Dear Site Principal Investigator and Laboratory Director:

All National Institutes of Health, National Institute of Allergy and Infectious Diseases, Division of AIDS-supported clinical trials involving human subjects must ensure compliance with federal regulations including procedures to protect the safety of all participants. These studies must be conducted in a manner to assure the sponsor and regulatory agencies that all data submitted are a true reflection of the results obtained during a study and that this data can be relied upon when making risk and/or safety assessments of study products.

DAIDS has determined that Good Clinical Laboratory Practices (GCLP) are the minimal requirements that clinical research laboratories should follow, as GCLP embraces both the research/pre-clinical and clinical aspects of Good Laboratory Practices (GLP). Complying with GCLP is an ongoing process that is central to optimal clinical research laboratory operations. DAIDS will monitor the progress toward GCLP compliance through annual audits and/or site visits for most laboratories. GCLP compliance will ensure that consistent, reproducible, auditable, and reliable laboratory results that support clinical trials will be produced in an environment conducive to study reconstruction.

To support the many laboratories that conduct quality laboratory testing for clinical trials around the world, DAIDS has developed, in collaboration with PPD, the attached “DAIDS Guidelines for Good Clinical Laboratory Practices (GCLP) Standards.” This guidance document is provided to clearly define the standards that encompass GCLP to include applicable portions of 21 Code of Federal Regulations (CFR) part 58, or GLP, and 42 CFR part 493, or Clinical Laboratory Improvement Amendment (CLIA) rules. Due to the ambiguity of some parts of these regulations, the attached document also includes guidance from accrediting bodies such as the College of American Pathologists and South African National Accreditation System. These GCLP standards should be applied to all laboratories performing testing that supports a clinical trial sponsored by DAIDS. Institutions must also meet sponsor-specific requirements as outlined in the Sponsor Statement of this document.

The first 37 pages of the document provide the GCLP standards. The next 66 pages are appendices that offer additional information and guidelines on how to implement some of these standards. This document can also be accessed on the DAIDS Clinical Research Policies and Standard Procedures Documents as an appendix to the Laboratory policies for Requirements for DAIDS Funded and/or Sponsored Laboratories in Clinical Trials (http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Pages/Laboratories.aspx).

I hope these GCLP standards become a useful resource for your clinical research laboratory operations. This document has been vetted through the DAIDS Management Group, Regulatory Affairs Branch, Office of Policy for Clinical Research Operations, DAIDS Clinical Laboratory Oversight Team (DCLOT), and the Cross Network Laboratory Groups. If you have any questions about the content of this document please contact your Network Coordinator or the DAIDS Clinical Lab Oversight Team (DCLOT’s e-mail: NIAIDDCLOT@niaid.nih.gov).

Sincerely,

Carl W. Dieffenbach, Ph.D.
Director, Division of AIDS, NIAID, NIH
DAIDS Guidelines
for
Good Clinical Laboratory Practice Standards

The development of these GCLP standards was a collaborative effort between PPD and the Division of AIDS (DAIDS). The authors that have contributed to this document are listed below:

**PPD, Inc.:**
- Global Government and Public Health Services, Laboratory

**DAIDS:**
- DAIDS Clinical Laboratory
- Oversight Team

The authors would also like to thank the following groups for their review and comments:

- Network Laboratory Groups
- Patient Safety Monitoring in International Laboratories (pSMILE)

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Good Clinical Laboratory Practices Standards

1. Sponsor Statement

Introduction
The mission of the Division of AIDS (DAIDS) of the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) is to help ensure an end to the HIV/AIDS epidemic by increasing basic knowledge of the pathogenesis and transmission of HIV disease, supporting the discovery and development of therapies for HIV infection and its complications, and supporting the discovery and development of vaccines and other prevention strategies. Clinical evaluation in humans provides the only means of determining whether a candidate product is safe and effective. DAIDS-supported clinical trials and studies involving human subjects must ensure compliance with federal regulations including procedures to protect the safety of all participants. There are multiple organizations conducting clinical trials for evaluation of therapies, vaccines, and other prevention strategies against HIV infection globally. In the absence of a single central laboratory that can perform endpoint and safety assays, it is imperative that the data from multiple laboratories performing assays are reliable and reproducible so that clinical trial data can be effectively compared. Many laboratories conducting clinical research do not fall under the oversight of any government regulatory authority. As an example, no standards or regulations exist for conducting immunogenicity assays for Phase 1 and 2 vaccine clinical studies. To bridge this gap, DAIDS, as the Investigational New Drug (IND) application sponsor, has determined that the Good Clinical Laboratory Practices (GCLP) are minimal requirements that must be followed. Institutions must also meet sponsor-specific requirements as outlined in the sections below. It should be noted that specific requirements from Network and Non-Networks may be more stringent than DAIDS requirements.

Food and Drug Administration’s Form FDA 1572
Before permitting an investigator to participate in a clinical trial for an IND, the sponsor must obtain a completed Food and Drug Administration’s Form FDA 1572, Statement of Investigator. This form serves to capture demographic information of the investigator, the specific protocol(s) to be conducted, information on the research facility where the trial will be conducted, and identification of the clinical laboratories to be used in the trial. In addition, the Form FDA 1572 provides documentation of the commitment of the investigator regarding compliance and the conduct of the trial. Form FDA 1572, Section 4 requires the entry of “Name and Address of any Clinical Laboratory Facilities to be used in the Study.” Section 4 must list the name(s) and complete physical address of ALL clinical laboratories or testing facilities that will be used for the clinical trial to process study related and/or study defined samples, which will directly contribute to or support the clinical trial. The official name of the laboratory (i.e., Department of Pathology) should be included. If multiple Clinical Research Sites (CRSs) and/or locations are listed on the Form FDA 1572, the corresponding clinical laboratories must be listed for each CRS and/or location. If a central laboratory is sending samples to its own satellite laboratories for additional testing, the satellite laboratories do not need to be listed as long as the central laboratory can trace, through written records, the samples to the satellite laboratories where the tests were performed. This information is necessary to ensure that the FDA and DAIDS can monitor the activities of all laboratories that provide data to support a DAIDS-sponsored trial. For clinical trials that are not conducted as an IND, a DAIDS Investigator of Record agreement must be completed.
Study Plans and Analytical Plans

Often, study protocols may not be adequate in addressing all tasks and processes that must be carried out by laboratory personnel when working with clinical trial specimens; in this case, a formal laboratory-specific supplement in the form of an analytical or a study plan should be developed. This plan is a technical document that describes all laboratory-specific components of the trial, defining study objectives and design for the conduct of the study within the laboratory setting. The study plan is a valuable source of information for many parties involved in the clinical trial (e.g., trial sponsor, laboratory director, laboratory personnel, specimen management coordinator, the Statistical Center, and the Quality Assurance Unit [QAU]). This comprehensive plan is written and approved by the laboratory director or designee and must include detailed information on the title of the study, purpose, authority and responsibility, key contacts, introduction and background, and instructions for:

- Specimen collection, chain-of-custody, and shipping instructions,
- Instrumentation and analytical methods to be used,
- Reference ranges, referral laboratory information, and transmission of results.

This version-controlled document must conform to an approved study protocol and its appendices, be updated as required by protocol revisions, and be in compliance with the U.S. FDA requirements and the Organization for Economic Cooperation and Development (OECD) regulations for Good Laboratory Practices (GLP).

Note: Please refer to Appendix 1 for an example template for a study plan.

Enrollment in External Quality Assurance Programs

All DAIDS funded and/or sponsored laboratories must participate in External Quality Assurance (EQA) programs for all testing used to support clinical trial research. Laboratories should enroll in EQA programs that cover all study protocol analytes. These programs must be approved by DAIDS and serve to 1) compare a laboratory’s performance with that of its peers performing the same type of testing, 2) assure the sponsor and regulatory agencies that the data generated is accurate and reliable to properly manage clinical trial volunteers’ safety, and 3) ensure that testing is performed with a rigor that will support product licensure in the U.S.. Laboratory performance in DAIDS-approved proficiency-testing programs will be monitored for successful performance by DAIDS or its designee.

Retention of Records

Laboratory records are paramount in reconstructing trial execution. 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 (http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/recordretention.pdf) states that clinical trial records belong to the Institution that conducts the DAIDS sponsored and/or funded trial. To determine how long to retain laboratory records refer to the DAIDS policy and the requirements of your Institution. Section 8 of these GCLP standards provides additional guidance on the types of laboratory documentation that should be archived.

Performance Specifications – Validation of Test Methods

DAIDS requires that all methods undergo testing activities to verify their performance specifications. This includes verification of accuracy, precision, sensitivity, specificity, linearity, and reference ranges. It is recommended that FDA-approved testing methods be employed when
possible, as validation exercises are less intensive and do not include verification of sensitivity and specificity performance.

**Good Clinical Laboratory Practices**

These GCLP standards should be applied to all laboratories performing testing that supports a clinical trial funded and/or sponsored by DAIDS to include safety, diagnostic, and endpoint laboratory assays. Safety assays are those tests that are performed to both monitor potential adverse events and to verify the study participants’ continued satisfaction of study inclusion/exclusion criteria, as appropriate, for each protocol. Endpoint assays are performed to aid in the monitoring of the trial’s efficacy for treatments and prophylaxis/prevention. DAIDS will audit most laboratories that are involved with its clinical trials on an annual basis (or as deemed necessary) to confirm GCLP compliance.

**2. Introduction**

Most laboratories in the clinical research arena do not fall under the oversight of any government regulatory authority. Often, in areas outside of Europe, Australia, and North America, there is no regulatory body devoted to laboratory science. In the areas where regulation exists, the targeted laboratories are either strictly “clinical” or “research” oriented. This type of scenario presents difficulties in discerning which regulations apply to laboratories engaging in clinical research.

GCLP is an approach to laboratory guidance which has been adopted by some European quality associations. The GCLP concept possesses a unique quality, as it embraces both the research/pre-clinical and clinical aspects of Good Laboratory Practices (GLP). DAIDS recognizes that consistent GCLP application is paramount in the success of any clinical trial. In most cases, clinical trial data is largely laboratory in nature to include study endpoints and participant safety data. Hence, if this laboratory data is called into question due to inconsistent practices, an entire trial effort could be deemed as a failure. As a precautionary element, and to ensure the sponsor’s confidence in the good quality of data produced by any laboratory performing study testing, DAIDS has overseen the development of GCLP standards which encompass applicable portions of 21 CFR part 58, or GLP, and 42 CFR part 493, or the Clinical Laboratory Improvement Amendments (CLIA). These regulations were intended to ensure the quality and integrity of safety data, allow accurate reconstruction of experiments, allow for safe, quality products, and allow data to be comparable regardless of where they were generated. These guidelines also help assure sponsors and regulatory agencies that all data submitted are a true reflection of the results obtained during a study and that this data can be relied upon when making risk and/or safety assessments. Due to the ambiguity of some parts of these regulations, these GCLP standards also include guidance from other organizations and accrediting bodies, such as the College of American Pathologists (CAP) and the International Organization for Standardization (ISO), which better define the intent of GCLP that is presently undefined by a single regulatory body. By recognizing these standards as the minimum requirements for DAIDS-funded laboratory operations, the expectation is that GCLP compliance will ensure consistent, reproducible, auditable, and reliable laboratory results that support clinical trials are produced in an environment conducive to study reconstruction.
3. Organization and Personnel

A. Introduction to Organization and Personnel

Laboratory management and staff share the responsibility of thorough documentation of the structure of the organization and the respective job descriptions and qualifications, as well as an 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.

B. Standards for Organization and Personnel

Documentation: The testing laboratory must have the following documents stored in the laboratory or readily available (e.g., within 24 hours) to authorized personnel, as appropriate:

- **Personnel policies** must be available that address such topics as orientation, training, continuing education requirements, performance evaluations, dress codes, and security. These policies detail employer and employee responsibilities as they relate to continued employment, employee and employer legal requirements, and protections.
- **Organizational and/or departmental policies** that describe how personnel can communicate existing issues which may affect quality of testing or safety of personnel must be available to ensure a non-retaliatory environment that encourages communication vital to the integrity of the study and the institution.
- **Job descriptions** that define qualifications and delegation of duties for all positions within the laboratory must be available to staff and other appropriate individuals (as defined below).
- **Personnel files** must be available to appropriate individuals (as defined below) that include a summary of the following items as they relate to each employee:
  - Orientation and training
  - Experience
  - Education
  - Applicable licensure/certification (if required)
  - Competency assessments
  - Continuing education records
  - Curriculum Vitae
  - Safety training
  - Attendance at job-related workshops and seminars

  *Note:* Please refer to Appendix 2 for an example of a Training Attendance Log.

  *Note:* Personnel files must be readily available (e.g., within 24 hours) only to authorized personnel such as the Laboratory Director, Quality Assurance (QA)/Quality Control (QC) Manager, Primary Investigator of protocol, and DAIDS officials and auditors.

- **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 staff understands communication path options and requirements.
Staff 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.

**Job-specific Training, Education, and Assessments**
- All personnel must receive direct and detailed training for the performance of all duties and tasks that they perform.
- Competency assessments must be conducted and recorded for all components of the employee’s training and functional responsibilities upon completion of initial training. Competency must be assessed every six months during the first year of employment, annually thereafter, or more frequently if laboratory management deems necessary. Competency assessments must compare employee performance against a documented standard and clearly verify competency or lack of competency for each evaluated task.
  - Competency assessments should assure that the staff maintains their competency to perform test procedures and report results promptly, accurately and proficiently.
  - The procedures for evaluation of the competency of the staff should include, but are not limited to:
    a. Direct observations of routine patient test performance, including patient preparation, if applicable, specimen handling, processing, and testing;
    b. Monitoring the recording and reporting of test results;
    c. Review of intermediate test results or worksheets, quality control records, proficiency testing results, and preventive maintenance records;
    d. Direct observation of performance of instrument maintenance and function checks;
    e. Assessment of test performance through testing previously analyzed specimens, internal blind testing samples or external proficiency testing samples; and
    f. Assessment of problem solving skills.
- A clinical laboratory continuing education program that is adequate to meet the needs of all personnel must be documented, and evidence of ongoing adherence by all laboratory personnel must be readily available. This documentation should include scheduling information such as how frequently personnel should attend a given course, the type of courses required, and the number of educational sessions personnel are required to attend over a given time period. Examples of training include, but are not limited to, topics such as blood-borne pathogens, shipping of dangerous goods based on International Air Transportation Association (IATA) regulations, and laboratory safety.

**GCLP Training**
- At this time, GCLP training is not a DAIDS requirement. However, it is highly recommended that all laboratory personnel receive training in GCLP. The frequency of this training must be sufficient to ensure that employees remain familiar with the GCLP requirements applicable to them.

**Job Performance Evaluations**
- Annual performance evaluations must be given to all laboratory personnel. These evaluations compare the employee’s overall performance of job responsibilities, duties, and tasks as outlined in the job description. These evaluations often take into
consideration many aspects of job performance in addition to technical competency, such as quality of interpersonal communication, attendance, and behavioral expectations.

**Staff Numbers:** The laboratory must employ an adequate number of qualified personnel to perform all of the functions associated with the volume and complexity of tasks and testing performed within the laboratory. The number of employees needed for optimal laboratory operations is determined by upper management in consultation with staff; this number is adjusted based on the scope and amount of workload.

**Staff Identification:** If signatures, initials, or codes are used as staff identifiers on any laboratory documentation, a documented list that links these identifiers to a printed name must be in place. Changes in staff signatures, initials, or codes, as well as identifiers for new staff must be immediately recorded in the laboratory’s documented list. The laboratory’s documented list should be a “controlled version” document that must be updated when applicable changes described occur in the laboratory. Signature logs should be archived so that those individuals who performed trial testing throughout the length of a trial may be identified. As an example, staff signatures, initials, or codes included in results from assays should be traceable to printed names available in the laboratory.

*Note:* Please refer to Appendix 3 for an example of a Signature Sheet.

**C. Record Retention**

Personnel records should be retained as outlined in Section 8 of these GCLP standards.

**References:**

- 42 CFR § 493.1413
- 42 CFR § 493.1451

**4. Equipment**

**A. Introduction to Equipment**

The laboratory staff 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 that demonstrate and provide evidence that all instrumentation and equipment are adequately validated, operated, inspected, cleaned, maintained, tested, and standardized to ensure optimal quality of assay results. 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.
There must be evidence that equipment performance, use, and maintenance are consistently and routinely documented and reviewed by the laboratory director or designee.

B. Standards for Equipment

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 should be readily accessible.
  - Retain preventive maintenance and service logs as outlined in Section 8 of these GCLP standards or until otherwise instructed.
- A supervisory staff member must review, sign, and date all documentation of equipment maintenance at least monthly.
- All laboratory equipment should be listed on an inventory document.

