.

e. Documentation Guidelines

The laboratory must maintain a written SOP for the operation of the LIS and should follow these guidelines:

- Procedures must be appropriate and specific to the day-to-day activities of the laboratory personnel as well as the daily operations of the information technology personnel. Current use of the LIS must match policy and procedure documents.
- The purpose of the computer program, the way it functions, and its interaction with other programs should be clearly stated.

f. Technical Support and Preparedness

The laboratory must have a documented backup system and accompanying procedure for the LIS based on the following guidelines in an effort to maintain integrity of data and reduce impact and severity of unscheduled downtimes and destructive events:

- The laboratory must have a procedure outlining the technical support personnel and/or vendor for the system including emergency contact information.
- Documented procedures and disaster-preparedness plans must exist for the preservation of data and equipment in case of an unexpected destructive event (e.g., fire, flood) or software failure and/or hardware failure, allowing for the timely restoration of service.
- Documented procedures must exist to ensure reporting of study participant results in a prompt and useful fashion during partial or complete LIS downtime, to include:
    - Steps to prevent the corruption and/or loss of active data.
    - Procedures for periodic backing up and storing of information.
    - Procedures for off-site storage of backup data.
    - Procedures for restoring information from backup media.
- The procedures must specifically address the recoverability of study participant information, the physical environment, and equipment and be tested periodically for effectiveness.
- The LIS should be run in a closed environment, as much as is practical, to protect participant confidentiality.
- If the facility uses a public network, such as the Internet, as a data exchange medium, there should be network security measures in place to ensure confidentiality of participant data.

11. Quality Management

Quality management (QM) is composed of the coordinated activities to direct and control an organization with regard to quality; it is a systematic approach to achieving quality objectives. A QM plan (or program) identifies the specific steps that a laboratory will take to ensure that data quality and study participant safety are being maintained.

External quality assurance (EQA) is an integral component of a total QM program. EQA specimens must be analyzed and reported just as study participant specimens are tested in the laboratory. EQA provides the opportunity for a laboratory to compare results and/or interpretations obtained on a set of specimens, photographic slides, and/or case studies with those of a peer group (a group of laboratories performing the same analyses with similar methodologies). If available, this external evaluation of the laboratory's analytical performance is paramount to a complete quality assessment of laboratory operations.

Standards for Quality Management

a. Quality Management Plan

- The laboratory must have a documented quality assurance plan/quality management program. This program must:
    - Be developed and maintained by an individual, or a group of individuals, that is separate and distinct from the testing personnel of the laboratory, if practical and possible.
    - Be integrated with the institutional quality assurance/quality management program, if applicable.
    - Detail an operational plan that describes the goals and objectives of the QM program.
    - Be accessible to all personnel.
    - Be designed to monitor, assess, and (when indicated) correct problems identified in pre-analytic, analytic, and post-analytic systems as well as general systems.
    - Address monitoring to include complaints and incidents.
    - Include all aspects of the laboratory's scope of care.
    - Address any problem that could potentially interfere with study participant care or safety while addressing risk assessment.
    - Include information on how the quality and safety information is to be collected and communicated.
    - Include control activities (e.g., QC and EQA).
    - Include any measurable key indicators of quality that are related to the laboratory operations that are explicitly targeted for improvement.
        - Key indicators must reflect activities that are critical to and/or have a significant impact on study participants or study outcomes. Examples of key indicators include: test turnaround time, specimen acceptability, test order accuracy, safety events.
        - The number of key indicators monitored by a laboratory should be proportional to the scope of the laboratory’s services. It is recommended that no more than five key indicators are actively monitored at any given time.

        - The laboratory must record investigation of key indicators and record corrective and/or preventive actions taken.
        - There must be evidence of appropriate follow-up action taken as a result of monitoring, as well as an evaluation of the effectiveness of corrective action undertaken with these key indicators.
    - Include results of ongoing measurement activities of these key indicators compared with internal or external benchmarks and trended over time (e.g., quality indicators should be measured and compared against defined quality goals).

