NEXIGHT GROUP

Georgia Tech

NSF

Research Infrastructure Needs to Support U.S. Leadership in Biomanufacturing

A report of the outputs from the NSF-funded Mid-Scale Infrastructure Workshops

June 2021

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Introduction

While significant progress has been made in developing next-generation vaccines and biologic therapies in recent years — including those for the 2019 novel coronavirus, SARS-CoV-2 — **there has been little progress toward developing the next generation of biomanufacturing research and development (R&D) and supply chain infrastructure for emerging therapies in the United States.** These infrastructure challenges became glaringly apparent during the SARS-CoV-2/COVID-19 pandemic, when shortcomings in raw material supply and quality, manufacturing capacity and scaling, logistics and product distribution, and workforce availability led to systemic failure of healthcare delivery despite rapid innovation in vaccines and therapies. Some of these shortcomings have been discussed in several recent biomanufacturing roadmap efforts led by organizations including the National Institute for Innovation in Manufacturing of Biopharmaceuticals (NIIMBL), the Advanced Regenerative Manufacturing Institute (ARMI)'s BioFabUSA, and the National Science Foundation (NSF) Engineering Research Center for Cell Manufacturing Technologies (CMaT ERC). Without a robust, established, national R&D and product development infrastructure for biomanufacturing and biologics supply chains, the United States will **continue to fall behind in its ability to scale emerging therapies and translate them from the laboratory to clinical and market applications**.

NSF recognized this challenge and has made significant investments into basic research and low- to mid-readiness level research in biomanufacturing, with the CMaT ERC (http://www.cellmanufacturingusa.org/) being one prime example. To build on NSF's efforts, the Georgia Institute of Technology (Georgia Tech) was funded by NSF to convene a mid-scale research engineering conference, **"Planning the Infrastructural Needs to Meet National Research Demand and Support the United States' Leadership in Biomanufacturing,"** to gather input from diverse, multidisciplinary stakeholders on building mid-size research infrastructure that would create a national hub and tools and technology warehouse for the biomanufacturing and supply chain of emerging therapies and next-generation vaccines.

With this funding, Georgia Tech organized a series of virtual workshops focused on four technical subjects:

- Cell Therapy Manufacturing Mid-Scale Infrastructure Workshop **—** November 10, 2020 3 – 5pm ET
- Virus and Gene Therapy Manufacturing Mid-Scale Infrastructure Workshop **—** November 12, 2020 12 – 2pm ET
- Emerging Vaccine Manufacturing Mid-Scale Infrastructure Workshop **—** November 13, 2020 3:30 – 5:30pm ET
- Mid-Scale Data Integration, Analytics, Security and Management Workshop **—** November 19, 2020 1-3pm ET

In these workshops, participants **identified the transformative infrastructure needed to fill the critical gaps in these technical subject areas and serve as a national resource** where researchers, product developers, clinicians, and companies can work together with regulatory and standards agencies, government entities, and patient groups toward a shared vision – and **enable scalable, cost-effective, rapidly-deployable, and adaptive biomanufacturing for the future.**

