TITLE: Quality Assurance Unit for GLP Nonclinical Laboratory Studies
SCOPE: Quality Assurance Staff
RESPONSIBILITY: Testing Facility Management, Quality Assurance Auditors
PURPOSE: Monitoring of GLP Studies

I. PURPOSE

1. The purpose of the Quality Assurance Unit for GLP Nonclinical Laboratory Studies (QAU) is to monitor all pre-clinical studies declared to support an application for research or marketing permits for products regulated by the FDA to assure management of the GLP Testing Facility (e.g., Center for Advanced Medical Learning & Simulation, CAMLS) that facilities, equipment, personnel, methods, practices, records, and controls are in conformance with the regulations in Title 21 Code of Federal Regulations of the Food and Drug Administration Part 58 Good Laboratory Practice for Non Clinical Laboratory Studies (21 CFR Part 58).

II. RESPONSIBILITY

1. The QAU is responsible for monitoring each declared non-clinical study to assure GLP testing facility management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with 21 CFR Part 58, testing facility standard operating procedures, and the approved study protocol.

III. PROCEDURES

1. For any given study, the QAU is appointed in writing by the Director of the GLP Testing Facility (e.g., CAMLS CEO) and shall be entirely separate from and independent of the personnel engaged in the direction and conduct of that GLP study. Assignments to each GLP study or function are made by GLP Testing Facility management, and will be indicated in writing.

2. Study Directors must be faculty of the University of South Florida. The Study Director is appointed by the Director of the Testing Facility (e.g., CAMLS CEO) in accord with 21 CFR 58. The Director of the Testing Facility shall replace the study director promptly if it becomes necessary to do so during the conduct of the study.

3. The QAU maintains a Master Schedule sheet of all nonclinical laboratory studies conducted at the testing facility having declared compliance with 21 CFR 58. This Master Schedule, indexed by test article, indicates the date
study was initiated, nature of the study, test article, test system, anticipated audit dates, current status of each study, identity of the sponsor, and name of the study director. The signed printed paper format of the Master Schedule is the official version of this record and will be maintained and archived as such.

4. The QAU maintains separate copies of all research protocols for which it is responsible.

5. The QAU will inspect each nonclinical laboratory study at intervals adequate to assure the integrity of the study and memorialize its inspections. The QAU will:
   a. Prior to the initiation of the study:
      1. Inspect all equipment designated for use in the study to determine that it has been adequately inspected, calibrated and maintained.
      2. Evaluate personnel to insure each individual engaged in the conduct of or responsible for the supervision of a nonclinical laboratory study shall have education, training, and experience, or combination thereof, to enable that individual to perform the assigned functions.
      3. Inspect the testing facility to determine that written SOPs are in place to insure the quality and integrity of the data generated in the course of the study.
      4. Determine the critical phases of the study and schedule audits at appropriate times for quality assurance.
      5. Review and evaluate the study protocol to insure it is complete (see #6).
   b. During the course of the study:
      1. Conduct study audits at the predetermined intervals listed on the Master Schedule.
      2. Re-inspect equipment at intervals to insure it remains calibrated/certified throughout the study for studies of long duration.
      3. Review personnel to assure anyone added to the study is adequately trained to perform their duties.
      4. Periodically submit to the Study Director and management written status reports of each study, noting any problems and the corrective actions taken.
      5. Determine that no deviations from approved protocols or standard operating procedures were made without proper authorization and documentation.
   c. After the conclusion of the study:
      1. Review the final study report to assure that such report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the nonclinical laboratory study.
      2. Prepare and sign a statement to be included with the final study report, which shall specify the date inspections were made and the findings reported to management and to the Study Director.
6. Study protocols are evaluated prior to initiation of the study to assess the following components are adequately described, when applicable:
   a. General Statement:
      1. Study number
      2. Study title
      3. Study objectives/methods
      4. Purpose of study
      5. Sponsor and address
      6. Testing facility and address
      7. Key personnel
      8. Signature of study director
   b. Compliance Statement
      1. GLP compliance
      2. Facility accreditation
      3. Animal Welfare Act
   c. Quality Assurance Monitoring
   d. Protocol Alteration
      1. Amendments procedures
      2. Deviations procedures
   e. Test/Control Articles
      1. Test article name
      2. Preparation of test article
      3. Source of test article
      4. Purity
      5. Stability
      6. Name of control article
      7. Preparation of control article
      8. Source of control article
      9. Stability
   f. Test System
      1. Source
      2. Characteristics
         a. Species/strain
         b. Sex
         c. Body weight
         d. Age
      3. Justification of test system
      4. Number
      5. Date of arrival
      6. Quarantine procedures
      7. Acclimation interval
      8. Method of unique identification
      9. Animal husbandry
         a. Facility conditions (SPF/VAF)
         b. Housing conditions
         c. Environmental conditions
         d. Feed and water description
         e. Food & water source & analysis
      10. Dates for clinical evaluations
      11. Dates for necropsy
   g. Proposed Study Dates
1. Study initiation date
2. Receipt of animals
3. Dates of critical phases
4. Study completion date

h. Test/Control Article Administration
1. Delivery system
2. Route and method
3. Justification of route and method
4. Preparation for administration
5. Concentration test article in carrier
6. Assay of test article
7. Vehicle (if used)
8. Amount of test article required
9. Frequency of administration
10. Method to determine absorption.

