intertek
Total Quality. Assured.

PHARMACEUTICAL BIOANALYSIS

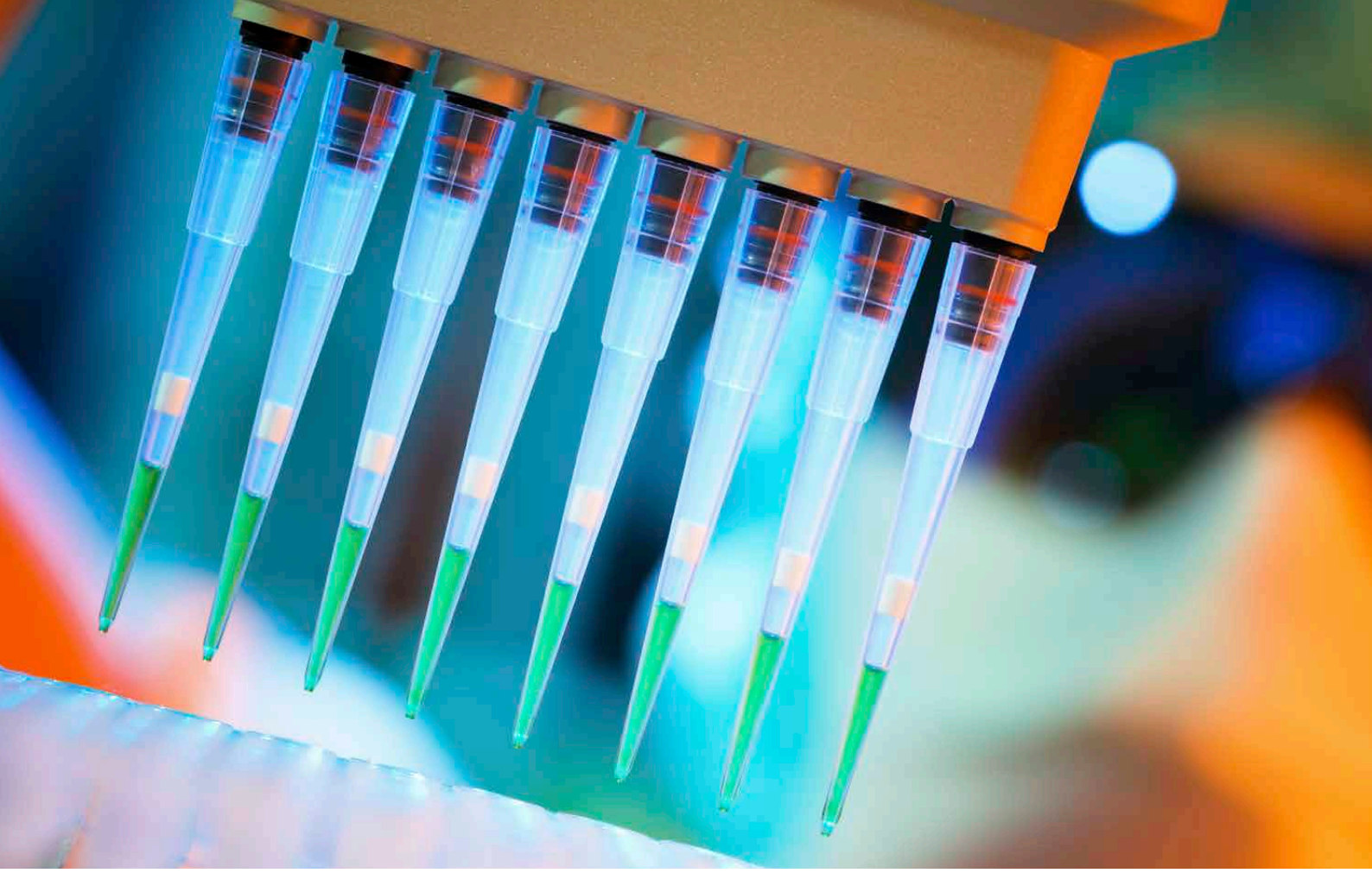
BIOANALYSIS SERVICES

Bioanalytical Expertise for Large and Small Molecules

Our Bioanalytical Expertise

Bioanalysis plays a critical role in the assessment of drug safety and efficacy. We understand that each project presents its own unique challenges, and by applying our 20 years of experience in conducting regulatory bioanalytical studies, our teams work closely with you to ensure that the best possible solutions are delivered, optimizing value for your programs.

