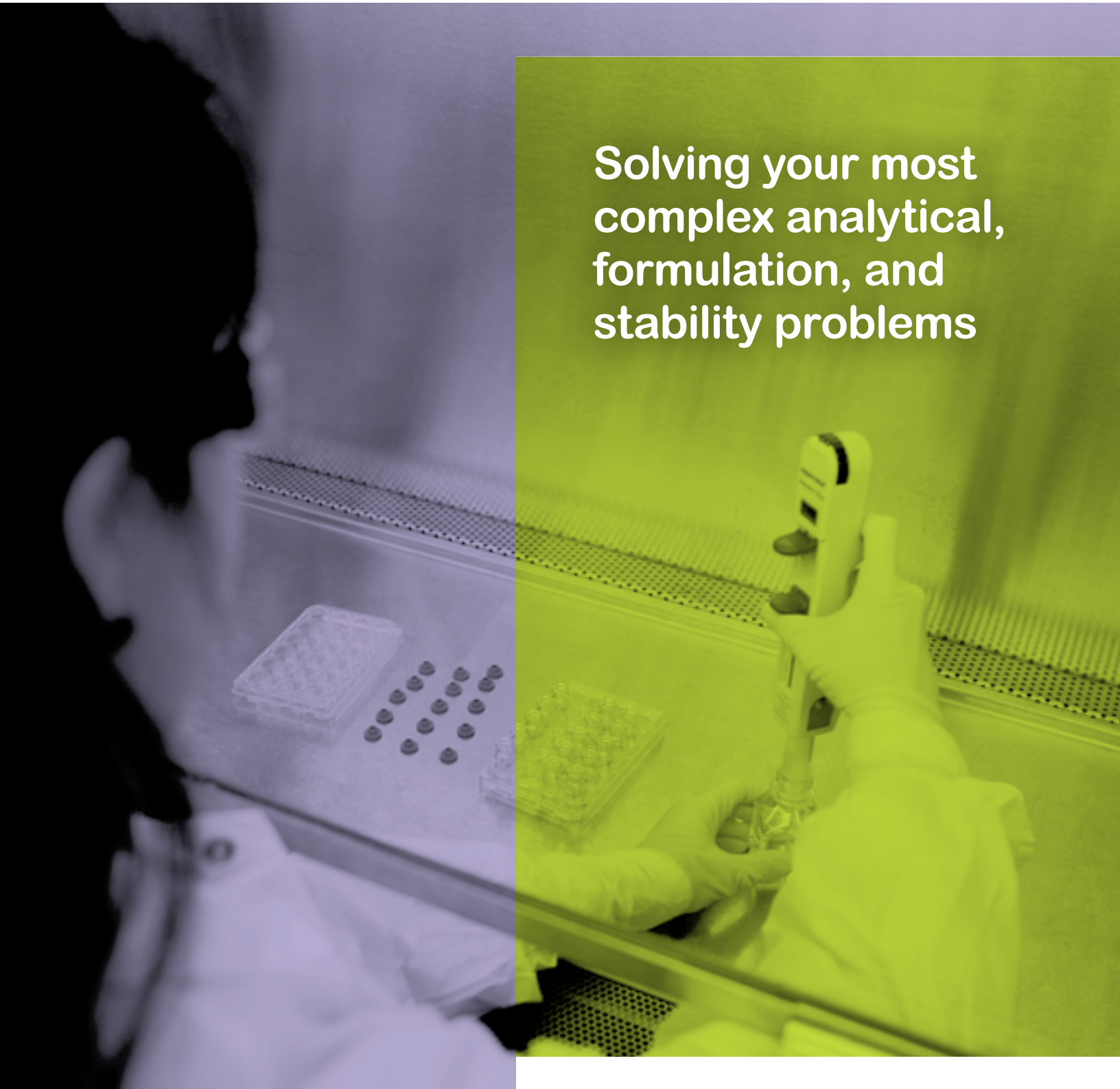
Analytical, Formulation, and Stability Services

CMC biologics
Right. On Time.



Solving your most complex analytical, formulation, and stability problems

Analytical Characterization

Profound Scientific Know-How.

State-of-the-Art Laboratories.

cGMP Services for Every Stage of Drug Development.

CMC Biologics has extensive experience, from Phase I through commercialization, developing and validating analytical techniques for complex proteins—glycoproteins, clotting factors, enzymes, growth factors, antibodies, and more.

Our innovative scientific team—with an average of 14 years' industry know-how—will provide you with the technical guidance needed to solve your most difficult analytical challenges. Our state-of-the-art equipment and laboratories enable us to deliver your customized solutions right, and on time.

As a global biopharmaceutical CMO, our expertise in analytical method development and validation, and formulation development for therapeutic proteins, ensures you the highest quality data in compliance with current cGMP requirements and ICH guidelines.

This powerful combination means faster, more flexible development to speed your product to market. Our collaborative mindset leads to long-lasting partnerships with customers across the industry.

Our broad capabilities allow us to characterize carbohydrates, monitor protein folding, verify primary structure, identify post-translational modifications, and more. With our talented staff, fully-equipped labs, and extensive experience with molecules from antibodies to complex glycoproteins, all under one roof—we are your number one resource for analytical protein characterization.

CASE STUDY BEYOND THE OBVIOUS

Problem: The Client experienced large changes in the ion-exchange profile of the drug candidate under moderate stress conditions.

Solution: Peaks were collected and characterized by a combination of intact LC/MS, peptide mapping and CD spectroscopy. The changes in the profile were attributed to post-translational modifications and low thermostability. The results of our thorough investigation provided guidance regarding a suitable storage temperature range for the product.

