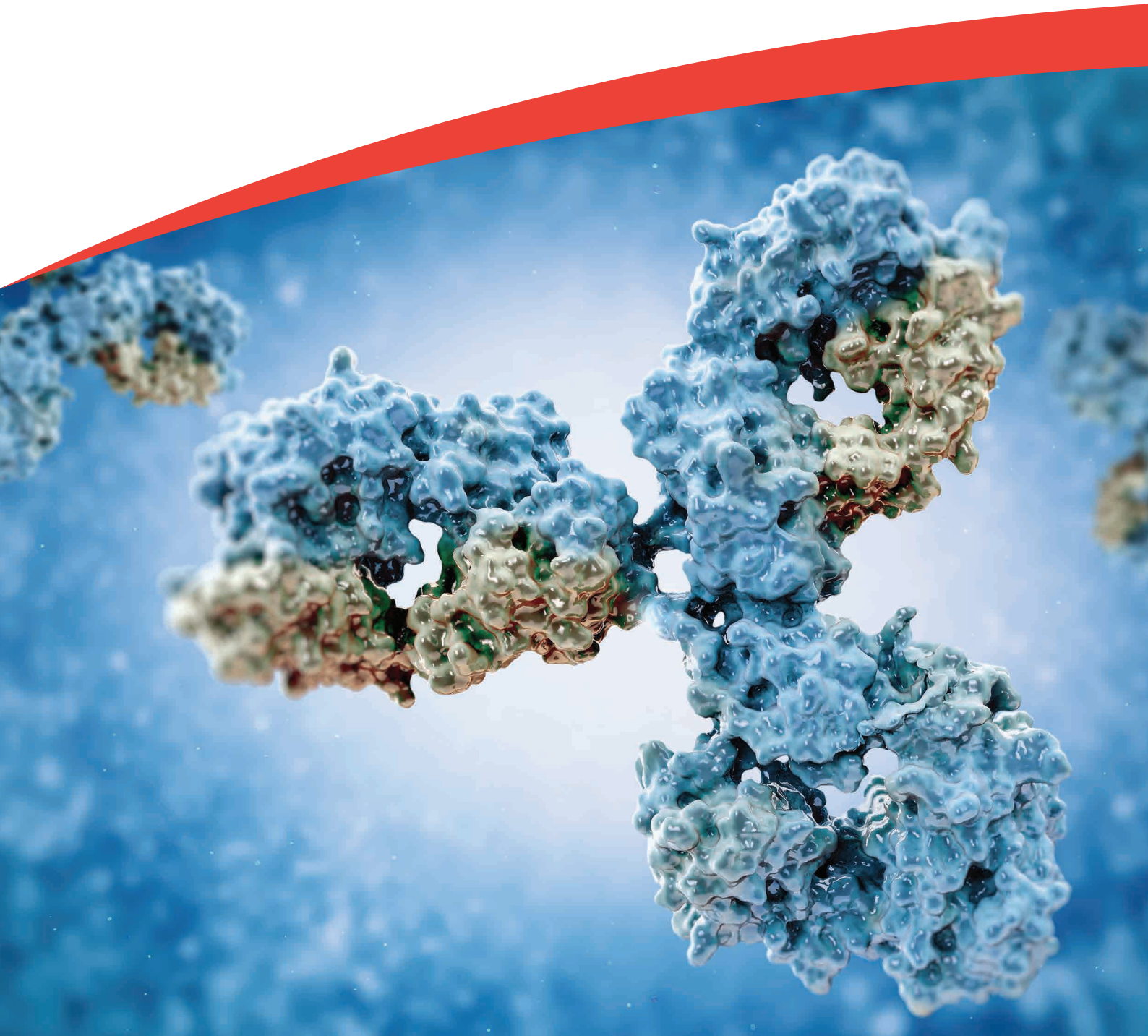
ALMAC

Partnering to Advance Human Health

Analytical solutions for biologics

Providing comprehensive and flexible analytical solutions to accelerate the development and approval of biologics



Analytical solutions for biologics

Providing comprehensive and flexible analytical solutions to accelerate the development and approval of biologics

- State-of-the-art analytical methods to thoroughly assess and characterise critical quality attributes
- Science-driven analytical data and characterisation packages for demonstration of biosimilarity and establishing totality of evidence
- Phase-appropriate lifecycle approach to analytics for method development, qualification and validation
- Release and stability testing to support clients' successful product launch in regulated markets including FDA, EMA and PMDA
- Global cGMP quality systems to support clinical and commercial biologics

Lot-release and stability testing

From our laboratories in Europe and the UK, Almac provides GxP release and stability testing services to support our clients' biologics drug substance and drug product programs for both novel biologics and biosimilars.