    Refer to the GCLP documents resource link in the reference list for an example of a quality management plan.

    - The laboratory must be able to use this QM document for guidance when conducting annual appraisals of effectiveness. The QM program documentation must demonstrate regular (at least annual) review by laboratory management. This review must ensure that recurrent problems have been addressed and that new or redesigned activities have been evaluated. The laboratory must be able to provide evidence of appraisal of its QM plan, to include:
        - Annual written QM reports.
        - Revisions to laboratory policies and procedures and to the QM plan.
    - The laboratory must provide evidence of implementation of this QM plan including:
        - Minutes of committee meetings.
        - Results of ongoing measurement.
        - Documentation-related complaint investigation.

b. Nonconforming Event (NCE) Management

- An NCE management program is based on principles of quality management, risk management, and study participant safety. It can be implemented through a manual means such as paper forms and tracking logs, or by using electronic database technology.
- The program should be structured, organized, and used consistently throughout the laboratory to:
    - Report nonconformances.
    - Investigate the causes of nonconformances.
    - Determine if any action is needed and, if so, perform necessary action.
    - Track and trend all nonconformances.
    - Identify opportunities to improve the efficiency and effectiveness of work processes.
    - Identify opportunities to reduce or eliminate risks and improve study participant safety.
- Reporting of problems as they are discovered is critical in an NCE

management program since unreported problems are likely to recur and continue unresolved, and this may cause harm to study participants.
- NCEs occur throughout the path of workflow from pre-analytical, analytical, to post-analytical activities
- Investigation of an NCE should be initiated promptly (e.g., within 48 hours) in order to facilitate collection of accurate information.
- A review of all NCEs should occur at regular intervals to look for potential patterns or trends.
- Once analysis of aggregated NCEs has been completed, a report should be prepared for laboratory management review.

c. Internal Audits

The laboratory's monitoring of the QM program must include an internal auditing program. Internal audits involve an individual or a group of laboratory personnel performing a self-assessment comprised of a comprehensive comparison of the actual practices within the laboratory against the laboratory's policies and procedures (e.g., personnel files, training documentation, QC performance, review of SOPs). These audits may also compare the laboratory's practices against a standard set of guidelines and/or standards. All findings (of both compliance and noncompliance) that result from the internal audit should be documented in an organized format to allow for appropriate corrective actions and follow-up through resolutions.

Periodic reviews of the internal audit program and its inherent processes may include:

- Trending and analysis of information from all audits.
- Feedback from auditees and personnel from the audited laboratory on the audit process.
- Preparation of a report of audit findings for the report period (e.g., quarterly, annually) for quality report and laboratory management review.
- Laboratory management review and assessment of the effectiveness of the audit program.

The final audit report of findings aids laboratory management in identifying opportunities for improvements and provides information for quality planning.

d. External Assessments

External assessments provide objective feedback on how well the laboratory is performing from a quality perspective, how its quality and operational processes are functioning, and whether the laboratory is meeting the needs of its customers.

External assessment refers to an audit, inspection, site visit, or survey performed by an organization external to the laboratory, such as those performed by governmental and accreditation organizations, to evaluate the effectiveness of the laboratory's quality management system.

Laboratories are strongly encouraged to participate whenever possible in national or regional laboratory accreditation programs; laboratories must participate in such programs, where required. The laboratory should have a documented process for handling external assessments conducted by governmental and accrediting organizations.

The laboratory's process for managing external assessments/inspections should include the responsibilities and activities for the following:

- Scheduling
- Preassessment paperwork
- Receiving assessors
- Facility access
- Records and material accessibility
- Assessor workspace
- Conducting the assessment
- Closing summary
- Follow-up response
- Implementing any needed corrective actions
- Verifying the effectiveness of the actions taken

e. Testing Turnaround Times

It is recommended that the laboratory have a list of assay turnaround times, if applicable. These turnaround times should be available to all laboratory personnel as well as to customers of the laboratory.

f. Laboratory Communication Plan

The institution or laboratory must have a non-retaliatory policy for personnel and study participants to communicate concerns regarding testing quality and/or laboratory safety to laboratory management. For laboratories that are part of healthcare systems, it may be appropriate to reference institutional or healthcare system-wide policies.