Bioassay Development

From ELISAs to cell-based bioassays, from antibodies to clotting factors to enzymes—we've seen it before. Whether you're starting from scratch, have a partly-developed method, or are transferring in a fully-developed method for validation, we can develop a method backed by the statistical power you need. Attention to every detail ensures that your bioassay is right, and on time.

CASE STUDY **BIOASSAY REBOOT**

Problem: The Client's existing potency assay demonstrated multiphasic response and poor assay performance, curve fitting, precision, and accuracy.

Solution: Based on the product's mechanism of action, additional cell lines were screened, an alternative cell line with a reproducible response was identified, and a release-ready cell bank was prepared. The cell culture conditions, plate layout, and readout mode were optimized to develop an assay with reproducible dose response curves that were suitable for reporting relative potency via parallel line analysis.

Formulation Development

We can design fast excipient screening studies using DOE principles and follow those up with real-time and accelerated stability studies as well as clinical in-use stability evaluation to deliver the perfect formulation. And we can design lyophilized drug product formulations accompanied by proven lyophilization cycle development in our two pilot-scale freeze-dryers. Whatever your protein—an antibody, antibody-drug conjugate, fusion protein, growth factor, hormone, or pegylated protein—we've formulated one like it.

CASE STUDY **STABILITY ENHANCEMENT**

Problem: The Client required better stability than provided by a previously-developed lyophilized formulation.

Solution: A cryoprotectant was identified that demonstrated enhanced stability under accelerated conditions over 12 weeks. A lyophilization cycle suitable for the new formulation was developed and successfully transferred to manufacturing scale.

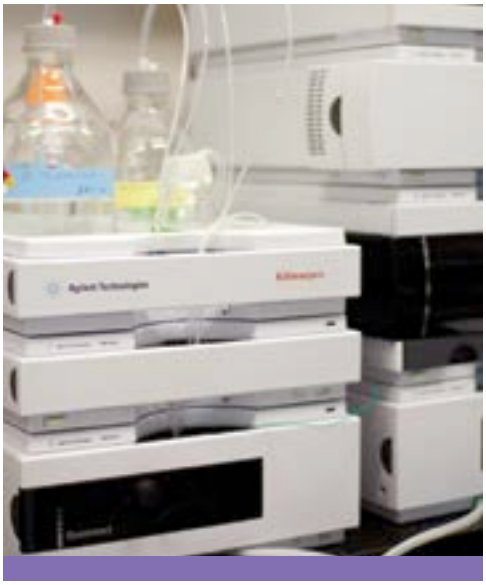
cGMP Stability

CMC Biologics transfers and validates the analytical methods needed to support your important regulatory efforts. Comprehensive characterization and bioassay development services enable us to provide data that includes validation and full documentation and meets all cGMP, ICH and international regulatory authority requirements.

CASE STUDY **ANALYSIS OF IN-USE STABILITY**

Problem: Client sought a protocol to establish short term stability.

Solution: Samples were pulled at 14 days at 2-8 °C + 2 days at 25 °C/60% relative humidity, 15 days at 2-8 °C + 1 day at 25°C/60% relative humidity and 16 days at 2-8 °C and then tested together to determine any possible degradation events that arose from the various stability conditions. Testing included Visual Appearance, pH, SDS-PAGE (reduced and non-reduced), peptide mapping, SEC-HPLC, IEX-HPLC, RP-HPLC, and Functional Activity testing.



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ANALYTICAL CHARACTERIZATION

Release Assays

- SE-, IE- and RP-HPLC
- SDS-PAGE and IEF
- CE-SDS using our Beckman PA-800
- icIEF using our Convergent iCE280
- N-terminal sequencing
- HPLC (UV) peptide mapping
- Carbohydrate analysis (quantitative sialic acid and monosaccharide analysis, N-glycan profiling)
- Polysorbate quantitation

Characterization Assays

- Protein intact mass profiling by LC-TOF MS using our Waters Acquity UPLC-Synapt HDMS (Q-TOF)
- Peptide mapping by LC-MS/MS using our Waters Acquity UPLC-Synapt HDMS (Q-TOF)
- Ion-trap, triple-quadrupole and MALDI mass spectrometers also available
- SEC-MALLS for aggregate characterization
- CD, fluorescence, and FTIR for secondary/tertiary structure characterization
- N-linked and N+O-linked glycan profiling by MALDI
- Western blotting

BIOASSAY DEVELOPMENT

Molecular Bioassay Development

- Quantitative ELISAs for titer determination
- Potency ELISAs, in direct-binding or competition formats
- Biacore
- Enzyme assays

Cellular Bioassay Development

- Examples include proliferation, viability, signal transduction, apoptosis, reporter gene assays, and CDC assays
- Ability to create release-ready cell banks

LIQUID AND LYOPHILIZED FORMULATION DEVELOPMENT

- Studies available include stress-degradation (including photostability), high-throughput formulation screening and optimization, formulation stability, in-use stability, and other studies upon request.
- Characterization and release assays listed above and to the left are available for formulation sample testing.
- Other assays available include subvisible particulates, and for lyophilized samples, residual moisture and reconstitution time.
- Two available pilot-scale lyophilizers for lyophilization cycle development: An FTS LyoStar II with SMART technology and a VirTis Genesis 35EL. Multiple cycles have been successfully transferred to production-scale.

cGMP STABILITY

- QC and QA reviewed Certificates of Analysis provided at each time point
- Capacity to support ICH long term, intermediate, and accelerated stability conditions (-70 °C, -20 °C, 2-8 °C, ambient, 25 °C/60% RH, 30 °C/65% RH, 40 °C/75% RH)
- 24 hour monitoring of all stability chambers and freezers with emergency backup