With Intertek as your partner, you have access to the scientific and regulatory knowledge of our bioanalytical experts, so that you can leverage the insight we bring to accelerate your drug development.



As time is of the essence, it is important to get your bioanalytical strategy right first time, to meet both regulatory requirements and the challenges presented by complex products and diverse biological matrices.

Helping you to meet your milestones

Our bioanalytical experts have developed methods for thousands of different compounds, providing phase appropriate, small molecule and large molecule bioanalytical support, high throughput sample bioanalysis, pharmacokinetic and toxicokinetic support, clinical sample management services, immunogenicity and biomarker assays.

Our teams are adept in method development, method validation and transfer of efficient and accurate methods that are optimized for your compound.

With a focus on evolving guidance, our bioanalysis thought-leaders design programs to generate regulatory-driven bioanalytical data to help you meet your next milestone.

To help you to make informed decisions, faster, our Good Laboratory Practice (GLP) and Good Clinical Practice (GCP) compliant laboratories provide clinical kit preparation, sample handling and management, integrated with automated data capture and reporting systems using the latest bioanalytical platforms.

Our experts

Our bioanalysis experts are thought-leaders in their field who actively contribute to progressing the bioanalysis community's knowledge of strategic and regulated approaches for bioanalysis. Our staff routinely present at conferences and contribute to peer-reviewed journal publications.

Our Centre of Excellence and bioanalysis facilities

Our Centre of Excellence in California, USA, spans 46,000 square feet of laboratories, offices and sample storage. It brings the benefit of high capacity strengthened by continued investment in the latest bioanalytical technologies to customers involved in preclinical and clinical development of small molecule drugs and biologic medicines. Our 30,000 square foot European Centre of Excellence is located in Manchester, UK and together our facilities are positioned to expedite delivery of fast and cost-effective bioanalysis results for global clients.

Diverse bioanalytical technologies delivering the best possible solutions

Our innovative use of bioanalytical technologies such as quantitative liquid chromatography-mass spectrometry (LC-MS/MS) and immunochemistry means that, no matter how complex your samples are, we can accommodate the chemistry or biology of your analytes as well as any matrix interferences across a diverse array of biological samples including plasma, blood, serum, urine, faeces, spinal fluid, skin, muscle, artery, myocardium, liver and kidney and a variety of tumor types. We also deploy GC-MS, qPCR, Nuclear Magnetic Resonance Spectroscopy (NMR), Inductively Coupled Plasma-Mass Spectrometry (ICPMS) and Surface Plasmon Resonance (SPR) in bioanalytical applications.

At Intertek, we have become experts at adapting analytical techniques to meet the growing demands of the bioanalytical industry, providing our clients with the best possible solutions.

Large Molecule Bioanalysis

We have extensive experience in the development, validation, and sample analysis of quantitative and qualitative GLP and non-GLP immunoassays in support of clinical and preclinical studies for the measurement of therapeutic drugs, synthetic peptides, humanized monoclonal antibodies, chimerics, conjugated drugs, growth factors, hormones, cytokines and biomarkers.

Specialist large molecule expertise:

- Quantitative Ligand Binding Assay Capabilities
  - Development, Validation and Optimization of Quantitative ELISAs for Proprietary Compounds
  - Transfer and Validation of Existing Methods
- Immunogenicity Studies using a Tiered Approach
- Neutralization Cell-based Assay Development, Validation and Sample Analysis
- Biomarker Solutions
- Radioimmunoassays (RIA)
- Enzymatic Assays
- Fluorometric Assays
- Biotinylations and Ruthenium Labeling capabilities
- Mode of Action Studies
- Bioanalytical LC-MSMS for proteins and biologics

Expertise across many product types

- Peptides
- Proteins, Monoclonal Antibodies
- Pegylated Proteins
- Biosimilars, Biospecifics, Biobetters
- Antibody-Drug Conjugates (ADCs)

Immunogenicity studies using a tiered approach

Our immunogenicity assay experts are experienced in the development and validation of qualitative and quasi-quantitative immunoassays. They utilize a multi-tiered approach to measuring ADAs and NAbs with the first tiers focused on detecting anti-drug antibodies (ADAs) that bind to the biologic drug. Samples are screened for the presence of antibodies, and antibody titer assessment followed by confirmation of the specificity of binding.

