2017

Roadmap Update to *Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells*

July 2017

About this Document

This document is designed to serve as an update to the *Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells* roadmap, which was published in June 2016 and launched by the White House Office of Science, Technology, and Policy (OSTP). This roadmap update provides a revised cell manufacturing industry strategy in response to recent cell manufacturing advances, the industry and clinical outlook, and emerging needs in the cell manufacturing industry. Both the roadmap and this update were developed by the National Cell Manufacturing Consortium (NCMC) with funding from the National Institute of Standards and Technology (NIST) Advanced Manufacturing Technology Consortia (AMTech) program.

The cell manufacturing industry has been changing rapidly since NCMC held workshops in 2015 to inform roadmap development. In the past two years, new cell-based therapies have received regulatory agency approval and others have demonstrated promising

This roadmap update focuses primarily on four areas that have been significantly impacted by industry change since roadmap publication: Process Automation and Data Analytics, Supply Chain and Transport Logistics, Standardization and Regulatory Support, and Workforce Development.

Other roadmap activity areas—including sections on developing and implementing advanced technologies and techniques in Cell Processing; Cell Preservation, Distribution, and Handling; and Process Monitoring and Quality Control—remain relevant and are critical focus areas of NCMC efforts. Please reference the full roadmap document for activities in these areas.

breakthroughs in clinical trials and received positive recommendations from advisory panels (e.g., the U.S. Food and Drug Administration [FDA] Oncologic Drugs Advisory Committee). The United States has also established several national public-private partnerships in this area, including the Marcus Center for Therapeutic Cell Characterization and Manufacturing (MC3M) at Georgia Tech and two new industry-led, bio-based Manufacturing USA institutes: the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) and BioFabUSA. To keep pace with innovations in the field, standards bodies—including NIST and the new Standards Coordinating Body (SCB) for Gene, Cell, and Regenerative Medicines and Cell-based Drug Discovery—have focused on developing standards that can more efficiently and effectively accelerate the availability of reliable and safe new cell-based products.

This momentum and rate of progress is expected to continue in coming years. Cell therapy manufacturing is projected to grow at an annual rate of more than 40 percent in the next 10 years, and is anticipated to be worth $4 billion in 2027.[1] The broader global regenerative medicine market, which was worth $18.9 billion in 2016, is projected to grow to more than $53.7 billion by 2021.[2] As advances in cell-based therapies, devices, diagnostics, and other biopharmaceutical products continue, these fields will facilitate the availability of life-changing treatments while also increasing the economic growth and competitiveness of U.S. manufacturing.

Recent U.S. Investments in Cell Manufacturing

The following select examples of public-private partnerships demonstrate increased U.S. emphasis and investment in the advancement of cell manufacturing, regenerative medicine, and biopharmaceuticals.

Marcus Center for Therapeutic Cell Characterization and Manufacturing (MC3M)

MC3M, which was formally launched in 2016 at Georgia Tech, is focused on establishing world-class collaborative infrastructure to facilitate the characterization and manufacturing of therapeutic cells. The Center, which used the *Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells* roadmap to inform its direction and focus, is funded by an initial investment of $23 million, including a $15.75 million philanthropic donation from the Marcus Foundation. MC3M aims to accelerate cell therapy research and technology, process and assay standards, and workforce development, particularly in the areas of critical quality attributes, process analytics, potency assays, sensors for non-destructive evaluation, process automation, and supply chain logistics.

[1] Roots Analysis, Cell Therapy Manufacturing Market, 2017–2027, March 3, 2017, https://www.rootsanalysis.com/reports/view_document/cell-therapy-manufacturing-market-2017-2027/158.html.
[2] Kelly Scientific Publications, Global Regenerative Medicine Market Analysis & Forecast to 2021; Stem Cells, Tissue Engineering, BioBanking & CAR-T Industries, May 2017, http://www.reportlinker.com/p04876076/Global-Regenerative-Medicine-Market-Analysis-Forecast-to-Stem-Cells-Tissue-Engineering-BioBanking-CAR-T-Industries.html.

