

High-Potent API Manufacturing Through Fermentation Technology

Combining its exceptional expertise in small molecule chemistry, biologics and high-potent compound handling, SAFC Pharma offers unique large-scale fermentation-based high-potent API manufacturing through its Jerusalem (Israel) manufacturing facility to help customers bring exciting new drugs to market.

Microbial fermentation is necessary for manufacturing such pharmaceutical and biopharmaceutical actives as small organic molecules, proteins, cell wall components (e.g. Lipopolysaccharides, Lipid A) and DNAs. Product diversity makes fermentation technology a multi disciplinary expertise associated with microbiology, organic chemistry, biochemistry and molecular biology. Other levels of complexity are revealed with Biosafety Level 2 Large Scale (BSL2-LS) fermentation utilizing Risk Group 2 (RG2) pathogens, and processing in explosion proof environments.



Strain Banking

Project-dedicated master and working strain banks of natural or recombinant microorganisms up to RG2 are generated using bio-hazard cabinets following stringent aseptic procedures to prevent the risk of cross contamination. All strain banks are subject to typing (identification) and strict homogeneity, viability and productivity testing. A secure, temperature-controlled biostorage area includes cryostorage in liquid nitrogen.

Microorganisms include:

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

SAFC® Pipeline Partners

Complex technologies

High-Potent API Manufacturing Through Fermentation Technology



Fermentation

SAFC Pharma has the ability to customize and optimize microorganism cultivation, media composition and growth conditions for product yields and scale them up as required. Submerged fermentation capabilities feature a 19 L, 100 L, 1,000 L and 4,000 L fermentation train, for batch or fed-batch operations. Monitored parameters include:

- Temperature
- PH
- D.O.
- Agitation
- Pressure
- Turbidity

Fermentation progress is closely monitored for microbial growth kinetics and culture homogeneity. Product/impurities accumulation and activity (enzymes only) are assessed through the entire fermentation process using appropriate analytical methods.



Recovery and Downstream Processing

Fermentation is harvested for biomass/broth separation upon reaching pre-determined criteria including physical, microbial and product accumulation endpoints.

Downstream processing is available for both aqueous and organic solvent based products. Core technologies include:

- Centrifugation
- Separation
- Homogenization
- Organic extraction
- Concentration
- Adsorption
- Process chromatography

SAFC gives special attention to working in conditions aimed at maximizing product recovery yield, minimizing volumes to be transferred to final purification while maintaining product integrity.



Purification

Final stage purification selectively separates and retains the desired product at the highest purity per its pre-determined specifications. Product specific purification menu and conditions include:

- Chromatography (e.g. affinity, ion exchange, size exclusion, hydrophobic interactions, normal or reverse phase)
- Filtration (direct or cross flow)
- Selective extraction and crystallization

Automated chromatography (MPLC, FPLC) and filtration systems (UF/DF) are monitored on-line allowing precision and reproducibility.

Purification is handled in a new fermentation facility designed to meet the most stringent containment and safety standards to accommodate high-potent fermentation manufacturing and purification.

Quality Management

Analytical services compliant with Pharmacopoeia (EP/USP) methods and ICH guidelines include:

- Analytical method development
- Validation and testing (HPLC, TLC, GC, UV-VIS, FT-IR, NMR, TOC, ICP, Moisture (KF), LAL, Polarimetry, ELISA, PAGE, enzymatic activity, microbiological testing)

All SAFC Pharma manufacturing activities are supported by dedicated Quality Assurance (QA) and Regulatory Affairs teams.



SAFC Pharma's fermentation technology supports customer programs from pre-clinical to commercial scale phases.

SAFC Pharma™
Inspiring Science

04516-506486
LAV
0108

www.safcpharma.com

Sigma-Aldrich® and SAFC® are registered trademarks and SAFC Pharma™ is a trademark of Sigma-Aldrich Biotechnology L.P. and Sigma-Aldrich Co.
© 2008 SAFC All rights reserved.

SIGMA-ALDRICH®