Overview

Meridian Life Science®, Inc. (MLS) is an industry leader in the commercial production of critical raw materials for diagnostic manufacturers. Core capabilities include both in vitro and in vivo methodologies. MLS has the resources to manufacture and purify monoclonal antibodies using a wide array of protein purification methods at quantities ranging from research (mg) to commercial (g) scale. All manufacturing is performed according to cGMP guidelines, with corresponding documentation and quality reviews.

Pilot to Commercialization Capabilities

1. **Pilot Studies**: MLS offers fixed-fee pilots based on final cell culture volume (1L, 5L, 10L, or 20L) or number of mice (minimum 20 mice) and is independent of antibody yield and purity.
2. **Cell Culture Optimization**: Extensive cell line optimization services, including conversion to serum free media, cell culture conditions (cell density, temperature, supplements, etc.), and antibody harvest methods.
3. **Cell Banking**: MLS offers cell banking services for your critical cell lines including generation and characterization of the bank, cryopreservation, and dual site storage.
4. **Downstream Process Development**: Extensive capabilities in filtration, centrifugation, and all forms of column chromatography from Protein A or G to SEC, HIC, and IEC.
5. **Validation Lots**: MLS understands the regulatory requirement to validate three successive production lots for critical biological reagents used in commercial products.
6. **Analytical Methods**: Vast experience in biochemical or molecular characterization (SDS-PAGE, Western, Silver, ELISA, HPLC, Protein concentration (BCA, UV-vis), cell viability/density).
7. **Commercial Production**: MLS has been manufacturing critical biological reagents for the diagnostics and biopharmaceutical industry for 25+ years with the quality systems and inventory management required to provide consistent supply.

Why Partner with MLS?

- Unparalleled experience and proven track record (25+ yrs)
- Core expertise in cell culture, ascites, protein production and purification
- Flexibility in scale and production systems
- Complete R&D and Process Development service
- Dedicated project management
- Complete confidentiality

We understand that the variable nature of most biological processes often requires ongoing R&D support. MLS has been and will continue to be a proactive partner to our clients working to ensure that projects receive the technical expertise required for successful execution.

For More Information on Contract Manufacturing and Custom R&D Development;
Contact a MLS Representative at contract-mfg@meridianlifescience.com.

WWW.MERIDIANLIFESCIENCE.COM
Custom *In Vitro* or *In Vivo* Monoclonal Development and Manufacturing Integration and Optimization of Customer Process (R&D to Commercial Scale)

**Development, Clonal Selection, and Adaptation**

- **Immunogen**
  - Immunization / Hybridoma fusion
  - Clonal selection / screening

- **Hybridoma Cell Line**
  - Tech Transfer / Optimization / Feasibility Study

- **Evaluation / Adaptation of Candidate Clones**
  - OPTION: Conversion to serum free media
  - OPTION: Sub-cloning
  - Analytical Testing
  - Selection of lead candidates for pilot study

- **Hybridoma Cell Bank**
  - Next Step: Optimization or Pilot Run

**Optimization**

- **Master Cell Bank**
  - 50 Vials

- **UPSTREAM OPTIMIZATION**
  - Cell Density & Viability
  - Media Selection
  - Physiological Conditions
  - Feeding Schedule
  - Production System
  - Harvest Conditions
  - Mouse Strain *(in vivo only)*
  - Injection Concentration *(in vivo only)*

- **DOWNSTREAM OPTIMIZATION**
  - Elution Methods
  - Filtration Methods
  - Final Buffer Conditions
  - Column Parameters

- **Next Step: Production**

**Manufacturing**

- **Pilot Runs**
  - (1L - 20L scale or 20 mice)

- **Testing & Batch Record**
  - (e.g.; yield, PTMs, purity)

- **3x Validation Runs**
  - (increasing in scale or at scale)

