COBBLESTONE

COURSE ID 2885

Protein Formulation and Stability

A Practical Approach for Stabilization of Biomolecules through Formulation and Processing Strategies

DIRECTED BY

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12 Hours

ACCREDITED COURSE

- Protein Chemistry
- Recombinant Synthesis
- Lyophilization/Spray Drying Techniques
- Injectable Drug Products
- Process Development
- Container Closure System

about the course

A significant portion of the pharmaceutical and diagnostic discovery groups are currently focusing on the development of biologically based molecules, such as monoclonal antibodies, proteins, and enzymes. These products, unlike small molecules, are highly susceptible to the usual stresses encountered during the product's shelf life and manufacturing process.

The success or failure of these products depends on various factors, including their formulation (such as stabilizers, surfactants, and pH) and the processing methods employed (such as reduced oxygen, lyophilization, spray drying, and minimizing shear).

This 12-hour, accredited training will begin with a brief overview of basic protein chemistry and degradation pathways followed by a short discussion on the different upstream techniques for growing and purifying the biomolecules of interest. The requirements for starting the development process will then be broken down followed by an in-depth discussion of the analytical tools necessary for development and finished product testing.

A discussion on the formulation development process for a biomolecule will be had, which will cover pre-formulation and formulation development strategies utilizing high throughput screening techniques. Process development will be discussed, including product compatibility with manufacturing equipment/product contact components, and lyophilization and spray drying as a means of long-term stabilization.

A section will be dedicated to discussing the importance of container closure systems and potential interactions with the product, followed by a discussion on aggregates and particulate matter issues and concerns.

Since this training is highly interactive, those attending the live training event must have a webcam on their computer as well as a microphone and speakers/headset to fully participate.

who should attend

This course is intended for professionals in the Pharmaceutical, Biopharmaceutical, Diagnostic, and Vaccine industries, especially those working in departments such as Chemistry, Biochemistry, Analytical, Engineering, and Biology.

Chemists, Biochemists, Biologists, Formulators, and Engineers working in product and process development and engineering will benefit greatly by attending this intensive training.

learning objectives

Upon completion of this course, you will be able to:

- Describe the complete process of developing stable biomolecule-based products including injectable drug products, diagnostics, and the like
- Explain the basics of recombinant synthesis, analytical requirements, pre-formulation, and formulation development strategies, process compatibility, and finished product manufacturing techniques including Lyophilization and spray drying
- Monitor and control aggregation during and after the manufacturing process

course outline

Review of Learning Objectives

Introduction

- Instructor Introductions
- Student Introductions
- Course Overview
- Goals of Course

Protein Chemistry

- Primary, Secondary, Tertiary, and Quaternary Structures
- Protein Characterization and Degradation Pathways
- Typical Stability Problems in Protein Products
- Thermodynamic vs. Kinetic Control of Protein Stability

Recombinant Protein Creation through E. coli and CHO Cells

- Expression Systems and Cell Line Engineering
- Upstream Process Development and Scale Up
- Downstream Processing: Protein and Peptide Purification
- Chemical and Genetic Modifications

Starting the Development Process

- Proteins as Drug Products, Vaccines, and Diagnostics in the Marketplace
- Required Resources for Development
- Analytical Requirements
- Pre-Formulation Development

Analytical Requirements for Characterization and Finished Product Testing

- Primary Structure Characterization (Peptide Mapping by LC-MS, AAA, Glycan Profiling)
- Physico-Chemical Properties (MW, Extinction Coefficient, Charge, Hydrophobicity)
- Biophysical Characterization of Secondary, Tertiary, and Quaternary Structure and Stability (CD, UV, DSC, FTIR, Fluorescence Spectroscopies)
- Product-Related Impurities

Designing an Optimized Formulation

- Theory of Stabilization
- Conformational vs. Colloidal Stability
- Excipient Considerations (Buffer Salts, pH, Ionic Strength, Counter Ions, Preferentially Excluded Stabilizers, Ligands, Surfactants, Etc.)
- Surfactants and Proteins
- Screening Techniques (Microcalorimetry, Fluorescence, UV, hHgh Temperature Multi-Well Plate Methods)
- Stabilizers and Preferential Exclusion (Cryo vs. Lyo Stabilization)
- Physical Stability in the Liquid and Dried States (FTIR, CD, Fluorescence)
- Formulation Robustness (Temperature, Freeze-Thaw, Shear Stress, Exposure to Hydrophobic Interfaces, etc.)