i. Experimental Design
1. Group designation
2. Method of group selection
3. Group Characteristics (#, age, sex/group)
4. Interim sacrifice (#/group)
5. Terminal sacrifice (#/group)
6. Types of measurements
7. Frequency of measurements
8. Record to be maintained
9. Specimens to be maintained
10. Statistical analysis

j. Post Mortem
1. Methods of euthanasia
2. Handling of animals found dead or moribund
3. Types of observations/measurements
4. Type of pathology (histology, cytology)
5. Type of laboratory test
6. Specimens to be maintained
7. Records to be maintained
8. Pathology facility, address, personnel
9. Archive location and period

k. Data, Records, and Specimen Retention

l. References

m. Signature Page

7. Study audits are conducted at intervals to assure the integrity of the study and shall consist of:
   a. In-process reviews of procedures to assess the performance of the study in compliance with the study protocol, standard operating procedures, and 21 CFR 58.
   b. Review of animal records such as:
      1. Arrival records
      2. Medical records
      3. Surgical records
      4. Room status sheets
   c. Review of protocol specific records such as:
1. Laboratory test/assay records
2. Surgical records
3. Implantation/Dosing records
4. Data measurement records
5. Test/control article records
6. Sacrifice/Tissue collection records
d. Animal and study protocol records are audited to determine:
   1. Completeness, to insure all data points and observations are accounted for.
   2. Data generated is recorded directly, promptly, and legibly in ink.
   3. All laboratory test, procedures, experimental evaluations, and assays take place as scheduled in the study protocol.
   4. Any changes in entries are made so as not to obscure the original entry, and shall indicate the reason for such change, and all changes are dated and signed at the time of change.
   5. All procedures are carried out accurately as described in the study protocol.
   6. Standard operating procedures are followed throughout the conduct of the study.

8. Final reports are evaluated by the QAU to assure that the report accurately:
   a. Describes the methods of the nonclinical laboratory study.
   b. Describes the standard operating procedures of the nonclinical laboratory study.
   c. Reflects the raw data of the nonclinical laboratory study.

9. Inspections, audits, and reports are memorialized in writing by indicating:
   a. Inspection number
   b. Date of the inspection
   c. Study inspected
   d. Phase or segment of the study inspected
   e. Person performing the inspection
   f. Findings and problems
   g. Any action recommended, and taken to resolve existing problems
   h. Any scheduled date for re-inspection

10. Inspections, audits and reports shall be conducted in the following format:
    a. The QAU periodically inspects, audits and reports on facilities, equipment, personnel, methods, practices, records and controls to insure management of conformance with 21 CFR Part 58 and that no deviations from approved protocols or standard operating procedures are made without proper authorization and documentation. These inspections will take place at intervals adequate to insure the integrity of the study. Any concerns or problems recognized are addressed to the Study Director and management in writing and copied to the Study Coordinator.
    b. The Study Director/Coordinator reviews the concerns and deviations found by the QAU and responds in writing back to the QAU, and they are copied to management, addressing each concern/problem and the corrective action taken within 30 days of the inspection report.
c. Any problems found during the course of an inspection, which are likely to affect the integrity of the study, shall be brought to the attention of the Study Director and management immediately.
d. Deviations from protocol or standard operating procedures without proper authorization and documentation will be memorialized in writing by the Study Director and included in the QAU study records indexed under Study Deviations.
e. The response of the Study Director/Coordination is submitted for review to the QAU which in turn issues a written report stating that the concerns/problems have either been adequately addressed and that no further action is necessary or that further action is needed.
f. All inspections, audits, and report records and their responses will be maintained in the QAU file entitled Audit Reports and archived according to 21 CFR Part 58.

11. All records maintained by the QAU will be in writing, and indexed in the following manner:
   a. Study protocol
   b. Master schedule
   c. Audit reports
   d. Deviations to study protocol
   e. Amendments to study protocol
   f. Background information
   g. Study equipment
   h. Study personnel
   i. Study forms
   j. Interim study reports
   k. Final report

12. All raw data documentation, protocols, specimens, and interim and final reports when archived within the testing facility are indexed to permit expedient retrieval. A testing facility may contract with commercial archives to provide a repository for all materials.

13. The Director of the Testing Facility must identify someone who is responsible for the archives, and only authorized personnel shall enter the archives.