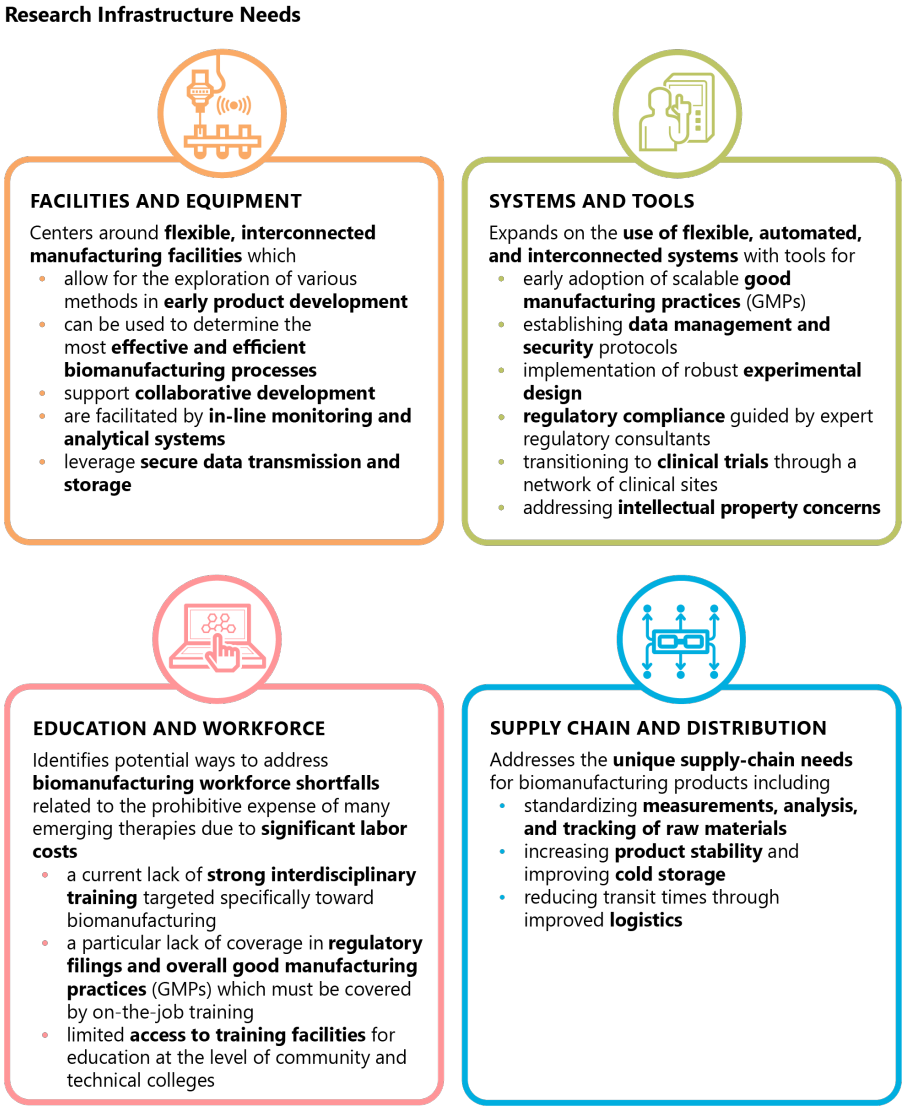
Executive Summary

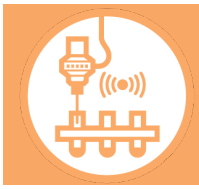
This whitepaper summarizes the results of the discussion from each of these workshops, organized into four overarching areas of infrastructure needs:

- Facilities and Equipment
- Systems and Tools
- Education and Workforce
- Supply Chain and Distribution

These areas cover major overlapping needs across cell therapy, virus and gene therapy, and emerging vaccines, as well as topics particular to each and the underlying data integration, analytics, and security infrastructure supporting them. Each infrastructure need includes a summary of **why it was identified as a need, the goals it will help achieve (or benefits it will provide), and how users from industry, academia, and clinical sites will access it**.

These needs **have not been prioritized** and are not presented in any specific order.





Facilities and Equipment Biomanufacturing Research Infrastructure Needs

The following section includes a compilation of workshop participant feedback on future needs for cell therapy, virus and gene therapy, emerging vaccines, and data **facilities and equipment infrastructure**. Needs are separated into ones that are **crosscutting** for each technical area, as well as ones that are more **specific** to certain technical areas.

These needs **have not been prioritized** and are not presented in any specific order.

Cross-Cutting Infrastructure Needs for Facilities and Equipment

Pilot-scale manufacturing facilities that allow rapid translation of lab-scale discoveries to Phase 1 and Phase 2 trials

Why a need:

- Early development requires flexible facilities to allow for the exploration of multiple platforms in determining the most effective, safe, stable, and scalable processes.
- Currently available contract manufacturing organizations (CMOs)/ contract development and manufacturing organizations (CDMOs) are often too specialized or too expensive for early development and do not provide enough overall capacity.

Goals/benefits of infrastructure:

- Provide access to equipment that is appropriate for phase 3 clinical trials and commercial manufacturing to decrease overall development cost and time.
- Couple formulation with analytics to facilitate comparability between processes and platforms.
- Support technology transfer and standardized quality control.
- Facilitate dissemination of products and data to connected facilities.
- Offer process-development expertise to assist smaller companies, academic researchers, and clinical centers with scale-up approaches that are Good Manufacturing Practice (GMP)-compliant, including guidance on manufacturing equipment and quality management system selection.
- Provide standardized regulatory guidance toolkits for IND filings and access to consultants with regulatory expertise.
- Provide a network for developers who wish to connect to contract testing organizations with the necessary equipment to perform quantitative analyses, particularly as related to identity, purity, and potency.