General Guidelines
Staff must conduct all preventive maintenance and service per manufacturer specifications by following these guidelines:
- Staff must keep all 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 for all equipment utilized, and record completion of these tasks on the appropriate logs in a timely fashion.

Temperature monitoring in absence of staff:
- There should be a written policy/procedure in place, explaining how temperatures are monitored during the absence of laboratory staff.

Backup instruments/Correlation Testing:
- If a laboratory uses more than one instrument to perform the same test, the primary and backup instruments should be compared to each other to determine the consistency of results. It is preferable that these comparisons be performed using study-participant samples. However, where availability or stability precludes the use of study-participant samples, the use of QC, EQA, or other reference materials may be necessary. Correlation testing should be performed on a semi-annual basis at minimum where applicable.
  Note: 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).

Service Guidelines
In addition to the above general guidelines, the laboratory must observe and document the specific service guidelines described below. Trained laboratory staff or certified contractors should perform the following:
- **Adjustable and fixed-volume automatic pipettors**
  Check for volumetric accuracy and reproducibility, and recalibrate as necessary before placing in service initially and at specific defined intervals. 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.
Therefore, DAIDS strongly recommends that laboratories perform checks for accuracy, reproducibility, and recalibrations four times per year.

- **Thermometers**
  Test thermometers against a standardized National Institute of Standards and Technology (NIST)-certified (or equivalent) thermometric device annually. For NIST-certified (or equivalent) thermometers, follow manufacturer’s recommendations for calibration and expiration date.

- **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 2-8ºC, and Reagent B’s acceptable storage temperature range is 3-10ºC, the tolerance limit for the refrigerator must be 3-8ºC.
  - Place liquid nitrogen freezers in facilities that are well ventilated or monitored for oxygen content.
  - Maintain daily (at a minimum) record of temperatures and/or levels of liquid nitrogen’ as appropriate.
  - Maintain appropriate documentation of corrective action for out-of-range temperatures and liquid nitrogen levels.

- **Incubators and water baths**
  - Establish tolerance limits for temperatures, carbon dioxide level, and humidity, as applicable.
  - Maintain daily (or “dates of use”) record of temperatures.
  - Maintain appropriate documentation of corrective action for out-of-range temperatures.

- **Centrifuges**
  - Measure operating speeds (appropriate for use in specimen processing) periodically (annually at a minimum; DAIDS recommends every six months) with a tachometer. Document the readings.
  - Maintain daily (or “date of use”) record of temperatures for refrigerated centrifuges.
  - Verify performance of centrifuge timers by comparing to a known standard (e.g., NIST traceable timer) every six months.

- **Autoclaves**
  - Verify content processing using heat-sensitive tape with each autoclave batch.
  - Verify effective sterilization with an appropriate biological indicator weekly.
  - 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.

- **Timers**
  - Check for accuracy by comparing to a known standard (e.g., NIST traceable timer) every six months.

- **Analytical balances**
  - Check accuracy with standard weights of the appropriate ANSI/ASTM (American National Standards Institute/American Society for Testing and Materials) class 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 so that vibration does not affect the readings.

- **Biosafety cabinets/laminar air flow hoods**
  - Verify air intake grills are not obstructed.
  - Certify cabinets/hoods annually by 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 hood’s 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 FPM inflow velocity. The actual airflow obtained on a daily basis would 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.
  - Note: Use of UV is recommended only when personnel are out of the room.
  - Document daily and weekly cleaning.

- **Generators**
  - Maintain and keep readily accessible records to verify that the back-up generator system is in place and operational.
  - Follow SOPs that detail generator maintenance.
    - a. Procedures should list the frequency and procedural steps of maintenance and testing.
    - b. Supporting logs should document monthly checks on critical generator components, including fluid levels (oil, coolant, and fuel), belts, battery, testing of start-up, and operation.

**References:**

**5. Testing Facility Operation**

**A. Introduction to Testing Facility Operation**

A testing facility must have written SOPs to ensure the consistency, quality, and integrity of the data generated from the 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. All SOPs must be readily available for use by testing personnel at the workbench. These SOPs must be of uniform format as determined by the laboratory director and must 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.
B. Standards for Testing Facility Operation

Current SOPs must be available in the work areas and accessible to staff.

The laboratory must write SOPs in a manner and language that is appropriate to the laboratory personnel conducting the corresponding procedures.

SOP Format
The laboratory must write SOPs in a standard format such as the format recommended by the Clinical and Laboratory Standards Institute (CLSI). This format may include the following:

- Document number
- Revision number and date
- Effective date of the document
- Number of pages
- Title, to include name of analyte, type of specimen, and method/assay and/or instrumentation
- Principle and/or purpose
- Scope
- Specimen requirements/collection methods
- Reagents, standards, controls, and media used
- Instrumentation, Calibration procedures
- QC
- Procedural steps
- Attachments (e.g., product inserts)
- Calculations
- Reporting results
- Reference ranges/critical values
- Limitations
- References
- Definitions
- Distribution
- Author
- Approval signatures and dates
- Document change history

Note: Please refer to Appendix 4 for an example of SOP in CLSI format.

SOP Distribution
The laboratory must distribute all new and revised SOPs to the appropriate laboratory staff 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 by signing and dating the SOP after their review.
- The laboratory must maintain this documentation in a system that readily allows for verification that personnel are knowledgeable of the new or revised SOPs.
Document Control Plan
The laboratory must maintain a current Document Control Plan that addresses and ensures the following vital elements of SOPs:

- Maintain a master list of SOPs currently used in the laboratory.
- Ensure SOPs are procedurally accurate and relevant.
- Keep the authorization process standardized/consistent, limiting approvals to laboratory management.
- Review SOPs annually and document the review.
- Remove retired or obsolete SOPs from circulation and identify them as retired or obsolete.
- Archive retired or obsolete SOPs for a period defined by the laboratory or institution. 
  Note: 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.

SOP Categories
The laboratory must have SOPs for all procedures being performed. Comprehensive lists of categories for SOPs may be found in reference literature.

General categories of SOPs within the department may include:

- Document Control: describe a plan that ensures relevance of all SOPs, as described earlier in this section.
- Organization and Personnel: detail policies that govern communication and administrative components of all employees of the organization, as described in Section 3.
- Personnel Training: explain required training and supporting documentation, as detailed in Section 3.
- Equipment Calibration and Maintenance: govern the physical maintenance and calibration of laboratory assets, as described in Section 4.
- Specimen Management and Chain-of-Custody: feature specimen transportation and handling steps required maintaining specimen integrity, positive identification of specimens, and audit trails from point of collection to delivery of results, as detailed in Section 10.
- Test Procedures: include the steps describing the performance of tasks, processes, and assays (safety, diagnostic, and end-point), formatted consistently as described earlier in this section.
- QC: express the components of establishing, performing, evaluating, troubleshooting, and documenting QC processes, as described in Section 6.
- QA: explain the systematic approach to ensuring continued improvement of the operations within the laboratory, as detailed in Section 13.
- Test Reporting and Records Management: oversee 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 8.
- Safety: describe the engineering controls, personal protective equipment (PPE), and processes to reduce risks to personal safety within the laboratory environment, as detailed in Section 11.
- Laboratory Communications: detail 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.
• Operations of Laboratory Information System (LIS): describe procedural stepwise
details of routine operation, as defined in Section 12.

C. Record Retention

Procedural documents should be retained as outlined in Section 8 of these GCLP
standards.

References:
42 CFR § 493.1251
42 CFR § 493.1407
42 CFR § 493.1105
College of American Pathologists Commission on Laboratory Accreditation, Accreditation
Checklists, 2012.
Clinical and Laboratory Standards Institute. (2006) Laboratory Documents: Development and
Control; Approved Guideline-Fifth Edition, [CLSI document GP2-A5, 26 (12)]. Wayne, PA:
Clinical and Laboratory Standards Institute.
Components; Approved Guideline-Second Edition. [NCCLS document GP22-A2]. Wayne, PA:
NCCLS.

6. Test and Control

A. Introduction to 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 materials 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.

B. Standards for Test and Quality Control

Quality Control Program
The laboratory must have a site-specific, written QC plan which clearly defines procedures for
monitoring analytic performance; this program ensures the consistent identification,
documentation, and resolution of QC issues. The laboratory director should be actively
involved in the design, implementation, and oversight of the QC program.

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 must 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 a few weeks, 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.

**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.

The laboratory director and/or designee 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’s 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 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 stain procedure. Other stains require daily or day of use QC, using a positive reacting organism and a negative, which could include the patient sample.

  *Note:* An analytical run spans the time interval over which the accuracy and precision of the assay is expected to be stable, must be based upon manufacturers’ instructions, and must not exceed 24 hours. For example, a given chemistry analyzer’s manufacturer may state that glucose reagents on their platform are stable for eight hours; in this case, QC must be performed every eight hours, or three times per day if operated 24 hours per day.

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 patient samples are tested.

For non FDA-approved tests, it is recommended that daily QC be run for testing used for primary endpoint and critical safety determinations. In addition, QC should be done in the following situations:

- If there are changes to device reagents, study populations and/or analytes
- When there are new operators performing testing on patient specimens
- 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 manufacturer’s recommended range
- If the temperature of the testing area falls outside manufacturer’s recommended range
- At periodic intervals as specified in a laboratory’s Quality Assurance program

At a minimum, laboratories should perform external QC weekly, whenever patient samples are tested in that week.
Review of Quality Control Data
QC must be run and reviewed 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.

QC results must be performed and acceptable results obtained (as defined in the written QC program) before test results are reported.

The laboratory personnel performing the testing must determine the appropriate corrective action to take for QC data that falls outside of established tolerance limits, using the QC program as a guide. Corrective action should 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 should evaluate study-participant results to determine if a significant clinical difference has occurred, in which case, the instrument QC should be re-established and the affected testing repeated.

Quality Control Logs
- QC logs must be present documenting control results assayed with each test, as described in each specific assay procedure.
  - Control records must be readily available to the staff 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., Levy 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 his or her initials, date, and time on all applicable QC records.
  - If QC materials are aliquoted, then they should be labeled in such a way that they can be traceable to the material name and lot, preparation date, expiration date and technician.
- QC records should contain detailed information to reconstruct establishment of ranges for each QC material used for monitoring analytic performance.

Note: Please refer to Appendix 5 for L-J Chart and Appendix 6 for QC Log examples.

Corrective Action Logs
The laboratory must ensure a corrective action log is present to facilitate documentation and resolution of QC failures.

Supervisor Review of Quality Control Documentation
Appropriate laboratory supervisory personnel must regularly review, sign, and date QC records and corrective action logs according to the following guidelines:
- A laboratory manager or designee must review, sign, and date the corrective action log at least monthly.
• The laboratory director or designee must review, sign, and date QC data at least monthly.
  
  *Note:* Documentation of all designees must be included in the current QC plan.

**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

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 FDA. Retention times are addressed in Section 8 of these GCLP standards.

**Labeling and Storage of Quality Control Materials and Reagents**

All QC materials and reagents must be properly labeled, as applicable and appropriate, with the following:

- **Storage requirements**
  - All QC materials and reagents 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 ambient temperature is maintained and corrective action taken when tolerance limits are exceeded. Ambient temperature logs should be utilized to document the acceptable ambient temperature range, record daily actual temperatures, and allow for documentation of corrective action taken should the acceptable temperature ranges be exceeded.
    
    *Note:* Ambient temperature tolerance limits must reflect the most stringent needs of all reagents, supplies, and specimens stored at ambient temperature; if Reagent A’s acceptable storage temperature range is 20-28°C, and Reagent B’s acceptable storage temperature range is 23-30°C, the tolerance limit for the room must be 23-28°C.
  - Date opened, prepared, or reconstituted by the laboratory, and the initials of personnel who prepared/reconstituted the QC material and reagents.
  - Expiration date.

Deteriorated or outdated (expired) QC materials 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. The manufacturer should be consulted should this situation arise. (Exception: Microbiological organisms; storage and sub-culturing techniques will determine time of use).

Calibrators must not be used as QC materials unless the laboratory is employing some other method when a separate control product is not available.

*Note:* If a calibrator is used as a control, it must be from a different lot number than that which is used to calibrate the method.
Inventory Control
The laboratory must have an established documented inventory control system in operation.

- 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.
- There must be evidence of a system which highlights the need to place supply orders, 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).

Parallel Testing
For each new lot of reagents, the laboratory must document that samples are tested in parallel with each current lot and that the comparable results are obtained before or concurrently with being placed in service.

- Parallel testing should include study-participant-based comparisons when possible. Use of study-participant samples should be restricted to assays that are required by the applicable clinical trial protocols and results obtained from new lot numbers retained for QA purposes only.
  Note: Use of study-participants for internal QA practices, such as parallel testing, may require approval by the applicable IRB or IEC.

Study-participant specimens tested on an established (current) lot number of reagents should be tested on the new lot number of reagents to assess comparability of results across lots. If study-participant specimens are not available for use, manufacturer-provided reference materials or proficiency testing materials with peer group means are acceptable.

- For quantitative tests, parallel testing should be performed by assaying the same study-participant specimens or reference materials with both the old and new lot numbers to assess comparability. QC materials must also be run when comparing old and new lots.
- For qualitative tests, minimum parallel testing must include re-testing at least one known positive (or abnormal) and one known negative (or normal) study-participant sample.

If study-participant specimens are not available for use, manufacturer-provided reference materials or proficiency testing materials are acceptable.

Note: A weakly positive sample must also be used in systems where study-participants’ results may be observed as weakly positive (e.g., Western Blot).

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. Laboratory water is classified as Type 1, 2, or 3 (defined by CLSI document C3-A4) and each type has different specifications for maximum microbial content, resistivity, maximum silicate contents, and particulate matter.

- 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) 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 due to contaminates.

References:
42 CFR § 493.1256
42 CFR § 493.1282
College of American Pathologists Commission on Laboratory Accreditation, Accreditation Checklists, 2012.

7. Verification of Performance Specifications

A. Introduction to Performance Specifications

Before reporting study-participant results, each laboratory that introduces a non-waived (a CLIA designation) test system must demonstrate that it can obtain performance specifications comparable to those established by the manufacturer (as found in manufacturer’s publications such as user manuals or package inserts). These steps ensure the assay is performing optimally within the environment the testing will be performed. Verification of performance specifications may also be referred to as validation of the method. Validation experiments should be performed for safety, diagnostic, and endpoint assays when implementing a new analyzer, new testing methodology, or new assay. All validation experiments should occur prior to testing study-participant specimens; documentation of experiment results and approval should be readily accessible. Methods that are defined as waived by CLIA do not require method validation. Endpoint assays, point-of-care testing, and “rapid” tests, if not classified as waived testing, require method validation as determined by their FDA-approval status as described above. Laboratories are not required to verify or establish performance specifications for any protocol-specific analytical test system used by the laboratory before April 24, 2003, provided the laboratories have documented acceptable Quality Control and external proficiency testing results.

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

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

**B. Standards for Performance Specifications**

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

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

Verification and documentation of both the Analytical Measurement Range (AMR) and the Clinically Reportable Range (CRR) must be performed when establishing the reportable range.

*AMR:* verifies 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.

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 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.

*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.
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 materials or control materials.
  - The laboratory may evaluate known samples of abnormal high and abnormal low values.

Note: Please refer to Appendix 7 for an example of how to determine the reportable range.

**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.

Note: Analytical sensitivity values that are smaller than the applicable standard deviation of the method are typically unreliable indicators of the method’s lower detection.

Note: Please refer to Appendix 8 for an example of how to determine analytical sensitivity.
**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 material 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.

*Note:* Please refer to Appendix 9 for an example of precision experiment.

**Analytical Specificity (Analytical Interferences):** estimate of the systematic error caused by other materials that may be present in the specimen being analyzed.

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.

*Note:* Please refer to Appendix 10 for an example of how to determine analytical specificity.

**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.

*Note:* Please refer to Appendix 11 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 validated is an unmodified, FDA-approved method, the manufacturer’s reference range may be verified. If the test is modified, or not FDA-approved, the reference range must be established.

- 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 published reference range(s).
- An appropriate number of specimens must 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 from patients that have been 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 must be evaluated to establish reference ranges. Typically, the minimum number of specimens required to establish reference ranges is 120 specimens per demographic group (e.g., if the laboratory wishes to establish gender-specific reference ranges, then the minimum number of specimens would be 240: 120 specimens collected from normal male patients, and 120 from normal female patients).
- Reference intervals 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 desires 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).

Note: Please refer to Appendix 12 for an example of how to determine reference ranges.

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

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 insure 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.

References:
42 CFR § 493.1253
College of American Pathologists Commission on Laboratory Accreditation, Accreditation Checklists, 2012.

