Laboratory software

Enabling data integrity in bioanalysis

Evolving scientific demands

There is continued growth in emerging scientific modalities, particularly the use of monoclonal antibodies and cell and gene therapies. Cell therapies are considered as “next generation” or “novel biologics” and are growing in quantity across development pipelines. A recent search in clinicaltrials.gov with the term “CART,” “TCR,” or “monoclonal antibody” yielded 106, 84, and 1,049 active/recruiting studies respectively. With such rapid growth, novel bioanalytical assays had to be developed and validated with only a draft guidance available as reference—stressing the importance of data quality and the ability to recreate a bioanalytical study.

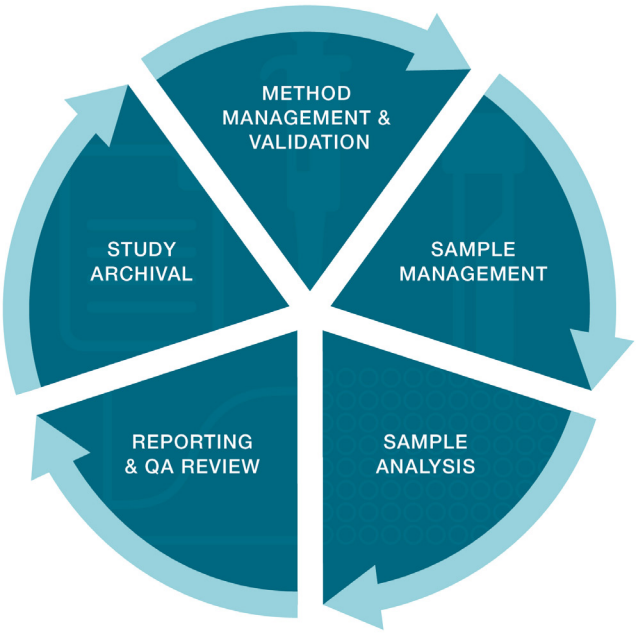
While there has been substantial growth within large molecule development, several trends have also emerged in recent years in regards to small molecule bioanalysis. One significant trend is the increasing demand for sensitivity and selectivity in small molecule analysis. Scientists are constantly striving to detect and quantify lower concentrations of analytes in complex biological matrices. This requires the development of more sensitive and specific analytical methods, such as **liquid chromatography-mass spectrometry (LC-MS)** and **gas chromatography-mass spectrometry (GC-MS)**, as well as innovative sample preparation techniques.

Across all molecule types there is an increasing need for the **integration of high-throughput automation systems**. With the common industry need to analyze large numbers of **samples efficiently, automated sample handling systems, robotic platforms**, and **Laboratory Information Management Systems (LIMS)** have become essential tools. These advancements help streamline the analysis process, reduce human error, improve quality, and increase productivity in laboratories. We partner with our customers to **address all of** these specific challenges to bioanalysis—***informatics, automation, sample prep and storage, antibody creation, instrumentation, and bioanalytical services***.

Producing data of high quality and integrity throughout bioanalytical studies

Laboratory analysis is just one component in controlling and ensuring data integrity during a bioanalytical study. Data integrity in a bioanalytical laboratory goes beyond nonclinical and clinical data capture, it stems into many other processes, such as record keeping, sample and analyte shipping, stability, study and sample management, method and instrument validation, training, and documentation. The data produced by bioanalytical laboratories is vital in supporting BLA and NDA submissions, as well as phase 1–4 clinical trials. The failure to adequately document Good Laboratory Practice (GLP) studies can result in regulatory agencies rejecting pieces of a submission and asking the Sponsor to re-conduct studies or, more seriously, a Refuse-to-File (RTF) as outlined in the guidance to industry "Refuse to File: NDA and BLA Submissions to CDER," causing a significant impact to the timeline and budget of a project. Section 21CFR601.2(a) states: "An application for a biologics license shall not be considered as filed until all pertinent information and data have been received by the Food and Drug Administration."[1]

The challenge for bioanalytical laboratories is ensuring that they are complying with the latest regulatory documents set forth by regulatory agencies in each of the countries where they plan to file. The most reliable way to help ensure the integrity of these components is by incorporating a dedicated bioanalytical LIMS, such as Thermo Scientific™ Watson™ LIMS Software.



Quality is not optional

The US Food and Drug Administration (FDA) reported in FY 2022 that out of the 29 nonclinical inspections conducted, significant observations were noted, resulting in the issuance of a Form FDA 483 Inspectional Observation during 13 inspections, with 78 significant observations noted. The trends and themes identified were:

- Inadequate training at multiple levels
- Failure to follow written procedures
- Lack of Study Director oversight[2]

Significant direct and indirect costs are accrued as a result of receiving a 483; the financial impact varies depending on the severity of the findings, ranging in costs from millions to multimillions of dollars to reconcile. Examples of direct costs include: hiring of consultants to mitigate and reconcile findings, government fines, re-validation of methods, loss of patient sample (particularly important in cases of rare disease), and repeat of clinical trial—on average, an individual pivotal trial for a new drug cost 19 million USD.[3]

In addition to the direct costs of receiving an FDA warning letter, there are also indirect costs:

- A damaged public reputation
- Competitor opportunity
- Severed contracts
- Distractions from growth
- Decreased employee morale and increased turnover

These direct and indirect costs can be mitigated by implementing a LIMS that is ***trusted by regulatory bodies and pharmaceutical Sponsors***. LIMS provide bioanalytical labs with a mechanism to help ensure that their scientific data is captured, documented, stored, witnessed, and archived in a safe and secure manor.