Pilot-scale manufacturing facilities that allow rapid translation of lab-scale discoveries to Phase 1 and Phase 2 trials

- Specific resources include cleanroom and sterilization facilities, equipment for downstream purification (including ultrafiltration and diafiltration), mammalian and bacterial cell bioreactors, and flexible storage capabilities (e.g. -70°C storage for RNA products).

Access approach:

- Establish centralized or regional facilities with harmonized analytics processes for phase 1 and 2 trials; this may include some support for technology transfer and transition into phase 3.
- Provide both "furnished" and "unfurnished" facilities for rentable suites; either provide full service or allow companies to use their own employees.
- Establish an internal, sponsor-quality system approach to isolate sponsors and accommodate multiple programs.

Shared centers designed for companies to participate in academia-industry or public-private partnerships for product development and manufacturing

Why a need:

- Collaboration is crucial to innovation and therapy development. Companies need a shared space to work together with academic researchers and clinical partners.

Goals/benefits of infrastructure:

- Wide-ranging facilities and manufacturing equipment would be shared among the users, including both standard and specialized manufacturing equipment, office space, laboratory environments, cleanrooms, and stockrooms.

Access approach:

- These would be available for any companies who want to partner or work in shared environments.

Consistent and secure data infrastructure and data standards

***Why a need*:**

- Aspects of product development, such as release assays, rely on standardized and reproducible data from common instruments.
- Due to a lack of interoperability, data must be manually entered and curated. This limits data integrity and thus impacts any analysis performed.
- Systems to protect security and privacy are critical for developers to adopt data-sharing and standardization measures without losing value.

Consistent and secure data infrastructure and data standards

- Data infrastructure needs span hardware, software, and data and metadata standards, including semantic definitions and inference capabilities.

Goals/benefits of infrastructure:

- Enable multi-modal analyses (e.g., flow and imaging data).
- Standardize datasets and increase data-sharing and collaboration.
- Incorporate provenance tracking, including data sources and collection methods, to control for variance in equipment and facilities.
- Collect data in a secure (e.g., encrypted) manner using data formats that can enable privacy-preserving analysis across organizations.
- Employ analytical methods, such as secure computation, that generate information and cross-performer pre-competitive comparisons without needing to solve issues of data use and sharing or to move data.

Access approach:

- Develop standards on data and metadata collection, cataloguing, and reporting to facilitate automated processes.
- Establish standards for data sharing, updating systems, and securing data.
- Ensure proper access control methods so user access is commensurate with their authority.
- Encourage manufacturers to provide APIs using the existing representational state transfer (REST) software architecture format.

Dedicated computing infrastructure/access (e.g., via cloud architecture or edge computing) combined with high-performance computing resources and security capabilities

Why a need:

- Connected facilities coordinating on a national level would be dealing with multiple terabytes of data.
- Cloud systems and decision support via AI tools will be critical to data management and innovation.

Goals/benefits of infrastructure:

- Support large-scale computation and national-scale data lakes.

Access approach:

- Integrate a national-level cloud system with smaller institutional and regional systems.

Sector-Specific Infrastructure Needs for Facilities and Equipment

Analytical/quality control (QC) lab infrastructure located close to production facilities

Why a need:

- In-process testing requires experience with specific analytics (e.g., flow cytometry with fresh cells).
- Critical quality attributes (CQAs) and related processes in cell therapy and molecular editing are still poorly understood.
- Developing QC assays (such as replication-competent virus and adventitious agent tests for vector lot release) is a time-consuming process.
- There is a pronounced need for standardization of assays and process control models.

Goals/benefits of infrastructure:

- Co-localize QC and analytics helps to understand relevant methods, data generation, and the relationships between testing and production.
- Increase in-line analytical abilities to characterize products and monitor processes.
- Standardize general assays.
- Broad characterization facilities will be able to facilitate concurrent CQA, mechanism of action (MoA), and critical process parameter (CPP) discovery.
- These facilities will also be able to generate potency methods, support release testing, inform process improvements/decisions, and increase understanding of CQAs of products and starting materials.

Access approach:

- Centralize testing in facilities within or near production sites.

Development of improved cell lines for vector production

Why a need:

- As the efficacy of gene therapy improves, commercialization will be limited by the current high production costs.
- Cell culture is an area of production that would benefit greatly from improved technology.

Goals/benefits of infrastructure:

- Focus on suspension rather than adherent cultures and serum-free or low-serum media to allow for easier scale-up and thus higher yields and cost efficiency.
- Equipment should support single-use bioreactors at a 3-7L working volume.

Development of improved cell lines for vector production

Access approach:

- A central facility would assist in basic infrastructure needs.
- Companies would bank their own cell lines after development.