Overview of Lyophilization and Spray Drying of Protein Formulations

- Description, Basic Theory, and Overview
- Characterization of the Thermal Properties (DSC/ FDM)
- Special Considerations for Choosing Excipients
- Cake Elegance and Other Physical Considerations
- Residual Moisture Considerations
- Tg and Storage/Shipping Conditions
- Controlled Nucleation as a Stabilization Technique and to Improve the Lyophilization Efficiency

Container-Closure and Protein Interactions (Packaging Concerns)

- Protein Adsorption to (Siliconed) Glass Containers, Container Delamination
- Hydrophobic Surface Interaction with Flexible Containers
- Phthalates and Latex Leachables and Immunogenicity
- Effects of Surfactants

Aggregates and Particulate Matter

- Theory of Protein Aggregation
- Soluble Aggregates vs. Insoluble Aggregates
- Screening Techniques for Aggregates and Other Particulate Matter
- Immunogenicity Issues with Protein Aggregates
- How and Where are Aggregates Formed Before, During, and after Manufacturing
- Special Regulatory Issues for Protein Formulations

Process Compatibility and Scale-Up

- Compatibility with Common Manufacturing Components (Stainless Steel, Glass, Silastic Tubing, Filter Membranes and Housings, etc.)
- Downstream Compatibility (Container Closure Systems, IV Bags and Tubing, Syringes, Etc.)
- Solution Hold Times (Pre-Filling and Post Reconstitution)
- Potential Sources of Shear Stress and Particle Generation/Shedding During Manufacturing
- Strategies for Improving Problematic Formulations when Scaling-Up

Questions & Answers

Assessment Opportunity

co-course instructors

J. Jeff Schwegman, Ph.D. is the founder and chief executive officer of AB BioTechnologies where he manages the day-to-day operations of the company.

Dr. Schwegman received his BS in Biochemistry from Indiana University in 1992 and began working at Cook Imaging in Bloomington Indiana, where he gained experience in analytical, formulation, and process development. In 1999 he began graduate study in the Department **of** Industrial and Physical Pharmacy at Purdue University under the direction of Dr. Steve Nail, where his focus of research involved studying changes in the physical structure of biological molecules during lyophilization. Dr. Schwegman received his Ph.D. from Purdue University in 2003 and returned to Bloomington where he worked at Baxter Pharmaceutical Solutions as a Research Scientist in the Pharmaceutical Development group. He specializes in speaking and consulting in parenteral pre-formulation, formulation, analytical, and lyophilization of both small molecules and large biomolecules.

In November 2005, he left Baxter and formed a life science company which specialized in developing new formulations and manufacturing processes for parenteral products. In February 2008, he formed AB BioTechnologies.

Dr. Marie-Eve Beaulieu, is Co-founder and Chief Scientific Officer, Peptomyc S.L.. Dr. Beaulieu has a strong background in R&D project management and coordinates the scientific team at Peptomyc. Her experience in biochemistry and peptide and protein structure and production enabled her to manage the in-house and outsourced scientific activities at Peptomyc since 2014. Marie-Eve developed the manufacturing protocols for OMO-103 (Peptomyc's innovative proprietary cell-penetrating Myc inhibitor) at lab scale and oversaw its swift implementation at the manufacturing CRO. She also previously worked in the pharmaceutical industry (Theratechnologies Inc.) where she contributed to the development and study of novel formulations for a now commercialized peptide-based drug. Marie-Eve co-authored 4 patent applications, 19 peer-reviewed publications (two as corresponding author), was awarded 9 prizes for presentations and recently (June 2018), a young entrepreneur award.

Accreditations

International Accreditors for Continuing Education and Training (IACET)
Cobblestone has been approved as a CEU Accreditor by IACET and awards CEUs for participation in qualified courses. Cobblestone has demonstrated that it complies with the ANSI/IACET Standards and is authorized to offer IACET CEUs for its programs. CEUs will be awarded for participation in Cobblestone's courses at the rate of .1 CEU per contact hour upon successful completion of the entire course and 70% accuracy in the required Learners' Assessment. A minimum score of 80% is required for all courses within a Cobblestone Certification Program. This course offers a total of 12 contact hours, or 1.2 CEUs. For further information, visit www.iacet.org