

Therapeutic Proteins - Development and Manufacture Through Fermentation Technology

Therapeutic proteins are a fast growing segment of the pharmaceutical industry. These include native proteins, recombinant and fusion proteins, peptides and antibody fragments, many of which are manufactured through microbial fermentation. Building on 30 years of experience, SAFC Pharma® offers contract development and manufacturing of fermentation-derived therapeutic proteins from pre-clinical to commercialization.



Microbial Systems

SAFC Pharma employs microorganisms up to Risk Group 2 and operates at Bio-safety level 2 large scale. Project specific master and working cell banks are safely deposited in temperature-controlled bio-storage. Strains, handled under strict aseptic procedures, are identified and characterized for homogeneity (absence of foreign growth), viability and productivity. Native or recombinant proteins may be recovered from the fermentation broth (secreted) or the biomass (e.g. intracellular, periplasmic, soluble, or in inclusion bodies). Yields are optimized through both upstream and downstream process development. SAFC Pharma has broad experience in microbial fermentation, including but is not limited to:

- Bacteria (e.g. *Escherichia coli*, *Staphylococcus aureus*, *Clostridium species*)
- Streptomycetes (e.g. *Streptomyces species*, *Actinomyces species*)
- Filamentous Fungi (e.g. *Nigrospora species*, *Aspergillus species*)
- Yeast (e.g. *Saccharomyces cerevisiae*, *Pichia pastoris*)

Manufacturing Capabilities

- The state-of-the art GMP fermentation facility in Jerusalem, Israel features:
 - Fully automated equipment
 - Cleaning and sterilization/sanitization in place (CIP, SIP) systems
 - Sanitary grade piping equipped with filters
 - Uniform fermentor geometry and pilot/production purification system consistency to ensure robust and scalable processes.

SAFC® Pipeline Partners

Complex Technology

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- Class 100,000 (ISO 8) Manufacturing suite:
 - Fermentors - 100 L / 1,000 L / 4,000 L
 - Continuous disc stack centrifuge
 - Automatic piston discharge high-speed centrifuge
 - High-pressure homogenizer
 - Temperature-controlled, stirred processing tanks up to 4,000 L



- Class 10,000 (ISO 7) segregated purification suites:
 - GE Uniflux™ tangential flow ultra/diafiltration, Unicorn™ software
 - Millipore® Liquid BioChromatography production and pilot-scale systems
 - BPG QuickScale high-performance columns
- Lyofast 5 pharmaceutical freeze dryer (Lyophilizer)



Quality Management

Dedicated Quality Assurance (QA) and Regulatory Affairs personnel are in place to handle:

- Document review and approval (e.g. MMF, SOPs, batch records, product release)
- Equipment qualification including 21CFR part 11 compliance
- Validation of manufacturing processes and cleaning procedures
- Investigation of non-conformances
- Change control implementation
- Corrective And Preventive Action (CAPA)
- Personnel training and Qualification program
- Drug Master File (CTD-DMF) filing with the regulatory agencies (e.g. FDA, EMEA)

Analytical Services

Therapeutic proteins analytical tests are compliant with Pharmacopoeia (EP/USP) methods and ICH guidelines. Managed via a validated Informatics System for Quality Control (QC) analytical data (SAP-QM), our services include:

- Analytical methods development and validation
- Testing of raw materials, in-process control, and final product release
- Stability testing
- Cleaning efficiency testing
- Selected protein analysis tests:

Test	Methods
Protein concentration	Biuret, Lowry, UV (A_{280}), W/C, Bradford
Molecular mass	ESI-MS
Protein identity	Western blot, LC-MS (Peptide mapping), Amino acid analysis
Protein purity	RP-HPLC, TLC, SDS-PAGE
Immunoassay	ELISA, Radioimmunoassay, Immunofluorescence
Potency/Activity	Bio assays (Enzymatic, Affinity, Attachment, Lytic)
Impurities	Heavy metals, Water (KF)
Residuals	qPCR (DNA), LC-MS/MS (Kanamycin), HPLC (IPTG)
Endotoxin	LAL
Microbial load	Bio-burden, Sterility



SAFC Pharma can support your fermentation derived therapeutic protein needs from the pre-clinical to commercialization

SAFC Pharma™
Inspiring Science

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