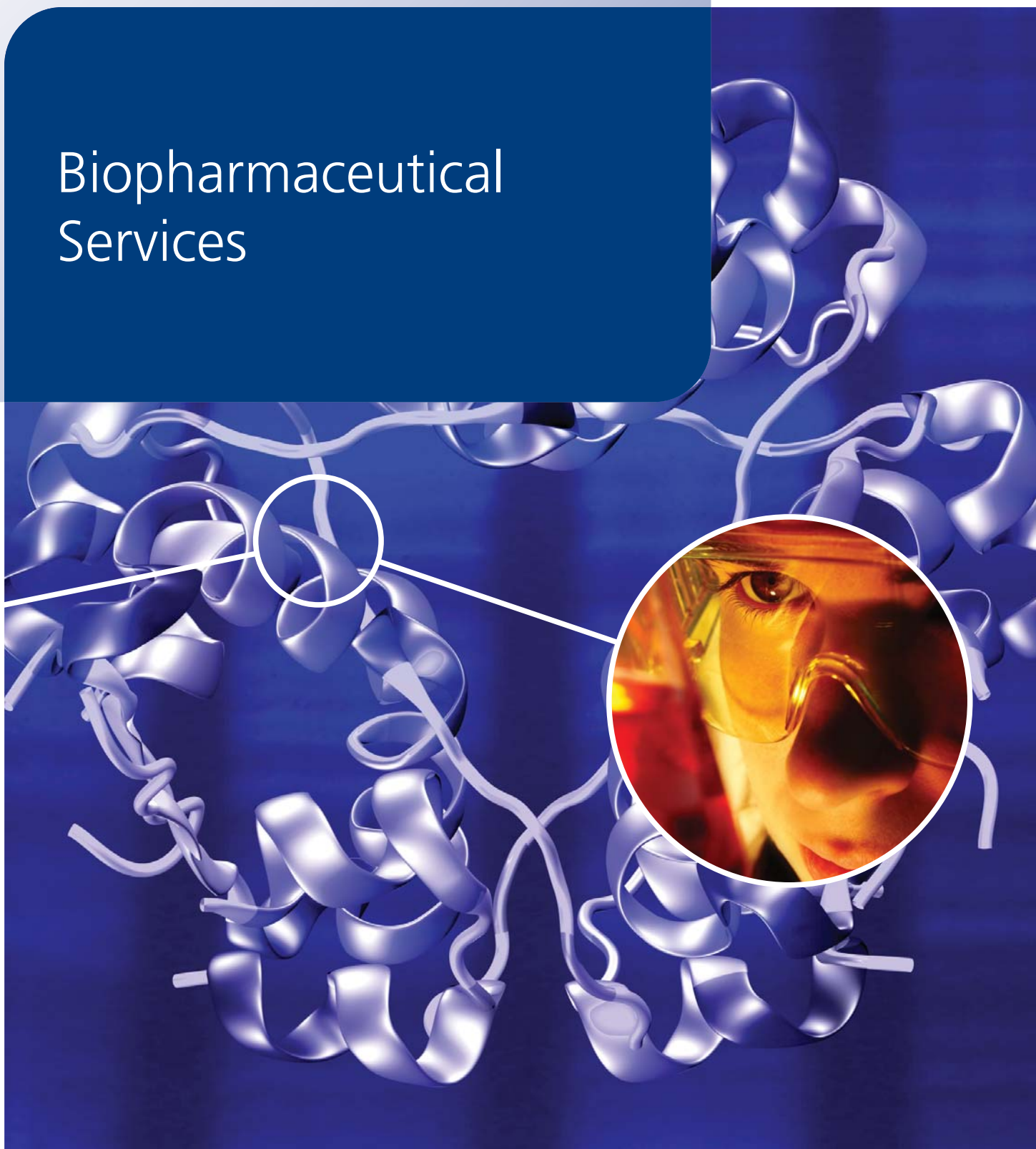


Intertek

Valued Quality. Delivered.

Expert Analytical & Bioanalytical
Services for Biopharmaceuticals

Biopharmaceutical Services



Biopharmaceutical Services

Ensuring the purity, identity, safety and quality of your biopharmaceutical product is critical to success. In an era where financial prudence is a necessity, getting your analytical or bioanalytical strategy right first time is more important than ever.

Intertek's GLP / GCP / cGMP compliant facilities provide comprehensive analytical and bioanalytical solutions for these complex products, helping you to navigate the challenges of development, authorisation and manufacturing. With over 30 years of providing high quality laboratory services for pharmaceutical and biotechnological products, Intertek offers a wealth of experience in working with biopharmaceutical APIs and finished products.