Hand-Off Communication: The laboratory should implement a procedure for effective “hand-off” communication that includes information about pending specimens, tests and participant-related laboratory issues when responsibility is “handed off” from one person to another, such as at a change in shift, or when the responsibility for a case is transferred from one pathologist to another, as applicable. The procedure should include provision for asking and responding to questions.

g. Standards for External Quality Assurance

For all laboratories participating in an EQA program, the following standards apply:

- Laboratories must enroll in EQA programs that cover all DAIDS protocol-related analytes, if available.
    - EQA programs for study protocol analytes must be approved by DAIDS.
    - Laboratory performance in DAIDS-approved proficiency-

testing programs will be monitored for successful performance by DAIDS or its designees.
    - Commercial EQA programs may be unavailable for specialized assays of protocol-specific analytes. In those cases, the laboratory should have a plan for alternative assessment of assay performance that is approved by laboratory management. Alternative assessments should be approved by DAIDS.
- EQA specimen testing should be handled in the same manner as participant samples.
- EQA specimens should be analyzed by the same methods routinely used for participant samples.
- EQA specimen testing should be rotated among personnel who routinely test participant samples.
- The laboratory must have written procedures for the proper handling, analysis, review, and reporting of EQA materials. There must be written procedures for investigation of each unacceptable EQA result to evaluate the impact on participant sample results and to correct problems identified in a timely manner.
- The date of EQA sample receipt in the laboratory and the condition of the samples must be recorded. When samples are missing or damaged, the laboratory must notify the EQA provider to obtain replacements.
- Every EQA process stage, from sample arrival to receipt of the report and any follow-up action, must be traceable with well-prepared documentation.
- The laboratory must have a procedure for assessing its EQA performance.
- The written EQA policies must strictly prohibit interlaboratory communications about EQA samples or results until after the deadline for submission of data to the EQA provider. EQA records must not be shared with and should be inaccessible to personnel of other laboratories, including affiliated laboratories, until after the deadline for submission of results. Laboratories that share a common computer system or personnel must have strict policies and procedures to ensure that personnel do not access EQA records from other laboratories.
- The written EQA testing policies must strictly prohibit referral or acceptance of proficiency testing specimens for analysis from other laboratories.
- When EQA results are submitted electronically to the provider, the attestation should be printed and signed by laboratory management and maintained for the retention time specified for EQA records.
- The laboratory should store the EQA samples in suitable conditions until the report for the specific event is received and the results are evaluated by the relevant laboratory personnel.
- All EQA results should be promptly reviewed by the appropriate personnel, as defined by the laboratory EQA plan. Such personnel may include the data analyst, supervisors, managers, quality specialists, and laboratory management.

- Regular supervisory review of EQA program results must be evidenced by:
    - Signature and date of review of *all* results.
    - Documentation of corrective action taken and appropriate preventive action in response to any unacceptable results.
- EQA performance results should be communicated to personnel because these results provide valuable information on the laboratory's performance.
- In addition to the review of EQA event performance, the laboratory should consider review of the entire EQA process over time. Trending the causes of EQA failures across laboratory disciplines and sections may identify patterns and trends that are not apparent in the evaluation of each event.
- Alternative External Quality Assurance (Alternative EQA)
    - If existing EQA surveys are not available, a suitable form of alternative proficiency assessments should be devised and proposed to DAIDS for approval. Such performance assessments include:
        - Splitting the samples included in a commercially available kit among two or more laboratories.
        - Splitting study participant specimens analyzed by a reference laboratory or other laboratory.
        - Periodic examinations on stored stable aliquots with known values, blinded to the testing laboratories.
        - Correlation testing of a backup method with an in-house primary method whose quality has been established using an external source.
    - Alternative EQA should be performed on a semi-annual basis at minimum where applicable.
    - Use of study participant samples should be restricted to assays that are required by the applicable clinical trial protocols and may require approval by the applicable IRB or IEC.