If you are looking for GMP release of clinical or commercial batches, our tailored services are flexible, timely and reliable.

Attributes to be assessed include:

- **Safety**
- **Purity**
- **Potency**
- **Glycosylation**
- **Identity**
- **Impurities**

Our stability programs for biologics are designed in accordance with ICH (Q5C) guidelines with most appropriate stability-indicating tests which are sensitive and robust. The most commonly used stability-indicating analytical methods include

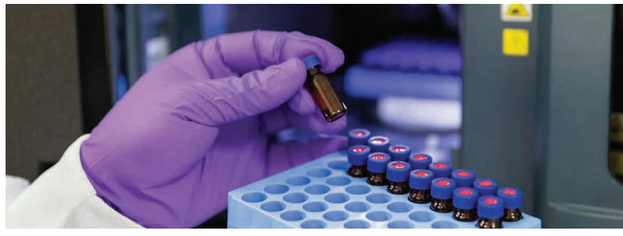
- **Size exclusion chromatography**
- **Ion-exchange chromatography**
- **Capillary Gel Electrophoresis (CGE)**
- **Biological assays**
- **Microbiological**

If required, ad-hoc temperatures and humidity conditions required to ascertain the shelf-life and comply with ICH guidelines can be provided.

Raw material testing

Almac offers comprehensive raw material testing services for microbial and mammalian expression systems that comply with pharmacopeial requirements and our clients' specifications.

Chemically defined media	Excipients and surfactants
• Amino acid analysis • pH, osmolality and appearance • Sugar, vitamin and metabolite profiles • Trace metal analysis by ICP-MS • Bioburden and endotoxin testing	Identity testing and characterisation of excipients and surfactants such as: • Polysorbate-80 • Polysorbate-20 • Triton • Anti-foam and Polyols



Management of analytical methods

Method development / optimisation

Fit-for-purpose analytical method development / optimisation based on AQbD paradigm. This approach allows Almac to develop sensitive yet robust analytical methods for release and stability testing of biologics.

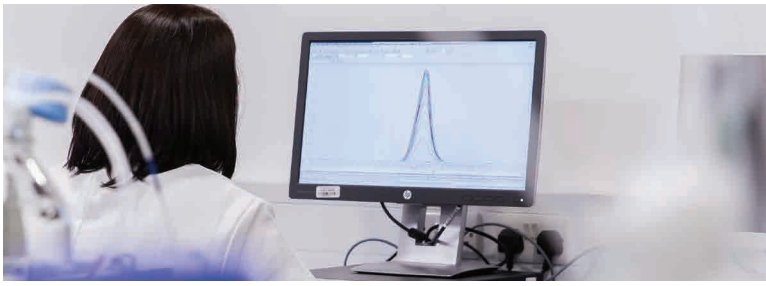
- **Quantity:** protein concentration by A280
- **Process related impurities:** host cell protein (ELISA), Protein-A leachate (ELISA), culture media components and detergents
- **Product related impurities:** protein oxidation, deamidation and degradation
- **Identity:** pI determination by cIEF, peptide mapping by UPLC
- **Glycan profile:** glycan analysis by UPLC, sialic acids, monosaccharide profiling
- **Excipients:** polysorbates, poloxamers, polyols, preservatives (phenol, benzyl alcohol) and buffering agents
- **Purity and heterogeneity:** aggregation (SEC), fragmentation (CE-SDS), charge variants (cIEF, CZE and IEX)
- **Potency:** binding ELISA assays, Fc functional assay

Method qualification / validation	Method transfer
Subsequent to successful method development, Almac offers phase-appropriate method validation according to ICH Q2 (R1) guideline recommended for the analytical procedure. We also perform gap analysis of previously validated methods at a different laboratory to de-risk the program and maximise the success of a regulatory dossier.	Almac offers method transfer services to support GMP clinical/commercial release and stability testing as well as characterisation methods. Our unparalleled expertise in seamless method transfers between laboratories through either comparative testing or co-validation of biologics ensures smooth transition.

Protein Characterisation

In line with the principles set out in ICH Q6B, using state-of-the-art Orbitrap mass- spectrometry, we can characterise your biological product allowing relevant specification to be established. This includes:

- **Determination of intact and reduced molecular mass**
- **Identification of gycoforms**
- **Extensive coverage of amino acid sequence**
- **Peptide mapping**
- **Terminal amino acid sequence**
- **Disulfide bridges and sulfhydroxyl groups**
- **Post translational modifications**



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