8. Records and Reports

A. Introduction to 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 specimens and attest to credibility of test results. These documents are also necessary in full study reconstruction and other similar auditing purposes. For this reason, laboratories involved in specimen testing that supports a clinical trial should maintain all applicable records and reports following the standards below.

B. Standards for Records and Reports

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 reports
- QC data (all records pertaining to proficiency testing, quality control, 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 results with reference intervals
• Raw data 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 [21 CFR §58.3(k)]
• 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, specimen management, protocols/manuals, Laboratory Information System (LIS), and specimen storage documentation)

**Record Retention**

Research documentation and final reports are transferred to archive during or at the end of the study [21 CFR §58.33(f)]. The space dedicated to archive will have limited access by authorized personnel only and allow expedient retrieval of documents. Storage conditions must ensure document preservation for the specified retention time. A commercial archive service may be contracted if required (21 CFR §58.190).

To determine how long to retain laboratory records, refer to DAIDS Policy on Storage and Retention of Clinical Research Records (http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/recordretention.pdf). Records may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records.

*Note:* Record retention is governed by multiple authorities, in both U.S. and non-U.S. settings. Local IRB/REC policies, regulations, and laws are to be followed if more stringent retention guidelines apply.

**Data Integrity**

Adequate 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

**Report Format**

The laboratory’s test report must indicate the following items:
• Either the study-participant’s name and/or a unique study-participant identifier
• The name and address of the laboratory location where the assay was performed
• The date and time of specimen receipt into the laboratory
• The assay report date
• The name of the test performed
• Specimen source (e.g., blood, cerebrospinal fluid, urine)
• 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
• Any information regarding the condition and disposition of specimens that do not meet the laboratory's criteria for acceptability
• The records and dates of all assays performed
• The identity of the personnel who performed the test(s)

**Pertinent Reference Ranges**

Pertinent reference ranges (relevant or applicable to the local or study population, as defined in Section 7, Verification of Performance Specifications), 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.

**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.

*Note:* Please refer to Appendix 13 for an example of Laboratory Test Method List.

**Assay Results**

• Information that may affect the interpretation of assay results (i.e., test interferences) must be provided upon request.
• Study-participants must be provided with pertinent updates on assay information whenever changes occur that affect the assay results or interpretation of test results. For example, if during a study a manufacturer improves the sensitivity of an assay so that result normal ranges are reported differently, this information must be communicated to the study-participants. This communication may require the combined efforts of laboratory staff, study coordinators, and Principal Investigators.
• Assay results must be released only to authorized persons and, if applicable, the individual responsible for requesting the test(s). Laboratories should maintain a list of locations to which results are reported.
• Alert and critical values
  – The laboratory director 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 staff when assay results fall within established alert or critical ranges.
  – Communication logs must be maintained that show prompt notification of the appropriate clinical staff after obtaining test results that fall within a critical range. Documentation on these logs must include:
    a. Date and time of notification
    b. Responsible laboratory individual performing notification
c. Name and credentials of person notified at the clinic and test results given
d. Any problem encountered in accomplishing this task

- 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. (See sponsor statement regarding laboratories listed on Form FDA 1572).
- All test reports and records must be maintained by the laboratory in a manner that permits ready identification and timely accessibility.

Result Modification Log and Errors in Test Results
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 intervals) 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 intervals 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 must 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 analyst performing and completing the test result modification, along with the date and time.
  - 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
  - A supervisor or designee must review, sign, and date the Result Modifications/Corrective Action Logs at least monthly.
  - The laboratory director or designee must review 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:
  - The laboratory must promptly notify the appropriate clinician and/or clinic staff member.
– The laboratory must issue corrected reports promptly to the authorized person ordering the test and, if applicable, the individual using the test results.
– The laboratory must maintain copies of the original report as well as the corrected report.

Archiving 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 the laboratory or institution. These documents may be archived either on- or off-site, based on the laboratory’s discretion. 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.
- Sole copies of research documents, defined as documents not having any back-up 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.).

References:
21 CFR §58.3(k)
21 CFR §58.33(f)
21 CFR §58.190
42 CFR § 493.1291
42 CFR § 493.1251

9. Physical Facilities

A. Introduction to Physical Facilities

The laboratory facility must be designed in such a manner that the safety of the employees and the quality of the work is not compromised. Proper space for instrument placement, ventilation, temperature control, and operation must be available. The laboratory design must ensure the safety of the personnel when they are moving through the work area, working with the equipment, and performing laboratory testing. Specimen movement and workflow through the laboratory must be such that opportunities for specimen loss, specimen mix-up, and exposure of laboratory personnel to biohazards are minimized.

B. Standards for Physical Facilities

General Space
- Laboratory work areas must have sufficient space so that there is no hindrance to the laboratory work.
- Laboratory walkways must be unobstructed.
Temperature and Humidity Controls
Laboratory room (ambient) temperature and humidity must be controlled so that equipment and testing is maintained within the tolerance limits set forth by the manufacturer.

Cleanliness of Facilities
All floors, walls, ceilings, and bench tops of the laboratory must be clean and well maintained.

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.
  Note: 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 FDA. Retention times are addressed in Section 8 of these GCLP standards.
- Laboratory storage areas must be allocated to adequately preserve the identity, purity, and stability of laboratory reagents, control materials, calibrators, and other laboratory materials.

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

References:

10. Specimen Transport and Management

A. Introduction to 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 the aforementioned procedures are carried out properly.

B. Standards for Specimen Transport and Management

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 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.

Laboratory Testing Request Form (Requisition)
A properly completed request form/log sheet 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.

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).

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 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 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 driver (if specimen transported);
• 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, site, 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
• Laboratory sample receiver name and signature
• 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
• Transporter name and signature, if applicable

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) to ensure specimen integrity
  – 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 (i.e., biohazard), packaging, shipping, and handling of specimens to ensure specimen integrity, while maintaining timely and safe shipment of specimens
  – Shipments must be prepared by following all federal and local transportation of dangerous goods regulations (e.g., 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
  – Certification of regulation training must be on file and readily available

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
  – The length of time the specimens must be retained, 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 the integrity of samples is maintained.
• A documented disaster recovery procedure must be available to ensure the continued integrity of specimens.

References:
49 CFR § 172
42 CFR § 493.1241
42 CFR § 493.1251
11. Personnel Safety

A. Introduction to Personnel Safety

Safety of laboratory employees 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 is 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. It should also address availability of prophylaxis measures, such as Hepatitis B vaccinations and post-pathogen exposure options.

B. Standards for Personnel Safety

Safety Equipment

- The following safety equipment must be in the laboratory to ensure the continued safety of laboratory staff and any authorized individual who may enter the laboratory:
  - Eye wash that may be plumbed (attached to sink or as “stand-alone”) or portable (sealed or refillable bottles)
  - Emergency shower/drench hose
  - Fire extinguishers
  - Sharps containers

- The laboratory must test and/or inspect equipment on the following schedule:
  - Plumbed eye wash (attached to sink or as “stand-alone”) must be flushed weekly
  - Portable (sealed bottles) eye wash must be inspected monthly for signs of contamination and replaced prior to expiration or as required by the manufacturer
  - Portable (refillable bottles) eye wash must be cleaned and refilled weekly or as required by manufacturer
  - Emergency shower/drench hose must be flushed weekly (preferred) but no less often than once per month
  - Fire extinguishers must be inspected monthly to ensure proper charge and recharged as required by local standards or the manufacturer’s requirements, if applicable
  - Sharps containers must be inspected daily and replaced when three-fourths full

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.
Evacuation Policy/Plan
Laboratory should have a comprehensive, documented and workable evacuation plan that is available to all laboratory employees and visitors. Laboratory employees should be appropriately trained in the evacuation plan/policy.

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 staff. 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 employees 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).

Material Safety Data Sheets (MSDS)
- To ensure proper handling and storage, the laboratory must have MSDS or equivalent in the workplace for each hazardous chemical that they use:
  - MSDS must include chemicals that are used for testing (e.g., Ficol-Hypaque).
  - MSDS must include chemicals that are for general use (bleach, disinfectants, etc.).
  - The laboratory must maintain each MSDS in the local language, although the laboratory may maintain copies in other languages as well.
  - Laboratory personnel must be trained on reading the MSDS. There is no standard format or order of information presented within MSDS; this training is necessary to ensure they can identify and locate the different types of information contained within an MSDS, such as Hazards Identification, First Aid Measures, Handling and Storage.
  - MSDS must be readily available to employees during each work shift and to employees when they are in their work area(s).
  - MSDS may be maintained electronically as long as no barriers to immediate employee access in each workplace are created by such options.

*Note:* It is recommended that an index of MSDS be maintained and that all MSDS should be updated periodically, within a two-year period, to ensure staff is equipped with the most current hazard and first aid information.

Safety Policies
Safety policies defined according to regulatory organizations such as the Occupational Safety and Health Administration (OSHA) or the International Organization for Standardization (ISO) must be present in the laboratory. The following safety policies must be in place to ensure the continued safety of laboratory staff and any authorized individual who may enter the laboratory:
- *Standard Precautions/Universal Precautions Policy:* This policy or group of policies defines all human biologic specimens as potentially infectious and addresses topics of consideration when dealing with potentially infectious specimens, such as hand care, PPE, working with open lesions, handling contaminated needles and other sharp objects, autoclaving, and disposal of materials.
• **Chemical Hygiene/Hazard Communication Policy**: This policy or group of policies addresses aspects of safe chemical handling. Chemical Hygiene policies typically address storage and utilization and disposal of chemicals, with the goal of minimizing exposures and risks associated with those chemicals. Hazardous Communication policies typically provide information about the identities and hazards of chemicals, required appropriate labeling, MSDS, 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.

• **General Safety Policies**: These policies address less specific topics as they relate to laboratory safety, such as fire and back safety.

• **Safety Equipment Policies**: These policies typically detail all available safety equipment, their purposes, and proper utilization.

### Safety Training

• All laboratory staff 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 employees 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:
    
    a. When PPE is necessary
    b. What PPE is necessary
    c. How to properly wear PPE
    d. What are the limitations of PPE
    e. The proper care, maintenance, useful life, and disposal of PPE
  - Chemical Hygiene/Hazard Communications (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

• Documentation of completion of safety training must be maintained.
  
  - Documentation of safety training must note the presenter, a brief description of the topics covered, 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. Ongoing safety training must take place each calendar year. Documentation of this training must be signed and dated by the employee.
Safety Incident Reporting

- Safety-related incidents must be documented and submitted to the Laboratory Manager or designee. 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

  a. Submitted safety incident reports must be reviewed and signed by the Laboratory Manager or designee 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.

  b. 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.

*Note:* To maintain employee confidentiality, all personal identifiers must be removed prior to submission to the QM team.

References:

29 CFR § 1910.1200


Refer to manufacturer’s websites for downloadable MSDS. Other websites for downloading MSDS are also available on the internet (i.e., [http://www.msds.com](http://www.msds.com), [http://www.msdssearch.com](http://www.msdssearch.com)).

12. Laboratory Information Systems

A. Introduction to Laboratory Information Systems

Clinical laboratories perform the laboratory tests, endpoint assays, and point-of-care testing as requested by physicians or as directed by clinical trial protocols. These laboratories must often generate the correct 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 of test ordering, delivery of necessary specimens to 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, report generation, and QC functions (e.g., Laboratory Data Management System, or LDMS). Reports generated by the LIS must be concise, readable, standardized in format, and chronological.
B. Standards for Laboratory Information Systems

Laboratory Information System Validation
The laboratory must maintain documented validation data for the LIS. All steps and results of validation must be documented and available for review.

- Document the installation of new computer programs when first installed. Any changes or modifications to the system must also be documented, and the laboratory director or designee must approve all changes before they are released for use.
- Document testing of all possible anticipated permutations of processes (for example, entry of normal, abnormal low, abnormal high, critical and absurd results).
- Document testing and validation of all calculations that are performed by an LIS.
- Document the validation of all data transmitted from the LIS to other computer systems and their output devices.
- Document the verification of reference ranges and comments as well as actual testing results.
- Document a validated emergency preparedness system.

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

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 result is entered into the LIS, the system must provide an audit trail to document each person involved (includes 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.

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 those 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 employees who will use the system should 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 employees’ access codes as a database from which hard-copy reports may be created.
  - User access codes should be inactivated upon termination of an employee. The user code, once inactivated, should not be used for another employee.
  - User codes must not be shared with coworkers.
• 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.

Documentation
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 staff as well as the daily operations of the Information Technology staff. Current use of LIS must match policy and procedure documents.
• The purpose of the computer program, the way it functions, and its interaction with other programs must be clearly stated.

Technical Support and Preparedness
The laboratory must have a documented back-up 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 staff and/or vendor for the system including emergency contact information.
• Documented procedures and disaster-preparedness plan 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 back-up data
  - Procedures for restoring information from backed-up media
  
  Note: The procedures must specifically address the recoverability of study-participant information, the physical environment, and equipment.
• The LIS should be run in a closed environment, as much as is practical, to protect participant confidentiality.

References:
21 CFR § Part 11
College of American Pathologists Commission on Laboratory Accreditation, Accreditation Checklists, 2012.
13. Quality Management

A. Introduction to 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 quality and study-participant safety is being maintained.

External Quality Assurance (EQA) is an integral component of a total QM Program. EQA specimens must be analyzed, quality assured 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.

B. Standards for Quality Management

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 (are) 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 staff
  - 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:
    a. Key indicators must reflect activities that are critical to and/or have a significant impact on study-participants or study outcomes.
b. **Examples of key indicators**: Test turnaround time, specimen acceptability, test order accuracy, safety events.

c. The number of key indicators monitored by a laboratory should be proportional to the scope of the laboratory's services.

d. The laboratory must record investigation of key indicators and record corrective and/or preventive actions taken.

e. 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).

**Note**: Please refer to Appendix 14 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 the laboratory director or designee(s). 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 report
  - 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

**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 or standards. All findings (of both compliance and noncompliance, or deficiencies) that result from the internal audit should be documented in an organized format to allow for appropriate corrective actions and follow-up through resolutions.

**Testing Turnaround Times**

The laboratory must have a list of assay turnaround times readily available to all laboratory staff as well as to customers of the laboratory.

**Laboratory Communication Plan**

The laboratory must have a non-retaliatory policy for employees to communicate concerns regarding testing quality or laboratory safety to laboratory management.
C. Standards for External Quality Assurance

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

- Laboratories should enroll in EQA programs that cover all study protocol analytes.
  - 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 designee.
- EQA specimen testing should be rotated among staff members.
- The laboratory director (or equivalent) or designee must review all external quality assurance data.
  
  Note: Documentation of the designee must be included in the current QC or QM program.
- Regular supervisory review of EQA Program results must be evidenced by
  - Signature and date of review of all results, and
  - Documentation of corrective action taken and appropriate preventive action in response to any unacceptable results.
- 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, split study-participant specimens analyzed by a reference or other laboratory, use of assayed material, or correlation testing of a back-up 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.
  
  Note: 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.

References:
42 CFR § 493.1233
42 CFR § 493.1701
College of American Pathologists Commission on Laboratory Accreditation, Accreditation Checklists, 2012.
**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.

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Glossary

accession: The process of identifying a specimen and entering a unique specimen identifier into laboratory records

accuracy: A measure of how close a measured value is to the true value

alert values: See critical values

aliquot: A portion of a specimen or product used for testing

aliquotting: The action of dispensing a product or specimen into smaller quantities. A portion of this product or specimen (aliquot) is typically used for testing or placed into long term storage.

American National Standards Institute: 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: Organization that develops and generates voluntary standards that are used worldwide (http://www.astm.org)

AMR: Abbreviation for Analytical Measurement Range

analyte: The substance being measured in an analytical procedure

Analytical Measurement Range: The range of analyte values that a method can directly measure on the specimen (without any pre-treatment not included as a procedural step of the assay)

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

analytical sensitivity: The estimate of the lowest concentration of an analyte that can be measured

analytical specificity (Analytical interferences): The estimate of the systematic error caused by other materials that may be present in the specimen being analyzed (e.g., lipemia, drugs)

ANSI: Abbreviation for American National Standards Institute

ASTM: Abbreviation for American Society for Testing and Materials

audit: An activity to determine through investigation the adequacy of, and adherence to, established procedures, instructions, specifications, codes, and standards or other applicable contractual and licensing requirements, and the effectiveness of implementation

audit trail: Documentation that allows reconstruction of the course of events

authorized persons/personnel: The staff designated by an authorizing organization that is responsible for a work activity’s technical and administrative objectives
**back up copy**: A magnetic copy of data, software, user-developed application, or operating parameters associated with an automated system and not considered the original

**benchmark**: A specific standard against which some aspect of performance can be compared

**blood-borne pathogens**: Microorganisms that are present in human blood and cause diseases in humans; while HBV, HCV, and HIV are specifically identified in the standard, the term includes any pathogenic microorganism that is present in human blood or other potentially infectious material that infects and causes diseases in persons who are exposed to blood containing the pathogen.

