



**Biologics Services:**  
**Process Development,**  
**Manufacturing, and Support Services**

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**VxP Biologics** provides product development, scale-up and manufacturing services as well as sterile fill finish capabilities to the global mammalian, microbial, and viral markets.



**Biologics Services: Development and cGMP Manufacturing**



## Biologics Services Overview

- **Research & Development**

- Protein Expression Services
- Antibody Development
- Process Development (Upstream/Downstream)
- Viral Vector Product Development
- Analytical/Bioanalytical & Characterization



- **cGMP Manufacturing & Fill/Finish**

- Final Product Development & Tech Transfer
- Cell Culture – Mammalian
- Cell Culture – Microbial
- Viral Cloning & Packaging Services
  - AAV, Lentivirus, Adenovirus
- Sterile Fill Manufacturing
  - Parenterals, Adjuvants, Vaccines
- Dedicated Facilities
  - Customized cGMP Production
  - Cytotoxic/Potent Compounds



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## Protein Expression Services

- **Molecular Biology**

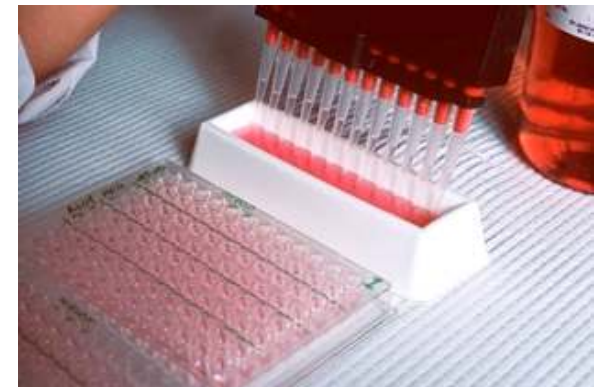
- Microbial Hosts: Bacterial (E. coli) Yeast (Pichia pastoris)
- Mammalian Hosts: CHO, HEK 293, etc.
- Gene cloning & Codon optimization
- Mutagenesis & Protein engineering

- **Lab Scale Protein Production**

- Expression optimization via Shake Flasks and Lab Reactors (inquire about details)
- Commonly Used Purification Tags: His6, GST, MBP, SUMO, FLAG, etc.
- Scale ranging from [micrograms – grams]

- **Diverse Protein Types**

- Size ranging from [3 kDa – 1000 kDa]
- Cytokines
- Monoclonal antibodies
- Membrane receptors
- Kinases & proteases



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## Antibody Development

- **Antibody Generation & Cloning**
  - Immunization and generation of hybridomas
  - Screening of Antibody Phage display libraries (client supplied ScFv/Fab libraries)
    - Cloning of variable regions of target antibody
    - Reformatting in IgG frame work
  - Cloning of heavy chain and light chain genes into suitable expression vector systems
    - From hybridoma
    - Client supplied and/or Codon optimized sequences can be provided, etc.
- **Fabs/Single Chain Antibodies (scFv)**
  - Cloning of Antigen Binding Domains or ScFv of target antibody
  - Expression and purification of E. coli, Pichia pastoris, or Mammalian cells



## Process Development Overview

- **Broad Range of Process Types**
  - Microbial (E. coli) & Mamalian (CHO); also Pichia, and other hosts
  - Secreted proteins, Intracellular soluble expression, Inclusion bodies
  - Pegylated and conjugated proteins
  - Development targeted for desired quality specifications, isoform selection
- **Process Development Services**
  - Process development, optimization and scale-up
  - Assay development and qualification
  - Formulation development and stability studies



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## Process Development cont.

- **Optimization & Scale-up (Upstream Production)**
  - Cell line development and scale-up for high product titer, stability and consistent manufacturing output
  - Manufacturing technologies and strategies (eg. Bioreactor design, disposable systems, fed-batch, perfusion, expression kinetics, etc.) for maintaining robust process performance
  - Optimized product harvest and recovery methods (eg. Centrifugation, tangential flow filtration (UF/DF), Depth filtration)
- **Optimization & Scale-up (Downstream Production)**
  - Purification technologies and recovery strategies (eg. Column chromatography using ion exchange, hydrophobic interaction (HIC), affinity, size exclusion, expanded bed absorption, hydroxyapatite, step or linear gradient elution, TFF for concentration or buffer exchange.
  - Impurity contaminant removal (viral, endotoxin, residual DNA, HCP)
  - Assay development and qualification



## Process Development cont.

- **Formulation development and Stability studies**
  - Referenced with current scientific knowledge, experience and expertise
  - Knowledge of improved methods of shelf life prediction and excipient testing
  - Experimentation of formulation based on strategy and analytical method development
  - Stability chamber storage and stability testing







## Viral Vector Product Development

- **Plasmid Cloning Service**
  - More than 15 destination vectors available, including multiple affinity and fluorescent tags
  - All clones will be fully sequenced to match your specifications
- **Adenoviral Cloning & Adenovirus Production Service**
  - Over 20 different destination vectors available for different fluorescent and affinity tags
  - Ready to transfect adenovirus can be produced within 2-3 weeks
- **Lentiviral Cloning & Lentivirus Production Service**
  - Complete service from gene cloning into lentiviral vector to lentivirus production
- **Adeno-Associated Virus (AAV) Service**
  - We offer the highest quality rAAV vectors and the most complete AAV Expression Systems
  - AAV Human cDNA ORF Cloning and AAV shRNA Cloning options available
- **Custom Cloning Service**
  - **CALL US TODAY** for further information on TALENs, shRNA Cloning, and Mutagenesis Services

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## Analytical Development & Product Characterization

- **Method transfer from client** – depends on prior development status
- **Full set of IPQC and lot release** – DS & DP method development
- **Product characterization** – including primary & higher order structure, glycosylation profile, impurities identification
- **Method qualification** – for release of Tox or Early phase clinical studies
- **Method validation** – for late stage products including late stage stability studies
- **Stability studies** – exploratory, formal, real time, accelerated, etc.





