CELL MANUFACTURING ROADMAP TO 2030

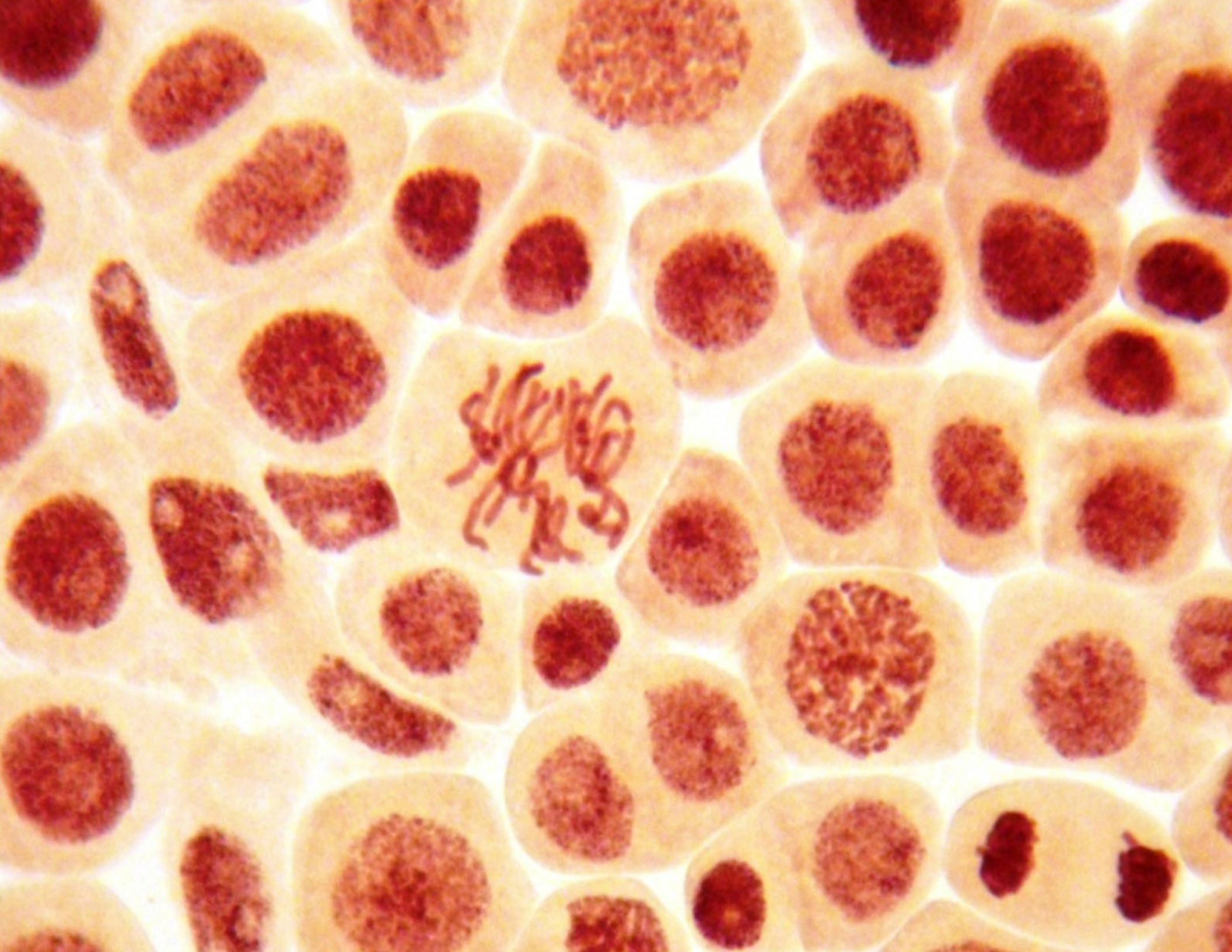
NOVEMBER 2019

National Cell Manufacturing Consortium

CMaT NSF Engineering Research Center for Cell Manufacturing Technologies

Georgia Tech Marcus Center for Therapeutic Cell Characterization and Manufacturing

PREPARED BY NEXIGHT GROUP



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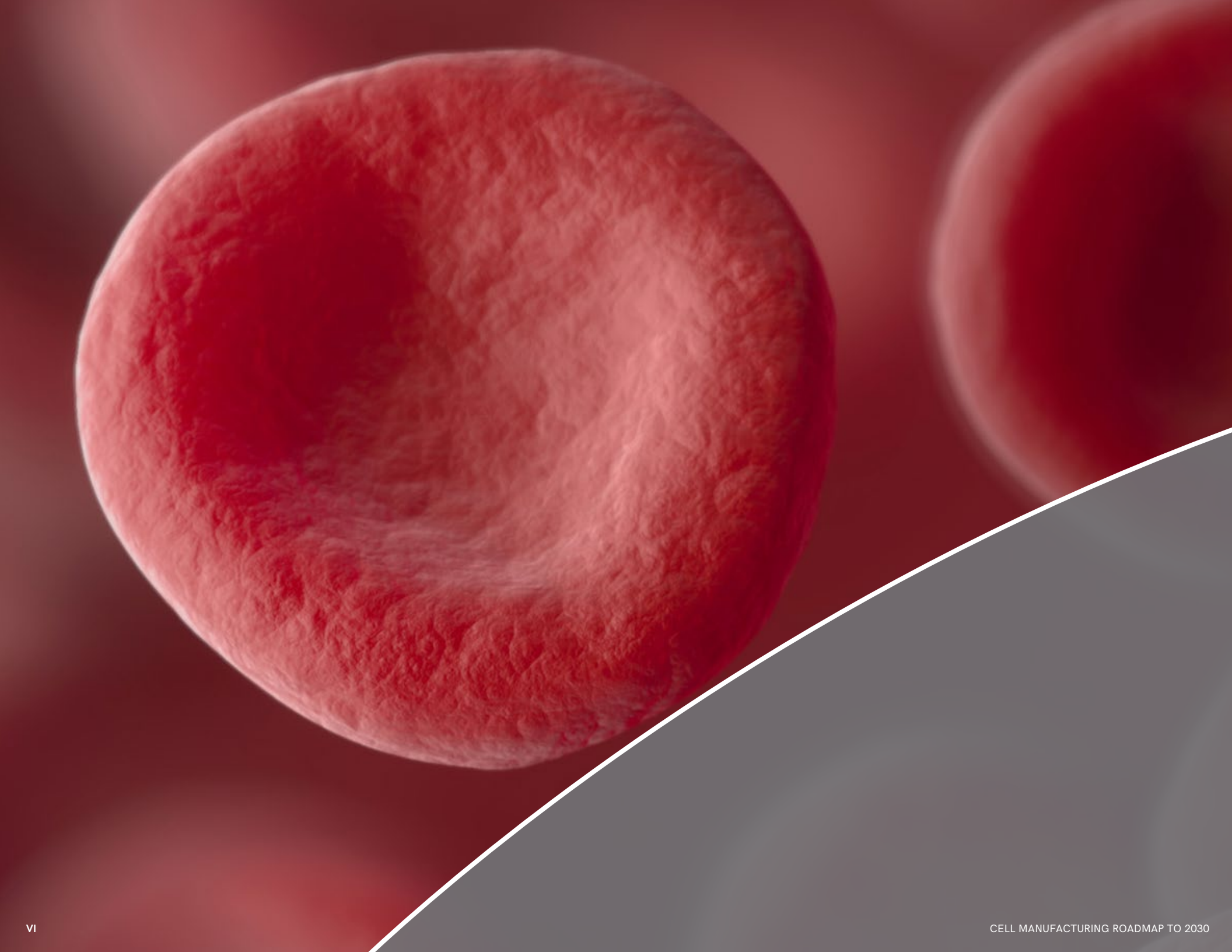
About this Roadmap