National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL)

Announced in December 2016 and launched in March 2017, NIIMBL's mission is to accelerate biopharmaceutical manufacturing innovation, support the development of standards that enable more efficient and rapid manufacturing capabilities, and educate and train a world-leading biopharmaceutical manufacturing workforce, fundamentally advancing U.S. competitiveness in this industry. NIIMBL is funded by a $70 million cooperative agreement from the National Institute of Standards and Technology and leverages $180 million in other commitments from more than 150 partners from industry, academia, and non-profits. The Institute plans to launch its first full project call by September 2017 and anticipates launching quick-start projects focused on accelerated technology and workforce development this summer.

BioFabUSA, administered by the Advanced Regenerative Manufacturing Institute (ARMI)

Announced in December 2016, BioFabUSA's mission is to de-risk and speed up the manufacturing of new engineered tissue technologies. The industry-led, public-private partnership, which is funded by an $80 million cooperative agreement from the Department of Defense and more than $150 million from industry, aims to develop an ecosystem with shared knowledge and assets from more than 110 members from industry, academia, and non-profit organizations. By focusing on five technical thrust areas—cell selection and culture, biomaterial selection and sourcing, tissue process automation and monitoring, tissue maturing technologies, and tissue preservation and transport—and education and workforce development, BioFabUSA will develop manufacturing platforms and processes to catalyze the development of therapeutic products.

Standards Development Partnerships

The International Standards Coordinating Body (SCB) for Gene, Cell, and Regenerative Medicines and Cell-based Drug Discovery was launched in September 2016. This public-private partnership of product developers, tools and service providers, professional societies, government entities, and academic centers is focused on supporting standards development via coordination, prioritization, resource compilation, inter-laboratory data generation, participation in consensus Standards Development Organization (SDO) activities, and education and implementation of standards.

Additionally, in response to the *21st Century Cures Act*, NIST and the FDA are collaborating on standards development and industry engagement—leveraging NIST's unique expertise in measurement science and analytics and the FDA's scientific, regulatory, and policy expertise—in the areas of biotechnology (ISO/TC 276), biocompatibility (ISO/TC 194), tissue engineered medical products (ISO/TC 150/SC 7), and medical and surgical devices (ASTM F04).

An Evolving Cell Manufacturing Industry Strategy

This roadmap update includes a refined strategy for achieving the cost-effective, large-scale, reproducible manufacturing of high-quality cells in response to recent cell manufacturing advances, the industry and clinical outlook, and emerging needs in the cell manufacturing industry. Industry changes and growth have necessitated revisions to the following cell manufacturing activity areas, which are the focus of this roadmap update:

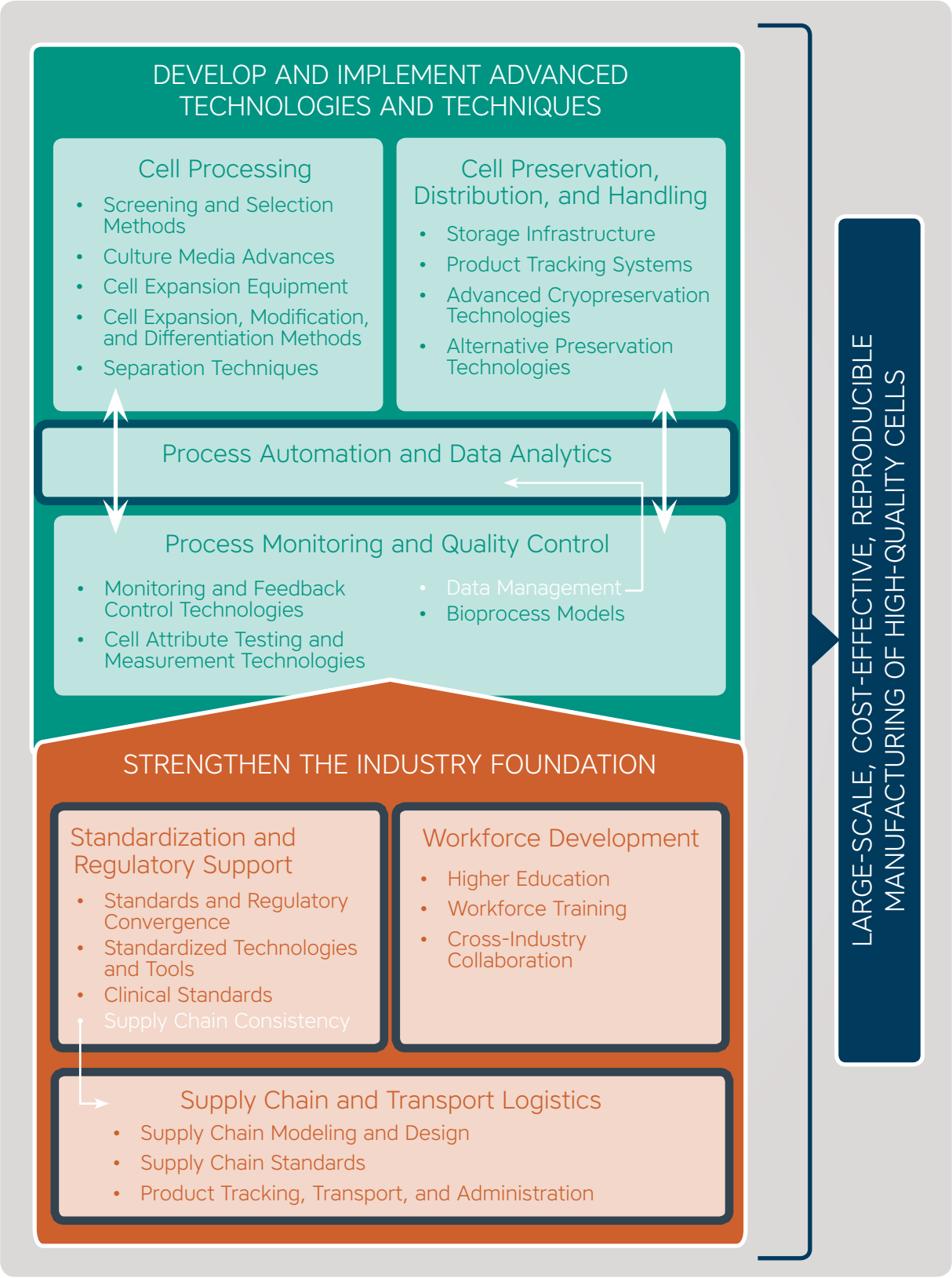
Process Automation and Data Analytics — Big data analytics holds significant promise to help identify critical quality attributes (CQA) and improve cell manufacturing processes, leading to efficient closed-system automation of unit operations and eventually whole bioprocesses. To realize these capabilities, the cell manufacturing community must improve measurement tools and electronic systems for data collection, develop or adopt advanced tools and systems for real-time data analytics, and collect more robust data from throughout the manufacturing process—from cell harvesting to delivery—both from the cells themselves as well as the process and the supply chain. Assessing cell function post-administration and the effect on the disease model in humans is also critical for identifying CQAs.

Supply Chain and Transport Logistics — The quality, affordability, and availability of cell-based products depends on the robustness of the cell manufacturing supply chain and the reliability and speed of product transport. To optimize the cell manufacturing supply chain, the cell manufacturing community should accelerate activities for advancing supply-chain-wide data collection, cell tracking technologies, and supply chain modeling. Given the importance of the supply chain and transport logistics to advancing cell manufacturing, this focus area was pulled out into its own activity area in the updated roadmap.

Standardization and Regulatory Support — With increased NIST and FDA focus on standards for cell-based products, and the launch of the International Standards Coordinating Body (SCB) for Gene, Cell, and Regenerative Medicines and Cell-based Drug Discovery, the cell manufacturing community should work to inform ongoing standards development activities that will increase the consistency of industry terminology, data collection and management, cell processing, and workforce training and certification. In particular, these regulatory entities should work with professional societies, patient advocates, clinicians, and industry to establish comprehensive, standardized clinical data registries to facilitate sharing of clinical outcomes and cell characterization data that can further accelerate identification of CQAs and inform updates to regulations and guidance.