## Formulation Characterization - Instrumentation

- iCE 280 Analyzer (imaged Capillary Electrophoresis)
- MALDI TOF/TOF (Matrix Associated Laser Desorption Ionization)
- Proteome 800 CGE (Capillary Gel Electrophoresis)
- Capillary Zone Electrophoresis (CZE)
- Isoelectric focusing (IEF)
- Biacore T100
- ELISA Reader with Micro plate well washer
- Freeze Drier
- HPLC
- RRLC (Rapid Resolution Liquid Chromatography)
- LC – ESI-MS/MS
- UV-Vis
- Karl Fischer Coulometric Titrator
- pH/Conductivity meter
- Electrophoresis systems
- TOC analyzer
- Endosafe PTS (mobile)
- Endotoxin Gel Clot & LAL





## Characterization - Techniques

### Identity

- Peptide mass finger printing
- Charge heterogeneity
- Intact Mass (MALDI-TOF & Electro Mass Spectrometry)
- Immunological methods (ELISA, Western blot)
- Electrophoresis (SDS-PAGE Reducing & Non-reducing)

### Protein Characterization

- Total Protein (Lowry, Bradford & BCA)
- Quantitation (Chromatography, SPR, UV-Visible Spectrometry, ELISA)

### Purity

- Electrophoresis (SDS-PAGE Native, Reducing & Non-reducing)
- Related Proteins (RPC)
- Aggregates (SEC, Light scattering)
- Charge heterogeneity (Imaged Capillary IEF, IEC)
- Fragmentation (Capillary Gel Electrophoresis)
- Host Cell Protein (ELISA)
- Rec-Protein A Leachate (ELISA)
- Host Cell DNA (qPCR, Hybridization)



## Characterization – Techniques cont.

### Potency

- Bioassay (*in vitro*)
- Specific binding assay

### Glycan Content

- N-Glycan Profiling (Normal Phase-LC with Fluorescent detection)
- Glycan composition (LC-ESI-MS)
- N-Glycan Profiling (Capillary Electrophoresis)
- Sialic acid composition (Reverse Phase-LC with Fluorescent detection)
- Monosaccharide composition (Reverse Phase-LC with Fluorescent detection)
- Glycosylation site determination (Peptide Mapping with LC MS & MS/MS approaches)

### Moisture Content

- Coulometry (KF)
- Relative Humidity (Computrac Vapor pro)

### Microbiological Attributes

- Bioburden
- Sterility
- Endotoxin (Gel clot & LAL)



## QC Testing and Stability Studies

- **Quality Control (QC) Testing**
  - QC testing on all incoming raw materials
  - Environmental monitoring and water quality testing
  - In Process testing services: cell growth, harvest titer, metabolite assays, etc.
  - Complete Batch release testing of Drug Substance and Drug Product
- **Stability Studies**
  - Stability chambers from -70C to +40C with humidity control
  - Standby cooling and heating system
  - Fully controlled with 24/7 monitoring and Alert system (21 CFR Part : Compliant)







## Drug Product Development Overview

- **Process Development Services**
  - Process development, optimization and scale-up
  - Assay development and qualification
  - Formulation development and stability studies
- **cGMP Manufacturing Services**
  - BSL-2 and BSL-3 containment
  - Cell and Virus seed banking
  - Research grade, preclinical and cGMP Phase I/II
  - Fill/Finish services
- **Consulting Services**
  - Process analysis and troubleshooting
  - Chemistry, Manufacturing and Controls (CMC)
  - **CALL US TODAY** to discuss Technology Transfer Packages



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## cGMP Manufacturing Services

- **State of the art, versatile pilot plant for GMP production of therapeutics to be used in clinical (Phase I/II) studies**
- **BSL-2 and BSL-3 containment**
  - AAV Vectors, Adenoviral Vectors, Attenuated Viruses, Lentiviral Vectors, Live Viruses, Retroviral Vectors, Vaccinia Virus, etc.
- **Cell and Virus seed banking**
  - Cell banks – master and working cells banks
  - Virus banks – vector stocks and clinical material
- **Research grade, Preclinical and cGMP Phase I/II**
  - Protein, VLPs, Monoclonal Antibodies, Peptides, etc.
- **Fill/Finish Services**
  - Custom, aseptic formulation/fill/finish with multiple presentations available
  - Batch sizes from **300 – 8,000 vials per day**



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## Mammalian Suite

- 50-1000L fermenters and associated downstream including viral inactivation and filtration
- Pre- and Post-viral removal steps in separate rooms for mammalian DSP
- Automated control of process steps, cleaning, CIP through Delta-V system



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## Microbial Suite

- 50-1000L fermenters and associated downstream intracellular soluble and IB expression
- Automated control of process steps, cleaning, CIP through Delta-V system



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# THANK YOU

For additional information:

**VxP Biologics**

[www.vxpbiologics.com](http://www.vxpbiologics.com)

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