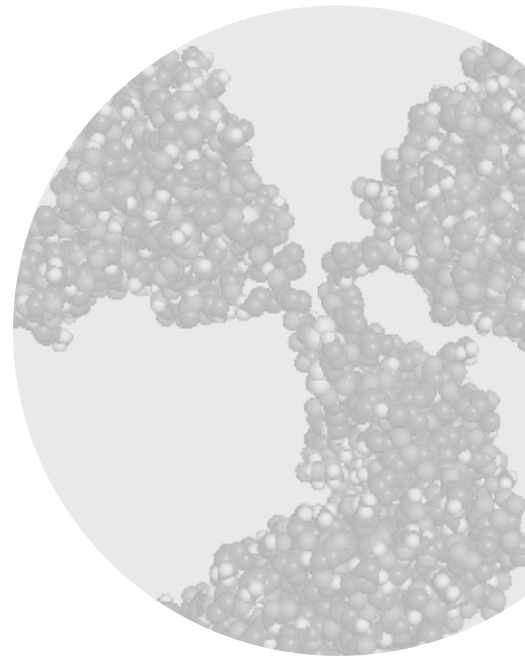




KYMOS
BIOTECH

Biologics

Biopharmaceutical testing



Biopharmaceutical testing

According to ICH Q6B, characterization of a biotechnological or biological product includes the determination of its physicochemical properties, biological activity, immunochemical properties, purity, and impurities by appropriate techniques in order to ensure safety, quality and efficacy.

Quality of biologics is a challenging issue that due to the high complexity of biopharmaceuticals cannot be established without the determination of the comprehensive analytical fingerprint, including many different aspects: structure, content, purity, impurities and stability.

Activity of the drug is a basic attribute that shall be determined to assess the drug efficacy, and it is mostly based in cell assays.

Safety is another key factor for biologics, as minor changes in the physicochemical properties, structure, conformation or impurity profile can cause an adverse or neutralizing immunogenic response.

CHARACTERIZATION AND COMPARABILITY

KYMOS is a CRO fully compliant with GLP offering reliable characterization and comparability services and a value proposition based on two different approaches:

- Testing Services focused on analytical results: Compendial Pharmacopoeia methods, Client's transferred methods, KYMOS' standard methods adapted to Client's product and specific method developed for the Client.
- Service Packs focused on the knowledge of the molecule, providing a full characterization of a particular aspect of the biopharmaceutical in an orthogonal analytical approach.

General testing

General tests are intended to have a preliminary overview of the quality attributes of the protein during the first development phases.

- Electrophoretic pattern by electrophoresis 1 and 2 dimensions, PAGE, SDS-PAGE, Bioanalyzer, IEF, Western blot
- Extinction Coefficient
- Protein quantification by Bradford, Lowry and BCA methods
- Amino Acid analysis by HPLC methods (Waters AccQ-Tag® and Agilent OPA®)
- Disulphide bonds by Ellman method
- Antibody isotyping



Structural analysis

The structure is important to obtain a complete identification of the molecule during the strain selection, cell bank stability, bioprocess improvement and characterization of the final product.

- Intact protein mass determination by electrospray MS and MALDI-TOF
- Peptide mapping and amino acid sequencing by LC-UV-MS/MS (QToF and QTRAP)
- Post-translational modifications such as deamidation, phosphorylation, oxidation and others by LC-UV-MS/MS
- N and C terminal sequencing of intact protein by ISD-MALDI-TOF and Edman degradation
- Glycosylation and phosphorylation sites by LC-MS/MS
- Glycosylation Profiles: monosaccharides, sialic acids, charge and glycan profiles by GC, LC with fluorescence and MS/MS detection and capillary electrophoresis with LIF detection



