

CALCET Company

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**ENGINEERING A PIVOTAL ROLE IN
BIOTECHNOLOGY AND
PHARMACEUTICAL INDUSTRIES**





Pivotal Role of Engineering

- “The process makes the product” and the process is designed-implemented-conducted by engineers
- Engineers use Computer Aided Design (CAD) and simulation tools to successfully expedite process development for pilot plant studies and optimize the process
- Engineers experiment on computer with alternative process set-ups and operating conditions to reduce cost & time consuming lab and pilot plant efforts



Pivotal Role of Engineering (cont)

- Engineers use process simulation tools throughout the life cycle of process development and product commercialization with benefits such as:
 - idea generation (when process ideas first conceived)
 - process development (while pre-clinical and clinical testing of candidate drug is on process development engineers look into many options available for manufacturing, purifying, characterizing the drug substance and mulating it as a drug product)



Pivotal Role of Engineering (cont)

- process undergoes constant changes (new syntetic routs are investigated, new recovery and purification options are evaluated, and alternative formulations are explored)

- Engineers evaluate environmental impact of process (environmental issues not addressed during process development may have serious consequences during manufacturing)



Pivotal Role of Engineering (cont)

- Engineers perform facility design and/or selection
- With process development nearing completion at the pilot plant level CAD and simulation tools are used to systematically design and optimize process for commercial production
- Good computer models are used to transfer process technology and facilitate design
- If a new facility needs to be built, process simulators are used to size equipment and supporting utilities



Pivotal Role of Engineering (cont)

- For a new facility, process simulators estimate the required capital investment options and select the optimal one based on leading process parameters
- In transferring production to existing manufacturing sites, simulators evaluate various sites from a capacity and cost point of view to select the most appropriate one
- The same applies to outsourcing of manufacturing to contract manufacturers



Pivotal Role of Engineering (cont)

- Engineers perform studies, design, construct, and perform testing of new manufacturing facility
 - In large scale manufacturing, simulation tools are primarily used for scheduling, debottlenecking, and on-going process optimization
 - Simulation tools track equipment utilization for overlapping batches and identify bottleneck areas and guide user through solutions



Pivotal Role of Engineering (cont)

- Engineers design full scale manufacturing facilities, utilities, processes, testing equipment, lyophilizers, and package and storage rooms
- Engineers design and optimize equipment, perform commissioning, transfer equipment and systems to owners, qualify (IQ, OQ, PQ) equipment and systems, perform pilot product and small/large scale trial lots.



CALCET Co. & CALCET Co. GmbH

- A consulting engineering and validation company
- Provides a wide range of specialized services to biotech and bulk pharmaceutical industries in US and abroad
- Have engineered projects from initial concept and design thru evaluation to final qualification
- Combines advanced engineering and analytical skills with experience



Company's Clients Summary

- Abbott Bioresearch Center, Inc.
- Abgenix
- Amgen Corp.
- Aradigm
- BASF Bioresearch Corp.
- Baxter Healthcare Corp.
- Bayer Corporation
- Biomarin Pharmaceuticals



Company's Clients Summary

- Dey, L. P.
- Genentech Corp.
- Genitope Corp.
- Impax Laboratories
- Martos.com SRL
- Novartis Corp.
- Novo Nordisk Delivery Technology
- Zogenix, Inc.



Company's Services

- Analysis and Design
- Process Engineering
- Reverse Engineering
- Commissioning (Engineering Check-out)
- Validation
- Plant Start-Up
- Training



Analysis and Design

- Utility/Facility Systems Design/Assessment
Plant steam/condensate, Glycol, Chilled/tower water, Distillation, Instrument air, Purified water, Water for Injection, Clean steam, Clean in Place/Clean out of Place, Process gases, Chemical Storage and dilution, HVAC, Air handling units, P&IDs and PFDs
- Reverse Engineering for Plasma Fractionation Facility and cGMP Design



Process Engineering

- Process Systems Design/Assessment (Media, Fermentation, Clarification/concentration, Buffer preparation, Purification, Cold storage, Lyophilization, Packaging)
- Development/upgrade Procurement Specs
- Commissioning and Start-up of equipment & systems for new production facility



Process Engineering (cont'd)

- Generation of P&IDs and PFDs
- Cycle development for CIP/COP, Automatic Control, PLC and Distributed Control Systems
- Develop Standard Operating Procedures, Manuals and Criteria Documents
- Use Analytical Procedures: HPLC, Electrophoresis, Infrared/Atomic Absorpt Spectroscopy, Bactereria Cell Culture, Virus Handling and Infectivity Assay



Process Engineering (cont'd)

- Root Cause Investigations and Non-Conforming Test Results and Implications
- Cold Room (-35°C) Storage Start-Up & Testing
- Viral Inactivation Full Design & Implementation
- Full Engineering Support for State-of-the Art Production of rFVIII at BAYER Building 60 Multi Purpose Biotechnology Plant in Berkeley



Validation

- Validation Strategy Formulation and Review
- Gap Analysis and Cleaning Studies
- Discrepancy Investigations (NOD, DER, NCM)
- Thermal Mapping (virtually all type equipment)
- Generation/Review of Technical Registration Dossiers (TRDs) to FDA
- Qualification of QC Laboratory Equipment



Validation (cont'd)

- Programmable logic control software qualification
- Generation/Development/Execution and Final Package Preparation of Test Plans/Protocols for: Scale-Up, Process Development, SOPs, Control System, Installation / Operational / Equipment and Process Performance Qualification (PD, IQ, OQ, EPQ, PQ)
- Viral Inactivation

Start-Up and Training

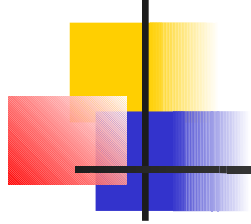


- Write start-up procedures to conform cGMP
- Start-up equipment and systems in any facility, utility and process biotechnology plant
- Organization, Generation, and Development of Training Courses
- Operational Training and Production Personnel
- Preparation of Training Manuals
- Seminar Presentations

Examples of Start-up and Training



- Design and Operation of Bayer's Building 60 Multipurpose Biotechnology Plant
- -35°C Cold Storage Room for Building 60
- Design and Operation of Viral Inactivation
- Clean-in-Place System Design, Operation, and Maintenance
- Prospective Maintenance for Corrosion Protection in Pharmaceutical Industry



THANK YOU!