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). The original roadmap, as well as the subsequent 2017 Roadmap Update, was developed with funding from the National Institute of Standards and Technology's Advanced Manufacturing Technologies (AMTech) Consortia Program.

Since these documents were published, the cell manufacturing field has experienced significant growth and innovation, necessitating an updated roadmap strategy in response to recent cell manufacturing advances, the industry and clinical outlook, and emerging needs. This *Cell Manufacturing Roadmap to 2030* assesses progress made in implementing roadmap activities, identifies current challenges the cell manufacturing community must overcome, and outlines activities needed to achieve large-scale, cost-effective reproducible manufacturing of high-quality cells—including both refined activities from the original roadmap and roadmap update, as well as new activities.

Roadmap development was sponsored by the National Science Foundation Engineering Research Center for Cell Manufacturing Technologies (CMaT), the Georgia Tech Marcus Center for Therapeutic Cell Characterization and Manufacturing (MC3M), and the National Cell Manufacturing Consortium (NCMC). Direct input from industry, academia, clinical facilities, private foundations, and government agencies during a facilitated workshop informed the updated roadmap strategy. The cell manufacturing experts who made vital contributions through workshop participation and roadmap reviews are identified in Appendix A of this report. Nexight Group supported the overall roadmapping process and prepared this roadmap.



Executive Summary

Since publication of the first cell manufacturing roadmap in 2016, the cell manufacturing field has grown significantly:

- There are more than 900 companies, ranging from small and medium businesses to multinational corporations, focused on the research and development of cell-based medical products.[1]
- Many new therapies have advanced to late-stage development: in the beginning of 2019, more than 1,000 clinical trials were under way.[2]
- Cell and gene therapy products, including Yescarta and Kymriah, are now available on the U.S. market. The U.S. Food and Drug Administration (FDA) expects more than 200 new Investigational New Drug (IND) applications for these therapies by 2020, with 10–20 approvals per year by 2025.[3]

1. Alliance for Regenerative Medicine, "Annual Regenerative Medicine Data Report," http://alliancerm.org/wp-content/uploads/2019/03/ARM_AR2018_Web_FINAL.pdf (accessed September 19, 2019).
2. Alliance for Regenerative Medicine, "Q1 2019 Data Report," https://alliancerm.org/publication/q1-2019-data-report/ (accessed September 25, 2019).
3. U.S. Food and Drug Administration, "Statement from FDA Commissioner Scott Gottlieb, M.D. and Peter Marks, M.D., Ph.D., Director of the Center for Biologics Evaluation and Research on new policies to advance development of safe and effective cell and gene therapies," https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics (accessed October 1, 2019).

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. It combines focused research and development to advance technologies and techniques with initiatives designed to support and sustain the cell manufacturing industry and growing bioeconomy. The roadmap strategy is built around five key cell manufacturing activity areas:

Cell Processing and Automation — The development of new cell-based products will demand better understanding and more efficient control of cell processing variables, including through increased process analytics and flexible feedback-controlled automation, to improve product consistency, potency, and reliability.

Process Monitoring and Quality Control — More consistent, reliable, and lower-cost cell manufacturing processes—through the use of sophisticated process simulation and modeling, in-line or at-line process analytical technologies, feedback control technologies, and big data analytics—will be critical to ensuring the highest quality of manufactured cells, particularly as demand for these cells grows.

Supply Chain and Transport Logistics — The affordability, availability, and access to a variety of cell-based products depends on the robustness of the cell manufacturing supply chain, the reliability of product storage, and the speed and reliability of product transport.

Standardization, Regulatory Support, and Cost Reimbursement — Existing and potential cell manufacturing best practices, standards, and regulations should encourage innovation, improve manufacturing quality across the value chain, and help ensure affordable treatment options for patients.

Workforce Development — An effective workforce needs to be capable of not only operating, but continuously improving, next-generation cell manufacturing technologies and their associated techniques with a data-driven multidisciplinary approach.

Cells are emerging as transformative therapeutics, but are also the building blocks of engineered tissues and organs. Resource investments in large-scale cell manufacturing are critical to fully realize the potential of this new industry and enable the next bioeconomy. Through a collaborative, strategic effort as called for in this roadmap and the support of public-private-philanthropic partnerships, the United States can accelerate cell manufacturing advances to ensure broader access to innovative, affordable, safe, and high-quality cell-based regenerative medicine products.