Workforce Development — Given the rapid growth of cell manufacturing, it is becoming even more critical for the cell manufacturing community to leverage and align existing higher education and workforce training programs and to continuously assess and ensure that training programs are focused on skillsets that industry needs most.

Figure 1. Updated Roadmap Strategy



**Activities related to Cell Processing; Cell Preservation, Distribution, and Handling; and Process Monitoring and Quality Control are not discussed in this roadmap update document but remain areas of NCMC focus. Please see the complete roadmap for activities in these areas.*

Process Automation and Data Analytics

The key to cell manufacturing process automation and the availability of generalizable technologies and tools that can be applied to a variety of cell types and applications is dependent largely on tools for data measurement and analysis. While all cell types and applications have unique processing needs, improved tools for big data analytics can enable increased control of process parameters and critical quality attributes (CQAs) to better understand, predict, and achieve desired cell modes of action (MOAs). To increase the robustness of available data and facilitate increased process automation, it will also be necessary to improve measurement tools, including sensors for non-destructive evaluation, and obtain and audit data from clinical trials. While much progress has been made since publishing the original roadmap to develop and implement advanced technologies and techniques, the integration and analysis of data from throughout the manufacturing process—from starting material to administration at a clinical site—has the potential to accelerate rapid progress toward achieving large-scale, cost-effective, reproducible manufacturing of high-quality cells.

Figure 2. Process Automation and Data Analytics Priority Activities

▲ MID **Changed time frame** ↑P **Changed priority level** ★ **New activity** **Bolded text indicates priority activities**

**Select activities from the original* Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells *roadmap were used to facilitate discussion related to Process Automation and Data Analytics.*

NEAR TERM (2017-2018)

CROSSCUTTING AUTOMATION AND ANALYTICS (CCAA)	
★	Establish expert subcommittees (e.g., sensors, classes of cell therapies) to explore technology options and their application to common problems
★	Assess and identify tools, analytic methods, processes, and in-process monitoring approaches that are generalizable or universal and can therefore advance the cell manufacturing field as a whole
★	Improve tools while also developing cell-type and disease-specific CQAs
★	Differentiate between tools available for understanding MOAs and CQAs, for process development, and for process control
★	Gather feedback from pre-clinical and clinical studies on cell characteristics to inform CQA determination
PROCESS MONITORING AND QUALITY CONTROL (PMQC)	
▲ MID	**Develop reliable real-time, image-based, in-line analytical methods for small volumes that collect comprehensive data about cells and media (e.g., activity base, morphology, phenotype, metabolism)** *(from Cell Attribute Testing and Measurement)*
	Apply smart manufacturing sensors and controls to monitor process conditions (e.g., exposure to high temperatures and humidity) that could impact cell quality *(from Monitoring and Feedback Control Technologies)*
▲ MID	Refine process monitoring software, including optical, metabolic, and dynamic scheduling software, based on feedback and design space *(from Monitoring and Feedback Control Technologies)*
★	Focus on the development of systems, sensors, and assays for known MOAs and cell identities, and choose a small number of test case areas to apply methods (i.e., big data analysis of T cell therapies to find CQAs that can be monitored or measured for efficacy)

