

Accessing Technologies via Analytical Laboratories: Evaluating Laboratory Quality Practices

ABRF

The Quality & Compliance Committee

Nadine M. Ritter, Abbott Diagnostics Division

Timothy K. Hayes*, Bayer Biological Products Division

Elizabeth Fowler, AutoImmune, Inc.

* Presenting author

Value of Core Analytical Resource Facilities

- Collection of experienced scientists with various analytical specialties in a single team
- Provides a developmental edge of continually evolving state-of-the-art technologies; easier to incorporate the newest methodologies
- Instrumentation needed to perform complex or unique analyses available with trained analysts, can shorten a part of product developmental timelines
- Enhance management of product development resources by using “just in time” partners at the appropriate phase

Types of Analytical Laboratories That Can Be Involved in Analyses to Support Product or Candidate Characterization

- **Internal Facilities:**
 - R&D or other labs within the manufacturing company that perform biomolecular analyses
- **External Facilities:**
 - Contract laboratories that perform analyses for customers
 - Academic/Government laboratories that perform analyses in addition to their sponsored research projects

Phases of Product Development & Types of Analyses Performed

- **DISCOVERY**

- **OBJECTIVE:** Determine the important molecular species in the system of interest
- **ANALYSES:** Track Isolation; Identification

- **DEVELOPMENT**

- **OBJECTIVE:** Identify & characterize the molecule(s) of interest, determine impurities, confirm stability
- **ANALYSES:** Track Process; Confirmation of Identity; Detailed Characterization

- **PRODUCTION**

- **OBJECTIVE:** Routinely analyze the preparation for the product and its impurities
- **ANALYSES:** Validation; Quality Assurance

Basic Elements of Laboratory Quality - Good Practices to Follow in All Labs

- Confirm proper functioning of instrumentation before and during use (ie. freezers, water baths and incubators).
- Store reagents/materials under proper conditions (ie. temperature, light)
- Follow effective system for filing/retrieval of samples
- Adequate documentation of protocols and data analysis for each sample
- Follow a system of filing/retrieval of analytical reports

Additional Quality Practices: Better yet...

GOAL: Greater assurance of reproducibility of analyses

- Routinely calibrate critical equipment (i.e. pipettors, pH meters and balances)
- Date reagents, solutions and other materials with expirations (i.e. do not use outdated items)
- Document maintenance activities (i.e. repairs, preventatives, water system tests)
- Perform routine system suitability checks for methods & instruments; document- and trend results
- Demonstrate competence of technical staff for the procedures they perform (i.e. CVs, training, tests)

Regulatory Compliance Standards for Analytical Laboratories

- FDA Good Laboratory Practices (GLP)
- FDA Current Good Manufacturing Practices (cGMP)
- ISO-9000 Series of Standards
- ICH Harmonization Guidelines

Good Laboratory Practices (GLP)

- Specific set of FDA requirements for non-clinical (i.e. animal based) studies that support pre-clinical safety testing
- Includes designation of a study director and quality reviewer, plus specific lab quality measures
- Applies to procedures used to analyze the “test article”, typically a formulation of the active product, for identity, stability, homogeneity and concentration.

Current Good Manufacturing Practices (cGMP)

- Specific sets of FDA requirements for the manufacture and testing of biologicals and pharmaceuticals
- Significant control of laboratory operations, including establishment of SOPs, validation of methods, use of data review and approval system, archiving of records, document change control, out-of-spec data handling, method failure analysis, and establishment of training procedures.
- Applies to laboratories testing a commercial product

ISO-9000 Series of Quality Standards

- ANSI/ASQC set of standards (9004 to 9001) that can be adopted by any business.
- Measures are aimed at establishment of a “quality system” designating responsible individuals and methods of information management; most useful in large organizations with multiple departments and numerous activities.
- ISO-9000 registration is achieved by passing inspections from designated certifying agencies: analytical labs might be certified if associated with larger entities (or large enough themselves).

ICH Harmonization Guidelines

- Regarded as the official minimum standards for registering pharmaceuticals
- Published by the FDA as guidances for industry
- Represent current inspectional trends
- Address analytical test methods from several viewpoints:
 - validation
 - specifications
 - impurities
 - stability testing
 - determining comparability of biotechnological pharmaceuticals

Being or Using a Service Lab: Key Issues

- Assess the level of quality measures in place; determine if they meet testing expectations
- Determine if the data integrity can be trusted- not based on emotion, but based on traceability
- Clearly ascertain the testing requirements for the samples, including any storage, handling and testing issues.
- Clarify the intended use of the data obtained in order to support development decisions and to meet any regulatory requirements that may apply