**calibrator**: A material of known composition or properties used for calibration of an analytical instrument or procedure.

**calibration**: The demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements

**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.

**certification**: Documented testimony by qualified authorities that a system qualification, calibration, validation, or revalidation has been performed appropriately and that the results are acceptable. Personnel certification is proof that a person has achieved a certain level of qualification.

**CFR**: Abbreviation for Code of Federal Regulations

**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

**Chemical Hygiene/Hazard Communications**: A written program developed and implemented that sets forth procedures, equipment, personal protective equipment (PPE) and work practices that are capable of protecting employees from the health hazards presented by hazardous chemicals used in that particular work place

**CLIA**: Clinical Laboratory Improvement Act/Amendments, 1988: Clinical Laboratory Improvement Act of 1967 (and amendments of 1988) which sets the guidelines for any clinical laboratory which tests material obtained from human clients, i.e., blood, tissue, swabs, etc. CLIA is administered through the U.S. Health Care Financing Administration (HCFA).

**Clinically Reportable Range**: The range of analyte values that a method can measure with additional pre-treatment of the original specimen and which thereby extends the reportable range of an assay/methodology

**Closed Information System**: A laboratory information system that requires no input from sources outside of the facility or its realm of control (i.e., all entries are made by the site’s laboratory staff; opposite of an Open Information System.)
**Code of Federal Regulations**: The general body of regulatory laws governing practices and procedures performed by federal administrative groups

**Coefficient of Variation (CV)**: A statistical representation of the precision of a test. The CV is often expressed as a percentage of the ratio of the standard deviation to the mean, (standard deviation/mean) X 100.

**competence**: Demonstrated ability to apply knowledge and skills

**compliance**: The act or process of fulfilling requirements

**confidentiality**: Prevention of disclosure, to other than authorized individuals, of information which is considered private

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

**control chart**: A graphic representation of a measured variable showing process generated control limits and data values as plotted points (See also Levy-Jennings Chart)

**control material**: A control solution that is available whose concentration is already known

**corrective action**: Steps that are taken to remove the cause(s) of a detected nonconformity or other undesirable situation in order to prevent recurrence or to achieve quality improvement at any stage of the process

**critical values**: Results that require prompt, rapid clinical attention to avert significant study-participant morbidity or mortality

**CRR**: Abbreviation for Clinically Reportable Range

**Curriculum Vitae**: A summary of academic and professional history and achievement.

**deficiency**: A situation in which a prescribed action was not carried out or an applicable requirement was not met

**designee**: One who has been indicated as responsible for a particular responsibility

**detection limit**: Lowest concentration of an analyte that can be reliably detected

**diagnostic assay**: Testing performed to aid in medical diagnosis (e.g., Hepatitis B Surface Antigen)

**Document Control Plan**: Description of steps to manage individual documents throughout their progression of development, including creation, organization, versioning, access control, and archiving

**documentation**: Written material that provides proof of work performed and/or and event that occurred

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

**engineering controls**: Well-designed work areas and equipment that minimize or eliminate exposure to hazards

**EQA**: Abbreviation for External Quality Assurance
**External Quality Assurance**: An external evaluation and comparative assessment of a laboratory’s analytical performance or proficiency in conducting laboratory assays. See also proficiency testing.

**FDA**: Abbreviation for Food and Drug Administration

**GLP**: Abbreviation for Good Laboratory Practice

**Good Laboratory Practice**: A world-wide quality management system for the design, conduct and reporting of studies in support of licensing/ product registration of drugs/food/chemicals for human or veterinary use

**guidelines**: A statement or other indication of policy or procedure by which to determine a course of action

**IATA**: Abbreviation for International Air Transportation Association.

**IND**: Abbreviation for Investigational New Drug.

**Investigational New Drug**: A drug that is under study but does not yet have permission from the U.S. Food and Drug Administration (FDA) to be legally marketed and sold in the United States.

**inspection**: The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources

**Key Indicators**: A significant and descriptive factor that reflects activities critical to patient outcome, affect a large proportion of the laboratory's patients, or that have been problematic in the past

**Laboratory Data Management System**: An information system that manages the collection, storage, and transportation of samples from clinical research units to either the researching laboratory or the specimen repository; the system is capable of recording the tracking steps of the specimen from the point of collection to the final disposition as consumed, discarded, or long-term storage

**Laboratory Information System**: consists of computer hardware, software, and data; it performs or assists with functions of test ordering, delivery of necessary specimens to 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, report generation, and QC functions

**LDMS**: Abbreviation for Laboratory Data Management System

**Levy Jennings Chart**: A commonly used control chart in which individual control measurements are plotted directly on a chart with limit lines drawn either as mean ± 2s or mean ± 3s. Time is displayed on the x-axis usually in terms of days or runs. This chart is used to assess precision as it reflects on the stability for a specific assay.

**licensure (certification)**: The granting of legal permission to provide a specific service by a regulatory body to an organization that meets certain expectations

**LIS**: Abbreviation for Laboratory Information Systems

**lot**: A quantity of homogeneous material assembled from uniform components under similar conditions that function in a uniform manner
**Material Safety Data Sheets**: Information provided by manufacturers describing the chemical and physical properties of a substance as related to its safe handling and storage

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

**mean**: The simplest statistic, an average, is calculated by adding all related data points, then dividing the resulting sum by the number of data points that were added together

**method validation**: The process of testing a measurement procedure to assess its performance and to validate that performance is acceptable

**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.

**morbidity**: The state of carrying a disease or the relative incidence of a disease

**mortality**: The number of deaths in a given time or place, within a population

**MSDS**: Abbreviation for Material Safety Data Sheet

**NIST**: Abbreviation for National Institute of Standard and Technology

**noncompliance**: A situation in which a requirement is not met

**non-waived test**: Laboratory tests that are not classified as 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)

**normal range**: By convention, the normal range is set to cover 95% of values from a normal population. Normal range has been replaced by the more neutral term, reference values. See reference range.

**OECD**: Abbreviation for Organization for Economic Cooperation and Development

**Open Information System**: A laboratory system that allows entry of information, such as orders or test results, from a remote location and by a third party; requires access to the onsite information system via internet, networking, or interfacing. Opposite of Closed Information System.

**Organization for Economic Cooperation and Development**: The OECD groups 30 member countries sharing a commitment to democratic government and the market economy. Best known for its publications and its statistics, its work covers economic and social issues from macroeconomics, to trade, education, development and science and innovation. In regards to GLP, “The primary objective of the OECD Principles of GLP is to ensure the generation of high quality and reliable test data related to the safety of industrial chemical substances and preparations in the framework of harmonising testing procedures for the Mutual Acceptance of Data (MAD)”. ([http://www.oecd.org](http://www.oecd.org))

**package insert**: The written pamphlet in every diagnostic test kit which includes instructions for proper use of the kit. In addition, the package insert contains some or all of the following: information on intended use; summary and explanation of the test; principles of the procedure; reagents provided; special precautions; specimen collection, storage and transport; materials provided/not provided with kit; procedural limitations; performance characteristics; results; and QC.
**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

**Personal Protective Equipment**: Specialized clothing or equipment worn by an employee to protect against health and safety hazard

**point-of-care testing**: A test conducted by a health professional during a patient encounter. Test results are typically available a few minutes after the specimen is collected.

**post-analytic variables**: Steps in the overall laboratory process between completion of the analytic phase of testing and results receipt by the requesting physician

**PPE**: Abbreviation for Personal Protective Equipment

**pre-analytic variables**: Steps in the process prior to the analytic phase of testing, starting with the physician’s order

**precision**: A measurement of the scatter or random error between repeated measurements expressed statistically as the standard deviation

**preventive (or preventative) actions**: Steps taken to eliminate the causes of a potential nonconformity or other undesirable situation in order to prevent occurrence

**preventive (or preventative) maintenance**: A time or cycle-based program with planned maintenance activities to prevent equipment malfunctions

**primary laboratory**: Laboratory determined to the main site of performing specimen assays for a given protocol; this laboratory is typically a local laboratory, often physically located on the site of the clinical trial facility

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

**proficiency testing**: The determination of laboratory performance by comparing and evaluating calibrations or tests on the same or similar items or materials by two or more laboratories in accordance with predetermined conditions

**QA**: Abbreviation for Quality Assurance

**QAU**: Abbreviation for Quality Assurance Unit

**QC**: Abbreviation for Quality Control

**QM**: Abbreviation for Quality Management

**qualitative tests**: Determining the presence or absence of analytes in the specimen without assigning numerical values

**Quality Assurance**: All the planned and organized activities implemented within the laboratory system to provide adequate confidence that the test results provided are as accurate and reliable as possible

**Quality Assurance Plan**: The document that provides guidance for the operation of a laboratory. This document generally contains, but is not limited to, information pertaining to: laboratory personnel, sampling procedures and sample rejection criteria, sample handling and chain-of-custody routines, the equipment employed by the laboratory, analytical methods, validation and reporting, calibration and QC procedures, equipment
maintenance, routine procedure for precision and accuracy, method validation, verification and corrective actions, and health and safety policy and training.

**Quality Assurance Unit**: Any person or organizational element, except the study director, designated by testing facility management to perform the duties relating to quality assurance of non-clinical laboratory studies (21CFR58.3)

**Quality Control**: The part of quality management focused on operational techniques and activities to determine whether the process exhibits nonrandom variation

**Quality Management**: Coordinated activities to direct and control an organization with regard to quality.

**Quality Management program**: Any management system that addresses all areas of an organization, emphasizes customer satisfaction, and uses continuous improvement methods and tools

**quantitative tests**: The accurate numerical determination of the quantity of an analyte present in a specimen

**Reagent Grade Water**: Water suitable for use in making up critical reagents or for use in sensitive analytical procedures

**reference intervals**: See reference range

**reference materials**: A material or substance in which one or more properties are sufficiently well established to be used for the calibration of an apparatus, for the assessment of a measurement method, or for assigning values to materials

**reference range**: The specified interval bound by two limiting values that contains 95% of the values found in healthy individuals. See Normal range.

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

**regulation**: A requirement having the force of law

**requirement**: Any rule, order, regulation, law, policy, or contractual agreement that directs or compels a specific action

**reportable range**: The useful analytical range of a laboratory method, i.e., the lowest and highest test results that are reliable and can be reported

**result modification**: Reports that contain any changes to study-participant results, accompanying reference intervals and interpretations, or study-participant identifiers, but not minor typographical errors that are not of any clinical consequence

**risk assessment**: The establishment of a relationship between the risks and benefits of potential hazards to which people may be exposed by identifying potential failure modes, determining severity of consequences, identifying existing controls, determining probabilities of occurrence and detection, and evaluating risks to identify essential control points

**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.

**self-assessment**: An assessment performed by the responsible organization to determine how well it is performing its job and meeting its responsibilities
**sensitivity**: The probability that a test will detect an analyte when it is present in a specimen

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

**SOP**: Abbreviation for Standard Operating Procedure

**source documentation**: Original documents, data, and records in electronic and hard copy formats

**specificity**: The probability that a test will be negative when an analyte is absent from a specimen

**sponsor**: The company, institution, government agency, group or individuals who assumes financial and legal responsibility for a clinical trial; the sponsor is also responsible for supervising and overseeing the trial

**stability**: The extent to which a product retains the same properties and characteristics that it possessed at the time of manufacture, throughout storage, and use

**standard**: A material of reference of known purity whose concentration is already known to a high degree of accuracy

**standard deviation**: A statistical measure of variation used to describe a frequency distribution; the square root of the average of the squared deviations from the mean; to calculate a standard deviation, the data points are first averaged, then this mean value is subtracted from each data point, giving the “difference score”; these difference scores are then each squared, and the squared difference scores are added together; the sum of the squared difference scores is then divided by the number of original data points less one, or “n-1”; a square root of the resulting quotient is the standard deviation

**Standard Operating Procedure**: Detailed, written instructions to achieve uniformity of the performance of a specific function

**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

**tolerance limits**: Specified interval giving upper and lower boundaries of permissible values

**traceability**: The ability to relate an identifiable measurement or value to a known standard, through an unbroken chain of comparisons all having stated uncertainties

**turnaround time**: Length of time from when a sample arrives in the laboratory and when the final result is issued to the ordering physician

**validation**: See verification

**verification**: The formal process of confirming and documenting that specified requirements have been met

**unmodified FDA-approved test**: 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**: Test that can be performed by technical personnel as well as non-technical personnel, and either in a clinical or non-clinical setting; the test is simple, relatively error-proof, and if error should occur, the test would cause little or no harm.
The tests that are listed in the original regulation are: (1) Dipstick or tablet reagent urinalysis (non-automated) for bilirubin, glucose, hemoglobin, ketone, leukocytes, nitrite, pH, protein, specific gravity, and urobilinogen; (2) Fecal occult blood; (3) Ovulation tests-visual color comparison tests for human luteinizing hormone; (4) Urine pregnancy tests-visual color comparison tests; (5) Erythrocyte sedimentation rate--non-automated; (6) Hemoglobin--copper sulfate--non-automated; (7) Blood glucose by glucose monitoring devices cleared by the FDA specifically for home use; (8) Spun microhematocrit; and (9) Hemoglobin by single analyte instruments with self-contained or component features to perform specimen/reagent interaction, providing direct measurement and readout. Since that time, new tests and methods are regularly gaining the designation of waived status; the manufacturers should provide documentation regarding the status of methods. The website for the Centers for Disease Control and Prevention (http://www.cdc.gov/index.htm) also contains up-to-date information regarding additions and revisions of testing complexity statuses.
References


Appendix Descriptions

Appendix 1: Template of a Study Plan Used for a Specific Laboratory Endpoint Assay
Quality First Laboratory officials have determined that a recently received study protocol is not adequate in addressing all tasks and processes that must be carried out by its laboratory personnel when working with clinical trial specimens. For this case, they have decided to create a formal laboratory-specific supplement in the form of an analytical or study plan. In order to ensure the plan describes all laboratory-specific components of the trial, defining study objectives and design for the conduct of the study within the laboratory setting, they will use a template to develop the study plan.

Appendix 2: Training Attendance Log
Velma Jones, fictitious manager of Quality First Laboratory, wishes to train the key operators on the ChemSmart 2000, by Ingenious. In an effort to capture full documentation of the training, she creates a training attendance log (TAL). This sample training attendance log provides an appropriate level of documentation for the training given to employees of the laboratory. This training log captures important details of the training such as topics, trainer information, and appropriate signatures verifying that the training was given/received. This log may be kept with personnel files for easy retrieval.

Appendix 3: Example of Signature Sheet
Within Quality First Laboratory, personnel often use their initials to document performance of a task; the laboratory information system employs “tech codes” to log identities of personnel who execute functions, such as result entry, within the system. Velma Jones, Laboratory Manager, must be able to quickly identify personnel by their printed initials or tech codes. This sample key is useful in linking signatures, initials, and tech codes (if applicable) as these identifiers are used throughout the laboratory’s documentation, to a legible printed name. This key ensures complete audit-ability of laboratory records.

Appendix 4: Example of SOP in CLSI Format
As a component of implementing a new assay within Quality First Laboratory, a stepwise procedure must be created for this assay to ensure consistently correct performance of the testing and to provide a reference to personnel for additional assay information. This SOP for HDL Cholesterol demonstrates an example of a standard format that is compliant with CLSI recommendations for SOP creation. Note the components of the procedure as they relate to the SOP format guidelines given in Section 5: Testing Facility Operation. Use of this or a similar format will also ensure ease of use of the SOP and consistency throughout a laboratory’s entire collection of SOPs.

Appendix 5: L-J Chart Example
Quality First Laboratory must document the results of all Quality Control runs. This Levy-Jennings (LJ) control chart is an example of an appropriate chart that may be utilized by personnel to document QC data. This chart allows for plotting of results by date of the month (on the horizontal or X-axis) according to these results’ relationships to pre-established value means, ± one standard deviations (the calculated standard deviation multiplied by positive one and negative one), ± two standard deviations (standard deviation multiplied by positive two and negative two), and ± three standard deviations (standard deviation multiplied by positive three and negative three).
A chart is created for each QC material used. The calculated mean and standard deviation results are manually entered for the corresponding fields on the vertical or Y-axis. This chart may also be created to record results by run number if multiple runs are performed on a given date. When completed appropriately, this record will also capture other vital QC documentation such as the control material description/lot number and routine managerial review.

These charts are used to document QC data to allow for determination of acceptability of QC run, and to aid in detection of shifts and trends in control data. The charts are a quick visual representation that assists with the evaluation of rule failures (e.g., if Westgard rules are employed by a laboratory, the graphing of data supports identification of 1-2S, 2-2S, and etc. failures). Often, the type of rule failure will assist with determining appropriate troubleshooting steps to effectively resolve the contributing instability within the testing system.