Version History

Modifications are made to DAIDS Guidelines for Good Clinical Laboratory Practice (GCLP) Standards via letters of amendment.

The table below describes the version history of, and modifications to, DAIDS Guidelines for Good Clinical Laboratory Practice (GCLP) Standards due to Letter of Amendment 1, dated 10 Jun 2011.

Document History and Modifications Date	Version	Modification	Item Number	Comment
21 July 2011	2.0	Letter of Amendment 1 (10 June 2011)	Item 1	Cover Page: author list revised
			Item 2	Section 1., Sponsor Statement – Introduction section, Food and Drug Administration's Form 1572: revised language, clarification of specific requirements in Section 4
			Item 3	Section 4., Equipment - Subsection B., Standards for Equipment, Documentation Guidelines: language added, clarification that all laboratory equipment should be listed on an inventory document
			Item 4	Section 4., Equipment – Subsection B., Standards for Equipment, General Guidelines: added language, clarification of policy/procedure for temperature monitoring in absence of staff

Document History and Modifications Date	Version	Modification	Item Number	Comment
			Item 5	Section 4., Equipment - Subsection B., Adjustable and Fixed-volume Automatic Pipettors: revised language, clarification of volumetric accuracy and reproducibility check requirements, as well as recalibration.
			Item 6	Section 4., Equipment - Subsection B., Thermometers: added language to indicate NIST-certified (or equivalent) thermometers follow manufacturer's recommendations for calibration and expiration date
			Item 7	Section 6., Test and Control - Subsection B., Frequency of Quality Control Testing and Types of Control Materials: language added, clarification of frequency for FDA-approved, CLIA-waived tests, as well as non-FDA-approved tests
			Item 8	Section 6., Verification of Performance Specifications - Subsection B. Standards for Performance Specifications: language added, clarification regarding precision validation for qualitative tests

Document History and Modifications Date	Version	Modification	Item Number	Comment
			Item 9	Section 8., Records and Reports - Subsection B., Standards for Records and Reports, Assay Results: language added, clarification of process to indicate the laboratories maintain a list of locations to which results are reported
			Item 10	Section 13., Quality Management - Subsection C., Standards for External Quality Assurance: language added, clarification of EQA specimen testing rotation among staff members in laboratories

The table below describes the version history of, and modifications to, DAIDS Guidelines for Good Clinical Laboratory Practice (GCLP) Standards due to Letter of Amendment 2, dated 09 July 2013.

Document History and Modifications Date	Version	Modification	Item Number	Comment
09 July 2013	3.0	Letter of Amendment 2 (09 July 2013)	Item 1	Cover page: Contract statement removed, NIH/NIAID and DHHS logos updated
			Item 2	Section 1., Sponsor Statement: revised language to DAIDS mission statement and Network requirements.
			Item 3	Section 3., Organization and Personnel – Subsection B., Standards for Organization and Personnel: competency assessments requirements

Document History and Modifications Date	Version	Modification	Item Number	Comment
			Item 4	Section 4., Equipment – Subsection B., Standards for Equipment: language added for back-up instruments/ correlation testing, centrifuge timer performance verification requirements
			Item 5	Section 8., Records and Reports - Subsection B., Standards for Records and Reports: revised language, refer to DAIDS Policy on Storage and Retention of Clinical Research Records
			Item 6	Section 11., Personnel Safety – Subsection B., Standards for Personnel Safety: language added, clarification on evacuation policy/plans
			Item 7	Section 13., Quality Management – Subsection C., Standards for External Quality Assurance: language added, clarification on Alternative External Quality Assurance

The table below describes the version history of, and modifications to, DAIDS Guidelines for Good Clinical Laboratory Practice (GCLP) Standards due to Letter of Amendment 3, dated 27 June 2019. DAIDS Guidelines for Good Clinical Laboratory Practice (GCLP) Standards Version 4.0 is equivalent to DAIDS Guidelines for Good Clinical Laboratory Practice Standards Document No.: MAN-A-OD-001.00.

