Laboratory Audits Conducted by NIAID HIV and Other Infectious Diseases Clinical Research Support Services (CRSS) Contractor

The CRSS Core Team is contracted by the Division of AIDS (DAIDS) to perform laboratory audits for Good Clinical Laboratory Practice (GCLP) compliance throughout the world. The DAIDS Laboratory Program staff is responsible for requesting audits. These audits may be triggered due to an immediate need, or may be driven by an established audit visit schedule. CRSS auditors contact the site staff to schedule the date(s) for the audit. An e-mail is then sent to the site staff to introduce the auditor, and confirm the audit date(s). After the audit date(s) are set, a pre-visit letter is provided to the site staff at least 10 calendar days prior to the audit date(s), which describes the agenda for the visit. In addition, a copy of the appropriate audit checklist is provided with the pre-visit letter to the site staff and all appropriate parties specified in the distribution list provided to the CRSS by DAIDS are copied (DAIDS, Network/Non-Network staff, and Patient Safety Monitoring in International Laboratories (pSMILE) staff).

The types of audits performed by CRSS include: General Laboratory, Central/Endpoint Laboratory, Peripheral Blood Mononuclear Cell (PBMC) Processing Laboratory, Histology/Cytology Laboratory, Tuberculosis/Acid-fast bacilli (TB/AFB) Laboratory, and Specimen Repository audits. The customized laboratory audit checklists utilized for each of these audits were developed using GCLP standards and cover regulations from 21 CFR Part 58 (GLP) and 42 CFR Part 493 (CLIA) and are augmented by guidelines from other organizations and accrediting bodies such as the Clinical Laboratory Standards Institute, the College of American Pathologists (CAP), and the International Organization for Standardization (ISO). The checklists take approximately three working days for a laboratory auditor to complete during the audit visit. The following GCLP Principles are covered, as applicable, in each document:

- External Quality Assurance
- Organization and Personnel
- Equipment
- Testing Facilities Operation
- Test and Control Articles
- Verification of Performance Specifications
- Records and Reports
- Physical Facilities
- Specimen Transport and Management
- Personnel Safety
- Laboratory Information Systems
- Quality Management

In addition, an audit of practice versus procedure (Vertical Audit) is conducted during each audit visit, where applicable. This exercise evaluates the accuracy of a particular laboratory in following their established standard operating procedure (SOP) for a particular assay that the auditor selects at the time of the visit, or is requested by DAIDS. When the audit visit is completed, a report is sent to the staff on the distribution list provided by DAIDS within 21 business days. The Distribution list will include DAIDS Clinical Laboratory Oversight Team (DCLOT) members and Network/Non-Network staff and may include pSMILE staff. The resolution of identified deficiencies found during the audit is then conducted between the site, DCLOT, pSMILE, and the Networks/Non-Networks as appropriate.

Laboratory Audit Checklists

There are six different checklists (audit shells) that are used by CRSS laboratory auditors.

All six of the checklists are similar in that they cover the same GCLP principles consistently for each facility type. This construction is in place to assist in the ongoing efforts to establish a global GCLP standard for all DAIDS-funded and/or sponsored laboratories. To that end, there are subtle differences to be noted. These differences are due to the distinct variation in the scope of services provided by each laboratory type. A summary of each audit approach is listed and found along with the corresponding checklists below.

General Laboratory

The General Laboratory Checklist was developed mainly for safety laboratories. This checklist is used globally for clinical trial site-operated, contracted, satellite, and back-up laboratories. It incorporates all of the aforementioned GCLP principles, and requires the auditor to address each principle for all testing activities funded and/or sponsored by DAIDS. This checklist is also used for Point-of-Care (POC) audits.

PBMC Laboratory

The PBMC Laboratory Checklist is tailored specifically for processing laboratories that work with PBMC. The questions are focused on all phases of PBMC testing, with a section dedicated to evaluating the actual performance of the PBMC processing steps versus the approved SOP.

Central Laboratory

The Central Laboratory Checklist is specific for laboratories performing endpoint assays, including non-FDA approved methods. The general checklist questions, as with all the checklists, are included as applicable along with specific topics related to endpoint testing.

Specimen Repository

The Specimen Repository Checklist is unique; although all applicable GCLP principles are covered, the focus is placed on specimen tracking and storage. The auditor is required to report more comprehensively in these areas. For example, in the other laboratory checklists, 5 to 10 random specimens are required to be audited from reception to final disposition. In this checklist, 50 randomly selected specimens will undergo this type of audit.

Histology/Cytology Laboratory

This is a comprehensive checklist specific to laboratories that specialize in Histology and/or Cytology work. It is a detailed checklist that addresses all Histology and Cytology laboratory areas of activity from specimen reception, preparation, examination, results issue, and specimen storage. The equipment section provides detailed questions on all Histology/Cytology equipment used in specimen processing and slide examination.

TB/AFB

This is a comprehensive checklist specific to laboratories performing Mycobacteriology testing such as: TB microscopy, culture, identification, and susceptibility testing. The checklist addresses specialized safety requirements for facilities performing such activities. The Quality Control, Quality Management, and Equipment sections also focus on specific requirements for TB testing.

Distribution of Audit Reports and Resolution

The final version of the laboratory audit report will be issued 21 business days from the end date of the audit to the staff on the distribution list provided by DAIDS that includes DCLOT, Network/Non-Network staff and/or pSMILE staff). Once distributed, the DCLOT staff may request assistance from pSMILE in generating the Action Plan (AP) that lists the audit findings with recommendations for corrective actions. The AP may be reviewed by the Networks/Non-Networks. A final AP is sent by DCLOT to the site staff with a request to respond within a time period deemed reasonable by DCLOT. The expectation is that the site staff will respond to any items in the report deemed to need corrective action by the site staff. The DCLOT, pSMILE, and Network/Non-Network staff will evaluate the response, including any corrective and preventative action (CAPA) measures, as applicable. If the DCLOT, pSMILE, and Network/Non-Network staff find the response or CAPA to be inadequate upon review, additional guidance may be given with a second response required from the site staff. This process will continue until all inadequacies have been addressed, and DCLOT and/or pSMILE will then communicate with the site that the audit report has been resolved.