Appendix 6: Quality Control Log Example
The QC log, as represented in this appendix sample, is a very close companion to the LJ Control Chart above. This sample QC log allows for Quality First Laboratory’s recording of the control material run information (date, time, technologist, and result) and links the data to the accompanying LJ chart. This document also allows for recording interpretation of the acceptability for the QC run and provides for complete documentation of appropriate corrective action.

The documented corrective action then becomes a tracking mechanism to help in discovery of larger testing system trends and issues with stability, and also allows users to review corrective action steps taken in the past to resolve similar issues they may be currently facing.

Like the LJ chart, this record will also capture the other vital QC documentation such as lot numbers, acceptable range, SD, and routine managerial review.

Method Validation
In the event a laboratory adopts a new method or assay, method validation must be performed. Typically, the experiments are performed in the following order:

- Reportable Range
- Analytical Sensitivity (if applicable)
- Precision, within-run
- Analytical Specificity (if applicable)
- Precision, across-runs
- Accuracy
- Reference Interval

The following example follows one course of action that could be taken by a fictitious laboratory, named Quality First Laboratory, and its manager, Velma Jones, to validate a cholesterol assay performed on a new analyzer acquired by the laboratory, the ChemSmart 2000, manufactured by Ingenious.
Appendix 7: Example of Reportable Range Experiment Results
This linearity evaluation example represents a set of tables that allows entry of an experiment’s results from analysis of five samples (CLSI recommends a minimum of five) that have assigned concentrations.

Quality First’s Laboratory Manager, Velma Jones, wishes to validate the manufacturer’s data regarding the useful analytical range (lower and upper limits of test results that are reliable for reporting purposes) of the new cholesterol method as it is performed on the ChemSmart 2000.

• Initially for this experiment, Ms. Jones obtains a standard kit that contains five samples with known (or assigned) concentrations of cholesterol that span the range documented by the manufacturer.

• Next, Ms. Jones performs five replicate tests for cholesterol on each sample.

• Ms. Jones then enters any descriptive information for the assay into the set of tables (e.g., analyte, method, units of measurement). Ms. Jones also inputs the definition (name or description) of the materials used and their assigned concentrations. Finally, she inputs the four replicate results obtained for each known sample.

  Note: Grey fields within the table indicate input cells (information or result entry fields).

• The set of tables calculates the mean, percent recovery (ratio of result obtained to assigned concentration), a linearity forecast (given the other data points for the curve, the expected result at a given concentration), and % bias (the relative difference between the forecast and the result obtained) for each of the five samples. These calculated values may assist Ms. Jones in discovering deviations from linearity (e.g., percent recovery for one set of replicates is very different from those of the rest of the sets, the forecast is dramatically dissimilar from the mean obtained, or the percent bias varies greatly for a set of data points). The table also creates a Linearity Scatter Plot and Percent Recovery Plot for user review.

• Upon review of the data and the plots, Ms. Jones may then enter her assessment of the linearity of each of the five samples and her overall evaluation of the assay’s linearity.

• Conclusion: In this experiment, Ms. Jones determines from a visual review of the graph of her experiment’s results, given the known concentrations available, which have verified linearity of the cholesterol to 995 mg/dL. The calculated values support her determination in that there are no outliers among the percent recoveries, the linearity forecast, and % bias. Ms. Jones and the laboratory director must then determine if this is comparable to the manufacturer’s data and sufficient for Quality First’s requirements.

Appendix 8: Example of Analytical Sensitivity Experiment Results
If the lower detection limit must be verified for the cholesterol assay, this example of the analytical sensitivity experiment results represents a table that allows the user to document verification of the manufacturer’s published sensitivity. This experiment will approximate the lowest concentration of cholesterol that Quality First Laboratory can expect to be able to measure with the ChemSmart 2000.

• Initially, Quality First’s Laboratory Manager, Velma Jones, determines from the package insert that the manufacturer’s (Ingenious) published sensitivity for cholesterol on the ChemSmart 2000 is 10 mg/dL, and that Ingenious
determined this sensitivity employing Lower Limit of Detection (LLD) methods based on 2 standard deviations. She enters this information into the table.

**Note:** Grey fields within the table indicate input cells (information or result entry fields).

- Next, Ms. Jones determines that the “blank” sample she will use for this experiment is the cholesterol diluent provided by the manufacturer; the blank sample contains no cholesterol. She also creates a “spiked” sample (using a material with a known standard concentration of cholesterol), creating a known concentration of 10 mg/dL cholesterol, to reflect the manufacturer’s published detection limit. She enters this information into the appropriate cells of the table.

- Ms. Jones then performs twenty replicates (minimum of 10 replicates recommended for statistical validity) of cholesterol for both the “blank” and “spiked” samples.

- Finally, Ms. Jones records the measurement response (raw data) generated by the method for the “blank” and “spiked” samples, and enters them appropriately into the table.

- The table then calculates the uncertainty in estimate of blank and spiked sample by multiplying the number of standard deviation(s) used by the manufacturer by the calculated standard deviations of the measured responses of the blank and spiked samples, respectively.

- The table then calculates the Calibration Factors by subtracting the mean of the blank measurements from the mean of the spiked sample measurement, then multiplying the resulting difference by the concentration of the spiked sample.

- The minimum detection limits are then calculated using the uncertainty and the calibration factors.

- In the case of Ms. Jones’s calculated results, the Lower Limit of Detection that has been calculated must now be compared with the manufacturer’s published LLD.

- Conclusion: In her experiment, Ms. Jones produced an LLD of 2.02 mg/dL (a value that is well below that of the manufacturer’s published LLD). Ms. Jones has therefore verified the manufacturer’s LLD.

**Note:** The table will also allow for comparison to Biological Limit of Detection (BLD), or Functional Sensitivity, if these methods were used by the manufacturer to determine analytical sensitivity.

**Appendix 9: Example of Precision Experiment Results**

This example of Precision Validation represents a sample set of tables that evaluates both short-term (within run) and long-term (across runs) precision for two specimens.

Velma Jones, Laboratory Manager, wishes to estimate the random error associated with performing the cholesterol assay on the ChemSmart 2000. She wants to determine the variability of repeat measurements and compare her laboratory’s analyzer with the performance guidelines (or data) published by the manufacturer, Ingenious.

- First, Ms. Jones decides to analyze control materials QualityTrol I and QualityTrol II for both short- and long-term components of this experiment. She based her choice for the number of materials on the levels of concentrations that are critical for the medical use of cholesterol. She chose controls over
study-participant samples as specimens for precision testing based on the convenience and the quantity of materials.

- Next, Ms. Jones enters the assay descriptive information (e.g., the analyte, unit of measure, method), and the sample information (e.g., name/description).
  Note: Grey fields within the table indicate input cells (information or result entry fields).
- She then performs the 20 within-run replicates (widely accepted as sufficient statistically, while maintaining costs); then she enters the results on the appropriate pages of the set of tables for each of the two specimens.
- Ms. Jones then assigns to team members the continued performance of the 20 across-run replicates for each of the two samples over a longer period of time (minimum of five days, introducing as much variation with environmental and operator conditions as is reasonable to represent a realistic working environment for the testing system). She enters these results on the appropriate pages of the set of tables for the two specimens.
- Finally, Ms. Jones enters the Ingenious’s data of precision (found in the package insert or in published method specifications) and the CLIA-defined Allowance for Total Error (this information may be found at http://www.westgard.com/clia.htm; 10% for cholesterol).
- The set of tables calculates the mean, standard deviation, and coefficient of variation for each set of results. It calculates outliers for each set of results based on an internal comparison of result with a running Standard Deviation “Index”, and displays a precision plot for each set. The set of tables also creates a report that includes the within-run and across-run statistics for each specimen; in addition this report compares the data to the manufacturer’s data and CLIA’s Allowance for Total Error.
- Conclusion: In the case of the sample data, the standard deviations and coefficients of variation would appear to be comparable to the manufacturer’s data for both within-run and across-run components. Likewise, the experiment passes on all counts for total error allowance. Ms. Jones and the laboratory director must evaluate the report data to determine if this performance is acceptable by comparison with the manufacturer’s data and sufficient for Quality First’s requirements.

Appendix 10: Analytical Specificity Experiment Results
If the analytical interferences (or analytical specificity) for an assay must be verified, this example represents a table that allows documentation of the results of these analytical specificity experiment(s).

Results of these experiments will assist Ms. Jones, Laboratory Manager, in approximating the systematic error caused by non-analyte (non-cholesterol, in this example) components/characteristics of specimens, such as icterus when performing the new cholesterol assay on these specimens. These experiments may also give Ms. Jones additional information regarding systematic error issues she may encounter when performing the accuracy experiments.

- Initially, Ms. Jones decides to verify that there is no interference from hemolysis, lipemia, and icterus for the cholesterol. She creates a table for each of these potential interferents, and enters the assay descriptive information as before (e.g., assay name, method, units of measure). The example reflects the studies she performed for lipemia effects on the cholesterol.
Note: Grey fields within the table indicate input cells (information or result entry fields).

- Next, Ms. Jones decides to use normal saline as a diluent (it contains no hemoglobin) for the purposes of this experiment. She also uses a known concentration of 1000 mg/dL Liposyn® III standard to perform the experiment. She inputs this information into the table.
- Ms. Jones then decides to create two sets of 1:2 dilutions of 10 samples: one set with the diluent and the other set with the interferent. The resulting concentration of Liposyn® III is then 500 mg/dL. She enters this information into the table.
- Next, the cholesterol assay is performed on the resulting total of 20 samples in duplicate, and all of the results are entered by Ms. Jones.
- Ms. Jones also enters the upper limit of the reference range and the allowable systematic error (from CLIA) for the assay into the appropriate cells.
- The table calculates the differences between the specimen/diluent mixtures and the specimen/interferent mixtures; it then calculates the average interference of the ten sets of data.
- Conclusion: The table calculates the allowable error at the upper limit of the reference range and evaluates the performance of the assay’s experimental results. In Quality First’s case, the lipemia at concentrations of 500 mg/dL is verified to not be an interferent at patient results of 130 mg/dL. This “Pass” evaluation is based on the fact that the calculated average interference is less than the allowable error at the upper reference range limit.

Appendix 11: Example of Accuracy Experiment Results
This example of Accuracy Validation represents a sample set of tables that allows comparison of the new cholesterol assay as performed on the ChemSmart 2000 with that of the analyzer currently in place within Quality First Laboratory. The comparison of methods will allow Velma Jones, Laboratory Manager, to approximate the systematic error (reflecting both proportional and constant error) that is inherent in the new assay. This comparison will also assist Ms. Jones in determining if the two assays will produce clinically comparable results.

- First, Ms. Jones enters the assay’s descriptive information (e.g., the analyte under investigation, reporting units, and the methods being compared for this experiment) into the set of tables.
  Note: Grey fields within the table indicate input cells (information or result entry fields).
- Ms. Jones then proceeds to analyze 40 samples (as recommended by Clinical and Laboratory Standards Institute) in duplicate (provides a check for validity of results) on both the comparative (reference) method and the test method over a period of days (five minimum per Clinical and Laboratory Standards Institute). These 40 samples should span the reportable range of the testing system, including abnormally low, normal, and abnormally high results, if applicable. She enters these samples’ results into the appropriate cells within the set of tables, along with specimen and run information (e.g., identification, date, time).
The set of tables calculates the means associated with each result pair, calculates the accompanying linear regression statistics, and creates comparison and bias plots.

Conclusion: Ms. Jones then reviews the statistics and plots, and enters her visual check of the comparison graph. In this case, she determines that the plot is linear. Ms. Jones and the laboratory director must now determine if the regression statistics and comparisons between the two methods are acceptable for Quality First’s requirements, or if additional steps must be taken.

Appendix 12: Example of Reference Range Experiment Results
This reference interval (normal range) verification example represents a set of tables that will assist Velma Jones, laboratory manager, in determining if the manufacturer’s reference intervals may be transferred to Quality First Laboratory during this final step of the performance specification verification. The verification of reference intervals is an important conclusion to the validation process in that it supports the interpretation of patient test results.

Ms. Jones enters the assay information (analyte name, method, units of measure) and the specimen identifiers from 20 pre-defined normal patients using inclusion/exclusion criteria (the minimum for transference per Clinical and Laboratory Standards Institute).

Note: Grey fields within the table indicate input cells (information or result entry fields).

Cholesterol assays are performed on all 20 samples, and Ms. Jones inputs the results into the appropriate cells of the set of tables. Ms. Jones must also input the proposed (manufacturer’s) reference interval.

Conclusion: The set of tables calculates the statistical analysis of the data, determines the number of results obtained that fell outside the proposed range, and evaluates the experiment’s results (Pass/Fail). In Quality First’s experiment, the data is evaluated as a “Pass” because no more than 10% of results fell outside of the proposed range, indicating that the reference ranges may be transferred. Velma Jones, Laboratory Manager, along with the Director of the Laboratory, must then assess the appropriateness of the ranges.

A similar set of tables that requires entry of 40 or 80 specimen results may also be necessary to use in the event this experiment fails (i.e., more than 10% of results fall outside of the proposed reference range). An additional set of tables that requires entry of 120 specimen results is necessary to use if reference ranges must be established.

References:

Appendix 13: Example of Laboratory Test Method List
This sample Laboratory Test Method List represents a catalog of available assays. This list is created so that, if requested, clients of the Quality First Laboratory may obtain a directory of assay-specific information that includes the test methods employed by the laboratory, accompanying reference intervals, and other performance specifications.
Appendix 14: Example of Quality Management Plan
This Quality Management Plan represents a comprehensively documented Quality Assurance/Quality Management program for Quality First Laboratory. The plan is written so that the context of the master document may change little from year to year, but the recorded attachment, “Quality Management Monitors,” will change as frequently as necessary to meet the quality requirements of the laboratory.
## Appendix 1: Template of a Study Plan Used for a Specific Laboratory Endpoint Assay

<table>
<thead>
<tr>
<th>Name of Institution</th>
<th>Study Plan</th>
<th>Protocol #</th>
<th>Name of Lab Endpoint Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Version:</strong></td>
<td>1.0</td>
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### Author(s): Name, degree, role in the protocol, affiliation

### Approval:

- **Approved By:** Name, degree, Head of Endpoint Assays
  - Date
- Name, degree, Head Central QAU
  - Date
- Name, degree, Principal Investigator and Study Director
  - Date

### Revision History:

<table>
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<tr>
<th>Version</th>
<th>Description</th>
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</table>
Appendix 1: Template of a Study Plan Used for a Specific Laboratory Endpoint Assay, continued

Protocol #, Name of Lab Endpoint Assay

PURPOSE/GOALS

This document describes the overall plan for the detection of ______ by name of the assay for Protocol #.

CONTENTS

1.0 Authority and Responsibility.................................................................pg
2.0 Distribution and Document Control.......................................................pg
3.0 Key Contacts/Agreements......................................................................pg
4.0 Introduction and Background...............................................................pg
5.0 Definitions.............................................................................................pg
6.0 Reagents and Materials.........................................................................pg
7.0 Specimens and Shipping.......................................................................pg
8.0 Instrumentation......................................................................................pg
9.0 Assay Protocol.......................................................................................pg
10.0 Analytical Plan (Statistical Analysis).....................................................pg
11.0 Timeline.................................................................................................pg
12.0 Record Keeping Specifics.....................................................................pg
13.0 References............................................................................................pg

1.0 Authority and Responsibility

The Head of Endpoint Assays, the Head of the Central QAU for the Endpoint Assay Laboratory, and the Principal Investigator of the provide name of the laboratory here have the authority to establish this procedure and are responsible for its implementation.

The Study Plan must be reviewed by the Central QAU.

The Central and Local QAUs are responsible for the distribution of this document (as described below).
Appendix 1: Template of a Study Plan Used for a Specific Laboratory Endpoint Assay, continued

Name of Institution
Study Plan
Protocol XX Name of Lab Endpoint Assay

2.0 **Distribution and Document Control**

This Study Plan may be distributed only by the name of Institution Laboratory Program QAU. It will be distributed to authorized personnel as described in the SOP for Writing and Implementing Study Plans. This Study Plan MUST NOT be copied and re-distributed by any of the primary recipients without prior authorization from the name of the Institution Laboratory Program Manager or the Director of the Laboratory Program.

3.0 **Key Contacts/Agreements**

Name(s), degree, affiliation

4.0 **Introduction and Background**

Protocol # is a phase____ to evaluate_____________________.
The name of the assay proposed in this study plan will help assess_____________.
This assay is composed of provide a brief description of the assay here.

5.0 **Definitions**

Provide key definitions (e.g., vaccine product being tested in the protocol)

6.0 **Reagents and Materials**

Reagents and materials specific to the name of the assay for Protocol # are listed here. For more detailed information refer to institution SOP for this assay.