Document History and Modifications Date	Version	Modification	Item Number	Comment
27 June 2019	4.0	Letter of Amendment 3 (27 June 2019)	Item 1	Section 1., Sponsor Statement: language added, clarification of GCLP approach and unique quality concept, expanded language for validation of test methods
			Item 2	Previous Section 2. Introduction: deleted, text moved to Section 1, Sponsor Statement. Sections that followed shifted upward
			Item 3	Section 2., Organization and Personnel – Subsection A., Introduction to Organization and Personnel: language added
			Item 4	Section 2., Organization and Personnel – Subsection B., Standards for Organization Personnel; language added for Job description standard information, Job introduction program and Job-specific Training, Education and Assessments, clarification of GCLP training
			Item 5	Section 3., Equipment – Subsection B., Standards for Equipment: language added, temperature monitoring, clarified check volume for adjustable pipettes
			Item 6	Section 4., Testing Facility Operation: language added; revised requirement for SOP review from annually to every two years
			Item 7	Section 5., Test and Control: language added, clarification of qualitative and quantitative non-waived tests, QC of media

Document History and Modifications Date	Version	Modification	Item Number	Comment
			Item 8	Section 6., Test Method Validation and Verification: language added, clarification of non-waived test validation or verification process and timing
			Item 9	Section 6., Test Method Validation and Verification: Addition of language for requirements for resuming testing for tests taken out of production and specimen collection container validation and verification
			Item 10	Section 6., Records and Reports: language added, emphasized participant's data confidentiality and security, clarified laboratory- developed tests (LDTs)
			Item 11	Section 8., Physical Facilities: language added, laboratory space security, liquid nitrogen monitoring
			Item 12	Section 10., Personnel Safety: language added, personnel responsibility, electrical grounding, gas cylinder storage, emergency preparedness policy, UV Light Exposure policy, safe work practices review
			Item 13	Section 11., Laboratory Information Systems: language added for audit trails, access and security
			Item 14	Section 12., Quality Management: language added, Nonconforming Event Management, Internal and External Assessments, Hand-Off Communication

The table below describes the version history of, and modifications to, DAIDS Good Clinical Laboratory Practice (GCLP) Guidelines due to Letter of Amendment 4, dated
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DAIDS Good Clinical Laboratory Practice (GCLP) Guidelines Version 4.1 is equivalent to DAIDS Good Clinical Laboratory Practice (GCLP) Guidelines Document No.: MAN-A-OD-001.01

Document History and Modifications Date	Version	Modification	Item Number	Comment
	4.1	Letter of Amendment ( )	Item 1	Document Title and Number - Changed from 'DAIDS Guidelines for Good Clinical Laboratory Practice Standards' to 'DAIDS Good Clinical Laboratory Practice Guidelines'; Document No. updated to MAN-A-OD-001.01
			Item 2	Dr. Carl Dieffenbach's letter - Removed
			Item 3	Sponsor Statement - Updated to reflect elements from Dr. Carl Dieffenbach's letter
			Item 4	Section 1., Organization and Personnel, b. Personnel Education and Evaluations, deleted language on Job Introduction Program
			Item 5	Section 1., Organization and Personnel, c. Job-specific Training, Education, and Assessments, updated language for training and personnel competence requirements
			Item 6	Section 1., Organization and Personnel, d. GCLP Training, clarification of training requirement for US specimen processing and endpoints laboratories and non-US personnel performing specimen processing and/or testing in

Document History and Modifications Date	Version	Modification	Item Number	Comment
				the clinic or clinical laboratory.
			Item 7	"Section 2., Equipment – Subsection B., Standards for Equipment: language updated for checking volume of adjustable pipettes and Backup Power Equipment options"
			Item 8	Section 3., Test and Control, B. Standards for Test and Quality Control, Frequency of Quality Control Testing and Types of Control Materials, language updated for frequency of external QC to weekly
			Item 9	Section 9., Personnel Safety, B. Standards for Personnel Safety, removed language on Electrical Grounding
			Item 10	Various replacements of "should" with "must" and, conversely, "must" with "should" throughout the document
			Item 11	Glossary – removed commonly-used terms plus words and abbreviations already defined within guideline text
			Item 12	Appendix Descriptions - Removed
			Item 13	Appendices - Removed

Glossary

alert values: See critical values.