Definitions: Types of Cells

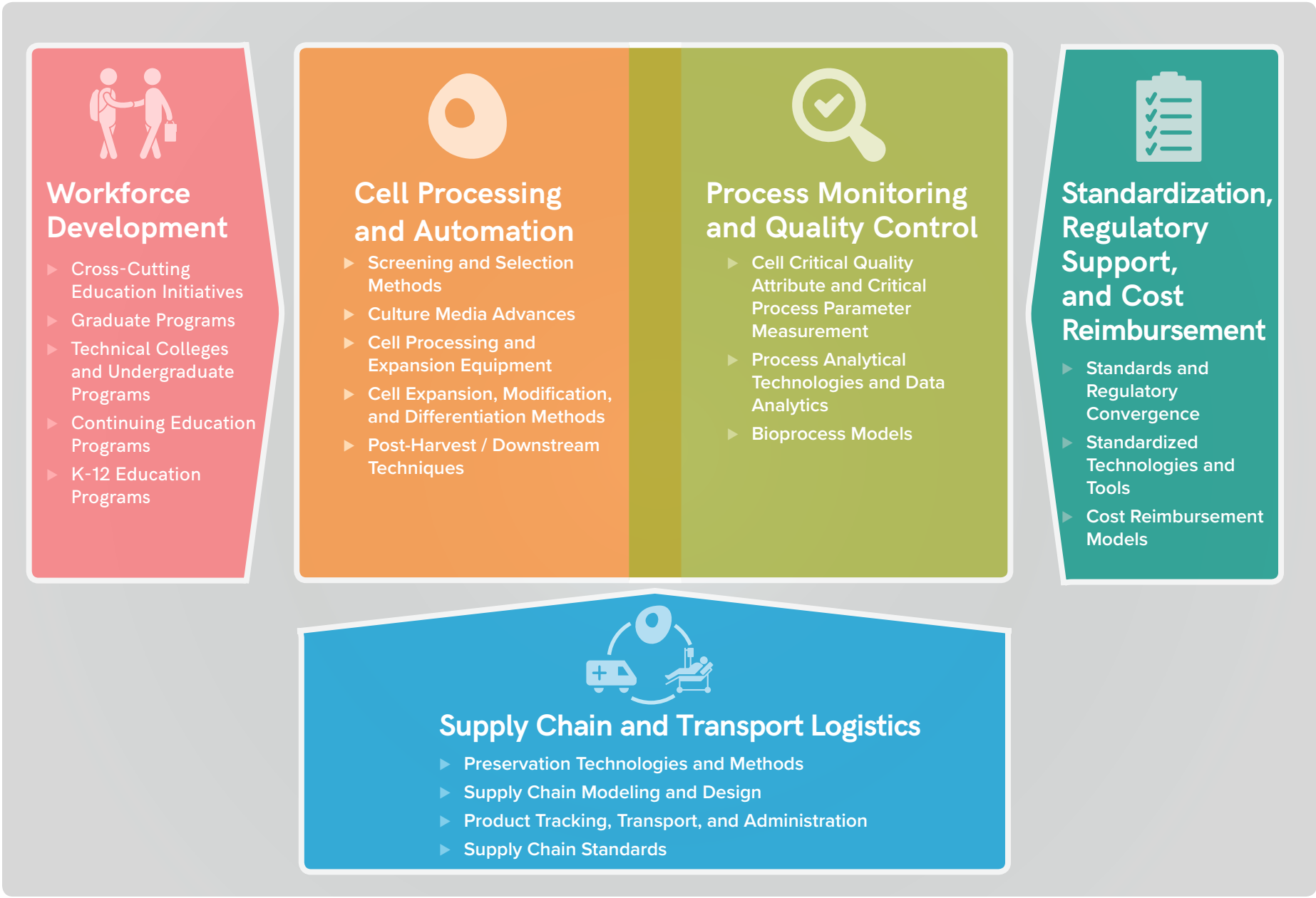
Cell manufacturing involves the production of a variety of cell types and their derivatives for use in final products, including cell therapies, engineered tissues, medical devices, and drug discovery and testing platforms. Though there are commonalities in the manufacturing of each of these cell types, manufacturing processes must be tailored to each specific cell type. This report divides cell types and the activities needed to advance their manufacturing into the following three areas:

Autologous—cells harvested, expanded, and later administered to the same patient as a point-of-care cell-based medical product

Allogeneic—cells from a donor that are expanded and banked for use in cell-based medical products

Pluripotent—unspecialized cells that can self-renew and are capable of differentiating into a variety of cell types with specialized functions, such as muscle cells, red blood cells, or cells of a particular organ

Figure 1. Roadmap Strategy



The high-priority activities included in this strategy—those with the greatest potential impact on cell manufacturing industry advancement in the next 10 years—are included in Figure 2.

Figure 2. High-Priority Roadmap Activities

Type of cell: Autologous, Allogeneic, Pluripotent, Crosscutting

		Timeline to Complete		
		2019-2021	2022-2025	2026-2030
Cell Processing and Automation				
⟷	**CULTURE MEDIA ADVANCES** Develop and optimize inexpensive, chemically defined media and universal feeder systems free of animal cells and components	→		
⟷	**CELL PROCESSING AND EXPANSION EQUIPMENT** Engineer bioreactors with increased capacity and integrated information technology systems that incorporate in-line and at-line monitoring and enable integrated feeds	→		
⟷	**CELL EXPANSION, MODIFICATION, AND DIFFERENTIATION METHODS** Identify method for low-cost, high-efficiency genetic modification that can engineer cells to elicit the desired response	→		
Pluripotent	**CELL EXPANSION, MODIFICATION, AND DIFFERENTIATION METHODS** Identify methods that can reduce the time needed to expand and differentiate pluripotent stem cells to 10%–20% of the current process time (i.e., several months)	→		
⟷	**POST-HARVEST / DOWNSTREAM TECHNIQUES** Develop closed-system, large-scale, label-free (or with removable labels) cell purification process and parallel cell purification system (including microcarrier separation and fill/finish)	→		
⟷	**POST-HARVEST / DOWNSTREAM TECHNIQUES** 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	→		
Autologous	**CELL PROCESSING AND EXPANSION EQUIPMENT** Develop tools for automated, feedback-controlled, closed-system, flexible bioprocessing that eliminate or reduce the need for cleanroom space and permit manufacturing in non-classified space		→	
⟷	**CELL PROCESSING AND EXPANSION EQUIPMENT** Achieve an integrated end-to-end automated and feedback-controlled closed-system process with integrated process analytical technologies (PAT)		→	
Process Monitoring and Quality Control				
⟷	**CELL CRITICAL QUALITY ATTRIBUTE AND CRITICAL PROCESS PARAMETER MEASUREMENT** Develop repositories or banks for acquiring and sharing reproducible cell source materials (e.g., tissues, cell lines, characterized cells) that can be used as references for comparing processes and donors and for assessing repeatability and reproducibility	→		
Allogeneic	**CELL CRITICAL QUALITY ATTRIBUTE AND CRITICAL PROCESS PARAMETER MEASUREMENT** Develop standardized, modular platform technologies and high-throughput assays or surrogates to ensure lot-to-lot consistency in terms of phenotype, functionality, quality, and potency over a range of time frames across the product lifecycle	→		