7.0 **Specimens and Shipping**

7.1 Specimen collection and processing
Indicate here:
Type of specimens collected
Type of containers used to collect samples
Labs/sites where specimens will be collected
Processing of specimens by labs/sites if applicable
Shipping from where to where (explain if shipping will include sending specimens to a central lab or facility for repository/re-distribution)
Other specific information pertaining to specimens and shipping
Appendix 1: Template of a Study Plan Used for a Specific Laboratory Endpoint Assay, continued

<table>
<thead>
<tr>
<th>Name of Institution</th>
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</thead>
<tbody>
<tr>
<td>Study Plan</td>
</tr>
<tr>
<td>Protocol XX Name of Lab Endpoint Assay</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7.2 Specimen Assay Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of the assay will be performed on all/subgroup/#/etc participants during the following schedule: indicate hours, days, months when assay will be conducted and their corresponding visit #. Indicate if special testing requirements are needed (e.g., positive signal during the first time point will determine further testing).</td>
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</table>

<table>
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<tr>
<th>8.0 Instrumentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>List equipment needed for name of the assay. Reference SOP for name of the assay for further details.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>9.0 Assay Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provide information of validation conducted for name of the assay as described in the name of the institution SOP. Provide any specific/relevant information regarding a special reagent or step needed for name of the assay. Provide information on the controls used in name of the assay (reference SOP for name of the assay for details)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>10.0 Analytical Plan (Statistical Analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Describe in detail the statistical analysis to be performed on the data set.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>11.0 Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Describe in detail the schedule of events (testing, obtaining results, statistical analysis, report of results) to be followed from the beginning to the end of the Study Plan.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>12.0 Record Keeping Specifics</th>
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</thead>
<tbody>
<tr>
<td>Include information on:</td>
</tr>
<tr>
<td><strong>12.1 Checklist</strong></td>
</tr>
<tr>
<td>Each assay will have a corresponding checklist. The checklist identifies the reagents’ lots used and confirms that each procedure’s step is done correctly.</td>
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</tbody>
</table>
Appendix 1: Template of a Study Plan Used for a Specific Laboratory Endpoint Assay, continued

<table>
<thead>
<tr>
<th>Name of Institution</th>
<th>Study Plan</th>
<th>Protocol XX Name of Lab Endpoint Assay</th>
</tr>
</thead>
</table>

Each checklist is signed by the technician performing the procedure as well as a witness.

Storage: The checklist is kept in the technician’s notebook (located in the laboratory) with the readout for each assay.

12.2 Raw Data
Indicate if raw data will be kept electronically (describe the system) and if it will also be stored as signed hard copies that will be kept in a protocol-specific notebook in the laboratory for each technician.

12.3 Data Calculation and Transfer
Indicate if data calculation is needed and if transfer of electronic and/or hard copies) will occur to authorized personnel (describe this staff).

13.0 References
Provide a list of SOPs and other documents cited in the Study Plan.
Training Attendance Log

Subject:
ChemSmart 2000: Key Operator Training

Description:
This classroom program is a comprehensive operational training course for the key operator of the Ingenious ChemSmart 2000. All aspects of operation and system maintenance are demonstrated and practiced during this 4-day course.

Topics/objectives include:

13.1.1 Communication with the System through the Control Unit
13.1.2 Interpretation of the error messages and appropriate actions
13.1.3 How to load reagents through Reagent Management and Configuration
13.1.4 Configuration features of the System through Options
13.1.5 Basic understanding of Diagnostics
13.1.6 Set up and review of quality control files through Quality Control
13.1.7 Use of stored patient data once samples have been run through Review Results
13.1.8 Calibration

Trainer: Velma Jones, MT

Date(s): 05, 06 May 2006

Continuing Education Units (if applicable): N/A

<table>
<thead>
<tr>
<th>Attendee Name</th>
<th>Attendee Signature*</th>
<th>Date Attended:</th>
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* By signing this Training Attendance Log, I confirm my attendance to the session(s) as detailed above. I understand that this training session will, if applicable, be followed by required demonstration of competencies I obtained during this training. These competency assessments will be recorded on a separate document.
Appendix 3: Example of Signature Sheet

Quality First Laboratory
123 Sunny Hospital Street
Johannesburg
South Africa

Signatures and Initials Key

<table>
<thead>
<tr>
<th>Name</th>
<th>Tech Code</th>
<th>Signature</th>
<th>Initials</th>
<th>Date of Signature</th>
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<tr>
<td>Frank Lee</td>
<td>111</td>
<td>Frank Lee</td>
<td>FAL</td>
<td>01Jan05</td>
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<td>Janice Wall</td>
<td>112</td>
<td>Janice Wall</td>
<td>JMW</td>
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<td>Beth Collins</td>
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<tr>
<td>Clyde Moore</td>
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Form Approved By: Laboratory Director

Review Date | Revision Date | Signature
-------------|---------------|-------------
APPENDIX 4: Example of SOP in CLSI Format

Quality First Laboratory
123 Sunny Hospital Street
Johannesburg
South Africa

Title: Serum/Plasma HDL Cholesterol, ChemSmart 2000® Chemistry System
Total Pages: 9
Origination Date: 03 December 2001
Effective Date: 08 August 2004
Prepared By: Velma Jones, MT
Supersedes Procedure Dated: 03 Dec 2001

Approved By: Frank Lee, Laboratory Director
Date: 08 August 2004
Approved By: Daphne Lane, M.D., Medical Director
Date: 08 August 2004

Distributed To
Quality First Chemistry
Quality First Phlebotomy

# of Copies
1
1

PURPOSE:
The HDL method used on the ChemSmart 2000® clinical chemistry system is an in vitro diagnostic test intended for the quantitative determination of high density lipoprotein cholesterol in serum and plasma.

PRINCIPLE:
The HDL Cholesterol assay is a homogeneous method for directly measuring HDL levels without the need for off-line pretreatment or centrifugation steps. The method is in a two-reagent format and depends on the properties of a unique detergent, which solubilizes only the HDL cholesterol lipoprotein particles, thus releasing HDL cholesterol to react with cholesterol esterase to produce color.

HDL measurements are used as an aid in the diagnosis of lipid disorders.

SCOPE:

Quality First Laboratories
Appendix 4: Example of SOP in CLSI Format, continued

SPECIMEN:

Type: Serum or Heparinized plasma  
Source: Venous blood collected by peripheral venipuncture  
Amount to be collected: 2 mL whole blood preferred, 1 mL minimum  
Collection Container: Red-top or green top tubes  
Sample Size: 28 µL

Patient Preparation:
Blood should be collected after a 12-hour period of fasting by normal procedures. Normal procedures for collecting serum and plasma may be used for samples to be analyzed by this method. Please refer to Specimen Collection Standard Operating Procedure located in the Phlebotomy Procedures Manual.

Specimen Handling Conditions:
Serum or plasma should be removed from cells within three hours of venipuncture. Serum or plasma may be refrigerated at 2-8°C for up to three days if not tested within 24 hours. For longer pre- or post-analytical storage, samples may be frozen at -20°C for up to one month or at -70°C for up to two years.

EQUIPMENT AND MATERIALS:

Analyzer or Test Kit: 
ChemSmart 2000® Chemistry Analyzer

Reagents and Media: 
Required Reagents and Media:  
HDL reagent cartridges, Cat. No. ABC may be obtained by ordering directly from Ingenious.

Special Safety Requirements:  
Used cuvettes contain human body fluids; handle with appropriate care to avoid skin contact and ingestion. For in vitro diagnostic use only.

Reagents and Media Preparation: 
Reagent cartridges are ready for use. Any reagent preparation is performed on board the clinical chemistry analyzer.

Storage Requirements:  
All reagents and test materials for this test are stored (at 2-8°C) in the main refrigerator located in the chemistry department. Overflow reagents are stored in the gray door refrigerator (at 2-8°C) located in the chemistry department. Refer to the carton for the expiration date of individual unopened reagent cartridges. Sealed or unhydrated cartridge wells on the instrument are stable for 30 days. Once wells 1 through 3 have been entered by the instrument, they are stable for 3 days. Once well 4 has been entered by the instrument, it is stable for 10 days. Once wells 5 and 6 have been entered by the instrument, they are stable for 15 days.
Appendix 4: Example of SOP in CLSI Format, continued

Supplies:
The HDL Cholesterol test also requires the following supplies:
Disposable pipettes, analyzer pipette tips, sample cups, gauze, and cuvettes.

EQUIPMENT CALIBRATION:

Calibration Details:
- Assay Range: 10 – 150 mg/dL
- Reference Material: HDL Calibrator, Cat. No. DEF
- Suggested Calibration Levels: 0, 50, 165 mg/dL
- Calibration Scheme: Three levels in triplicate
- Calibration Frequency: Every new reagent cartridge lot. Every 3 months for any one lot
- Assigned Coefficients: C0 0.000  C1 2.000

Performing a Calibration:
1. To access the calibration software, from the Main Operating menu on the analyzer monitor,
   b. Press Calibration.
   c. Press SETUP and RUN.
2. Select the test method to be calibrated.
3. Enter all information on the screen.
   a. Press QC yes/no to change to yes.
   b. Press Assign cups.
   c. Press Load/run.
4. Load samples as indicated on the load list.
5. Press RUN.

Reviewing a Calibration:
1. To access the calibration software, from the Main Operating menu on the analyzer monitor,
   - Press Process Control.
   - Press Calibration.
   - Press Enter.
   - Press Review Data.
2. Select the test to be reviewed.
Appendix 4: Example of SOP in CLSI Format, continued

3. Press **Calculate**.
4. Evaluate m (slope) and b (intercept) using the following guidelines:
   
   **Acceptance Criteria for Use in Review of Calibration:**
   
   - Precision: No obvious outliers
   - Slope (m): Calibrated: Linear: 0.97-1.03
     Logit: 0.95-1.05
   - Intercept (b): Close to zero or clinically insignificant
   - Correlation Coefficient (r): 0.990-1.000
   - Quality Control (QC): within acceptable range

5. Press **Accept Data** or **Reject Data**.
6. Enter QC into the laboratory computer system if run along with the calibrators.

**Troubleshooting Calibrations:**
1. Ensure you are using the correct calibrator insert sheet for the lot you are calibrating.
2. Review calibrator preparation, storage conditions, and the expiration date on the calibrator product’s package insert sheet. For the lyophilized products, the preparation steps must be followed precisely.
3. Check that the sample cups were loaded into the segments in the correct order. If not, press **Reject Data** and rerun the calibration.
4. Review instrument maintenance logs and the system counters screen for overdue maintenance. Check the cycle count for the sample probe tip, especially if the problem is on a method with low sample volume.
5. Check that all temperatures are within range on the Daily Maintenance screen. Check the temperatures with a calibrated thermometer using the temperature calibration procedures in Module 3: Maintaining in the *ChemSmart 2000® Operator’s Guide*.
6. Compare the C4 term on the calibration Review Data screen to the C4 value on the method insert sheet. If it is not the same, contact the Technical Assistance Center. Only logit methods have a C4 term.
7. If calibration problem remains unresolved, contact the Chemistry Resource Technologist or the site Manager.

**QUALITY CONTROL:**

**Frequency**
Perform QC runs at least once daily

**Number of Control Materials**
Solutions at two levels of a QC material with known concentrations
Appendix 4: Example of SOP in CLSI Format, continued

Description of Control Materials
QualityTrol Unassayed Chemistry Control (Human), Levels 1 and 2 supplied by Ingenious, catalog # 601 and 602.

Storage of Control Materials
QualityTrol Unassayed Chemistry Controls are stable until the expiration date when stored unopened at -10º to -20º C. Once thawed and opened, all analytes will be stable for 6 days when the control is stored tightly capped at 2-8º C.

Preparation and Handling of Control Materials
QualityTrol Unassayed Chemistry Controls should be treated the same as patient specimens. Before sampling, allow the control to thaw completely at room temperature for 15-20 minutes. Once thawed, gently invert the vial 4-5 times to ensure homogeneity and use immediately. Do not use a mechanical mixer.

Control Criteria
QC ranges are established using the laboratory’s cumulative mean as well as the peer group reported standard deviation. QC is reviewed weekly by the key operator and submitted monthly for manager and peer review.

If control values are unacceptable, do not report patient results; instead:
1. Determine whether the QC failure(s) is/are the result of systematic or random error, and troubleshoot based on this determination.
2. Implement corrective action based on investigation results.
3. Rerun QC materials to evaluate effectiveness of corrective action. If issue resolution is successful, perform patient testing and determine accuracy of patient results released since the last successful QC run. If repeat of the QC run is unsuccessful, repeat steps 1–3 as necessary to resolve issue(s).
4. Document all steps taken, both successful and unsuccessful attempts at resolution.

HDL CHOLESTEROL TESTING PROCEDURE:

Instructions for Processing Samples

Bar-Coded Tubes
1. Place bar code labels on tubes. 10 mL tubes may be put directly in a segment with the bar code facing the bar code reader. 7 mL and 5 mL tubes must be placed in appropriate adaptors. Brown adaptors are for 7 mL tubes; green adaptors are for 5 mL tubes. Check for sufficient sample volumes using the tube fill gauge.
2. Short bar-coded tube samples can be transferred into the clear plastic small sample containers (SSC). The SSC is then put in the corresponding bar-coded sample tube. Place tubes in segments with the bar codes facing the bar code reader.

Sample Cups
3. Samples without bar codes can be put in plastic sample cups and placed in either brown or green adaptors. Enter patient information manually.
4. Urine and CSF specimens can be processed in sample cups. Patient information must be entered manually. Place in either brown or green adaptors.
5. Manually entering patient information:
Appendix 4: Example of SOP in CLSI Format, continued

a. From the main operating menu, press **Enter Data**.
   - **POSITION** Enter the segment letter (if applicable) position that you want to use.
   - **PATIENT NAME** Enter the name (if applicable).
   - **SAMPLE NO** Enter the patient accession number (if applicable).
   - **LOCATION** Entry optional.
   - **TEST** Select test by pressing method keys on keyboard.
   - **MODE** Select the sample container you are using. Sample cup primary tube, SSC, etc.
   - **PRIORITY** Routine, stat, etc.
   - **DILUTION** Enter the dilution factor (if applicable).
   - **FLUID** Serum, urine, plasma, or csf.

b. To run a single specimen, enter the patient information. Place the specimen in the segment position you have selected and press **Process Single**.

c. If you have more than one sample to enter manually, press **New Sample** after each entry. After entering all samples, press **Load List**. Place samples in the designated segment positions and press **Run**.

d. Segments that are in use are highlighted in red at the top of the screen. Any segments in red should not be taken off the instrument.

e. To initiate processing of down-loaded samples:
   - From the Sample Status screen, move the cursor to the double-asterisked sample.
   - Enter the segment position for the sample.
   - Press **Enter**.
   - Load barcoded samples.
   - Press **Run**.

f. The cursor will change to a box.
   - Enter the segment position for the sample.
   - Press **Enter**.
   - Load barcoded samples.
   - Press **Run**.

7. Sampling, reagent delivery, mixing, processing, and printing of results are automatically performed by the ChemSmart 2000® system. For details of this processing, refer to your ChemSmart 2000® system manual.

**METHOD PERFORMANCE SPECIFICATIONS**

**Analytic Sensitivity**
The sensitivity of the HDL method is 10 mg/dL, and is defined as the concentration at two standard deviations above the mean of the Level 1 Chem1 Calibrator (0 mg/dL). See package insert for detailed information regarding the analytic sensitivity.

**Analytic Specificity**
Interference from icterus (bilirubin 60 mg/dL), hemolysis (hemoglobin 1000mg/dL), and lipemia (1000mg/dL) was less than 10 %. See package insert for detailed listing of substances having no measurable effect on the HDL method.

**Reportable Range**
10 – 150 mg/dL

**Dilution Protocols**
- Maximum dilution for samples: 1:10
- Diluent: Normal Saline
Appendix 4: Example of SOP in CLSI Format, continued

CALCULATIONS

Formulas:
cLDL is a reported chemistry test that is calculated and not directly measured by the analyzer.
Calculate the cLDL by the following formula:

\[
cLDL = Chol - HDL - vLDL \\
vLDL = \frac{Trig}{5}
\]

Examples:
Chol = 185 mg/dl  
LDL = 185 – 45 - (300 ÷ 5)  
Trig = 300mg/dl  
LDL = 185 – 45 - 60  
HDL = 45mg/dl  
LDL = 80 mg/dl

Calculation Notes:
Calculation is inaccurate with triglyceride > 400mg/dl. In such cases, ultracentrifugation at a specialized lab may be desired.

