



LakePharma
The Biologics Company



Process Development Services

LakePharma Development Center and microBiomufacturing Center

November 2019

LakePharma Provides Integrated Solutions for Biologics Development



- LakePharma is a US-based biologics contract discovery, development, and manufacturing organization (CRDMO) with a proven track record of performance
- LakePharma does not develop pipeline for own drug development

Key PD Related Services

Large-Scale Antibody/Protein Purification	Mammalian & Microbial Expression + Purification	<ul style="list-style-type: none"> • Gram scale IgG enrichments, 3 L – 50 L (mammalian). • Gram scale purification of untagged proteins – 100 L, microBiomufacturing scale (microbial).
Upstream PD	Cell Culture Optimization	<ul style="list-style-type: none"> • Parallel Bioreactor screening via Ambr 15. • Scale up/down process optimization, & tech transfer.
Downstream PD	Purification Development	<ul style="list-style-type: none"> • Optimize purification processes for CMO transfer. • Small scale chromatography and UF/DF development.
Analytical & Formulation Sciences	Biophysical Characterization	<ul style="list-style-type: none"> • Developability, stability, & characterization studies. • Formulation development

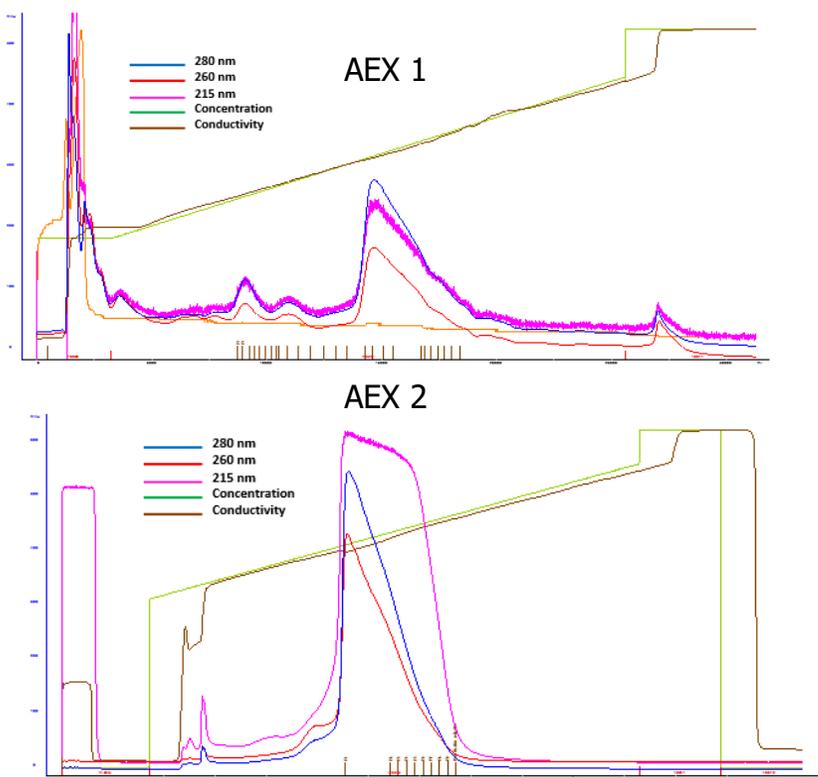
Purification Columns for All Scales



1.6	2.6	3.5	5.0	7.0	10	14	20	30
4-120	10-320	20-600	40-1,200	80-1,150	160-2,400	310-4,600	630-9,400	1,400-21,000
			column diameter (cm)					
			effective bed volume range (mL resin)					

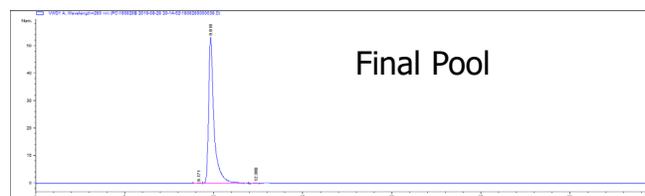
Case Study: Protein Refold & Enrichment of Untagged Protein

- Process development performed at 500 g inclusion body (IB) scale followed by 1500 g scaleup
- Purification process involved protein refolding, 4 UF/DFs, and 3 chromatography steps (AEX, AEX, HIC)
- Chromatography performed on AKTA Pilot with between 0.8 and 1.6 L columns with either 70 or 100 mm diameter (Millipore QuickScale 70, 2 x GE BPG 100)
- RP-HPLC, SE-HPLC, A280, SDS-PAGE, endotoxin analysis on column fractions steered pooling to avoid deamidated and other undesired species