Type of cell: Autologous	Allogeneic	Pluripotent	Crosscutting	Timeline to Complete 2019-2021	2022-2025	2026-2030
Process Monitoring and Quality Control, continued						
⟷	**PROCESS ANALYTICAL TECHNOLOGIES AND DATA ANALYTICS** Conduct big data analysis to identify critical quality attributes (CQAs) for modes of action (MOA) and link critical process parameters (CPPs) to CQAs and needed measurements			→		
⟷	**CELL CRITICAL QUALITY ATTRIBUTE AND CRITICAL PROCESS PARAMETER MEASUREMENT** Develop real-time CQA and CPP monitoring systems (e.g., with smart sensors and real-time in-line or at-line PAT and controls) that non-destructively gather and transmit CQA data and adjust process parameters to drive cell populations to the desired functional state				→	
⟷	**CELL CRITICAL QUALITY ATTRIBUTE AND CRITICAL PROCESS PARAMETER MEASUREMENT** Develop and validate all-in-one (customizable, flexible, and modular) non-destructive rapid test method with sensors and imaging technologies for assessing CQAs					→
⟷	**PROCESS ANALYTICAL TECHNOLOGIES AND DATA ANALYTICS** Generate a registry of patient history and clinical outcomes, linking cell data to patient data and disease characteristics					→
⟷	**BIOPROCESS MODELS** Define experimental and computational data science methods and data required to identify CQAs and CPPs and develop associated bioprocess modeling for novel cell therapies					→
Supply Chain and Transport Logistics						
	PRESERVATION TECHNOLOGIES AND METHODS Improve understanding of cell responses to cryopreservation and thawing interactions			→		
	PRESERVATION TECHNOLOGIES AND METHODS Engineer end-user-friendly formulation that allows for higher-temperature storage alternatives to cryopreservation			→		
	PRESERVATION TECHNOLOGIES AND METHODS Develop processes for large-scale (i.e., number of units, unit volume) cell cryopreservation that improve cell quality, functionality, and batch homogeneity			→		
	SUPPLY CHAIN MODELING AND DESIGN Integrate adaptive, real-time machine learning approaches into supply-chain modeling			→		

Type of cell:  Autologous  Allogeneic  Pluripotent  Crosscutting

	Timeline to Complete		
	2019-2021	2022-2025	2026-2030
Standardization, Regulatory Support, and Cost Reimbursement			
STANDARDS AND REGULATORY CONVERGENCE Engage with the FDA (i.e., Center for Devices and Radiological Health [CDRH], Center for Biologics Evaluation and Research [CBER]) on issues of single-patient personalized medicine and regulatory requirements, potentially through existing liaison meetings, including with the Foundation for the Accreditation of Cell Therapy (FACT) and Alliance for Regenerative Medicine (ARM)	→		
STANDARDIZED TECHNOLOGIES AND TOOLS Define and regulate tests for common assays in cell manufacturing (e.g., counting, viability, flow cytometry)	→		
COST REIMBURSEMENT MODELS Develop new payment models and coverage policies relevant to cell therapies	→		
COST REIMBURSEMENT MODELS Continue to engage organizations—including FDA, Centers for Medicare and Medicaid Services (CMS), professional societies, industry groups, and other clinical centers and organizations—to address third-party payer issues	→		
Workforce Development			
CROSS-CUTTING EDUCATION INITIATIVES Develop a detailed, periodically updated roadmap to collect data to delineate the necessary skill sets for various levels of the cell manufacturing workforce and to inform better collaboration across industry and education programs (i.e., K-12, 2-year, 4-year, Masters, Ph.D., post-doctorate students)	→		
TECHNICAL COLLEGES AND UNDERGRADUATE PROGRAMS 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	→		
GRADUATE PROGRAMS Compile a description of different jobs and required skill sets that students with various education levels could aspire to in the cell manufacturing industry and post them in a centralized space	→		
TECHNICAL COLLEGES AND UNDERGRADUATE PROGRAMS Supplement current biological sciences and engineering curricula with areas of focus for cell manufacturing (e.g., specific technologies, Good Manufacturing Practices [GMPs], regulations, business management)		→	

The Need for Expanded U.S. Investment

In 2018, global regenerative medicine revenues totaled $13.3 billion.[4] By 2025, the industry is projected to grow to more than $48.97 billion.[5] The United States is currently at the forefront of biomedical research and technology development, and therefore well positioned to lead advances in cell manufacturing needed to realize the potential of the rapidly growing regenerative medicine market. 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. Large-scale cell manufacturing and the resulting increased commercialization of cell-based products will also accelerate the widespread achievement of several important national goals.

Improved health and reduced disease burden

Large-scale cell manufacturing can help bring more effective treatments to market that address the underlying causes of many diseases and conditions rather than only managing their symptoms. These emerging and next-generation cell-based medical products could cure or significantly change the course of diseases, reducing the need for life-long treatments and ultimately improving the quality of life of millions of people.

Increased competitiveness of U.S. manufacturing

Currently, there are more than 900 companies, ranging from small and medium businesses to multinational corporations, focused on the research and development of cell-based medical products.[6] Increased U.S. investment in cell manufacturing could grow the number of U.S. companies and jobs in this field, building a skilled workforce that can secure the United States' lead in the emerging field of cell-based medical treatments. Additionally, for every worker employed in biopharmaceutical manufacturing, another 4.9 jobs are created across other industries.[7]

More affordable healthcare

The United States spends nearly $3.5 trillion each year on healthcare.[8] Many diseases currently require life-long care and management, creating a significant financial strain to consumers and the government over the course of patients' lives. This economic burden could be reduced by the advancement of large-scale cell manufacturing and the resulting increased availability of cell-based medical treatments that can minimize the need for long-term management of diseases impacting the U.S. population.

