



Bioanalytical sciences

Helping you get the most from your precious samples

analytical quality • measurement accuracy



regulatory testing • chemical measurement • bioanalysis

standards • GLP GCP cGMP

Every project is unique, and every sample precious

The challenges in drug development put increasing emphasis on generating safety and efficacy information quickly and reliably.

Planning and conducting preclinical and clinical studies is costly and time-consuming and the return on your investment is often measured in terms of pharmacokinetic (PK) and/or pharmacodynamic (PD) results generated by the bioanalytical laboratory.

This means you need a laboratory partner who you can trust and who shares your passion and enthusiasm to progress your project.

LGC has one of the world's most extensive bioanalytical facilities and a team of scientists dedicated to providing on time, high quality data to help you make critical decisions on the safety and efficacy of your molecule.

Working with a team committed to open, transparent communication, we give you access to flexible resources with the capacity to handle the requirements of small discovery projects through to the most complex clinical studies.

Supported by the latest mass spectrometry and immunochemistry technologies, and a full range of microbiology and flow cytometry services, our team offers you in-depth expertise spanning small molecules, biopharmaceuticals, molecular biology and antimicrobials. Operating from state-of-the-art facilities to GLP, GCP and cGMP.

Case study

Complex biomarker project combining LC-MS/MS, ELISA and clinical analyser technologies

Challenges:

- 48 biomarkers in Phase I/IIa programme.
- No existing methods for many of the biomarkers.
- Limited sample volume.
- Rapid data turnaround times critical.

Science:

- Developed novel LC-MS/MS methods for the determination of up to 7 steroid biomarkers in one analysis.
- 31 individual LC-MS/MS, ELISA and clinical analyser methods validated fit-for-purpose in our GLP accredited labs.
- Input to sample management and handling to help finalise clinical protocol.
- Detailed planning of sample analysis sequence to maximise the utilisation of limited sample volume.

Solutions and output:

- New methods developed and validated on-time.
- >180,000 analyte determinations across the Phase I/IIa programme requiring fast results reporting.
- All data was delivered on, or ahead, of time.

With a dedicated team of scientists committed to service excellence, you benefit from open channels of communication.



Unique track-record

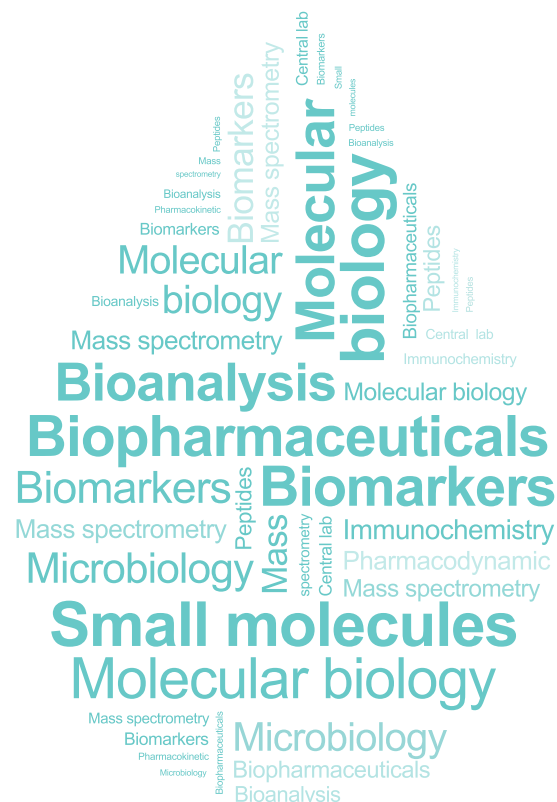
LGC has been at the forefront of analytical science for more than 50 years and has provided specialist microbiology services for antimicrobial development for more than 25 years.

We have a unique heritage as a pharmaceutical contract laboratory that has developed from the world's leading sports drug surveillance laboratory. This background has given us a special insight into high quality, challenging method development and adopting new technologies for the quantitative determination of drugs and biomarkers in biological fluids.

Combining this proven track record in bioanalysis and biomarkers with microbiology, molecular biology and central lab services gives you access to a broad-based laboratory capability and customised service to help you get the most from your precious samples.

Flexible resources

LGC's team of more than 150 bioanalytical scientists are supported by a flexible infrastructure including more than 20 LC-MS/MS systems, extensive immunochemistry, molecular biology, microbiology and flow cytometry services. This broad capacity allows us to allocate resources to match your needs, from small method development projects to large, complex multicentre clinical trials.



Pioneer in science and new technologies

LGC is unusual amongst contract laboratories in the high number of papers, oral presentations and posters that we present each year.

This reflects the fact that our scientists do not only provide testing services, but also pioneer the development of novel methods and the adoption of new technologies.

We are regularly invited by instrument manufacturers to evaluate new systems. This gives us an excellent opportunity to assess the latest bioanalytical techniques and instruments.