Conformational analysis

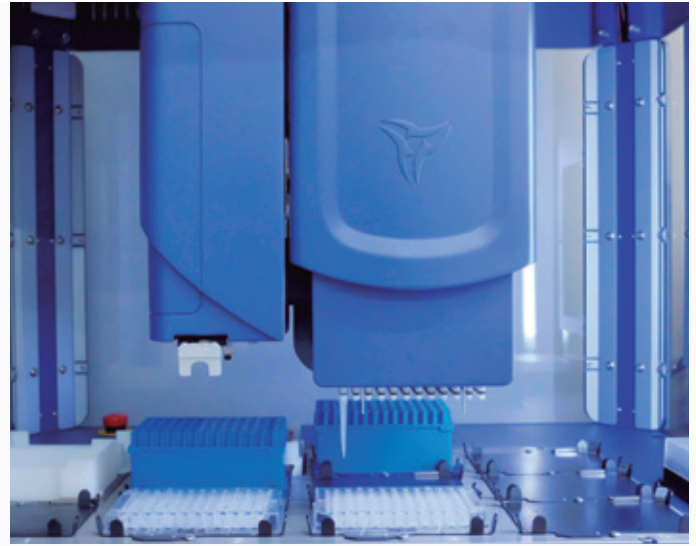
The 3D conformation and the folding of the protein play an important role on protein activity and may have a strong impact on the biological activity and immunogenicity.

- Circular Dichroism (CD)
- Ultraviolet spectroscopy (UV)
- Fluorescence spectroscopy (FL)
- Infrared spectroscopy (FT-IR)

Identity, content and protein related impurities

The chromatographic pattern is very powerful when comparing a biosimilar with the original in order to detect any possible difference. It is also the way to check the quality of the purification process.

- Liquid chromatographic patterns: RP-HPLC/UPLC, SEC-HPLC/UPLC, affinity-HPLC/UPLC (detection by diode array, fluorescence, refractive index, evaporative light scattering, electrochemical and MS detection)
- Capillary electrophoresis with UV and laser induced fluorescence (LIF)
- ELISA, electrochemiluminescence and radio-immunoassay



Process related impurities

Process impurities are also a measure of the quality of the purification process and an important topic because of potential safety concerns.

- Host Cell Proteins by commercial and specific ELISA
- Chemical contaminants by HPLC and GC
- Elemental impurities by AAS and ICP-MS
- DNA by colorimetric commercial kits
- Mycoplasma by PCR commercial kits
- Mycotoxins by colorimetric or gel-clot test
- Bioburden

Biological activity

Biological tests are key to confirm the molecule activity. This kind of tests is completely different to the rest of analytical methods and requires a very specific expertise.

- Binding studies by ELISA, ECLA (MSD®), RIA and SPR (Biacore®)
- Potency assays cell based assays
- Competitive inhibition ELISA assays for vaccines

KYMOS is fully compliant with GMP to provide routine quality control services for investigational, animal and human medicinal products. KYMOS has the authorisation to import and provide Certificates of Analysis and Release to products from non-European manufacturers.

Stability studies

Biopharmaceuticals may suffer aggregation, truncation, protein folding changes and other modifications that may have a potential impact on safety and efficacy. Stability studies are essential to detect potential risks and KYMOS offers its experience under the guideline ICH Q5C.

- Design, storage and management
- Development and validation of stability indicating methods
- Stability testing for APIs and drug products
- All ICH conditions available
- Photostability
- Holding time, temperature cycling and transportation stability
- In use stability
- Leachables & extractables
- Ongoing stability



Batch testing and release

KYMOS performs method development and validation or method transfer of Clients' methods required for batch certification and release. KYMOS also carries out tests against Pharmacopeia monographs and test methods. KYMOS' experience covers a wide range of biotechnological products such as **biosimilars, therapeutic proteins, monoclonal antibodies, oligonucleotides, ADC, hormones and peptides**. The release tests usually cover the following quality requirements:

- Appearance
- Identity
- Purity
- Impurities
- Potency
- Quantification
- General tests: pH, osmolality, particulate matter
- Endotoxins and Sterility
- Specific tests, case by case

Kymos also has wide experience in **polysaccharides** (SPR of heparin interactions, disaccharide mapping, Pharmacopoeia chromogenic tests of antifactor IIa and Xa) and in **vaccines** (characterization of adjuvants, development and validation of potency ELISA assays).



www.kymos.com

Kymos Pharma Services, S.L.
Parc Tecnològic del Vallès
Ronda Can Fatjó, 7B
08290 Cerdanyola del Vallès
Barcelona, Spain

Phone (+34) 93 548 18 48
Fax (+34) 93 170 29 99
info@kymos.es