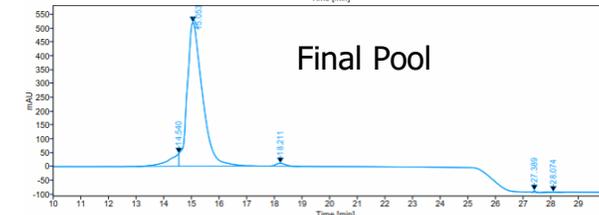
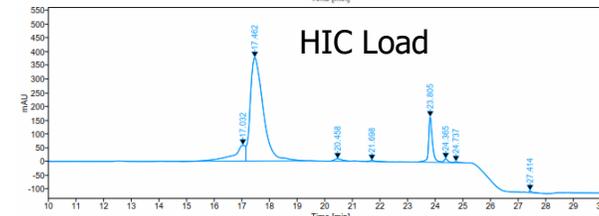
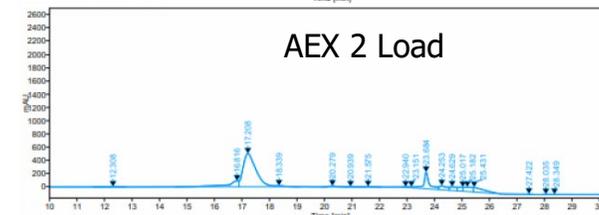
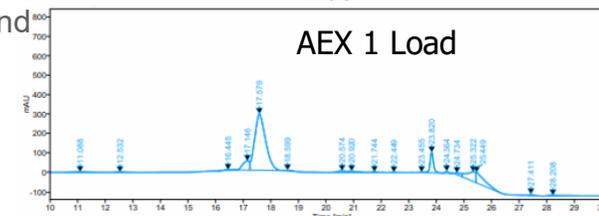
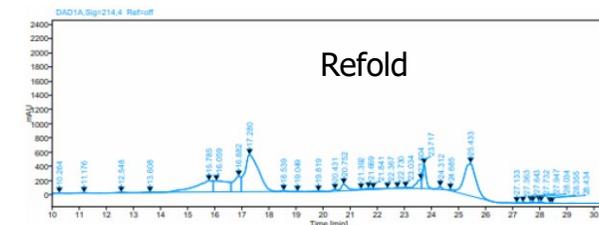


AKTA Pilot chromatograms

Summary Information	
Expression Scale	10 L, <i>E. coli</i>
Enrichment	UF→Refold→UF/DF x 2→ AEX→AEX→HIC→UF/DF→Endotoxin reduction
Total Protein	1.8 grams
Purity	>99.5% (SE-HPLC)
Endotoxin	0.08 EU/mg



SE-HPLC chromatogram



RP-HPLC chromatograms

CHO Expression Systems at LakePharma

TunaCHO™

**7-14 day transient
High Yield**

10 mL – 20 L
Can reach >1 g/L

CHO-ASAP™

Fast Stable

Transfection through
40 L production
in 6 weeks

CHO-GSN™

**High Performance
Stable**

Multiple programs
at clinical stage

- Support discovery, development, and manufacturing
- The same CHO-K1 parental is used for all platforms so products from the different platforms have similar activity & PTM profiles

Pipeline for Mammalian GMP Manufacturing: Upstream PD in Hayward, CA Transfers to Hopkinton, MA

Preliminary Upstream Media and feed screening

- DoE for media and feed screen:
 - 5 basal media x 3 feeds

Best condition resulted in 2x improvement



Sartorius ambr® 15 Microbioreactor Clone & Parameter Screening

- DoE of Parameters
 - 6 parameters evaluated

Best condition identified to scale up in 2L SUB



2L SUB Confirmation Run

1.5X achieved in 2L bioreactor run



50L SUB Scale Up

Results & protein quality identical to 2L SUB results



Highlighting LakePharma's Full Offering

Antibody Center	Gene-to-Protein (GTP) Center	Development Center	Vector Center	microBiomufacturing™ Center
San Carlos, CA	Belmont, CA	Hayward, CA	Worcester, MA	Hopkinton, MA
Antibody discovery with hybridoma, phage, and yeast display	DNA cloning and production	CHO-GSN™ stable cell line development	AAV and Lentivirus engineering and process development	Bioassay and analytics
Antibody characterization (Octet, Carterra, DSC, etc.)	Protein and antibody production using TunaCHO™ and Tuna293™	Upstream, downstream process, analytical and formulation development	DNA cloning and production	Upstream, downstream process development
Antibody developability	Protein analytics	Bioassay development	Stable cell line generation	GMP production, GMP QC lab including USP sterility and bioburden testing, bioassay and analytical testing and method validation
<i>de novo</i> antibody sequencing by mass spec	CellSpot™ antibody screening and characterization	Protein conjugation and characterization	Protein and antibody production using Expi293™ and ExpiCHO™	Biorepository (GMP)

Contact Us Today



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