Automated technology to support the establishment of highly integrated, distributed production with interoperable equipment

Why a need:

- Getting hardware to communicate in automated manner is a significant challenge.

Goals/benefits of infrastructure:

- Establish a universal translator to automate data entry into a repository, which could be part of an overall standardized API that would allow different instruments to communicate with each other.
- Facilitate information sharing on overall facility performance to help develop best practices.
- Include a research function that would focus on new automation technologies to support the field, which could be adapted or applied to the biomanufacturing facilities (or be specific to a particular company).

Access approach:

- Within a facility, establish remote monitoring capabilities and a central dashboard that would update with real-time production metrics and improve system security.

Systems and Tools Biomanufacturing Research Infrastructure Needs

The following section includes a compilation of workshop participant feedback on future needs for cell therapy, virus and gene therapy, emerging vaccines, and data **systems and tools infrastructure**.

These needs **have not been prioritized** and are not presented in any specific order.

Flexible automation technologies and in-line monitoring tools to support research in new, improved, or disruptive manufacturing technologies for cells, vaccines, and viruses at scale (or within a system allowing for scaling)

***Why a need*:**

- Current technologies are expensive and carry increased risks of batch failures and inconsistent product quality.
- Enhanced monitoring technology reduces the requirement for operator intervention and the level of training needed for operators, which is currently a major expense in cell and gene therapy manufacturing.
- Scaling up will require systems to minimize variability between research and process development and increase consistency for smoother technology transfers.
- Technology parameters must be adaptable until processes have been streamlined.
- Initial development should focus on robustness/value rather than cost.

Goals/benefits of infrastructure:

- Establish flexible, scalable platforms that offer sampling and sensing mechanisms for process and product quality monitoring, preferably in real time.
- Provide quality-driven feedback control of the manufacturing process to minimize footprint and manufacturing costs.
- In-line monitoring allows for more rapid and straightforward process characterization and validation to establish critical process parameters (CPPs).
- Enhanced monitoring allows adaptability to patient-to-patient variation.
- Generate pooled analyses of critical raw materials (e.g., tangential flow filtration membranes and high flow cartridges) which currently suffer from variable quality.
- Consider GMP compliance for all systems and tools from the outset to facilitate scaling.
- Develop standardized analytical methods, quality management systems, and documentation processes.
- Develop data-management and AI tools that facilitate in-process learning.

Flexible automation technologies and in-line monitoring tools to support research in new, improved, or disruptive manufacturing technologies for cells, vaccines, and viruses at scale (or within a system allowing for scaling)

- Allow developers remote access and control for programming and monitoring on automated platforms, which will require highly secure systems that permit processes to be online.

Access approach:

- Provide a centralized space with a variety of flexible tools.
- Initial facilities should be focused on specific processes and applications that would most benefit from standardization.
- Automation and feedback control need to be decided locally based on parameters derived from big data.

Internet-of-things (IoT) for biomanufacturing

Why a need:

- As the amount of data captured from biomanufacturing processes grows, incorporating IoT is crucial for correlating manufacturing data and clinical outcomes, and ultimately improving understanding of the underlying biology and how to adjust existing manufacturing processes.
- Enabling cross-platform communication is important for both combining batch records from various systems during a single manufacturing run and linking manufacturing platforms with logistics technologies.
- Multi-owner laboratory information management systems (LIMS) can coordinate data between multiple facilities but require streamlined processes and enhanced security.
- The anonymous sharing of process analytical data is also vital in generating large datasets for artificial intelligence (AI) and machine learning (ML) applications.
- Most IoT cannot currently handle the magnitude of data required for process support; as IoT tools continue to develop, security must also keep pace.
- Incorporating IoT is often an expensive endeavor for small and early-stage developers.

Goals/benefits of infrastructure:

- Develop powerful AI/ML tools linked to in-line monitoring (e.g., monitoring of empty capsid ratios).
- Provide predictive supply chain modeling and development expertise.
- Employ robust cyber-security tools.

Internet-of-things (IoT) for biomanufacturing

- Establish registry/database information for continual improvement of modeling and monitoring power.

Access approach:

- Provide large, secure storage clouds and secure edge computing systems to support IoT and use of sensory data.
- Develop secure IoT devices with means to update and authenticate security protocols.
- Provide a centralized database for universal access for data mining and analytics.