Enhanced national security

The increased availability of novel cell-based medical treatments could enable faster and more effective treatment of military personnel and first responders. Large-scale U.S. cell manufacturing could also help to better accommodate surge demands for cell-based medical treatments in response to emergency incidents—including natural disasters, transportation accidents, exposure to hazardous materials, and terrorist attacks—while reducing the risk of supply disruptions from dependencies on overseas resources.

4. Alliance for Regenerative Medicine, "Annual Regenerative Medicine Data Report," http://alliancerm.org/wp-content/uploads/2019/03/ARM_AR2018_Web_FINAL.pdf (accessed September 19, 2019).
5. Zion Market Research, Regenerative Medicine Market by Product (Gene Therapy, Cell Therapy, Small Molecule & Biologic, and Tissue Engineering), by Material (Biologically-Derived Material, Synthetic Material, Pharmaceuticals, and Genetically Engineered Material), and by Application (Oncology, Cardiovascular, Musculoskeletal, Dermatology, Ophthalmology, Neurology, Wound Healing, and Others): Global Industry Perspective, Comprehensive Analysis, and Forecast, 2018–2025, May 2019, https://www.zionmarketresearch.com/report/regenerative-medicines-market.
6. Alliance for Regenerative Medicine, "Annual Regenerative Medicine Data Report," http://alliancerm.org/wp-content/uploads/2019/03/ARM_AR2018_Web_FINAL.pdf (accessed September 19, 2019).
7. TEConomy Partners, prepared for the Pharmaceutical Research and Manufacturers of America (PhRMA), "Biopharmaceutical Manufacturing in the U.S.: Making Cutting-Edge Medicines Today and Leading the Way on Medicines of Tomorrow," March 2019.
8. Centers for Disease Control and Prevention, "National Health Expenditures 2017 Highlights," https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf (accessed September 19, 2019).

Although U.S. progress can and will be made to address the activities outlined in this roadmap through individual research efforts, a more extensive and coordinated cell manufacturing community, supported by public-private-philanthropic partnerships, will be critical for maximizing U.S. cell manufacturing industry progress and ensuring success of the emerging bioeconomy. 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.

National Science Foundation (NSF) Engineering Research Center for Cell Manufacturing Technologies (CMaT)

CMaT, announced in September 2017, is an NSF-funded engineering research center supported by a consortium of universities, which is led by the Georgia Institute of Technology (Georgia Tech). CMaT's mission is to enable cell therapy product manufacturing scale-up by developing innovative tools, systems, and technologies that better ensure product quality, potency, safety, and cost effectiveness. The center also focuses its efforts on workforce development in collaboration with industry partners such as GE, ThermoFisher Scientific, and Lonza, among others.

Marcus Center for Therapeutic Cell Characterization and Manufacturing (MC3M)

MC3M, which was formally established 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.

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 additional commitments from partners from industry, academia, and non-profits. The Institute issued its third call for projects in July 2019.

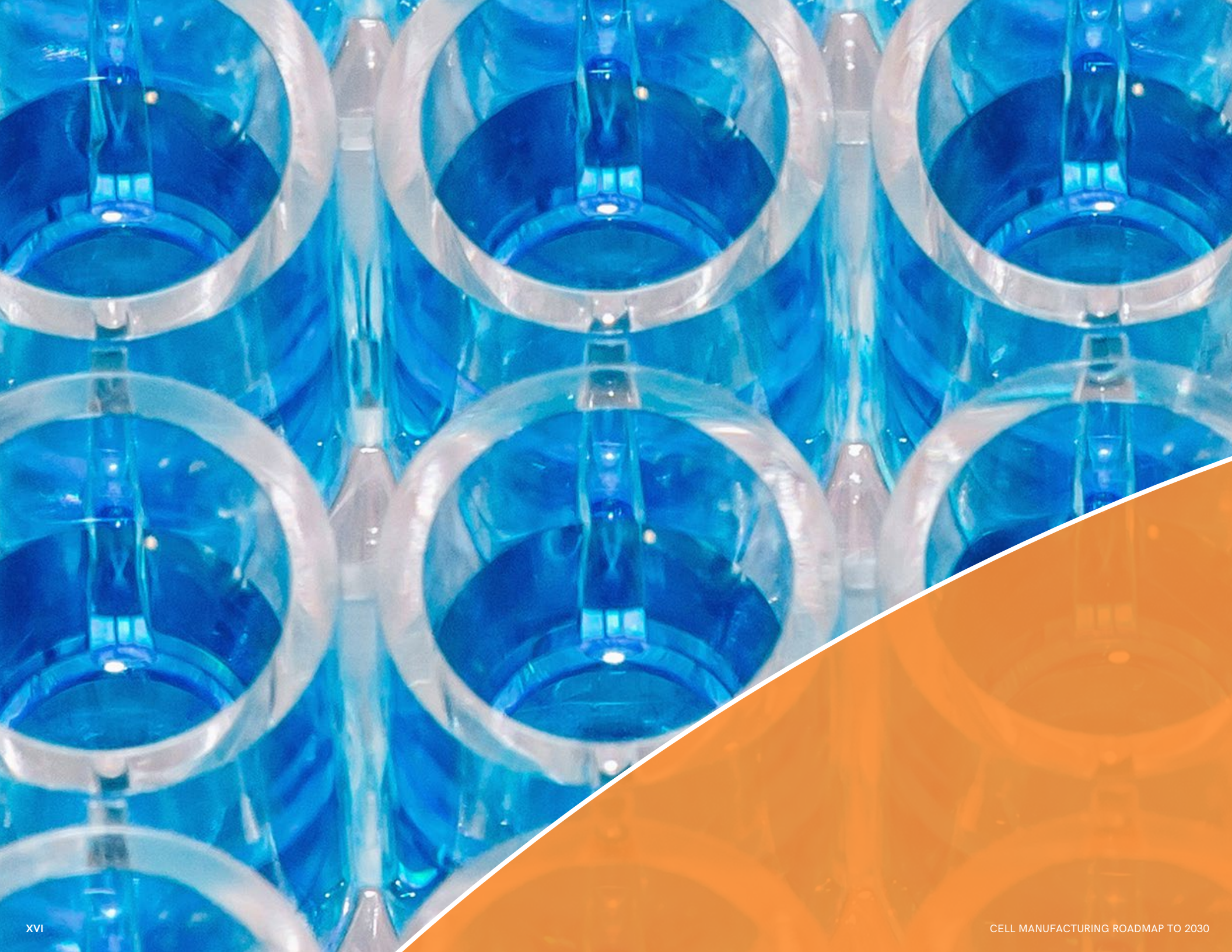
BioFabUSA, administered by the Advanced Regenerative Manufacturing Institute (ARMI)

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 150 members from industry, academia, and non-profit organizations. By focusing on four technical thrust areas—removing existing hurdles to reproducible tissue biomanufacturing, producing modular and scalable GMP-compliant manufacturing processes and integrated technologies, developing and standardizing manufacturing by providing training opportunities for all ages, and disseminating knowledge and technologies to enable continued innovation—BioFabUSA will develop manufacturing platforms and processes to catalyze the development of therapeutic platforms and products.