LGC's bioanalytical experts also contribute to the development of standards, harmonised procedures and sharing knowledge with industry colleagues and we actively support key industry bodies such as the European Bioanalysis Forum (EBF), The Global Bioanalysis Consortium (GBC) and The Global CRO Council (GCC).

Case study

Identification of *in-vivo* and *in-vitro* derived antibody-drug-conjugate (ADC) metabolism

Challenges:

- ADC's are antibodies (or antibody fragments) with a specific payload conjugated to the molecule via a labile chemical linker.
- Quantitative methods are required for the intact ADC molecule as well as the released payload, which cannot be done solely using immunochemistry based techniques.

Science:

- Enzymatic digestion of an ADC can generate a cleaved antibody backbone with its payload still attached and in an intact form. The subsequent LC-MS/MS analysis of a digested ADC will allow the quantitation of the intact payload at a specific conjugation site within the ADC molecule.
- This technique enables an assessment of payload stability, as a drop in signal of the full length, digested and conjugated peptide relative to a digested peptide generated from elsewhere in the ADC (giving total Ab concentration) will point to specific degradation / metabolism of the payload, or deconjugation of the drug from the antibody.
- This approach can therefore help identify metabolism events during the course of a PK study.

Solutions and output:

- The digestion approach was used to identify protease action on an antibody peptide conjugate in a mouse PK study.
- A payload specific metabolite was confirmed by analysis of extracts on an Orbitrap high resolution MS system.
- This approach can help identify potential weak points in payload design, and indicate where unwanted metabolism is occurring in *in-vivo* and *in-vitro* environments.



Discovery

Pre-clinical

Phase I/IIa

Phase II-IV

Post-marketing

Bioanalysis (small and large molecules)

Small molecules

With a focused Strategic Science Team, and one of the largest, purpose-built bioanalytical facilities in the world comprising over 20 LC-MS/MS systems, we continue to pioneer new method development techniques (such as small molecule biomarkers by LC-MS/MS) and apply novel technologies to answer your analytical challenges.

With experience spanning a variety of species and novel matrices, our flexible service includes comprehensive feasibility, method establishment, development and transfer capabilities, validation and sample analysis. Working to meet the shortest possible sample analysis timelines, we are totally committed to providing bioanalytical data and reports of the highest quality.

Biopharmaceuticals

Biopharmaceuticals, are becoming ever more complex, evolving from monoclonal antibodies and cytokines to bispecific and multi-domain therapeutics. The next generation of biopharmaceuticals biosimilar and biobetters are coming through the drug development pipelines. Development and validation of bioanalytical assays to support your biopharmaceutical development programme, whether it be pharmacokinetic (PK), Anti-Drug-Antibody (ADA), Neutralising Antibodies (nAbs) or Pharmacodynamic (PD) is core to our business. LGC has combined first hand industry knowledge and academic expertise with state of the art technology such as Electrochemiluminescence (ECL), Erenna and Gyrolab to provide a unique combination of capabilities to help you develop your biopharmaceutical.

Biomarkers

Biomarkers

Biomarkers are increasingly important in early phase decision-making, as indicators of safety or efficacy. At LGC, we have a wealth of experience in detection and quantitation of biomarkers in a wide variety of matrices. Our therapeutic specialities include metabolic disorders (including diabetes and cardiovascular disease), inflammatory disorders (such as rheumatoid arthritis), respiratory diseases (including COPD) and anti-infectives. We have significant experience in establishing validated fit-for-purpose methods using our comprehensive analytical platform, often combining LC-MS/MS, immunoassay and clinical laboratory techniques to achieve project objectives. Whatever biomarker questions you have, LGC's flexible and innovative team has the answer.

Microbiology and molecular biology

Antimicrobials

With over 25 years of experience in the provision of antimicrobial drug development services, we offer a truly expert service from our purpose built, containment level 3 facility in the UK. Fully GLP compliant and boasting an extensive isolate collection, our microbiologists provide a bespoke and specialised service. Supporting all phases in the drug development pipeline, we have particular strengths in discovery screening, preclinical efficacy and safety, veterinary products, clinical trials support, molecular biology and global surveillance programmes.

Molecular biology

Our dedicated molecular biology team offers specialist expertise and capabilities which integrate seamlessly within the LGC Group and beyond. Our particular strengths lie in the application of qPCR for the analysis of genetic biomarkers for clinical trials and quantitative gene expression of metabolic enzymes. Other specialist areas include development of molecular methods for pathogen detection and quantification, DNA fragment analysis for point mutations, and genotyping. We are proud of our position at the cutting edge of molecular diagnostics.

Flow cytometry

Flow cytometry services

The flow cytometry service provides a range of assays including: immunophenotyping, receptor occupancy, intracellular cytokines, phosphor-flow, nAbs and cellular activation. All can be validated to GLP/GCP guidelines.