Regulatory consultants to assist small-to-mid-sized companies and academic developers in FDA and other regulatory filings

Why a need:

- Small companies experience issues with submitting product approval applications—especially with chemistry, manufacturing, and controls (CMC) data, which takes the longest and is often the most foreign to start-up companies—that end up delaying the product review and approval process.
- Product developers need to be able to demonstrate that they use valid production processes, especially on emerging platforms, and describe the analytical tools and assays they use to prove product quality.
- Various federal requirements may impact data lifecycle management, such as maintaining records on product batches and GMP materials.
- The regulatory landscape for new biomanufacturing platforms is shifting, and regulations as written can be interpreted in different ways. There is difficulty in establishing adequate case studies for both applicants and regulators.

Goals/benefits of infrastructure:

- Provide a basic framework for regulatory approval and consideration of international standards.
- Outline CMC development processes and optimization, including documentation and validation.
- Support developers in characterizing the process and the product, developing Critical Quality Attributes (CQAs) and Critical Process Parameters (CPPs)
- Develop rapid release assays
- Integrate new technologies and data-driven improvements in the manufacturing pipeline.
- Establish methods for efficiently transferring and retaining data, determining critical versus non-critical data, and facilitating cross-functional analysis.

Regulatory consultants to assist small-to-mid-sized companies and academic developers in FDA and other regulatory filings

- Support regulatory scrutiny and inspections to clarify regulatory concerns for both regulators and developers.

Access approach:

- Provide A-to-Z assistance when interacting with the FDA, from Initial Targeted Engagement for Regulatory Advice on CBER Products (INTERACT) meetings up through submitting product approval applications.
- Include record-keeping and compliance guidance in SOP management.
- The facility should have a Facility Master File (FMF) on file with the FDA to facilitate CMC for products produced in the central facility.
- Connect academic developers and small businesses through office hours or retired experts to avoid the costs associated with hiring full-time experts.
- Establish a centralized contracting process connecting developers with CMOs, other manufacturing support facilities, and clinical trial sites.

Design of experiments (DOE) software and multiplexed small-scale bioreactors for rapid process development

Why a need:

- Many academic developers and small companies do not have expertise in DOE and rely on simpler, one-factor-at-a-time (OFAT) approaches to experimental design that can overlook potential interactions between factors.
- Product development can be cost-prohibitive without having access to DOE software for designing appropriate small-scale studies or performing multifactor DOE such as response surface methodology.

Goals/benefits of infrastructure:

- Reduce development time and costs by reducing the number of production runs needed during development.

Access approach:

- Allowing developers access to automated software, data scientists, and other technical experts to facilitate their understanding of DOE.

GMP compliance support for all systems, tools, and materials

Why a need:

- Many tools used at a small scale, such as the ÄKTA avant chromatography system, are for process development and are not GMP-compliant. There is a need for validated instrumentation that can run at smaller scales.

Goals/benefits of infrastructure:

- Validate instrumentation qualification to help ensure that companies can document GMP.
- Incorporate electronic quality management and batch record systems.

Access approach:

- Require authorization and two-factor authentication to access secure electronic systems, and the ability to firewall records from independent entities.

Intellectual property (IP) guidelines/protocols

Why a need:

- IP disputes and uncertainty around rights can stall development. Integrating a strategy for handling IP-related concerns would help promote additive, accelerated manufacturing advances.

Goals/benefits of infrastructure:

- Create a pre-competitive space in which new shared processes and resources (e.g., cell lines and plasmids), including potential new IP generated by the center, would be made accessible to all participants.
- Establish guidelines to clarify the distinctions between inventorship and ownership with associated rights to IP to use and operate globally.

Access approach:

- Establish open-source access at a national center which would keep its own IP rights.

Support for clinical trials with access to clinical trial sites, and infrastructure for study conduct

Why a need:

- For vaccine products developed for clinical studies, manufacturers must be connected to clinical trial sites with expertise across phase 1-3 studies.
- The funding requirement to bring a vaccine or cell, gene, or biologic therapy to clinical trials largely falls on the developer, but academic developers and small companies may not have the capacity to identify which vaccine candidates have potential to succeed as commercial products.

Support for clinical trials with access to clinical trial sites, and infrastructure for study conduct

Goals/benefits of infrastructure:

- Generate a master cell bank (MCB), good laboratory practice (GLP) material to support toxicology studies, and cGMP drug products (DP) to support Phase 1 clinical studies.
- Identify promising vaccines or cell, gene, or biologic therapies in laboratory development that deserve more translational studies.
- Provide access to experts with knowledge in protocol development, implementation, study conduct, and regulatory compliance for human testing to facilitate the advancement from product development to clinical trials.
- Improve clinical research site infrastructure: investigational drug services; quality and data management; recruitment and retention capacities; and clinical, administrative, and laboratory processing.