Standards Development Partnerships

The Standards Coordinating Body for Gene, Cell, and Regenerative Medicines and Cell-Based Drug Discovery (SCB) was formally launched in January 2017. This public-private partnership of product developers, tools and service providers, professional societies, government entities, and academic centers is focused on supporting standards development by engaging with community stakeholders to identify and prioritize needs, coordinating standards advancement efforts, participating in consensus standards development organization (SDO) activities, and educating and building awareness of standards.

Additionally, in response to the *21st Century Cures Act*, the National Institute of Standards and Technology (NIST) and 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), medical and surgical devices (ASTM F04), and pharmaceutical and biopharmaceutical manufacturing (ASTM E55).



Cell Processing and Automation

Each parameter of cell processing, including the vessel, media, nutrients, and physicochemical environment, influences the properties that cells require to be effective therapeutically. The development of new cell-based medical products will demand better understanding and more efficient control of cell processing variables, with advancements such as increased process analytics and flexible feedback-controlled automation, to improve product consistency, potency, and reliability.

Recent Progress

- Improving understanding of the cell types present in various cell therapies and the properties of these cells
- Documenting impacts of trace elements in culture media on product quality
- Designing and developing closed, automated, small-footprint cell processing systems
- Developing allogeneic and universal T-cell therapies
- Improving the scale of mesenchymal stem cell (MSC) production
- Increasing understanding of the limits of population doubling, senescence, and exhaustion
- Using synthetic biology to better control development of cell therapies

2030 Targets

Higher Productivity and Yield

Total post-culture process yields > 90%

2X – 5X increase in media productivity

Identification of highest quality cells (efficacy and safety) to reduce scale-up and dose requirements

Improved Process Automation and Speed

25% reduction in time for end-to-end batch production

Quality-driven, feedback-controlled, flexible automation for both autologous and allogeneic cells that can adjust process based on in-line or at-line real-time analytics, increasing reproducibility and reducing labor costs

Reduced Cost

90% reduction in cost of culture media and reagents

5X reduction in cost of goods and services (COGS) per patient compared with current costs

Core Challenges

Difficulty scaling research to large-scale production

- Scaling up allogeneic cell culturing research to a bioreactor environment, which can be 1,000 times the scale of a typical research flask, requires proof of comparability of the process and of product quality at these larger scales.
- The cell manufacturing community lacks small-scale bioreactor models to accommodate smaller lot sizes and bridge the gap between small-flask research and large-scale production.
- The cell manufacturing community lacks flexible, feedback-controlled automation and in-line and at-line process analytical technologies needed for large-scale processing.

Inefficient cell separation and purification methods

- Cell separation and purification is challenging, particularly because desired cells are often the same size as unwanted particles.
- Desired cells are also fragile and subject to shear, further adding to the complexity of cell separation.

Increased potential for contamination in open-culture settings

- Every opening of a culture vessel poses the potential for contamination from molds, yeasts, viruses, mycoplasma, and other cell lines.
- Maintaining a sterile environment is time- and labor-intensive, necessitating access to innovative closed systems.

Inadequate surrogate markers for understanding cell critical quality attributes (CQAs)

- There are no validated surrogate markers for reliably evaluating cell CQAs—including purity, potency, identity, stability, and viability—to define the safety and efficacy of therapeutic products made from these cells.
- Processes and measurement selection criteria vary across researchers and product developers since products and applications differ significantly, making it difficult to compare measurement outcomes.

Activities

Type of cell: Autologous, Allogeneic, Pluripotent, Crosscutting

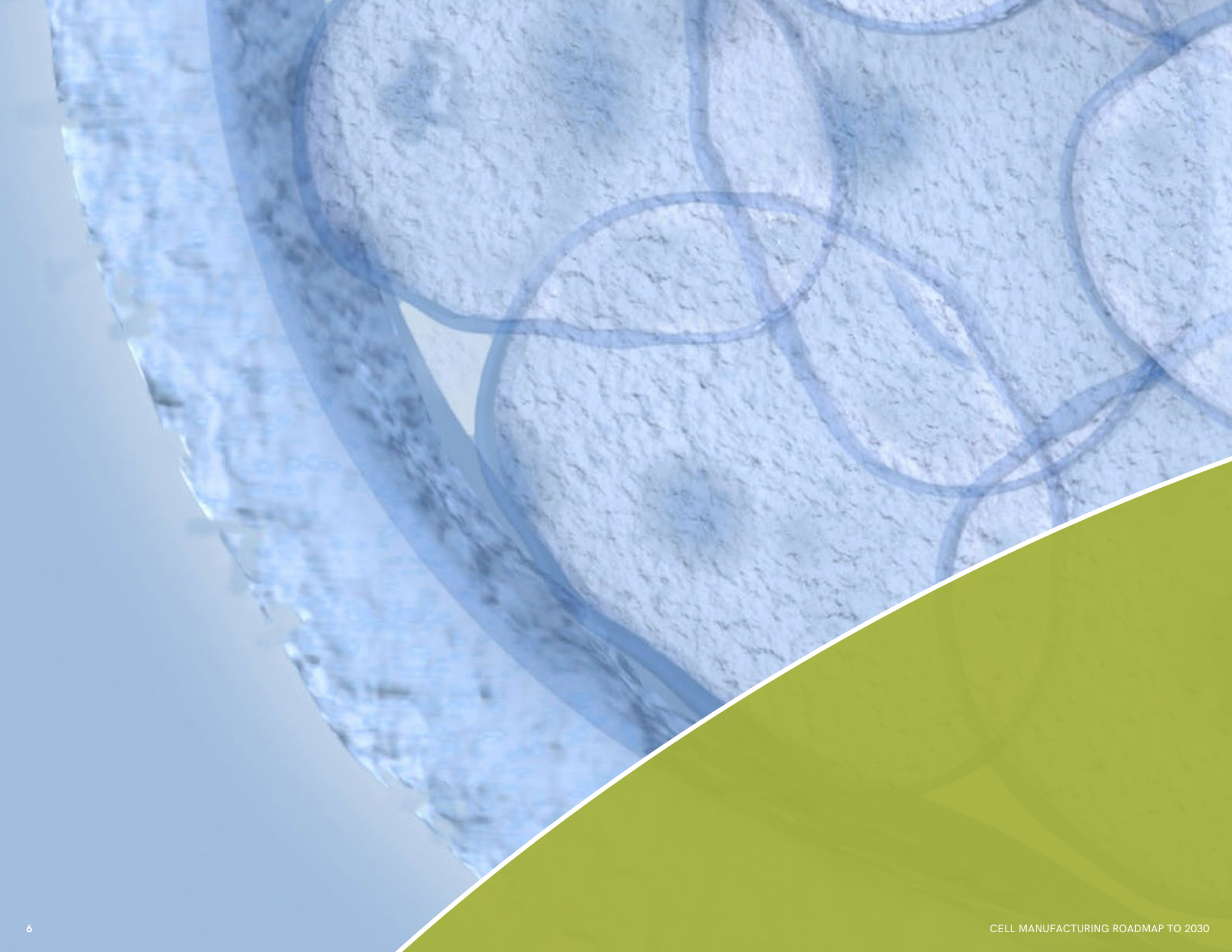
Bold = high-priority activity
✶= new activity