NEAR TERM (2017-2018)	DATA ANALYTICS (DA)	★	**Develop platform technology (i.e., cell-based assays) to automate/accelerate assays**
			Improve analytics for pattern recognition, CQA determination, and key performance parameter determination
		★	Conduct big data analysis to find CQAs for MOAs, develop measurement technology for CQAs, and conduct process analysis to link critical process parameters to CQAs and measurement needed to develop automation and advanced sensors
MID TERM (2019-2021)	CELL PROCESSING (CP)	LONG ↑P	**Improve closed-system, non-manual, and efficient technology for automated tissue processing** *(from Cell Expansion Equipment)*
			Develop automated, closed systems that allow for parallel manufacturing of multiple patient samples *(from Cell Expansion Equipment)*
			Collect and analyze upstream processing image data to automate clonal selection and remove subjectivity in decision-making *(from Screening and Selection Methods)*
		NEAR ↓	Develop approaches for automating visual inspection methods to distinguish between cells and extraneous matter, including particulates and inactive products, reducing labor requirements and the cost of goods sold *(Separation Techniques)*
	PMQC		**Develop standardized platform technologies or high-throughput assays and surrogates to ensure cell-to-cell consistency in terms of phenotype, functionality, quality, and potency over a range of time frames** *(from Cell Attribute Testing and Measurement)*
		LONG ↑P	**Develop real-time CQA monitoring systems (e.g., with advanced sensor technology) that adjust process parameters to drive cell populations to a functional state** *(from Monitoring and Feedback Control Technologies)*
			Advance and integrate sensors that can non-destructively gather and transmit data *(from Monitoring and Feedback Control Technologies)*
			Build an easy-to-operate, automated central controller that can accommodate multiple units for parallel processing *(from Monitoring and Feedback Control Technologies)*
LONG TERM (2022-2025)	CP		Develop high-efficiency automated graft fractionation technology *(from Separation Techniques)*
	PMQC	MID ↓ ↑P	**Develop and validate all-in-one non-destructive rapid test method with sensors and imaging technologies for assessing CQAs** *(from Cell Attribute Testing and Measurement)*
			Develop sensors that can be embedded in the matrix to visualize cells grown on a microcarrier *(from Monitoring and Feedback Control Technologies)*

Supply Chain and Transport Logistics Action Plan

To ensure the availability of current cell-based products and keep pace with anticipated industry growth in coming years, the cell manufacturing community must identify and implement optimized supply chain models. It will be critical to capitalize on recent developments in cell tracking; accelerate the integration of real-time data collection and analysis in supply chain models; and improve shipping conditions to achieve the large-scale manufacturing and distribution of reliable, high-quality cells. By leveraging lessons learned from other industries (e.g., Amazon, grocery deliveries) with large, distributed, rapid delivery networks and by building cloud-based industry databases, the cell manufacturing industry could more quickly identify potential solutions for coordinated cell product distribution. In the near term, a balance of both distributed and centralized supply chains will help improve affordable, timely access to cells for a variety of applications. In the long term, an optimized supply chain with more sophisticated transport capabilities could significantly expand product access by accommodating a range of delivery mechanisms, from the delivery of individualized treatments via drones or self-driving vehicles to the international transport of life-saving therapies.

Figure 3. Supply Chain and Transport Logistics Priority Activities

▲ MID Changed time frame | ↑P Changed priority level | ★ New activity | **Bolded text indicates priority activities**

NEAR TERM (2017-2018)

SUPPLY CHAIN MODELING AND DESIGN (SCMD)	▲ LONG	**Define and standardize the optimal supply chain design, defining data inputs, model types, and scenarios/ constraints for supply chain modeling of several transport designs**
	★	Assess Amazon's approach for fast fulfillment and economies of scale and identify aspects of this approach that could be applied to autologous cell manufacturing
	★	Model the supply chain and identify bottlenecks associated with integration with electronic medical records and cloud-based enterprises
SUPPLY CHAIN STANDARDS (SCD)		**Publish a paper that clarifies definitions (e.g., serum free, xeno-free, chemically defined) for media composition, cytokines, and all other ancillary materials**
		Initiate regulatory standards to ensure consistency of raw materials (e.g., serums) from different suppliers and reduce dependency on sole source providers, while standardizing data quality attributes and shipping
PRODUCT TRACKING, TRANSPORT, AND ADMINISTRATION (PTTA)	★	**Educate customs agents to facilitate international transport of cells**
	★	Gather data from FedEx, UPS, Amazon, and grocery shopping services on what products are held in transport and rules for biologics in each country
	▲ LONG	Develop and integrate an automated reading device (e.g., bar coded or radio-frequency identification [RFID]) to gather data inputs from different sources and points during the workflow—including at manufacturing and clinical sites—and enable 100 percent chain-of-custody recording
		Generate electronic batch records and develop raw material control for numerous processes in parallel to facilitate the tailoring of existing systems