Access approach:

- Provide high-level biosafety facilities.
- Supplement screening with a mechanism to attract attention from the pharmaceutical industry, venture capital, BARDA, or others.
- Establish a screening committee with credibility and connections to attract funding opportunities.

Edge computing to accommodate disparate locations

Why a need:

- Datasets in biomanufacturing consist of a relatively small number of large files (hundreds of terabytes in volume) relative to the higher volume of smaller transactions in many cloud computing systems.
- Edge computing limits the magnitude of data transactions to and from the cloud and makes running real-time analytics more efficient for multiple locations.
- Edge computing can also help detect and counter cyberattacks at local levels to reduce the damage to biomanufacturing systems.

Goals/benefits of infrastructure:

- Integrate edge computing with internet of things (IoT) and cloud computing to facilitate faster real-time decision making while minimizing bandwidth costs.
- Create and share methods for data integration of commonly collected data types in various locations.
- Encourage laboratories to record the same information across similar studies and share this information with other laboratories.
- Develop edge-based analytical tools specific to biomanufacturing, including tools for querying and filtering data for analysis and review

Edge computing to accommodate disparate locations

- Establish secure methods for pushing analytical methods down and for rolling our security updates to infrastructure in the edge.

Access approach:

- Establish a spectrum of computational, networking, and storage capabilities, ranging from single-laboratory to nationwide scale.
- Build in security verification protocols for data and analysis pushdowns from the cloud to ensure validity and security (e.g., model checking).
- Employ authentication mechanisms across locations to prevent unauthorized access of networks.
- Develop edge-based analytical tools proving the return on investment for using edge computing approaches in biomanufacturing.

Development and use of techniques and tools to build biomanufacturing threat models, secure systems, security testing, and share cyber incidents

Why a need:

- An equipment and software supply chain inventory with provenance is needed to comply with federal security requirements.
- Export control requirements can also apply to data.
- Increasing integration of facilities and adoption of automated equipment and internet of things increase cybersecurity risks.

Goals/benefits of infrastructure:

- Study cybersecurity approaches, tools, and best practices from other industries such as finance and manufacturing to evaluate their potential applications to biomanufacturing.
- Enable sites to predict attacks and share related information (e.g., attack modes) with other sites.
- Develop demonstration systems to test cybersecurity approaches that comply with requirements for supply chain and export control.
- Engage biomanufacturing equipment manufacturers and vendors to increase their awareness of cybersecurity and develop the equipment and devices necessary for infrastructure with built-in security and resilience.

Access approach:

- Establish a central resource for cybersecurity best practices and up-to-date information on cyber threats and incidents.

Education and Workforce Biomanufacturing Research Infrastructure Needs

The following section includes a compilation of workshop participant feedback on future needs for cell therapy, virus and gene therapy, emerging vaccines, and data **education and workforce infrastructure**.

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Convergent knowledge and expertise base for the emerging and existing workforce

***Why a need*:**

- It will be critical to build base knowledge and multidisciplinary capabilities across the workforce in areas ranging from biology to bioprocessing, manufacturing sciences, quality control and assurance, automation and analytical tools, clinical trials, and data sciences. Operators must be comfortable working with data and processes, and statisticians must understand the constraints unique to cell therapies.
- Many academic centers do not have a knowledge base in manufacturing processes; to date, education in industry has been primarily on-the-job training, with GMP training timelines averaging 3–6 months, or longer.
- The current supply of workers with biomanufacturing operations and cleanroom experience is very limited, and the lack of appropriate degree programs at the community-college and technical-school levels forces employers to hire operators with 4-year or advanced degrees, incurring increased labor costs and lower employee retention.
- Addressing these issues requires engagement with prospective partners from academia and industry to target resources and build the workforce.

Goals/benefits of infrastructure:

- Bridge the language gap with a holistic curriculum that conveys the critical nature of GMP, CMC, assay development, etc. to academic centers and partners that want to do translational work.
- Develop technical expertise in isolation, culture (bioreactors), characterization, cryopreservation, shipping and packaging, quality assurance (QA) and QC, financial analysis, product-specific in vivo analysis, and product instrumentation.
- A centralized training program provides a head start for operators and reduces the burden of on-the-job training for clean room and aseptic handling techniques.
- Establish an advisory group with knowledge about formulation, regulatory approvals, and stability testing.