- **Production**

**MLS Regulatory and Quality Systems**

- ISO 9001:2008 certified
- EC 1774/2002 approved
- Regulatory Affairs and Quality Assurance/Quality Control:
  - √ Provide necessary support for R&D to cGMP production
  - √ Support tech transfer, batch records and release, and Certificates of Analysis

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In Vitro and In Vivo Monoclonal Antibody Custom Services

**Development and Clonal Selection**

**Development Services:**
- Immunization and hybridoma fusion services offered through partnership with trusted lab
- Multiple mouse strains: BALB/c or strain of choice
- Clonal selection and screening
- Cell line sub-cloning to ensure homogenous population
- Master and Working cell bank production and maintenance
- Specificity analysis by ELISA: methods can be developed or tech transferred
- Additional analytical testing available (SDS-PAGE, HPLC, mycoplasma, sterility, etc.)
- Customizable program

**Adaptation and Optimization**

**Upstream Optimization:**
- Conversion from ascites to cell culture
- Adaptation to growth in serum-free media
- Scale-up conditions
- Matrix analysis studies – compare effect of variables on yield:
  - Production system
  - Media selection
  - Seeding cell density
  - Fed-batch method vs. terminal harvests
  - Physiological conditions (e.g., dissolved O₂)

**Pilot, Validation, and Routine Manufacturing**

**Custom Services:**
- Flexible scheduling
- Dedicated project manager
- Fixed-fee pilot projects: 1L, 5L, 10L, 20L
- Quotes on a per mg or gram basis can be provided for validation runs and routine production (once yield is confirmed by pilot study)

**Culture Systems:**
- CL-1000 flasks
- Tissue culture flasks
- Cell Factories
- Roller bottles - smooth or ridged
- Spinner flask
- Wave Bioreactor®

**Overview of In Vivo Services**

**Cell Line Service:**
- IgM Cell line production and purification
- Mycoplasma Testing
- Viability Monitoring
- Multi site Master or Working Cell Bank

**Cell Line Rescue:**
- Old or low yielding cell lines
- Yield optimization improvements
- Previously unsuccessful cultured cell lines

**Ascites Service:**
- Large facility with 55,000 mice capacity
- Pilot program – 20 mice minimum
- Large scale production of up to 5,000 mice per lot
- Lot-to-Lot Consistency
- Fixed pricing after pilot run
- Competitive Bulk Pricing
- Flexibility in Custom Options
- Fast turnaround time

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Meridian Life Science, Inc. (MLS) and Vybion have entered into an exclusive agreement to offer a stand-alone technology platform for the development of antibodies that can be engineered into a flexible range of formats. ProCode has demonstrated the ability to select binders from libraries and affinity mature these binders.

ProCode works in two formats allowing for Co-expression Selection of scFv and target as well as a familiar Display Selection format to accommodate a range of targets. Library construction strategies utilized ProCode’s solubility optimized human scFvs (HuSelect) that comprise multiple frameworks and randomized and multiple length CDR inserts. The ProCode technology permits engineering of selected MAbs, develop cell lines and optimize culture through process development.

HuSelect scFv libraries with novel modified leaders are expressed on the inner *E. coli* membrane. Fluorescent antigen target binds, and is selected, for example, by FACS after the cell wall is permeabilized.

HuSelect scFv libraries with novel leaders are co-expressed with target antigen fused to antibiotic resistance gene. Only soluble scFvs that bind to target confer antibiotic resistance following transport. Antibiotic pressure selects, in multiple rounds, for higher affinity.

**ProCode Advantages:**
- Rapid affinity maturation to low pM
- Complete panels of high affinity binders in a few weeks. More effective functional screening.
- Stand-alone technology
- Better stability, lower aggregation
- Effective in oxidizing and reducing environments
- Reduced time to market

**ProCode Technology Features:**
- Novel transport ‘self edits’ for folded proteins only
- Solubility optimized scFv libraries
- Multiple libraries each with unique frameworks and synthetic randomized CDRs
- Two selection modes can accommodate a range of targets or specific target epitopes
- Target binding epitope mapping by display of overlapping target sequences