
Guidelines For Good Research Practices in Research Laboratories Conducting Sample Analysis in Support of a Clinical Trial

PURPOSE

The purpose of this document is to provide guidelines to research laboratories at the University of Miami (UM) establishing minimum quality standards for conducting sample analysis in support of a clinical trial conducted under an Investigational New Drug (IND) application.

SCOPE

The guidelines described in this document must be followed when conducting sample analysis in support of a clinical trial being conducted under an IND.

Although recommended, it is not required to follow these guidelines for other research taking place in the laboratory.

ABBREVIATIONS

CV	Curriculum vitae
ELISA	Enzyme Linked Immunosorbent Assay
FDA	Food and Drug Administration
HPLC	High Performance Liquid Chromatography
IND	Investigational New Drug
LIMS	Laboratory Information Management System
SOP	Standard Operating Procedure
UM	University of Miami

RESPONSIBILITY

It is the responsibility of all personnel conducting sample analysis in support of an IND to implement and adhere to the guidelines in this document.

All personnel conducting research in UM research laboratories, including laboratory Directors, research associates, students, etc. have the responsibility to:

- Protect human and animal subject safety
- Ensure and maintain data integrity
- Ensure data reliability and reproducibility
- Protect and secure research records (both paper and electronic format)
- Protect UM's intellectual property

Guidelines For Good Research Practices in Research Laboratories Conducting Sample Analysis in Support of a Clinical Trial

STANDARD OPERATING PROCEDURES (SOPs)

Written procedures must be available and easily accessible to describe and define the sample analysis process, including the reporting of data and use of equipment. It is recommended to save the SOPs in BOX or One Drive for easy access.

Written procedures describing the following must be available:

- Assay qualification process
- Assay procedures for sample analysis (e.g. ELISA), including solution preparations
- Acceptance criteria for assays
 - e.g. 2 out of 3 control samples must be within established range
- Acceptance criteria for samples
 - e.g. sample value must be within standard curve range
- Criteria for the maximum number of repeat analyses allowed
- Criteria for reporting repeat analysis data
- For example:
 - report the mean of all repeat values
 - use outlier test to omit a value
- Instructions for use of analytical equipment

SAMPLE TRACKING & REAGENT INVENTORY

There must be a system in place to log the samples and reagents received and to document their storage temperature and location.

A tracking system may consist of any of the following:

- paper log sheets
- spreadsheets in electronic format
- database such as LIMS (Laboratory Information Management System)

Note: Human subject samples must be labeled with the subject number and must not contain the subject's name.

Guidelines For Good Research Practices in Research Laboratories Conducting Sample Analysis in Support of a Clinical Trial

EQUIPMENT

Calibration and Maintenance:

Establish an equipment calibration and maintenance schedule, especially for critical equipment.

The frequency of calibrations may vary for different types of equipment depending on the sensitivity of the equipment and the frequency of use.

Documentation of calibrations and any maintenance performed must be maintained. Place calibration stickers on equipment to note the date of calibration and the next due date.

Defrost freezers on a regular basis or as needed. This may require making arrangements to move items into a temporary cold room or alternative freezer while the defrost cycle is in effect.

Equipment Verification:

For critical steps or solution preparations, verify the accuracy of equipment such as balances, pH meters and pipettes prior to use, even if the equipment has already been calibrated.

Temperature Monitoring:

Establish acceptable temperature ranges for refrigerators, freezers, liquid nitrogen tanks and incubators. Critical refrigerators, freezers, liquid nitrogen tanks and incubators (while in-use) must be monitored to ensure that the correct temperature is being maintained.

Temperature monitoring may be continuous via the use of data-loggers or min/max thermometers. Recorded temperatures must be reviewed by personnel to ensure that unacceptable temperature excursions have not been occurring. Captured data must be saved to an electronic file and/or printed and maintained.

Alternatively, a manual process can be used whereby the temperature is recorded by personnel on a daily basis. For example, temperature readings may be taken twice daily. Maintain a log book of manually recorded temperatures.

