LakePharma
The Biologics Company

microBiomanufacturing™ Services

LakePharma Hopkinton

NR-7349.20200127

Introducing the microBiomanufacturing™ Approach

- GMP manufacturing of biologics: small scale, single use, and flexible
  - Early-stage manufacturing that bridges the gap between development and late-stage manufacturing
  - Can be commercial supply for certain niche products

- Part of LakePharma's Integrated Solution approach for biologics development
  - Rapid advancement from process development to clinical supply
  - Manufacturing collaborates closely with process development, bioassays, QC
  - Unmet market need

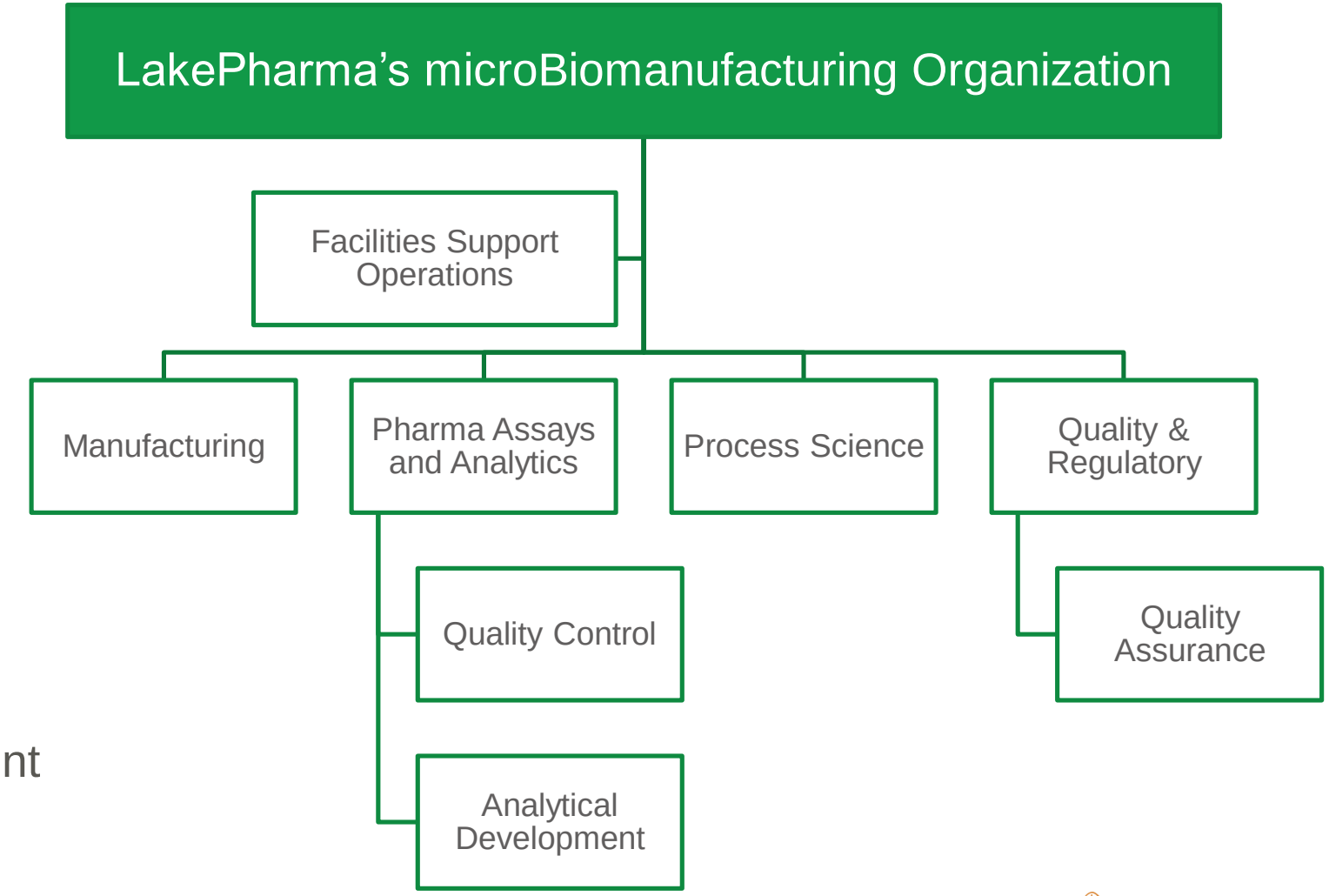
To the customer, this approach offers

- ☑ Fast turnaround time from RCB to GMP in 4 months
- ☑ Shorter queue and flexible scheduling
- ☑ Small-scale production as little as 1-10 mg

microBiomanufacturing™ Organization

LakePharma Hopkinton
69,000 sq.ft. cGMP/R&D site

- East Coast based- Hopkinton, MA
- 60+ employees, several positions in active recruitment



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GMP Manufacturing

Process Design & Development

- Proof of concept
- Small-scale models
- Seamless tech transfer
- Analytical Development