We deploy strategic approaches to increase drug tolerance: such as MSD Bridging Mastermix with acid dissociation, ECL/ELISA based Solid phase extraction with acid dissociation (SPEAD), Affinity Capture Elution (ACE), "BEAD" (use of nanoparticles or magnetic beads) assays.

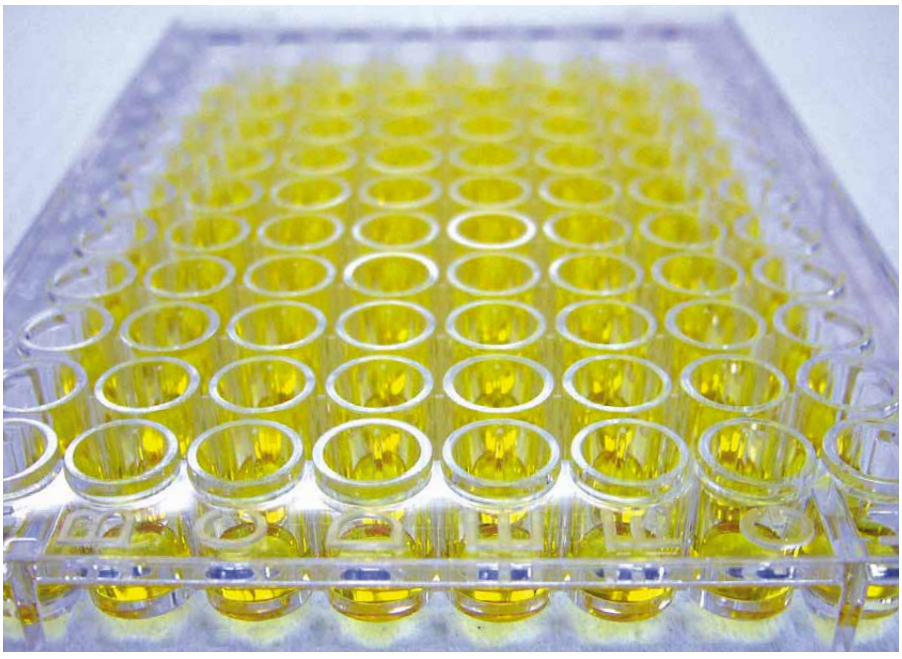
Immunogenicity assessment of NAb activity can be performed by utilizing cell based assay or competitive ligand binding assay (LBA). Cell-based neutralization assays are used to detect the presence of ADA which interferes with the biologic activity of the drug. Our GLP compliant immunogenicity laboratories are equipped with established industry immunoassay platforms such as ELISA, Radioimmunoassays (RIA), Electrochemiluminescence (ECL) and cell-based neutralization assays.

Biomarker assays

We deliver discovery and clinical biomarker solutions from our dedicated team which has expertise in the qualification and validation of biomarkers using ELISA, and ECL platforms (including multiplexing, prototypes and custom multiplexing from MSD and Luminex) in multiple matrices and anticoagulants.

Examples of validated assays include:

- Anti-KLH IgG and IgM
- Anti-tetanus toxoid (TT)
- IgG and IgM
- E-Selectin
- FGF
- HGF
- ICAM-1
- IL-6
- IL-8
- IP-10
- Leptin
- MCP-1
- MMP-3
- MMP-9
- TNF-alpha
- VCAM-1
- VEGF C
- VEGF
- VEGF R2
- Multiplexing (Vascular Injury I & II)



Bioanalytical LC-MS Services

We apply our bioanalytical expertise and industry insight to design strategic and efficient bioanalytical programs

Applying over 20 years of experience in the development and validation of quantitative LC-MS/MS methods for novel drugs and metabolites our scientists deliver robust and reproducible bioanalysis solutions.

Our laboratories support all phases of regulated pre-clinical and clinical bioanalysis development, applying validated methods in a high throughput environment to accelerate development times for proprietary and generic drugs across many types of biological matrices. With automated data capture, data management and reporting that meets regulatory needs, our laboratory is an established leading center of excellence for bioanalysis.