At Intertek, we understand the need to have a responsive, flexible analytical resource, with experienced project management to meet your critical milestones and deliver regulatory compliant data every time.

Purity. Identity. Safety. Quality.

- Structural Characterisation
- Physicochemical Properties
- Comparability Studies
- Process Residuals Determination
- Product Related Impurities
- Aggregation Studies
- Immunochemistry
- Potency Testing
- GMP Microbiology
- Extractables / Leachables
- QC Release Testing
- ICH Stability Studies
- Method Development & Validation

Specialist Services for:

- Recombinant Proteins & Glycoproteins
- Monoclonal Antibodies
- Antibody-Drug Conjugates
- Biosimilars & Biobetters
- Oligonucleic Acid Therapeutics
- Vaccine



Post Translational Modifications (PTM)

Intertek offers strategic approaches to PTM analysis. With intelligent application of enzyme or chemical digestion coupled with highly sensitive LC-MS, the detection and identification of a range of PTMs can be explored:

- Deamidation
- Glycosylation
- Phosphorylation
- Acetylation
- Alkylation
- Sulfation
- Glycylation
- Methylation
- Oxidation
- Mis-matched S-S bridges
- Truncation
- N/C-terminal modifications

Immunochemistry Services

Intertek's Immunochemistry capabilities are world renowned for developing and validating quantitative ligand-binding assays for novel biologics and biosimilars. Our extensive expertise in the development and validation of quantitative ligand-binding assays (immunoassays) for use in PK (pharmacokinetic) and TK (toxicokinetic) studies including immunogenicity and biomarker studies for novel biologics and biosimilars:

- Biomarker Assays
- Cell Based Neutralization Assays
- Immunogenicity Assays
- Quantitative Immunoassays
- PK & TK Studies

Process Related Impurities

Process related impurity are typically present in trace levels in challenging sample matrices. Intertek apply a range of highly specific and sensitive analytical techniques including LC-MS or LC-MS/MS, GC-MS, NMR and ICP-MS to detect:

- Kanamycin
- Tobramycin
- Gentamycin
- Amoxicillin
- Chloramphenicol
- Methotrexate
- Glutathione
- Dithiothreitol
- IPTG
- Triton-X
- Tween

Secondary and Tertiary Structure

Determination of secondary structural attributes (α -helix, β -sheet, β -turns) using, Circular Dichroism (CD), FTIR, Fluorescence1D / 2D High field 500MHz NMR studies (NOESY & TOCSY).

Potency Assays

Potency bioassays are an integral part of release and stability testing. Intertek has experienced specialists performing cell based potency and ligand binding assays. These assays can be performed to GMP for regulatory submissions or as a non-regulatory study under the same high quality standards.

Comparability Studies

The FDA and EMEA require demonstration of comparability compliant with the ICH Q6B and Q5E guidelines. Intertek has undertaken many detailed comparability studies since 1999. There is a regulatory expectation that "orthogonal" approaches will be applied such that conclusions for key quality attributes are based on multiple technologies.

ICH Stability Testing

Biopharmaceuticals require stability storage integrated with advanced analytical capabilities. Intertek experts offer strategically planned studies - In particular identification of degradation products such as deamidation or oxidation, may be included in the analysis package for either short term, long term studies or forced degradation.

QC Release Testing

Important for both bulk lots and finished products, Intertek's suite of release tests includes assays for purity, quality and endotoxin testing. Release tests can be developed and validated in house, transferred from clients or include Pharmacopeia Monograph testing.

Aggregation Studies

Aggregation can have serious implications for the safety and efficacy of a biopharmaceutical. A comprehensive range of analytical techniques such as SEC-MALLS or DLS can be applied.

Product Related Impurities

Isolation of product related impurities using FPLC, HPLC or SEC for characterisation and use in release assay validation. Host cell protein utilising ELISA methods and Host cell DNA options are also available.

Expertise in Protein Analysis

Protein therapeutics can present significant analytical challenges. Intertek characterisation packages reflect the requirements of ICH Q6B Guidelines and aim to meet the analytical challenges of a 'well characterized' or 'specified' biological product.