American National Standards Institute (ANSI): Organization that oversees the creation, proliferation, and use of thousands of rules and guidelines that affect a broad range of businesses; also engaged in accrediting programs that assess conformance to standards, such as ISO 9000 management systems (http://www.ansi.org).

American Society for Testing and Materials (ASTM): Organization that develops and generates voluntary standards that are used worldwide (http://www.astm.org).

analytical run: An interval, period of time, or number of specimens for which the precision and accuracy of the method is expected to remain stable.

authorized persons/personnel: The staff designated by an authorizing organization that is responsible for a work activity's technical and administrative objectives.

auto-verification: A process whereby the LIS or instrument system performs verification of result data according to laboratory-defined rules and logic.

central laboratory: Laboratory (or a group of laboratories) utilized by all sites participating in a given clinical trial for performance of certain assays, typically as a result of desired standardization of results and/or assay complexity.

chain-of-custody: Procedures to account for the integrity of each specimen by tracking its handling and storage from point of specimen collection to final disposition of the specimen.

Clinical Laboratory Improvement Amendments of 1988 (CLIA): Federal standards applicable to all U.S. facilities or sites that test human specimens for health assessment or to diagnose, prevent, or treat disease.

contract laboratory: Laboratory used on contractual basis to perform limited list of assays associated with a clinical trial.

endpoint assay: Testing performed to aid in monitoring of a trial's effectiveness for treatments and prophylaxis/prevention.

laboratory management: Personnel performing supervisory and/or managerial functions within the laboratory.

matrix: All the physical and chemical constituents of the material or specimen, except the analyte.

modified FDA-approved test: Assay, procedure or system that does not follow the manufacturer's procedure without deviation or is used for clinical indication(s) that is (are) not approved by the manufacturer.

nonconforming event: An occurrence in which established policies, processes, or procedures are not met.

non-waived test: Laboratory tests that are not classified as CLIA-waived; often referred to as tests of moderate- or high-complexity (e.g., a complete blood count with a manual differential is considered to be test of high-complexity).

parallel testing: Side-by-side comparison of existing and new product lots to

demonstrate the reproducibility of the new product lot within defined acceptance criteria.

post-analytic: Of or relating to steps in the overall laboratory process between completion of the analytic phase of testing and results receipt by the requesting physician.

pre-analytic: Of or relating to steps in the process prior to the analytic phase of testing, starting with the physician's order.

processing laboratory: Laboratory that serves to perform primarily the pre-analytical tasks associated with study-participant specimens, such as collection, centrifugation, aliquoting, and storage.

read-back: The repetition of a message one has received, in order to acknowledge it.

referral laboratories: A laboratory that conducts tests for other laboratories; reference laboratories are usually large and may be independent or hospital based.

safety assay: Test that is performed to both monitor potential adverse events and to verify the study-participant's continued satisfaction of study inclusion/exclusion criteria, as appropriate, for each protocol.

sharps: Any object that can penetrate the skin, including, but not limited to, needles, scalpels, and broken capillary tubes.

standard precautions: An approach of infection control in which all specimens containing or contaminated with human blood and body fluids are treated as if infectious; formerly known as Universal Precautions.

unmodified FDA-approved test: An FDA-approved assay, procedure or system that follows the manufacturer's procedure without deviation and is used only for the clinical indication(s) approved by the manufacturer.

waived test (or CLIA-waived): Simple tests with a low risk for an incorrect result. They include: certain tests listed in the CLIA regulations, tests cleared by the FDA for home use, tests that the manufacturer applies to the FDA for waived status by providing scientific data that verifies that the CLIA waiver criteria have been met.

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