All temperature excursions will need to be evaluated for their impact on each product stored in the respective equipment, based on the duration of the excursion and the available stability data of that product.

Guidelines For Good Research Practices in Research Laboratories Conducting Sample Analysis in Support of a Clinical Trial

Alarm System:

Critical equipment such as refrigerators, freezers, liquid nitrogen tanks and incubators that are used to store or incubate critical samples/cells must be connected to an alarm system and back-up power.

SOLUTIONS

Solution Preparation:

Document how the solution was prepared. Include the following:

- Name of solution
- Date of preparation
- Expiration date
- Names of components
- Amount of components
- Lot number and expiration date of components
- Total volume prepared
- pH value (if applicable)
- Storage condition
- Name/initials of investigator/person who prepared it

Solution Labeling:

In addition to UM's Environmental, Health and Safety requirements, prepared solutions and reagents must be labeled with the following information:

- Name of solution
- Concentration
- pH value (if applicable)
- Date of preparation
- Expiration date
- Storage condition
- Name/initials of investigator/person who prepared it

Guidelines For Good Research Practices in Research Laboratories Conducting Sample Analysis in Support of a Clinical Trial

ASSAY QUALIFICATION

To demonstrate that an analytical procedure is reproducible, conduct the following:

- Establish an acceptable quantitative range for the control samples.
- Perform the procedure a minimum of three (3) times using standards and control samples, as described in your Assay Qualification SOP.
- Repeat the procedure using different operators to test for inter-operator reliability.

Points to consider:

A final acceptable quantitative range may be established for each control sample by using the overall mean value of each control sample from all three (3) or more assays.

For example: A control sample prepared at a target concentration of 10mg/mL may be determined to have a concentration of 10.8 mg/mL obtained from the overall mean of the three (3) or more assays.

It may then be decided to have a +/- 20% range from 10.8 mg/mL as the final established quantitative range.

Documentation of Assay Qualification:

Maintain all documentation of the qualification effort. Documentation should include the following:

- Written assay procedure that was followed
- Name of operators
- Preparation of solutions and reagents
- Concentration of prepared standards and control samples
- Raw data printouts/electronic files from analytical equipment (e.g. ELISA reader)
- Tabulated results and conclusion

SAMPLE ANALYSIS DOCUMENTATION

When analyzing samples, document the procedure that was followed, the solutions used, and the samples that were analyzed.

Sample analysis source /raw data generated by equipment such as ELISA reader, HPLC, etc. must be maintained as follows:

- Raw data must be printed and initialed and dated by operator. The printouts must be maintained in a dedicated binder for this study protocol number.

Guidelines For Good Research Practices in Research Laboratories Conducting Sample Analysis in Support of a Clinical Trial

- Electronic files must be saved in BOX or One Drive. A naming convention for electronic files should be established to ensure records are organized and easily found.
- Samples of human tissue/fluid must be de-identified, referenced by subject number, and must not contain the subject's name.

RECORD RETENTION

Sample analysis data must be maintained in a dedicated binder for a specific study protocol number. At the end of the study, sample analysis data will be archived together with the clinical trial records under that protocol number, for a time period to be specified by the Sponsor of the trial

TRAINING

A training file for each operator performing the sample analysis must be maintained to document their qualifications and experience. Each file should contain, at minimum, the following:

- Current CV
- Current job description
- Copies of certifications or licensure
- Training records indicating training on:
 - the study protocol and any amendments related to the sample analysis
 - the assay procedure/SOP
 - the equipment SOP
 - any other SOP related to the sample analysis

SIGNATURES

Prepared by: _____ *Signature on file* _____ Date: _____ *20 Jul 2017*
Helen Miletic, MA, CHRC, RQAP-GCP
Quality Assurance Manager, RCQA

Approved by: _____ *Signature on file* _____ Date: _____ *04 Aug 2017*
John L. Bixby, Ph.D.
Vice Provost for Research