Structural Characterisation

Amino acid sequence:	Sequencing studies using a broad range of digest strategies and LC-MS/MS (including enhanced scan techniques with Intelligent Data Acquisition)
Amino acid composition:	IC (HPAEC-PAD), HPLC, UPLC Methods
Terminal amino acid sequence:	N- and C-terminal sequences e.g. by LC-MS/MS sequencing of peptide fragments from digests containing N- and C-termini. LC-MS allows confirmation of an expected C-terminus. Also can be similarly used to deduce the presence of "ragged ends"
Peptide map:	Peptide mapping by protease digestion followed by LC-MS, LC-MS/MS, MALDI-MS. For batch release the LC-UV profile can be compared directly with that of a highly characterised batch of reference material
Sulfhydryl groups & disulphide bridges:	Sulfhydryl groups & disulphide bridge mapping using protease digest and chemical modification experiments followed by MALDI-MS. Necessary to establish formation of expected and "mis-matched" interactions as well as the amount of free sulfhydryl groups
Carbohydrate structure:	Glycosylation studies by enzymatic glycan cleavage and fingerprinting by ion chromatography or MALDI-MS

Physico-chemical Properties

Molecular weight:	Molecular weight by MALDI-MS, ESI-MS and LCMS
Isoform pattern:	Isoform and impurity studies using PAGE, SDS-PAGE, IEF, CE, HPLC
Extinction coefficient:	Validated Extinction Coefficient studies if required
Liquid chromatographic patterns:	For ID, homogeneity, purity – HPLC, UPLC, SEC, RP HPLC, IEX
Spectroscopic patterns:	FTIR, 1D & 2D NMR, Fluorescence, UV-vis, CD
Electrophoretic patterns:	CE(CZE), CIEF, Gel IEF
Quantity:	Absorbance at 280nm, Bradford or Lowry Total Protein Assay, Quantitative amino acid analysis, BCA, Total Nitrogen
Aggregation studies:	SEC, SEC-MALLS, SEC-Viscometry-RALLS, DLS, Zeta Potential, CE, Gel electrophoresis

Glycoprotein Characterisation

Influenced by the cell line, Glycosylation can potentially affect the bioactivity, safety and efficacy of the product. In line with the ICH Q6B guidelines Intertek offers analytical packages throughout development to the final product covering:

- Carbohydrate content (neutral, amino sugars, sialic acid)
- Determination of glycosylation sites
- Structure of the carbohydrate chains (antennary profile)
- Composition of the glycan moieties

Monoclonal Antibodies

The complex geometries of the antibody domain and their glycans mean that even relatively small changes in carbohydrate structure can lead to functionally significant changes in protein structure. Intertek's expertise include:

- Isolation, purification & characterisation of Fab/Fc fragments by Gel Electrophoresis or HPLC
- Identification of glycopeptides following digestion and analysis by MALDI or LCMS
- Sialylation analysis by ion chromatography and normal or reverse phase chromatography.
- N- and O-glycan characterization
- Purity of intact antibody by 1D Gel Electrophoresis

Drug Delivery Technology

Our experts routinely work with clients helping them to understand and develop drug delivery technology such as encapsulation and novel formulation microstructure through physical characterisation techniques such as DSC, Cryoelectron microscopy and Optical microscopy.

Biosimilars & Biobetters

Biosimilars ('follow-on biologics') are complex protein structures. Extensive testing is required to demonstrate a comparable profile to a reference product as minor changes in bioprocessing can alter the product's character, safety and efficacy. Intertek's Biosimilar testing services include:

Analysis Services -

- Comparability Studies
- Protein Analysis ICH Q6B
- ICH Stability Testing
- Release Testing
- PEGylation Analysis

Bioanalytical Services -

- Immunochemistry Services
- Immunogenicity Assays
- Ligand-Binding Assays
- Clinical & Preclinical
- Pharmacokinetics

Vaccines

Intertek's BSL2 vaccine analysis facility is aligned for characterisation of vaccines based on recombinant viral vectors, protein antigens, polysaccharides, semi-synthetic poly- or oligosaccharide-protein conjugates and novel nucleic acid (DNA and RNA) constructs. Comprehensive technology coverage facilitates carbohydrate, lipopolysaccharide, lipid, peptides, protein, glycoprotein, and lipoprotein components of vaccines throughout the development process to manufacturing and post-marketing surveillance.

Oligonucleic Acid Therapeutics

Intertek offers a comprehensive suite of GLP/cGMP analytical characterisation and strategies for assessing composition and purity underpinned by considerable experience for the different classes of oligo-based drugs (siRNA, Antisense oligonucleotide (DNA-like) or Aptamer):

- Detailed Structural Characterisation
- Determination of impurities
- 31P NMR characterization of APIs & product related P containing impurities



Excellence in Protein Analysis

Our Centre of Excellence for protein structure & physico-chemical characterisation has been inspected by the UK MHRA for GLP and GMP compliance and by the US Food and Drug Administration (FDA) for GMP compliance.



Globally grounded where you need us most.

Whatever your target market, Intertek's global network of experts is ready to help you reach it. For more information, email biopharma@intertek.com, or contact one of our regional head offices:

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