Good science requires good record keeping. Good record keeping promotes both accountability and integrity.

Bioanalytical laboratories are required to comply with regulatory guidance documents, such as Guidelines for Bioanalytical Method Validation (EMA and FDA), 21 CFR 58, and 21 CFR 11, from method development through study archival. Procedural elements for data integrity in a bioanalytical laboratory can be broken down into three elements: integrity of the analyte and data produced, integrity of the sample identity, and integrity of documentation.[4] Integrity of the analyte or drug product needs to be maintained from manufacturing of the drug product to handling, shipment, and storage procedures. This includes tasks such as confirming that the product certificate of analysis is attached to each analytical run and that the same lot of drug product is used from method development throughout sample analysis, providing consistency across data sets. Without complete knowledge of the conditions that an analyte has been through, the accuracy of assay data will be called into question by an inspector. It is crucial to have full chain of custody for any movement that is made to the analyte, for example, temperature monitoring records must be included with shipping records, and all movements into and out of storage must be tracked and monitored. Failure to track these methods accurately can jeopardize the credibility of the bioanalytical study due to incorrectly following procedures. It can also affect the stability or change the composition of an analyte.

Ensuring integrity in the sample identity and sample data encompasses many different bioanalytical processes, such as instrument validation, method validation, sample management, and laboratory analysis. Validation of computerized systems and laboratory equipment is a key factor in establishing the accuracy and reliability of data that is generated or produced from those systems. Laboratories must conduct validation of systems according to 21 CFR Part 11, this provides assurance that the system is consistently producing expected results and complies with security requirements, enabling high data integrity.

The Guideline for Bioanalytical Method Validation explicitly details all analytical methods that must be conducted for assays used in clinical analysis. The rigor of the method validation guidance provides credibility and integrity in the data that is generated from clinical assays. If a method fails to comply with the bioanalytical guidance, then the results produced in clinical analysis cannot be fully accepted by auditors due to a lack of confidence in the performance of the assay.

It is vital that a Study Director in a bioanalytical study can walk an auditor through the complete life cycle or chain of custody of a nonclinical or clinical sample. This allows the auditor to review the sample accessioning process, which must comply with GLP principles and Good Clinical Practice (GCP) standards. Auditors must be able to see documentation related to how the sample was received and stored, documentation of any discrepancies in the shipment or sample manifest, and each freeze/thaw of the sample, including movement for analytical runs (i.e., time at benchtop and temporary refrigerator storage). Without a complete chain of custody, the credibility of the sample and therefore the analytical results can be called into question. GLP studies must be fully documented, including training records on all SOPs for instrument use, reagent creation, analytical methods, and data analysis

So why leave data quality up to chance? Leave it to the experts

Satisfying compliance with many different regulations is a challenging task for the bioanalytical community, but with the right partner these challenges turn into strengths. Thermo Fisher Scientific has been serving the bioanalytical community for over 20 years and has the regulatory acumen and domain expertise required to effectively drive success. We support bioanalysis in many different avenues—whether it's integrating data analysis with Watson LIMS software, running an assay on a Thermo Scientific™ Orbitrap™ Mass Spectrometer, storing critical reagents in a Thermo Scientific™ Ultra Low Temperature freezer, purchasing an antibody, or utilizing our best-in-class bioanalytical laboratory services.

Watson LIMS software is the market-leading bioanalytical LIMS, trusted by top pharmaceutical Sponsors and CROs for decades. It is designed for enhanced traceability, compliance, and control from the first method development to the final study completion across clinical or nonclinical studies and large or small workflows. Unlike the competition, Thermo Fisher can tap into the bioanalytical expertise of our more than 120,000 colleagues to create industry-trusted, reliable solutions.

We help our customers accelerate innovation and enhance productivity, underpinned by quality, always.

References

1. US Department of Health and Human Services (2017) Applications for biologics licenses. Procedures for filing. Vol. 7, 21CFR601.2.
2. US Food and Drug Administration. FY 2022 good laboratory practice, FDA 483 observation trends. https://www.fda.gov/media/172783/download
3. Johns Hopkins Bloomberg School of Public Health (2018) Cost of clinical trials for new drug FDA approval are fraction of total tab. https://publichealth.jhu.edu/2018/cost-of-clinical-trials-for-new-drug-FDA-approval-are-fraction-of-total-tab

Choose Watson LIMS software for precise bioanalysis, when it matters.

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