MID TERM (2019–2021)	SCMD		**Integrate adaptive, real-time big data machine learning approaches into supply-chain modeling**
			Establish long-term supply of critical components to address issues related to single-source supply, reduce cost, and increase the ability to supply the quantity required to manufacture a cell component
	SCD	★	**Build business case for return-on-investment for sharing supply chain data**
		LONG ▲	Establish metrics for comparing tissue and blood processing practices across manufacturers and companies
		★	Scale up production of high-quality reagents for use in cell therapy products
		★	Assess and identify gaps in current industry standardized definitions of media composition and reagents
		★	Develop standards for quality and purity of raw material
	PTTA	★	**Develop fool-proof packaging to reduce variability in administration**
		★	Train hospital staff in the administration of cell therapies and the collection of tissues/cells
		★	Develop standards for collection of starting materials
		★	Establish best practices for coordinated distribution process with consensus metrics for success
		★	Define improved shipment conditions
			Develop reusable distribution solutions such as easy-to-sterilize capsules that transmit location and record critical environmental encounters and tracking information
		NEAR ▼	Define methods to segregate and securely track products, patient information, and global footprint in a multiproduct manufacturing facility
LONG TERM (2022–2025)	SCMD	★	Design a distributed model for case management and a tiered approach to supply that incorporates scheduling
		★	Achieve fast fulfillment connectivity from point-of-care to manufacturing pathway through a distributed supply chain like the Amazon model
	PTTA	★	Develop technology to make cells “hibernate” and enable transport at room temperature
		★	Develop technology for nitrogen- and dimethyl-sulfoxide-free transport and storage
		★	Generate global passport or standard for international transport of cell therapies
		★	Achieve delivery of cells via drones or self-driving vehicles, and establish related logistics standards

Standardization and Regulatory Support Action Plan

Much has happened in the area of standards development for cell therapies, devices, diagnostics, and other biopharmaceutical products since the publication of *Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells*. In response to requirements of the *21st Century Cures Act*, which was passed in December 2016, the U.S. Food and Drug Administration (FDA) and the National Institute of Standards and Technology (NIST) are collaborating on the development of standards and consensus definitions for cell-based and regenerative medicine products. In late 2016, the International Standards Coordinating Body (SCB) for Gene, Cell, and Regenerative Medicines and Cell-based Drug Discovery, which is co-chaired by Krish Roy, Technical Lead of NCMC, was also launched. In the next few years, standards development for cell-based products and biopharmaceuticals will be further accelerated in coordination with the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) and BioFabUSA.

By working closely with the SCB, NIST, FDA, the Alliance for Regenerative Medicine (ARM), NIIMBL, and BioFabUSA, NCMC can help inform standards development and accelerate the implementation of standards for the manufacturing and administration of cell-based products. NCMC should implement activities focused on informing the standardization of cell manufacturing technologies and tools, including criteria, definitions, assays, and data collection; and the development of standards for clinical registries, guidance, and reimbursement. Such standards activities will be critical to increasing the consistency of industry terminology, data collection and management, cell processing, and workforce training and certification, which will more efficiently and effectively facilitate the development and availability of reliable and safe new cell-based products.