		Timeline to Complete		
		2019-2021	2022-2025	2026-2030
Screening and Selection Methods				
Pluripotent	Establish a method for rapid donor screening (e.g., assay technology) for use early on in the culturing process to assess the quality of cells and their suitability for process integration	→		
Pluripotent	Collect and analyze upstream processing image data to automate clonal selection and remove subjectivity in decision-making by standardizing methods for selecting suitable induced pluripotent stem cell colonies		→	
Pluripotent	Ensure starting material (i.e., cell) quality, consistency, and quantity		→	
Culture Media Advances				
Crosscutting	**Develop and optimize inexpensive, chemically defined media and universal feeder systems free of animal cells and components**	→		
Allogeneic	Eliminate need for feeder cells or uniform conditioned media and identify paracrine factors to increase understanding of cell functionality and facilitate increased process efficiency	→		
Allogeneic	Produce a panel of quality assays for serum cultures to ensure serum consistency and assess safety	→		
Cell Processing and Expansion Equipment				
Crosscutting	**Engineer bioreactors with increased capacity and integrated information technology systems that incorporate in-line or at-line monitoring and enable integrated feeds**	→		
Allogeneic	✶Develop scaled-down manufacturing systems for R&D use, especially for process development and optimization	→		
Allogeneic	Generate devices that automate adherent cell cultures, including seed trains and expansion phase	→		
Allogeneic	Extend holding times of final formulation to enable large lot sizes	→		
Autologous	**Develop tools for automated, feedback-controlled, closed-system, flexible bioprocessing that eliminate or reduce the need for cleanroom space and permit manufacturing in non-classified space**		→	
Crosscutting	**Achieve an integrated end-to-end automated and feedback-controlled closed-system process with integrated process analytical technologies (PAT)**		→	

Type of cell: Autologous, Allogeneic, Pluripotent, Crosscutting

Bold = high-priority activity
✶= new activity

		Timeline to Complete		
		2019-2021	2022-2025	2026-2030
Cell Processing and Expansion Equipment, continued				
Crosscutting	✶Develop small- and medium-scale automated, closed systems (i.e., to support Phase I and Phase II)	→		
Crosscutting	Create modular, flexible systems capable of producing several cell types simultaneously			→
Crosscutting	✶Develop standards around sterile connections, with the long-term goal of integrating specific unit operations			→
Cell Expansion, Modification, and Differentiation Methods				
Crosscutting	**Identify method for low-cost, high-efficiency genetic modification that can engineer cells to elicit the desired response**	→		
Pluripotent	**Identify methods that can reduce the time needed to expand and differentiate pluripotent stem cells to 10%–20% of the current process time (i.e., several months)**	→		
Allogeneic	Develop a reagent and method for large-scale T-cell activation and transduction	→		
Pluripotent	Improve automated, closed systems for more efficient tissue processing	→		
Allogeneic, Pluripotent	Advance closed-system gene delivery technology for transduction/ transfection, screening, and selection	→		
Crosscutting	Improve understanding of the effects of environmental and media conditions	→		
Pluripotent	Develop high-sensitivity and rapid differentiation assays	→		
Autologous	Develop automated, closed systems that allow for parallel manufacturing of multiple patient samples		→	
Post-Harvest / Downstream Techniques				
Crosscutting	**Develop closed-system, large-scale, label-free (or with removable labels) cell purification process and parallel cell purification system (including microcarrier separation and fill/finish)**	→		
Crosscutting	**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**	→		
Allogeneic	✶Push cell upper and lower limits for separation techniques and expand the range of possible volumes	→		
Crosscutting	Identify potential areas for process streamlining or biopreservation to extend holding or process times of cells during downstream processing	→		



Process Monitoring and Quality Control

A single process alteration during cell manufacturing could yield cells with properties that deviate from those required for a specific cell-based medical product. More consistent, reliable, and lower-cost cell manufacturing processes—through the use of sophisticated process simulation and modeling, in-line or at-line process analytical technologies, feedback control technologies, and big data analytics—will be critical to ensuring the highest quality of manufactured cells, particularly as demand for these cells grows.

Recent Progress

- Evaluating process analytical technology (PAT) advances from CHO cell process industry for application in cell therapy manufacturing
- Increasing cell-based assay automation, including with the use of robotics, scheduling software, and imaging
- Advancing modeling software to simulate CAR-T manufacturing processes to better control cell properties and quality

2030 Targets

Faster Availability of Safer and Higher Quality Products

< 1% sterility fails

Reduce time for release testing and stability studies by 50% – 75%

Critical quality attributes (CQAs) and critical process parameters (CPPs) are well established to improve quality, reduce batch failures, and reduce scale-up requirements

< 5% quality control failures of CQAs for cell function

Integrated PAT with flexible feedback-controlled automation for CQAs and CPPs

More Robust Data

By 2022: Establish international, anonymized repository of standardized data

Core Challenges

Difficulty identifying the most appropriate CQAs and CPPs to measure

- The cell manufacturing community lacks sufficient understanding of which cell attributes to measure in both starting and final cells, in part because manufactured cells differ from cells in the human body.
- This can hinder efforts to define properties that manufactured cells must possess to be appropriate for therapeutic use.