Convergent knowledge and expertise base for the emerging and existing workforce

Access approach:

- Consider government-sponsored retraining of workers to support cell and gene therapy manufacturing operations.
- Integrate multiple institutions, connecting companies that manufacture final products with community colleges, technical colleges, and other institutions with training needs.
- Connect developers with potential future employees participating in facility programs.
- Establish a training unit within the centralized facility with its own labs and clean room space, allowing for materials production and workforce training to occur simultaneously.
- Hands-on training would be available for biomanufacturing operators without four-year degrees.
- Consider supporting underserved geographic locations when possible..

Integrated educational and training modules to support future workforce requirements, including regulatory compliance

Why a need:

- Much of the equipment used for cell therapy manufacturing requires highly trained personnel to operate, but these required skills are not standardized. A lack of national and international standards prevents training credentials and certificates from being transferrable and stackable.
- Current curricula in this area do not provide enough training on how to scale production, nor do they provide transferable skills. It is unclear what level of training is most needed.
- Integrating training modules into existing curricula, or developing new curricula, would help reduce both training costs for new employees and variability from operator to operator. The large number of operators and analysts needed for autologous cell therapy due to its high-throughput nature presents a particular training challenge.
- Current workforce education programs and on-the-job training have very little emphasis on regulation, quality, and good documentation practices. Incoming staff have often never seen completed regulatory documents and have no grounding in the level of content or quality of writing required for regulatory filings.
- Understanding regulatory requirements for study design and reporting, including identifying proper milestones and controls, is critical to developing complete product submissions that will be accepted by the FDA and other regulatory bodies.

Integrated educational and training modules to support future workforce requirements, including regulatory compliance

- Graduate-level students need to understand these requirements as they join the workforce to help reduce the onboarding needed.

Goals/benefits of infrastructure:

- Reduce the need for on-the-job training and produce a skilled workforce with transferable skills.
- Establish manufacturing operator and quality control (QC) analyst training that also ensures an understanding of GMP compliance. Facilitate academic-industry consortia.
- Training programs would outline the entire documentation process, such as writing and maintaining DMFs for the facility and GMP requirements for facility design/layout.

Access approach:

- Virtual reality (VR) modules could be used in community colleges for initial stages of training such as aseptic techniques, while advanced training would still require access to a facility.
- Develop bachelor's and master's degree-level programs focused on manufacturing and industry.
- Provide short courses and certificates for doctoral degree-level workers at smaller organizations.
- The basics of preparing and submitting regulatory documents can be integrated into core training.
- Facilities would employ or have access to experts who are experienced in regulatory filings.
- A centralized team with multiple experiences with regulatory filing at a single site would allow feedback from the FDA to be easily shared, though this requires the facility to allow information to be shared between programs.
- Work with 2-year colleges, the National Association of Community Colleges, and relevant professional associations to develop stackable and transferrable certification programs including standards, training, evaluation, re-certification, and a national accreditation or endorsement mechanism.

Enabling cross-industry collaborations and emergency response

Why a need:

- It will be critical to build cross-industry collaborations and public-private partnerships in areas ranging from biology to bioprocessing, cybersecurity, practical AI/ML applications, data engineering, and other relevant emerging technologies and areas.
- IP-related concerns disincentivize collaboration, so encouraging people to participate in a community forum will be an essential first step.

Enabling cross-industry collaborations and emergency response

- Individuals across industry, national labs, and the United States government must be trained to respond in times of need and available to collaborate on national biomanufacturing efforts in response to emergencies.

Goals/benefits of infrastructure:

- Establish secure channels for data sharing between industry and clinical and research partners.
- Identify crosscutting issues between organizations and laboratories.
- Create cohorts of collaborators and networks among industry that are ready to be leveraged in a time of need to help specific facilities.
- Create opportunities for social gatherings and trust-building.

Access approach:

- Use existing methods for data sharing without sharing IP or core technology; clarify that some information may not actually be considered IP.
- Focus on connecting companies down to the working members.
- Some emergency functions (e.g., pandemic response) may require an anti-trust act or other legislation.

Education programs to train tomorrow's data management experts

Why a need:

- Data management for biomanufacturing requires a highly multi-disciplinary workforce, including training in biotechnology, information technology, and data analytics. Labor is a primary driver of production costs due to this requirement.
- There is a lack of relevant cybersecurity training for biomanufacturing; for example, NC State has a Biomanufacturing Training and Educational Center, but they currently do not offer cybersecurity education.
- As AI technologies develop, there will also be a need for training on ethical, responsible, and sustainable use of AI.
- Useful data infrastructure depends on accurate records and data integrity, which can be difficult to validate without standard formats.