EXPECTED RESULTS

The instrument automatically calculates and prints the concentration of HDL in mg/dL using the calculation scheme illustrated in your ChemSmart 2000® system manual. Reportable ranges as determined by Quality First and Quality First Satellite laboratories:

Results are reported in mg/dL and rounded to the nearest whole number.
Normal range: HDL = >35 mg/Dl

INTERPRETATION OF RESULTS

cLDL cholesterol normal range: < 130 mg/dl is desirable
Borderline High Risk 130 – 159 mg/dl
High Risk >159 mg/dl

The National Cholesterol Education Program recommends against use of combined risk factor indices. Each risk factor should be evaluated separately

PROCEDURE NOTES, REFERENCES, AND ATTACHMENTS

Procedure Notes:
Fibrin in the sample may cause sampling problems. Rim the sample with a wooden applicator to remove the fibrin. Re-spin the sample and re-analyze.
Routine test orders should be completed within four hours from collection.
Stat test orders should be completed within one hour from collection. If testing will be delayed beyond these limits, the attending physician or nurse must be notified and the specimen stored appropriately.
Appendix 4: Example of SOP in CLSI Format, continued

References:
2. Gotto Am. Lipoprotein metabolism and the etiology of hyperlipidemia, Hospital Practice 1988; 23: Suppl.1, 4.
4. NIH Consensus Conference, Triglyceride, high-density lipoprotein, and coronary heart disease, JAMA 1993; 4:505-510.

Attachments:
1. ChemSmart 2000 ® Maintenance Log
2. ChemSmart 2000 ® Calibration Worksheet
3. ChemSmart 2000 ® Reagent Log

DOCUMENT RETENTION

ChemSmart 2000® Maintenance log is kept in the QC/Maintenance notebook at the analyzer. This is to be stored for the life of the instrument plus seven years. ChemSmart 2000® Calibration Worksheet is kept in the Calibration notebook. This is to be stored for seven years.

<table>
<thead>
<tr>
<th>Review Date</th>
<th>Revision Date</th>
<th>Signature</th>
</tr>
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<tbody>
<tr>
<td>07 August 2005</td>
<td></td>
<td>Frank Lee</td>
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END
Appendix 4: Example of SOP in CLSI Format, continued
Quality First Laboratory
ChemSmart 2000 ® Maintenance Log
Month: ______________________ Year: ______________________

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<th>Daily Maintenance Task</th>
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<th>As Needed Maintenance</th>
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<td>Wash Cuvettes</td>
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Reviewed: ______________________ Date: ______________________

Good Clinical Laboratory Practice Standards 75 of 105
Final Version 3.0, 09 July 2013
Appendix 4: Example of SOP in CLSI Format, continued

<table>
<thead>
<tr>
<th>Acceptable Ranges:</th>
<th>Lot #</th>
<th>Slope (m)</th>
<th>Intercept (b)</th>
<th>Correlation Coefficient (r)</th>
<th>QC Acceptable? (Y/N)</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear: 0.97 – 1.03</td>
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<td></td>
<td>Approx. 0</td>
<td>0.990 – 1.000</td>
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<td></td>
</tr>
<tr>
<td>Logit: 0.95 – 1.05</td>
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<td></td>
<td>-Or- Clinically Insignificant</td>
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</table>

Date

Reviewed: ___________________________ Date: ___________________________

Reviewed: ___________________________ Date: ___________________________
Appendix 4: Example of SOP in CLSI Format, *continued*

Quality First Laboratory
ChemSmart 2000 ® Reagent Log
Reagent Name: ____________ Order Number: ________

<table>
<thead>
<tr>
<th>Lot #</th>
<th>Date Receive</th>
<th>Expiration Date</th>
<th>Date 1&lt;sup&gt;st&lt;/sup&gt; Calibration</th>
<th>Comments</th>
<th>Initials</th>
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</table>

Reviewed: ____________ Date: __________

Reviewed: ____________ Date: __________
Appendix 5: L-J Chart Example

Levy Jennings Quality Control Chart
Analyzer: ChemSmart 2000 Month/Year: July 2006
QC Material/Level: QualityTrol Level 1 Lot Number: ABX-128
Date:

Reviewed:
## Levy Jennings Quality Control Log

**Analyzer:** ChemSmart 2000  
**Month/Year:** July 2006  
**QC Material/Level:** QualityTrol Level 1  
**Lot Number:** ABX-128  
**Mean Value:** 150  
**SD Value:** 5.0  
**Units:** mg/dL  
**Acceptable range:** 140 to 160

<table>
<thead>
<tr>
<th>Date</th>
<th>Time (HHMM)</th>
<th>Tech Initials</th>
<th>Result</th>
<th>Plotted on LJ Chart? (Y/N)</th>
<th>Acceptable? (Y/N)</th>
<th>Corrective Action Log/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0815</td>
<td>FAL</td>
<td>151</td>
<td>Y</td>
<td>Y</td>
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<tr>
<td>2</td>
<td>0900</td>
<td>BKC</td>
<td>148</td>
<td>Y</td>
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<td>0823</td>
<td>VJ</td>
<td>149</td>
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<tr>
<td>7</td>
<td>0805</td>
<td>VJ</td>
<td>139</td>
<td>Y</td>
<td>Y</td>
<td>1-2S rule failure; warning only, will observe closely</td>
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<td>8</td>
<td>0810</td>
<td>FAL</td>
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<td>Y</td>
<td>N</td>
<td>2-2S failure; shift possible, lamp damaged; replaced lamp, next run of 150 acceptable</td>
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Reviewed by: ________________________________  Date of Review: ________________________________
Reviewed by: ________________________________  Date of Review: ________________________________
Appendix 7: Example of Reportable Range Experiment Results

**Linearity Evaluation**

<table>
<thead>
<tr>
<th>Linearity Material</th>
<th>Assigned Concentration</th>
<th>Accuracy/Recovery Mean</th>
<th>Accuracy/Recovery % Recovery</th>
<th>Linearity Forecast</th>
<th>Linearity % Bias</th>
<th>Visually Linear?</th>
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<tbody>
<tr>
<td>Level 1 Standard 1</td>
<td>25</td>
<td>23.0</td>
<td>92.0</td>
<td>15.8</td>
<td>-31.4</td>
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<td>Level 2 Standard 2</td>
<td>100</td>
<td>95.0</td>
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<td>91.0</td>
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<td>Level 3 Standard 3</td>
<td>250</td>
<td>225.0</td>
<td>90.0</td>
<td>241.3</td>
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<td>Level 4 Standard 4</td>
<td>500</td>
<td>495.0</td>
<td>99.0</td>
<td>491.9</td>
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<td>Yes</td>
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<tr>
<td>Level 5 Standard 5</td>
<td>1000</td>
<td>995.0</td>
<td>99.5</td>
<td>993.1</td>
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<td>Yes</td>
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**Experiment Results**

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<th>Level 1</th>
<th>Rep 1 Result</th>
<th>Rep 2 Result</th>
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**Regression Analysis**

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<th>Intercept</th>
<th>Standard Error</th>
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<td>1.00233871</td>
<td>-9.277016129</td>
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**Visual Check for Linearity:** Yes
**Analyst:** Velma Jones
**Date:** 4-Apr-06

Approval: Date:
Appendix 7, continued
Linearity Scatter Plot

![Linearity Scatter Plot](chart.png)
Appendix 7, continued
Linearity Percent Recovery

% Recovery

Assigned Concentration (units)
Appendix 8: Example of Analytical Sensitivity Experiment Results

### Sensitivity Experiments

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Units</th>
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<tr>
<td>&quot;Blank&quot; Material Used:</td>
<td>0 mg/dL</td>
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<tr>
<td>Spiked Sample 1:</td>
<td>10 mg/dL (Note: should represent manufacturer’s detection concentration)</td>
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</tbody>
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### Experiment Results

#### Measurement Response

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<th>Replicate #</th>
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<th>Spiked Sample 1</th>
<th>Spiked Sample 2</th>
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<td>1</td>
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<tr>
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</tr>
<tr>
<td>20</td>
<td>1100</td>
<td>2025</td>
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</table>

**Lower Limit of Detection**
- Manufacturer's Multiple of SD used in determination of LLD: 2
- Uncertainty in Estimate of Blank: 200.1 measurement response
- Calibration Factor: 1 mg/dL per 99.095 measurement units
- **Minimum Detection Limit (LLD): 2.02 mg/dL**

**Biological Limit of Detection**
- Manufacturer's Multiple of SD used in determination of BLD: 2
- Uncertainty in Spiked Sample: 399.8 measurement response
- Calibration Factor: 1 mg/dL per 99.095 measurement units
- **Minimum Detection Limit (BLD): 6.05 mg/dL**

**Functional Sensitivity**
- SD in Concentration Units, Spiked Sample 1: 2.02 mg/dL
- **CV Spiked Sample 1:** 20.2 %
- Note: Target for CV is 20% to determine Functional Sensitivity.
- Additional Spiked Samples may have to be analyzed until desired 20% CV reached.
- **Functional Sensitivity:** 10 mg/dL
- SD in Concentration Units, Spiked Sample 2: 
- **CV Spiked Sample 2:** %
Appendix 9: Example of Precision Experiment Results

### Short-Term Precision

<table>
<thead>
<tr>
<th>Method</th>
<th>Selectra XL</th>
</tr>
</thead>
<tbody>
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<td>Biosmart</td>
</tr>
<tr>
<td>Analyte</td>
<td>Cholesterol</td>
</tr>
<tr>
<td>Units of Measure</td>
<td>mg/dL</td>
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<td>Date</td>
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</tr>
<tr>
<td>Analyst Name</td>
<td>Velma Jones</td>
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#### Experiment Results

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<th>Outlier?</th>
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<td>211</td>
<td>-0.7</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
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#### Precision Plot

![Precision Plot]

#### Preliminary Estimate of Precision, Short Term

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<td>CV%</td>
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Appendix 9: Example of Precision Experiment Results, continued

Long Term Precision

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Experiment Results

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Preliminary Estimate of Precision, Long Term

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Precision Plot

Good Clinical Laboratory Practice Standards
Final Version 3.0, 09 July 2013
Appendix 9: Example of Precision Experiment Results, continued

Precision Evaluation

Method: ChemSmart 2000
Manufacturer: Ingenious
Analyte: Cholesterol
Units of Measure: mg/dL

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Short-Term (within run)

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Manufacturer’s Data (within run)

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CLIA Allowance

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<tr>
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Long-Term (across runs)

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<tbody>
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<td>1.2</td>
</tr>
<tr>
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Manufacturer’s Data (across runs)

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CLIA Allowance

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Approval: ________________________________

Date: ________________________________
Appendix 10: Example of Analytical Specificity Experiment Results

Analytical Specificity

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<th>mg/dL</th>
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<td>Resulting Concentration:</td>
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Experimental Results

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<th>Result</th>
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<th>Volume</th>
<th>Volume</th>
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Differences Between Diluent and Interferent

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</table>

Average Interference: 12.5 mg/dL
Upper Reference Limit: 130
Allowable Systematic Error (%): 10
Allowable Error at Upper Reference: 13
Pass / Fail: Pass
Approval: Date:

Analyst: Velma Jones
Date: 4-Apr-06
### Appendix 11: Example of Accuracy Experiment Results

#### Accuracy (Method Comparison)

**Analyte:** Cholesterol  
**Units of Measure:** mg/dL

#### Experiment Results

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### Regression Analysis

- **Slope**: 0.498
- **Intercept**: 0.618
- **Standard Error**: 1.397
- **Correlation Coefficient**: 1.000

**Visual Check for Comparison**: YES

**Approval**:  
**Date**:  

---

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Appendix 11, continued
Comparison Graph (Scatter Plot, Means of Replicate Results)
Appendix 11, continued
Bias Plot for Means of Replicate Results
## Appendix 12: Example of Reference Range Experiment Results

### Verification of Reference Interval

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Analyst: Velma Jones  
Date: 4-Apr-06

### Statistical Analysis

- **Mean:** 145.2  
- **Standard Deviation:** 7.13  
- **Median:** 145.5  
- **Range:** 135 to 160

### Reference Interval

- **Proposed:** 125 to 155  
- **Number of Results Less Than 125:** 0  
- **Number of Results Greater Than 155:** 2  
- **Total Results Outside Proposed Range:** 2  
- **Percentage Results Outside Proposed Range:** 10%  
- **Pass/Fail:** Pass

### Approval:

Date: ________________________________
Appendix 12: Example of Reference Range Experiment Results, continued

Verification of Reference Interval

**Analyte:** Sodium  
**Method:** ChemSmart 2000

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Analyst:  
Date:  

**Statistical Analysis**  
Mean: 142.725  
Standard Deviation: 11.35  
Median: 143.5  
Range: 121 to 160

**Reference Interval**  
Proposed: 125 to 155  
Number of Results Less Than 125: 6  
Number of Results Greater Than 155: 6  
Total Results Outside Proposed Range: 12  
Percentage Results Outside Proposed Range: 60%  
Pass/Fail: Fail  

Approval:  
Date:  

---

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Appendix 13: Example of Laboratory Test Method List

Quality First Laboratory  
123 Sunny Hospital Street  
Johannesburg  
South Africa

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<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>Rate</td>
<td>50 - 136 U/L</td>
<td>15 – 500 U/L</td>
<td></td>
<td>Routine: 4 hours; STAT: 1 hour</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td>ALT (SGOT)</td>
<td>Rate</td>
<td>19 - 55 U/L</td>
<td>5 – 500 U/L</td>
<td></td>
<td>Routine: 4 hours; STAT: 1 hour</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
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<tr>
<td>AST (SGPT)</td>
<td>Rate</td>
<td>15 - 37 U/L</td>
<td>5 – 500 U/L</td>
<td></td>
<td>Routine: 4 hours; STAT: 1 hour</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td>Bilirubin, Total</td>
<td>Endpoint Colorimetric</td>
<td>0.2 - 1.3 mg/dL</td>
<td>0.05 – 40.0 mg/dL</td>
<td>Hemolysis, any degree</td>
<td>Routine: 4 hours; STAT: 1 hour</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
</tbody>
</table>
### Appendix 13: Example of Laboratory Test Method List, continued

<table>
<thead>
<tr>
<th>Test</th>
<th>Methodology</th>
<th>Reference Ranges</th>
<th>Reportable Ranges</th>
<th>Interferences</th>
<th>Turnaround Times</th>
<th>Specimen Requirements</th>
</tr>
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<tbody>
<tr>
<td><strong>Chemistry</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Blood Urea Nitrogen (BUN)</td>
<td>Colorimetric</td>
<td>7 - 18 mg/dL</td>
<td>1.5 – 50.0 mg/dL</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
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<tr>
<td>Calcium</td>
<td>Colorimetric</td>
<td>8.5 - 10.5 mg/dL</td>
<td>Critical Values: &lt;7.0 or &gt;13.5 mg/dL</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td>Chloride</td>
<td>Integrated Multisensor Technology</td>
<td>98 - 108 mmol/L</td>
<td>50.0 – 155 mmol/L</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
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<tr>
<td>Carbon Dioxide</td>
<td>Enzymatic Endpoint</td>
<td>21 - 32 mEq/L</td>
<td>9 – 40 mEq/L</td>
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<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td>Cholesterol, High Density Lipoprotein</td>
<td>Colorimetric</td>
<td>29 - 83 mg/dL</td>
<td>5 – 400 mg/dL</td>
<td>Lipemia, moderate to gross</td>
<td>Routine: 4 hours</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td>Cholesterol, Total</td>
<td>Colorimetric</td>
<td>&lt;200 mg/dL</td>
<td>5 – 400 mg/dL</td>
<td></td>
<td>Routine: 4 hours</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
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<tr>
<td>Creatinine</td>
<td>Rate</td>
<td>0.5 - 1.2 mg/dL</td>
<td>Critical Values: &gt;9.9 mg/dL</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
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### Appendix 13: Example of Laboratory Test Method List, continued