Figure 4. Standardization and Regulatory Support Priority Activities

▲ MID Changed time frame ↑P Changed priority level ★ New activity **Bolded text indicates priority activities**

NEAR TERM (2017-2018)

STANDARDS AND REGULATORY CONVERGENCE	
★	**Inform the standards development efforts of the SCB, NIST, and ARM, including addressing Section 3036: Standards for Regenerative Medicine and Regenerative Advanced Therapies of the *21st Century Cures Act***
↓P	Form a working group to engage with the Office of Tissues and Advanced Therapies (OTAT), Office of the Director, on cell therapy policy issues
	Work with SCB on engaging the International Conference on Harmonisation (ICH) to change Drug Substance to Drug Product in the Common Technical Document, Module 3 for investigational new drugs (INDs)
STANDARDIZED TECHNOLOGIES AND TOOLS (STT)	
★	**Develop information management standards**
	Work with the SCB on establishing quality-by-design principles for cell product manufacturing
	Identify differences between smaller-scale autologous and larger-scale allogeneic manufacturing processes that would affect FDA regulatory interactions
↓P	Work with the SCB and NIST on establishing reference materials for in-process and release assays to contribute to the testing of candidate materials
★	Develop reference standards for characterizing cell identity, potency, and purity
★	Build consensus on standardized analytical methods for measuring cell properties

NEAR TERM (2017-2018)	CLINICAL STANDARDS (CS)	★	**Generate a registry of patient history and clinical outcomes**
		★	Develop standards for workforce coordination, leveraging crossover with the Foundation for the Accreditation of Cellular Therapy (FACT), the American Association of Tissue Banks (AATB), and the American Association of Blood Banks (AABB), for local deployment of cell therapies and INDs
		↓P	Engage with the FDA on issues of single-patient personalized medicine and regulatory requirements (e.g., synthetic DNA using patient's gene sequence and viral vector delivery), potentially through existing liaison meetings, including with the International Society for Cellular Therapy (ISCT) and Alliance for Regenerative Medicine (ARM)
			Support the FDA's existing efforts on quantitative definitions for a material to be xeno-free, serum-free, and free of other animal components
			Establish a working group to define the regulatory pathway for cellular products through the FDA—addressing their unique challenges and requirements—and develop regulatory plan tools (e.g., templates, checklists, and limited population studies)
		★	Work with the FDA on guidance on minimally manipulated definitions (e.g., homologous use, autologous) and allogeneic products
		★	Build consensus among stakeholders on requirements, specifications, and best practices for classified space for various cell manufacturing applications
MID TERM (2019-2021)	STT	↑P	**Develop commercially available reference standards for various cell types through collaborations to test candidate materials and develop materials**
		↑P	**Define and regulate tests for tissue and organ functionality**
		↓P NEAR	Establish standards for acceptable levels of residuals and impurities in final products (e.g., single-use products), working with the FDA to define impurities and their impact and identify relevant tests
		↓P NEAR	Develop guidelines regarding cell genetic stability and chromosomal aberrations (i.e., pass/fail)
		NEAR	Establish standards with FDA, the European Medicines Agency (EMA), NIST, and the International Organization for Standardization (ISO) for protein and DNA/RNA quantification
			Work with the International Society for Stem Cell Research (ISSCR) to define acceptance criteria and tests for embryonic stem cell and induced pluripotent stem cell pluripotency
	CS	NEAR	Establish a working group, including FDA, the Centers for Medicare & Medicaid Services (CMS), ARM, and ISCT, to address third-party payer issues, leveraging the Kidney Health Initiative's engagement of CMS in their development of a renal replacement roadmap
		★	Develop a general project plan outline/task list for getting to pre-IND and IND filing
LONG TERM (2022-2025)	STT	★	**Develop high-throughput, low-cost tools and assays for reliable assessment of potency, including processing (i.e., form potency toolkits)**
		★	Assess how to standardize validated, automated processes in a de-centralized setting

Workforce Development Action Plan

Given the rapid growth of cell manufacturing, it is becoming even more critical for the cell manufacturing community to leverage and align existing training programs and to continuously assess and ensure that training programs are focused on skillsets that industry needs most. Training programs must address a broader set of skills beyond cell therapies, including intellectual property, business management, regulations, and data management and analysis. These topics must be included in curricula at all levels of biomedical engineering and biological science programs and reinforced through internships from the undergraduate to post-doctorate level to provide the next-generation workforce with real-world experience. To ensure that the existing workforce can keep pace with industry advances, the cell manufacturing community should incorporate these skills in standardized and integrated certificate programs, short courses, and training modules that allow workers to accumulate stackable credentials. Such advances in cell manufacturing training are critical to establishing and implementing industry best practices and ensuring continued innovation and consistency in the manufacturing of high-quality cells.