Case study

High-throughput bioanalysis to support preclinical development of a novel mAb

Challenges:

- Provide bioanalytical support for a 26 week toxicology study with a novel monoclonal antibody (mAb).
- Rapidly establish and validate a bioanalytical method, after the in-life phase had initiated.
- Large dynamic range 51.2 – 11,000,000 ng/mL.
- High throughput analysis of > 5,000 samples.

Science:

- Analytical strategy was carefully reviewed to meet the challenging requirements of this study.
- LGC became the first CRO to establish a GLP validated method on the Gyrolab platform.

Solutions and output:

- Transferred method to the Gyrolab platform in 4 days.
- Established 1 to 9,000 assay dilution to achieve the large dynamic range.
- Validation completed in < 2 weeks.
- 5,200 samples analysed in 135 analytical batches.
- All QA'd data delivered on time.

Case study

Bioanalytical project with high throughput sample analysis

Challenges:

- Analysis and reporting audited data from 3320 samples, >216 ISR samples and Sponsor requested repeats using 2 highly sensitive bioanalytical methods in < 8 weeks.
- Requires robust assays to achieve this.
- Fluticasone
 - Short column lifetime (regeneration required every 96 injections).
 - No alternative (longer lifetime columns) could be identified.
 - LLOQ of 1 pg/mL using SPE and Xevo TQS.
- Formoterol
 - Contamination matrix, required some screening.
 - Easy contamination of reagents, required additional care.
 - Instability observed in both solutions and matrix.
 - LLOQ of 0.25 pg/mL using SPE and API5000.

Science:

- In house assays developed for Fluticasone and Formoterol, both common inhaled drugs.
- Pass rate metrics were 96.5% for Formoterol and 88.8% for Fluticasone.
- Weekend working was undertaken to keep instruments running 24/7 and utilise other equipment.
- Regular checking and issuing of data to Sponsor to enable repeat selection.
- Regular auditing of data to reduce time required at the end of the study.

Solutions and output:

- QA audited data provided by the date initially proposed as the best case scenario for delivery.
- Enabled the Sponsor to decide whether or not to conduct an extension phase in a short time frame.
- LGC performed analysis of a further 3320 samples for a subsequent study to even tighter timelines and will be supporting others.



Highest quality

At LGC, we have an absolute commitment to the highest quality in everything we do. We are proud of our 100% success record in regulatory GLP and GCP inspections, but we recognise that quality is not just about compliance with international quality standards.

Quality is at the heart of our operation, focusing on “Right First Time” and cost savings to our clients.

We follow the same rigorous principles and standards for all experimental work, so whether you require non-regulated discovery bioanalysis or full regulatory studies, you know that your samples are in safe hands.

Case study

Ongoing “Right First Time” initiative in bioanalysis

Challenges:

- Reduce timelines and costs whilst maintaining the highest quality standards.
- The need to analyse increasing numbers of samples in shorter timeframes for complex PK/PD protocols.

Science:

- Recognising the similarity between our bioanalytical activities and manufacturing organisations, LGC has embraced a number of LEAN approaches to monitor and improve systems and processes.
- We have also taken an innovative approach in developing a single quality system with common SOPs and shared laboratory facilities delivering services to ISO17025, GLP and GCP.

Solutions and output:

- LGC has increased instrument utilisation, whilst maintaining high levels of batch success as measured by Right First Time – improving quality and cost efficiency.
- 100% success in regulatory inspections.
- Cost savings have been passed on to clients.



Your team at LGC

The smooth running of your outsourced project is dependent upon the skill and experience of the people you are working with. Above all, however, the success of the collaboration relies on great communication.

At LGC, we are committed to ensuring that you have a great experience working with us and this, we believe, is a major factor in maintaining our excellent record of repeat business. Our goal is for 100% of our customers to return to us where they have a need for our services.

With a dedicated team of scientists working on your project, you benefit from open channels of communication with a project manager who is close to the experimental work. In the challenging world of drug development, things don't always go as planned, so everyone at LGC is encouraged to be open and honest about problems as they arise and proactively offer solutions.

About LGC

LGC is an international science-based company and market leader in the laboratory services, measurement standards, genomics, reference materials and proficiency testing marketplaces. LGC operates in a variety of markets – including, but not confined to, Food & Agriculture, Government, Pharmaceuticals and Biopharmaceuticals and Sports - which underpin the safety, health and security of the public and the regulation of industry, for both private and public sector clients.

With headquarters in Teddington, South West London, LGC employs over 2,000 staff, operating out of 22 countries worldwide. Its operations are extensively accredited to international quality standards such as ISO/IEC 17025.

Set up in 1842 as the Laboratory of the Government Chemist, for more than 100 years LGC has held the unique function of the Government Chemist in the UK. LGC was privatised in 1996 and is now majority-owned by KKR a leading global investment firm.

From biomarkers to small molecules, biopharmaceuticals and antimicrobials, we are ready to answer your questions.

Science for a safer world

For more information about **LGC** – our latest results, news, details of our products and services, please visit the Group's website at www.lgcgroup.com



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