<table>
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<tr>
<th>Test</th>
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<td><strong>Chemistry</strong></td>
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</tr>
<tr>
<td>Glucose</td>
<td>Colorimetric</td>
<td>72 - 112 mg/dL</td>
<td>10 – 1000 mg/dL</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Critical Values: &lt;50 mg/dL or &gt;350 mg/dL</td>
<td></td>
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<td></td>
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<tr>
<td>Magnesium</td>
<td>Endpoint</td>
<td>1.6 - 2.4 mg/dL</td>
<td>0.1 - 8.0 mg/dL</td>
<td>Hemolysis, any degree</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Critical Values: &lt;1.3 mg/dL or &gt;5.0 mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sodium</td>
<td>Potentiometric</td>
<td>136-146 mmol/L</td>
<td>115 – 165 mmol/L</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
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<tr>
<td></td>
<td></td>
<td>Critical Values: &lt;125 mmol/L or &gt;155 mmol/L</td>
<td></td>
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<tr>
<td>Phosphorus</td>
<td>Colorimetric</td>
<td>2.2 - 4.6 mg/dL</td>
<td>0.5 – 20 mg/dL</td>
<td></td>
<td>Routine: 4 hours; STAT: 1 hour</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Critical Values: &lt;1.5 mg/dL</td>
<td></td>
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<tr>
<td><strong>Chemistry</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Potassium</td>
<td>Integrated Multisensor Technology</td>
<td>3.7 - 5.2 mmol/L</td>
<td>1.0 – 9.0 mmol/L</td>
<td>Hemolysis, any degree</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td>Potassium</td>
<td>Integrated Multisensor Technology</td>
<td>Critical Values: &lt;3.0 mmol/L or &gt;6.0 mmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein, Total</td>
<td>Endpoint Colorimetric</td>
<td>6.1 - 8.0 g/dL</td>
<td>1.5 – 30 g/dL</td>
<td></td>
<td>Routine: 4 hours; STAT: 1 hour</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>Colorimetric</td>
<td>female: 1.9 - 8.2 mg/dL, male: 2.5-9.2 mg/dL</td>
<td>0.5 – 20 mg/dL</td>
<td></td>
<td>Routine: 4 hours; STAT: 1 hour</td>
<td>Serum, or Lithium Heparin Plasma, 0.5 mL</td>
</tr>
<tr>
<td><strong>Hematology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit (HCT)</td>
<td>Calculated by Analyzer</td>
<td>female: 36.0 - 47.0 %, male: 40.0 - 52.0 %</td>
<td>N/A</td>
<td>Hemolysis, any degree</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>EDTA Whole Blood, 1 ml</td>
</tr>
<tr>
<td>Hemoglobin (HGB)</td>
<td>Absorption Spectrophotometry</td>
<td>female: 12.0 - 16.0 g/dL, male: 14.0 - 18.0 g/dL</td>
<td>3.0 – 30 g/dL</td>
<td>Hemolysis, any degree</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>EDTA Whole Blood, 1 ml</td>
</tr>
<tr>
<td>Hemoglobin (HGB)</td>
<td>Absorption Spectrophotometry</td>
<td>Critical Values: &lt;5 g/dL</td>
<td></td>
<td></td>
<td></td>
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</table>
### Appendix 13: Example of Laboratory Test Method List, continued

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<tr>
<td>Hematology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean Corpuscular Hemoglobin (MCH)</td>
<td>Calculated by Analyzer</td>
<td>27.5 - 33.0 pg</td>
<td>N/A</td>
<td>Hemolysis, any degree</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>EDTA Whole Blood, 1 ml</td>
</tr>
<tr>
<td>Mean Corpuscular Hemoglobin</td>
<td>Calculated by Analyzer</td>
<td>32 -36 g/dL</td>
<td>N/A</td>
<td>Hemolysis, any degree</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>EDTA Whole Blood, 1 ml</td>
</tr>
<tr>
<td>Concentration (MCHC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean Corpuscular Volume (MCV)</td>
<td>Calculated by Analyzer</td>
<td>female: 81.0 - 99.0 fl; male: 80.0-98.0 fl</td>
<td>N/A</td>
<td>Hemolysis, any degree</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>EDTA Whole Blood, 1 ml</td>
</tr>
<tr>
<td>Platelet (PLT)</td>
<td>Optical Scatter</td>
<td>145 - 400 K/ml</td>
<td>15 – 1000 K/ml</td>
<td>Lipemia, gross</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>EDTA Whole Blood, 1 ml</td>
</tr>
<tr>
<td>Optical Scatter</td>
<td></td>
<td>Critical Values: &lt;50,000 - &gt;800,000 K/ml</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Red Blood Cell (RBC)</td>
<td>Electrical resistance</td>
<td>female: 4.00 - 5.40 M /mL; male: 4.60 - 6.10 M /mL</td>
<td>1.50 – 15.0 M/mL</td>
<td>Lipemia, gross</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>EDTA Whole Blood, 1 ml</td>
</tr>
</tbody>
</table>
### Appendix 13: Example of Laboratory Test Method List, continued

<table>
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<tr>
<td><strong>Hematology</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>White Blood Cell (WBC)</td>
<td>Optical Scatter</td>
<td>4.8 - 10.8 K/mL Critical Values: &lt;1.0 or &gt;25.0 K/mL</td>
<td>0.5 – 25.0 K/mL</td>
<td>Lipemia, gross</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>EDTA Whole Blood, 1 ml</td>
</tr>
<tr>
<td>Clarity</td>
<td>Manual</td>
<td>Clear</td>
<td>N/A</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
</tr>
<tr>
<td>Color</td>
<td>Manual</td>
<td>Yellow, Straw, Amber</td>
<td>N/A</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>Refractometer, mass gravity meter, or reagent strip</td>
<td>1.001 - 1.035</td>
<td>1.000 – 1.055</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
</tr>
<tr>
<td>pH</td>
<td>Reagent strip</td>
<td>4.5 - 8.0</td>
<td>3.5 – 9.0</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
</tr>
<tr>
<td>Ketones</td>
<td>Reagent strip</td>
<td>Negative</td>
<td>N/A</td>
<td>Bloody specimen, sulfamethoxazole</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
</tr>
<tr>
<td>Glucose</td>
<td>Reagent strip</td>
<td>Negative</td>
<td>N/A</td>
<td>Bloody specimen, sulfamethoxazole</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
</tr>
<tr>
<td>Protein</td>
<td>Reagent strip</td>
<td>Negative, Trace</td>
<td>N/A</td>
<td>Bloody specimen, sulfamethoxazole</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
</tr>
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</table>
### Appendix 13: Example of Laboratory Test Method List, continued

<table>
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<tr>
<th>Test</th>
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<td><strong>Hematology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Bilirubin</td>
<td>Reagent strip</td>
<td>Negative</td>
<td>N/A</td>
<td>Bloody specimen, sulfamethoxazole</td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
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<tr>
<td>Microscopic Examination</td>
<td>Manual</td>
<td>WBC: 0-3 HPF RBC: 0-3 HPF</td>
<td>N/A</td>
<td></td>
<td>Routine: 4 hours; STAT: 1 hour</td>
<td>Urine, no preservatives, 1 mL</td>
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<tr>
<td>Urine Pregnancy</td>
<td>Immunoassay</td>
<td></td>
<td>N/A</td>
<td></td>
<td>Routine: 4 hours; STAT: 30 minutes</td>
<td>Urine, no preservatives, 1 mL</td>
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### Test Methodology

<table>
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<tr>
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<th>Specimen Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3+/CD4+</td>
<td>Flow Cytometry</td>
<td>Absolute Lymphocyte: 1,000 - 4,800/uL</td>
<td>Absolute CD3+ T-Lymphs: 55% - 84%</td>
<td>CD3+/CD4+ T-Lymphs: 690 - 2,540/uL</td>
<td>CD3+/CD4+ T-Helper: 31% - 60%</td>
<td>Absolute CD3+ T-Lymphs: 50 - 5,000/uL</td>
</tr>
</tbody>
</table>

Note: CD3+/CD4+ Flow Cytometry

- Absolute Lymphocyte: 1,000 - 4,800/uL
- CD3+ T-Lymphs: 55% - 84%
- Absolute CD3+ T-Lymphs: 690 - 2,540/uL
- CD3+/CD4+ T-Helper: 31% - 60%
- Absolute CD3+/CD4+ T-Helper: 410 - 1,590/uL
Appendix 14: Example of Quality Management Plan

Quality First Laboratory
123 Sunny Hospital Street
Johannesburg
South Africa

<table>
<thead>
<tr>
<th>Title:</th>
<th>Quality Management Plan – Quality First Laboratory</th>
</tr>
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<tbody>
<tr>
<td>Origination Date:</td>
<td>January 1996</td>
</tr>
<tr>
<td>Effective Date:</td>
<td>04 January 2004</td>
</tr>
<tr>
<td>Written By:</td>
<td>Velma Jones, MT (ASCP)</td>
</tr>
<tr>
<td>Supersedes Policy/Procedure Dated:</td>
<td>26 Sept 2001</td>
</tr>
<tr>
<td>Approved By:</td>
<td>Frank Lee, Network Laboratory Director</td>
</tr>
<tr>
<td>Date:</td>
<td>04 January 2004</td>
</tr>
<tr>
<td>Approved By:</td>
<td>Daphne Lane, M.D.</td>
</tr>
<tr>
<td>Date:</td>
<td>04 January 2004</td>
</tr>
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<tbody>
<tr>
<td>Quality First Laboratory</td>
<td>1</td>
<td>Quality First Satellite Central Laboratory</td>
<td>1</td>
</tr>
</tbody>
</table>

Purpose:
The Quality Management Program is established to fulfill the department’s responsibility to have a planned and systematic program for the monitoring and evaluation of the quality and appropriateness of the laboratory’s contribution to support clinical trials and study participant care. Each section of the laboratory is responsible for identifying important issues in study participant care and safety and for ensuring the integrity of clinical trial data generated within the laboratory.

Responsibilities:
Each member of the Laboratory Staff is responsible for:
- Assuring the quality of work they perform, correcting errors when observed, and suggesting methods to prevent reoccurrence of any observed issues; and
- Assisting in the implementation of the Quality Management Plan.

Each Lead Technologist is responsible for:
- Assisting the Manager in the development and implementation of Quality Management plans,
- Identifying important or potential problems in their sections or shifts of responsibility, and
- Monitoring implemented plans for desired outcomes and reporting follow up activities to the Laboratory Manager.

The Quality Assurance/Quality Control Officer is responsible for:
- Overseeing all areas of Quality Management and facilitating data collection activities conducted within each department section;
Appendix 14: Example of Quality Management Plan, continued

- Documenting activities and reporting these to the Laboratory Management Team, Laboratory Medical Director and Quality Management department; and
- Monitoring follow up activities, assuring that the desired results have been achieved and sustained.

Each Manager is responsible for:
- Identifying important or potential problems in their assigned lab areas;
- Objectively assessing the cause and scope of problems and prioritizing investigations and resolution activities, giving highest priority to those problems with the greatest impact on study-participant care and study trial data;
- Evaluating trends to further identify problem areas;
- Implementing decisions or actions that are clinically useful to address and correct identified problems;
- Monitoring follow up activities, assuring that the desired results have been achieved and sustained; and
- Enhancing communication among co-workers, departments, and physicians in order that interrelated issues receive appropriate and expedited solutions.

The Laboratory Medical Director is responsible for:
- Overseeing ongoing departmental Quality Management activities,
- Ensuring that the program is implemented throughout the laboratory,
- Representing the Medical Staff in clinical issues that impact patient care, and
- Reporting Quality Management activities to appropriate Medical Staff committees.

Scope of Services:
The scope of services of the Clinical Laboratory is defined by the task or analytical workload presented to the Laboratory, and by the needs of the study-participant, sponsors, and those identified by the study protocol.

Laboratory evaluation of specimens is necessary to enable physicians and principal investigators involved in caring for study-participants and conducting clinical trials to monitor study-participants’ progress while under therapy. Routine testing is performed in the Clinical Laboratory, while testing requiring technology not available within the hospital institution is forwarded to accredited Reference Laboratories approved by the Medical staff. A full range of testing is thus available, either in the Laboratory sections of Hematology, Chemistry, Molecular Pathology or at approved reference laboratories.

Important Aspects of Services:
Laboratory testing is dependent upon appropriately collected and positively identified specimens which are either analyzed immediately upon collection, or appropriately transported and preserved for later analysis. To assist the medical staff and hospital personnel who collect specimens, a Laboratory Services Manual is available via electronic format locally and off campus at outreach sites via the internet. Study-participant identification is assured by only collecting specimens on study-participants who are appropriately identified by the policy on identification of study-participants. The study-participant’s name and unique identification number is recorded on each LIS (Laboratory Information System)-generated specimen label. The initials of the individual collecting the specimen, the time of collection, and the date are required for each specimen. Specimens are accessioned into the LIS by manual entry. The progress of each specimen/test is available through the Care Manager system for order entry. Before results are released, pre-processing Quality Assurance ranges are used to evaluate results, such as delta checks, critical values, and technical ranges. Depending on the method/analyzer used for testing, results that pass the established QA checks may be auto-verified or manually released by staff technologists.
Appendix 14: Example of Quality Management Plan, continued

The integrity of the analytical system is crucial to the testing service. This is assured by an appropriate preventive maintenance schedule and the utilization of an extensive QC program to establish the accuracy of the testing as it is performed. Clearly written, legible policy/procedure manuals, which include procedures for maintaining and appraising the function of all department testing modalities concurrent with their use, are available for every process in the department and are located at the site of the testing process. Furthermore, the department participates in inter-laboratory comparison programs to promote uniformity across the field and in proficiency testing programs that assay both the analytical systems and the quality of the individuals operating them.

The credentials and qualifications of both the department and its staff are established in order to underwrite appropriate testing quality. The network laboratories are approved by the College of American Pathologists (CAP). Interim CAP self-inspections are conducted by the laboratory staff in an effort to document and correct deficiencies noted using current CAP guidelines. The interim self-inspection is an important aspect of education and laboratory process improvement. Department personnel have clearly written position descriptions which define credential requirements for each position and establish the credentials of employees in those positions. Continuing education experiences and communication through departmental e-mail are used to keep staff current with the field.

Adequate reporting mechanisms are required to bring department testing to bear on study-participant care. Certain analytical procedures are identified for which abnormal values are defined as critical values and reported immediately to physicians or clinic staff when prompt intervention on the trial volunteer’s behalf may be indicated by an aberrant laboratory value. More routine reporting mechanisms include computer-generated reports printed at the clinics and at outreach sites.

The adequacy of the facility is critical to quality testing. The Quality First Network laboratories maintain technological competence through the utilization of technologically current, well-maintained instrumentation throughout the department, and selected by hospital personnel for its compatibility with the demands of testing in the facility. The Biomedical Engineering department provides maintenance and service by utilizing qualified technical engineers.

Method:

Each department of the Laboratory participates in Quality Management using the following reporting methods:

1. Specific departmental indicators are monitored on a monthly or quarterly basis and are reported at the Department of Laboratory meetings. Each specific indicator is categorized by type, which includes the following:
   - Efficacy
   - Appropriateness
   - Continuity
   - Safety
   - Effectiveness
   - Efficiency
   - Availability
   - Timeliness
   - Respect and Caring

2. The Risk Management Variance Report is used for all laboratory employees to report variations from standard operating procedures and physician concerns relating to all phases of testing (pre-analytical, analytical, and post-analytical). This is completed online utilizing Inciport, a risk management software program, and provides immediate notification to all coordinators, managers, and directors of departments involved. The actions taken are documented within the Inciport system.

Tracking of Variances: Monthly variance reports are given to the Management Team for review and development of action plans if indicated, then forwarded to the laboratory director and the Principal Investigator for review. Specific queries are generated by Risk Management as needed to identify potential problems related to processes or procedures that are identified as High Risk, High Volume, or High Dollar.
Appendix 14: Example of Quality Management Plan, continued

The PDSA Process

After a specific quality issue has been identified by Risk Management Variance Reports or the departmental indicators, a team consisting of individuals directly related to the issue will be formed. Members of the team will meet as necessary to examine the entire process around the particular issue. Members may consist of laboratory personnel and/or personnel from other areas of the hospital. Each team has a facilitator who directs the activities and keeps the team focused on the issue. The clinical laboratory will have Quality Management teams throughout the year as need is identified. All departmental staff members participate in the process as determined by management.

The Laboratory Department’s Quality management plan is based on the Plan/Do/Study/Act (PDSA) method of problem identification and resolution. The plan will:

1. **Plan** the improvement.
   a. Determine benchmarks and best practices.
   b. Describe current practices.
   c. Measure and Analyze.
   d. Generate and choose solutions; use Root Cause Analysis as a tool.

2. **Do** the improvement.
   a. Map out trial run.
   b. Implement trial run.

3. **Study** the results of the improvement.
   a. Evaluate the results.
   b. Draw conclusions.

4. **Act** to consistently achieve any improvements gained and continue to improve the process.
   a. Standardize the change in practice.
   b. Monitor and consistently achieve any improvements gained.

**Communication of findings**

1. Graphical tools are used to communicate quality findings and simplify comparisons across time.
2. Activities, progress, and resolutions are reported to Clinical Outcomes as needed.
3. Monthly variance reports are collated for each department manager.
4. Bulletin boards are utilized to display monthly departmental indicators and other quality management activity information.

**Annual Evaluation**

A summary of the previous years’ activities is performed with recommendation for changes and continuation of activities as indicated by the effectiveness of the overall institutional plan. The summary is forwarded to the Principal Investigator for signed review and a copy is sent to the Quality Management Department.

**Attachments or Appendices**

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<tr>
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<td>GL 05.3</td>
<td>Risk Management Variance Report</td>
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