Our LC-MS bioanalysis services

- Method Development & Validation
  - High Throughput GLP Sample Analysis
  - Pre-clinical Bioanalysis
  - Clinical Bioanalysis
  - Bioequivalence Studies
  - Bioavailability Studies
- Non-GLP Rapid Discovery-Phase Bioanalysis
  - In Vitro Screening Bioanalysis
  - Tissue Bioanalysis
  - Early Pharmacokinetic (PK) Studies
  - Lead Optimization Studies
- Bioanalysis in Ocular Tissues & Fluids
- Clinical Kit Preparation, Sample Handling & Management

Projects are assigned to and managed by experienced Principal Investigators with support from teams of Project Managers, Project Coordinators, Senior Scientists and Chemists. Our project teams ensure that your methods are properly validated, and study samples are accessioned, analyzed and reported in a timely and cost efficient manner.

Non-regulated bioanalysis

Our non-GLP, rapid non-regulated bioanalysis services are optimized to support in vitro screening, tissue bioanalysis, early pharmacokinetic (PK) studies and lead optimization. Our dedicated team of bioanalytical scientists have in-depth experience in many classes of compounds and different matrices including plasma, blood, ocular tissues, tumor tissues, and other unusual matrices providing highly optimized programs that are flexible, fast and cost effective.

Rapid discovery bioanalysis includes LC-MS/MS instrument optimization with rapid analysis of your samples employing a generic protein precipitation method with a broad range of calibration standards.

Lead optimization / early PK services includes a more rigorous evaluation of assay performance and calibration curve range prior to analysis of your samples. Samples are analyzed under more stringent guidelines using freshly prepared calibration curves and QC samples.

A range of established and proven generic discovery phase methods have been developed for broad screening applications with rapid turnaround times

CASE STUDY

Novel Approaches for An Enzyme Activity Assay

A client desired an activity assay for a PEGylated enzyme for which a commercial colorimetric assay was available. The colorimetric assay did not meet the performance criteria for regulated work. An immunoassay was then developed but was subject to significant matrix effects.

Our Solution

Development of a replacement assay was complicated by endogenous substrate and enzymatic product. To overcome this, the specificity of LC-MS/MS was employed and an activity assay developed using a stable labeled substrate which produced a labeled product, which could be differentiated from the endogenous analyte.

Benefit Delivered to our Client

A enzymatic activity LC-MS/MS assay was developed and successfully validated to regulatory standards. The method was used in multiple pharmacokinetic studies and enabled the client to move forward with their drug development program.

Our Innovative Use Of Bioanalytical Technologies

Regulated and lead optimization bioanalysis in ocular tissues & fluids

For over 15 years, our teams have developed and validated highly specific and sensitive approaches for a wide variety of compounds in multiple ocular matrices. Diverse homogenization and extraction techniques are available for processing ocular tissues and fluids to ensure optimal recovery of analytes. Technologies such as multi-tube bead homogenization and high energy ultrasonication are often employed individually, or in conjunction with more traditional processing techniques. Non-GLP studies are also routinely conducted to support discovery, lead optimization and proof of concept programs of ocular drugs. We have experience across these ocular matrices:

- Aqueous humor
- Vitreous humor
- Retina
- Choroid
- Sclera
- Cornea
- Conjunctiva
- Ciliary body
- Lacrimal gland
- Eyelid
- Sclera
- Lens

Oligonucleotide bioanalysis services

Ensuring a safe and efficacious product, Intertek are experienced in GLP or GCP bioanalysis supporting toxicokinetic (TK) and pharmacokinetic (PK) studies for preclinical and clinical development of oligonucleotide products. Our GLP laboratories typically apply a range of bioanalytical techniques including ELISA, mass spectrometry approaches (LC-MS/MS and UPLC-MS/MS) and capillary gel electrophoresis (CGE).

Biosimilar bioanalysis studies

Intertek's GLP immunochemistry capabilities are world renowned for developing and validating assays for pharmacokinetic (PK), toxicokinetic (TK), pharmacodynamic (PD), immunogenicity studies for biosimilar products. Using diverse immunochemistry technologies (e.g. ligand binding assays), radioimmunochemistry (RIA) and functional (e.g., enzymatic and cell-based assays) assay platforms we have experience across a wide range of products including Erythropoietin (Epoetin), Insulin, GCSF, Interleukin, Avastin, Bevacizumab, Trastuzumab, Rituximab, Enbrel, Infliximab, Adalimumab and more.