GMP Manufacturing

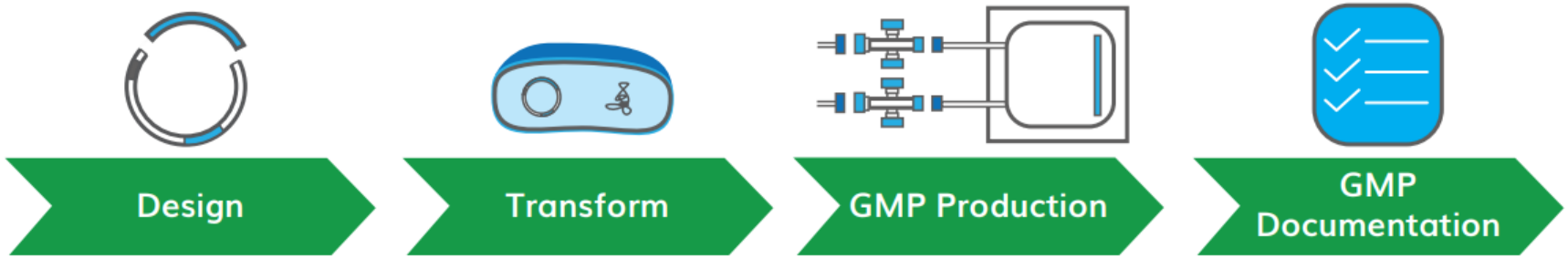
- Validated equipment and utilities
- ISO classified clean rooms
- Upstream and downstream processes
- Single use materials

Three Independent Suites

- Suite C – Plasmid DNA
- Suite A – Mammalian
- Suite B – Flexible; coming online in 2022

GMP-Grade Plasmid DNA Manufacturing

LakePharma offers integrated services from vector engineering to GMP manufacturing



- Construct design
- Gene synthesis
- Clone gene into plasmid vector

- Transform plasmid into *E. coli* strain
- Generate cell bank

- Upstream and downstream processing
- In-process and release testing

- Batch records
- QC results
- QA release

Key Highlights

4 Four grades available: research to GMP grades

Single-use technologies to reduce potential cross-contaminations

Integrated platform technologies to deliver best-in-class materials

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Summary of Plasmid DNA Grades

Features	Research Grade	Bioprocessing Grade	GMP Ready Grade (10 – 500 mg/batch)	Full GMP Grade (100 – 500 mg/batch)
Single-use material	✓	✓	✓	✓
Animal source free		✓	✓	✓
Raw material documentation		CoA and/or some QC testing and review	Material specifications CoA and/or some QC testing and review QA disposition	Material specifications CoA and/or some QC testing and review QA disposition
Operating space	R&D	Dedicated space in R&D	Clean Room	Clean Room
Independent verification		✓	✓	✓
QC testing		Optional	✓	✓
Documentation in batch record/forms/protocols		✓	✓	✓
QA oversight			Limited	✓
QA approval and issuance of batch record/forms			✓ - protocol	✓ – batch record
QA final review and disposition of batch record/forms/protocols			Limited – CoA, batch summary report	✓ – CoA, CoC
Quality Systems (deviations, OOS etc.)			✓ – discrepancies documented	✓ – must be closed prior to disposition

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Quality Control Laboratories

- To support bioprocessing, GMP Ready, and full GMP grades
- Equipment qualification completed
- Method validations completed
- Support release and stability testing

Partial List of GMP Tests

- Visual Appearance
- Identity (FTIR)
- Sterility (USP <71>) Bacteriostasis/Fungistasis
- Purity (260/280 Ratio)
- Concentration (UV spectrophotometry)
- DNA Homogeneity (densitometry of EtBr Stained agarose gel)
- pH, Osmolality
- Bioburden (USP <61>)
- Raw Material Testing
- Identification (e.g. gel electrophoresis)
- Mycoplasma (qPCR)
- Endotoxin (Kinetic Turbidimetric or Chromogenic LAL)
- Residual Host Genomic DNA (qPCR)
- Residual Host Protein (Micro BCA)
- Residual Host RNA (SYBR Gold agarose gel electrophoresis, densitometry)
- Restriction Digest
- GMP DNA Sequencing

Quality Systems

- The Quality organization is independent of the development and manufacturing organizations
  - QA: Documentation, Systems, and Compliance
  - QC: Microbiology, Analytical, PCR, Bioassay, Raw Materials
  - AD: Develops/transfers assays from research or client into QC (GMP method qualification / validation)
- Quality Policy in place
- Quality System Manual effective
  - Ensures compliance to applicable portions of 21 CFR Parts 210, 211, 600, 610 and 820 and ISO 13485 for execution of GMP processes
- ISO 13485:2016 certified
- Quality Agreements: define the duties with respect to quality of LakePharma and Client for contract GMP activities specified at the LakePharma Hopkinton facility:
  - Plasmid DNA manufactured under GMP
  - Bulk drug substance (API) for clinical use only
  - Diagnostic reagents to be used as kit components
  - GMP testing services

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GMP Biorepository Services

Dedicated short- and long-term storage with segregated areas that are fully validated and cGMP compliant. *Natural disasters and blackouts can happen. Protect high value samples in a GMP environment can avoid loss of million of dollars and years of recovery.*

- **What do we store?**
  - Cell banks (RCBs/MCBs/WCBs), client samples or materials such as reagents or antibodies
- **What storage conditions?**
  - LN_2 vapor phase. Ultra Cold -80C (liquid CO_2 back-up), -20°C and 2-8°C .
  - All equipment calibrated, validated, and on a PM program
- **What about security?**
  - 24/7 temperature monitoring and alarm notification
  - Badge access system controls entry to the biorepository area
  - All equipment on emergency generator power; full power redundancy

Contact Us Today

888-406-5658 (Toll free)

Inquiries@LakePharma.com

www.lakepharma.com

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