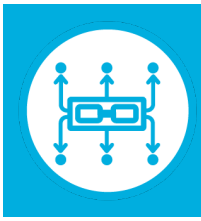
Goals/benefits of infrastructure:

- Establish a foundation of general, inclusive education on infrastructure and technology that also covers foundational concepts like edge, cloud, and distributed computing to help standardize nomenclature.
- Emphasize cybersecurity, including the vulnerabilities that arise at the intersection of supply chain, digital infrastructure, and biological workflows.
- Encourage instrument manufacturers to write to an industry-standard format or at least publish instrument output standards.

Education programs to train tomorrow's data management experts

Access approach:

- Certificate programs are a possible approach, especially for targeting the existing workforce.
- Certificate programs led by big IT companies (Google, Facebook, Microsoft) can provide a model.



Supply Chain and Distribution Biomanufacturing Research Infrastructure Needs

The following section includes a compilation of workshop participant feedback on future needs for cell therapy, virus and gene therapy, emerging vaccines, and data **supply chain and distribution infrastructure**.

These needs **have not been prioritized** and are not presented in any specific order.

Inventory and stable supply of raw materials, including tracking and certification

***Why a need*:**

- A limited or unstable supply of critical, GMP-quality raw materials such as media can delay production.
- Many small-scale pilot facilities lack storage space and rely on just-in-time delivery of raw materials, which also causes product delays during iterative manufacturing.
- Small companies may also lack the capacity to establish secondary sources for GMP-compliant critical raw materials and reagents during scale-up and transition to clinical trials.
- Insufficient tracking and certification of raw materials affects both the sourcing of reagents (i.e. switching suppliers) and the downstream effects of contaminants and defects

Goals/benefits of infrastructure:

- Strategize with major suppliers and expand supplier base to ensure adequate pools of GMP-quality raw materials and reduce lead times in production and development.
- Ensure batch and reagent identification numbers are readily retrievable: e.g., for a given batch of vaccine, information should be available on the exact batch of NaCl used in the buffers.
- Incorporate standardized certificates of analysis (COA) into supply chain data management.

Access approach:

- Create a central resource connecting suppliers with manufacturers.
- Standardize certification procedures to enter the supply chain, using safety equipment or medication procedures as models.

Storage facilities and product stability for biomanufacturing supply chains

Why a need:

- Stable materials that cannot be manufactured quickly must be produced in advance and stockpiled.
- Early clinical trials may need a small capacity for cool chain and transportation.
- Cell therapies using a cryopreserved product typically rely on bone marrow transplant labs at hospitals to thaw and formulate the cells for dosing. These labs present a space constraint for processing and storage that can be a significant bottleneck for clinical development beyond Phase I, which limits patient access.
- Product stability is a hurdle for global vaccine development and deployment.
- Expanding cold-chain capabilities would also facilitate easier cell collection from patients.

Goals/benefits of infrastructure:

- Assist developers during early formulation and process development to increase product stability and design products that require less complex supply chain and distribution practices.
- Improving storage and shelf-life extension would enable cell banking to become more useful for allogeneic therapies.
- Establish best practices in cold-chain management, systems for minimizing thawing events, and automation of freezing and inventory.
- Facilitate dose preparation capabilities as well as support to move to thaw-and-inject formulations and the ability to send samples to a sponsor.
- Focus on defining and enhancing product stability.

Access approach:

- Potential warehouses with controlled-rate freezers and freezer farms able to store products from room temperature down to liquid nitrogen storage temperature.

Data infrastructure and logistical support for supply-chain planning

Why a need:

- Times of acute need require an ability to access up-to-date information, including data on manufacturing capacity and supply quality.
- Chain-of-custody and chain-of-identity tracking is critical for the security of the product lifecycle, from monitoring critical reagents supplies to patient harvesting and delivery logistics.

Goals/benefits of infrastructure:

- Establish a system for change notifications; upstream changes (e.g., a patient's status or diagnosis) should propagate through the data management systems to flag affected downstream, derived data.
- Standardize shipping strategies with validated vendors, including international shipping.
- Link inventory and disposition systems to a manufacturing execution system (MES).

Data infrastructure and logistical support for supply-chain planning

Access approach:

- Employ data structures for provenance and tracking, possibly using blockchain for supply chain transactions.
- Connect users with consultants to identify supply chain and distribution strategies.
- Establish an automated tracking system with easy-to-understand interfaces for patients to check on the status of their material.