Antibody-drug conjugate bioanalysis

Antibody-Drug Conjugates (ADCs) present unique bioanalytical challenges as they tend to be complex heterogeneous mixtures of multiple species with a range of drug-to-antibody ratios. ADCs typically incorporate both large and small molecule characteristics, and so our bioanalytical teams apply diverse bioanalytical methods, including ligand-binding assays and LC-MS methods, to quantify these species in serum/plasma for PK studies and strategies for assessing immunogenicity. Intertek provides complete bioanalytical capabilities for ADCs:

- Quantitative bioanalytical assays for preclinical and clinical studies
- Total antibody assays
- Total conjugated ADC assays
- Unconjugated (free drug) assays
- Immunogenicity assessment

PEGylated small and large molecule bioanalysis

PEGylation greatly increases the molecular size of the drug molecule and introduces challenges for bioanalysis by standard techniques at the low concentrations such as those observed in biological samples like plasma or serum. Intertek can offer direct bioanalytical approaches that are either Good Clinical Practice (GCP) or Good Laboratory Practice (GLP) compliant with minimal sample preparation.

- Quantification of PEGylated drugs in biological matrices by Nuclear Magnetic Resonance Spectroscopy (NMR)
- Immunogenicity assays against the intact PEGylated protein or against individual fragments
- Pharmacokinetic (PK) assays for PEGylated proteins to determine the concentration of the PEGylated drug product by using a bridging / sandwich ELISA assay platform.

Unique areas of bioanalytical expertise

- Demonstrated Expertise in Ocular Tissue Bioanalysis for Large and Small Molecules
- Post Marketing Antidrug Antibody (ADA) assays
- Clinical Kit Prepartation, Sample Handling & Management
- Immunogenicity and Neutralizing Antibody Assays
- Antibody Drug Conjugate (ADA) LC-MS and Immunochemistry Services
- Long History of Bioanalytical Support of Biosilmilar Drug Development
- Excellent Regulatory History

CASE STUDY

Novel Approaches for Immunogenicity Assessment

A client desired an immunogenicity package for the assessment of Anti-drug antibodies to infliximab. The method was developed using a traditional bridging ELISA with ECL endpoint however there were concerns over the ability to detect low affinity ADAs.

Our Solution

Our experts designed and developed an immunogenicity package using Surface Plasmon Resonance (SPR). Due to SPR being a real time assessment of binding, without the need for wash steps, this allowed for the instantaneous visualisation of ADA binding even with low affinity antibodies.

Benefit Delivered to our Client

Both a traditional bridging ELISA and novel SPR method were developed and qualified. The methods provided an orthogonal approach to immunogenicity assessment allowing the client to meet the safety requirements needed for their phase of clinical trials

CASE STUDY

Re-evaluating Assays to Minimise Risk and Meet Timelines

The client desired a pharmacokinetic (PK) study to evaluate a potential antibody drug product. We developed a method to analyse the drug concentration in rat serum using a traditional direct sandwich ELISA. However, during development it became evident that, with the proposed reagents and expected parameters, the assay would need to use undiluted rat serum, a potential logistical problem in rodent studies.

Our Solution

Our experts re-evaluated the assay reagents and conditions and were able to introduce a different detection antibody that permitted the use of diluted serum without compromising the sensitivity and quality of the assay.

Benefit Delivered to our Client

Our improved assay, conserved precious samples and minimized the risk of data-loss and logistical problems, allowing the client to meet milestones with high quality data that facilitated their decision making process.

CASE STUDY

Novel Approaches for PEGylated Drugs

A developer of a novel PEGylated drug required a robust and sensitive bioanalytical method which avoided observed issues with sample matrix interference.

Our Solution

Our experts assessed and validated appropriate 1H NMR methods achieving a method suitable for a GLP study. A high-resolution 600MHz spectrometer achieved suitable LOQs whilst presenting a highly specific method for the analyte. Quantitation repeatedly produced statistically accurate results.

Benefit Delivered to our Client

The client was able to progress safety and efficacy studies with confidence in this highly specific and sensitive bioanalytical approach.

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