Figure 5. Workforce Development Priority Activities

MID Changed time frame | P Changed priority level | ★ New activity | **Bolded text indicates priority activities**

NEAR TERM (2017-2018)

HIGHER EDUCATION (HE)

★	**Develop certificate programs in cell therapy manufacturing and quality control (at two-year colleges, technical colleges, or universities)**
	Establish modular, bi-directional (i.e., continuous engagement between industry and academia), dynamic curriculum development processes in areas of cell manufacturing knowledge, including logistics, revenue, intellectual property, and confidentiality, at high schools, community colleges, four-year universities, and graduate and post-doc programs
★	**Supplement current biological sciences and bioengineering curricula with areas of focus for cell manufacturing (e.g., specific technologies, good manufacturing practices [GMPs], regulations, business management)**
	Engage local community colleges, technical colleges, and universities to help train the entry-level workforce in the skills that industry has identified as critical to advancing cell manufacturing
MID	**Pilot undergraduate internship or cooperative education program with preparatory courses**
★	Develop data handling and analysis curriculum (e.g., biostatistics) applied to biomanufacturing to build a cell-therapy-centric software workforce that extends beyond bioinformatics and cultivates a role for "cell therapy industrial engineers"
	Launch graduate and postdoctoral industry internships that include preparatory curriculum with instruction on industry skills for productivity (e.g., how to keep a laboratory notebook, how to manage intellectual property), case studies of successful and failed processes and products, and rapidly changing guidance documents such as those from the U.S. Food and Drug Administration (FDA)
	Leverage existing training networks and industry to plan inter-institutional training programs (e.g., online courses and massive open online courses [MOOCs]) that address specifics of cell therapy manufacturing and policies and logistics
★	Develop a career track for "cell manufacturing managers" with managerial internships focused on management skills such as decision-making

NEAR TERM (2017-2018)	WORKFORCE TRAINING (WT)	★	**Develop flexible, rapid retraining programs, including certificates with stackable credentials, that leverage existing training networks (e.g., community colleges)**
			Launch a MOOC short course with stackable certifications to train manufacturing personnel on emerging cell biomanufacturing topics
		★	Assess who should drive the development of entry-level workforce training centers and collaborate with these entities on center setup, leveraging lessons learned from the biologics industry and other proven models
		★	Assess industry workforce needs (regulatory and technical) and map these needs to the skillsets provided by currently available training
		★	Assess reasons for current industry personnel turnover
		★	Develop workforce development programs focused on data management and regulatory issues
MID TERM (2019-2021)	HE		Implement responsive programs that address identified knowledge gaps in cell biomanufacturing and engage the appropriate industry instructors across disciplines (e.g., business, regulatory, intellectual property, software, statistics, bioinformatics)
			Build global awareness on challenges and opportunities in cell therapies through coursework and internships, including industry case studies on global regulatory issues and ethical considerations on how cell therapies are viewed or allowed in various countries
			Implement inter-institutional training programs at the graduate level
		★	Establish post-military training programs for cell manufacturing technologist/specialist positions
	WT	★	Develop customer discovery programs and consortia to connect aspiring entrepreneurs to existing stakeholders
		★	Monitor the current status of workforce diversity and target programs to address any deficiencies as the industry expands
LONG TERM (2022-2025)	HE	↑P	**Institutionalize responsive educational programs that address identified knowledge gaps**
			Institutionalize internship or cooperative education program for two- and four-year undergraduate programs
			Implement inter–institutional training program for two-year and four-year undergraduate degrees
	WT	NEAR ↓	Formalize a mechanism for transferring legacy knowledge to the next-generation workforce and facilitate interactions between the existing and emerging workforce through an existing or new professional society

Appendix: Roadmap Update Contributors

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