Inadequate PATs and assays to assess cell characteristics

- Existing measurement and data analysis tools are not sufficiently advanced to allow for real-time analysis of cell characteristics, including viability and purity.
- A lack of physiologically relevant potency and safety assays will make it difficult to detect and consequently mitigate inconsistencies or issues in cell processing.

Difficulty detecting contaminants quickly and accurately

- The primary way to detect contaminants in cell cultures—visually inspecting them—requires several days to determine if a culture has been compromised.
- Certain contaminants (e.g., viruses, mycoplasmas) are difficult to detect until they achieve high densities. By the time contamination is identified, it may have spread more widely, altering cell behavior and function and ruining entire cell lots.

Insufficient bioprocessing models to predict the impact of manufacturing conditions and materials on cell behavior

- Current bioprocessing models are inherently incapable of simulating all relevant bioprocess parameters due to the variability in both cells and patients.
- This prevents the community from determining how to improve or scale processes while ensuring high-quality and reproducible outputs.

Lack of reference materials for assay development, quality control, and cross-laboratory comparison

- The cell manufacturing industry does not have a reference bank of materials (e.g., National Institutes of Health cell banks) to use when developing and validating assays and other quality control tests.
- Without easy access to these materials, the community cannot easily ensure that the tests they create are accurately measuring cell attributes across platforms, laboratories, and companies.

Activities

Type of cell:  Autologous  Allogeneic  Pluripotent  Crosscutting

Bold = high-priority activity
✶= new activity

		Timeline to Complete		
		2019-2021	2022-2025	2026-2030
Cell Critical Quality Attribute and Critical Processing Parameter Measurement				
	✶**Develop repositories or banks for acquiring and sharing reproducible cell source materials (e.g., tissues, cell lines, characterized cells) that can be used as references for comparing processes and donors and for assessing repeatability and reproducibility**	→		
	**Develop standardized, modular platform technologies and high-throughput assays or surrogates to ensure lot-to-lot consistency in terms of phenotype, functionality, quality, and potency over a range of time frames across the product lifecycle**	→		
	Industrialize reliable real-time, in-line quantitative analytical methods for small volumes that collect comprehensive data about cells and media (e.g., activity base, morphology, phenotype, metabolism)	→		
	Develop sensors that can visualize cells grown on a microcarrier	→		
	**Develop real-time CQA and CPP monitoring systems (e.g., with smart sensors and real-time in-line or at-line PAT and controls) that non-destructively gather and transmit CQA data and adjust process parameters to drive cell populations to the desired functional state**		→	
	✶Develop and test a standardized cell-based assay platform for T cell therapies that enables the relevant gene of interest to be added for CQA assessment		→	
	**Develop and validate all-in-one (customizable, flexible, and modular) non-destructive rapid test method with sensors and imaging technologies for assessing CQAs**			→
Process Analytical Technologies and Data Analytics				
	**Conduct big data analysis to identify CQAs for modes of action (MOA) and link CPPs to CQAs and needed measurements**	→		
	Use data mining to extract data about equipment use, maintenance, calibration, and critical process parameters from electronic batch records, electronic notebooks, and other electronic databases	→		
	Improve analytics for pattern recognition, CQA determination, and key performance parameter determination	→		
	Conduct a gap analysis of cell manufacturing data and supporting information technology using generic process maps (one each for autologous, allogenic, and pluripotent cell types) of relevant data sources, process inputs and outputs, and software types and languages across the workflow (i.e., from raw materials sourcing to clinical trials)	→		

Type of cell:  Autologous  Allogeneic  Pluripotent  Crosscutting

Bold = high-priority activity
✶= new activity

		Timeline to Complete		
		2019-2021	2022-2025	2026-2030
Process Analytical Technologies and Data Analytics, continued				
	✶Develop a software standard for exchanging manufacturing process and cell quality data between labs to better enable large-scale bioinformatic analysis that connects process steps and conditions with results	→		
	Automate analytics for product release, including gene editing, human leukocyte antigen typing, sterility/ mycoplasma removal, and tissue compatibility testing		→	
	✶Develop software solutions to automate harmonization of batch data and assay results to facilitate batch release		→	
	✶**Generate a registry of patient history and clinical outcomes, linking cell data to patient data and disease characteristics**			→
Bioprocess Models				
	Identify, evaluate, and modify bioprocess modeling software suite (e.g., with chemical engineering characterization, fluid dynamics modeling, and cell shear modeling) for modeling cell manufacturing processes—including the impact of scale-up on material handling, quality control, and inventory/shipping (in-process for CAR-T cells, needed for allogeneic)	→		
	Model effects of bioreactor mechanical force, pH, carbon dioxide, and oxygen levels on complete pluripotent stem cell (e.g., HSCs, T cells) manufacturing	→		
	Improve or expand on in vitro models (e.g., cell matrix measurement) for predicting cell characterization and performance	→		
	✶Define method and data required to identify CQAs and develop associated bioprocessing modeling for CAR-T cells	→		
	Develop models and assays needed to conduct accelerated shelf-life stability studies		→	
	Build models that include more complicated regenerative medicine manufacturing processes and technologies, including tissue engineering, whole organ engineering, and cell-based combination products		→	
	Establish methods for using validated bioprocess models to quickly troubleshoot manufacturing failures and drive corrective and preventative actions		→	
	✶**Define experimental and computational data science methods and data required to identify CQAs and CPPs and develop associated bioprocess modeling for novel cell therapies**			→

Supply Chain and Transport Logistics

The affordability, availability, and access to a variety of cell-based products depends on the robustness of the cell manufacturing supply chain, the reliability of product storage, and the speed and reliability of product transport. The growing demand for cell-based products will require developing robust and reliable cell preservation methods, identifying and implementing optimized supply chain models, and improving cell tracking technologies to ensure the timely delivery of high-quality therapies.

Recent Progress

- Establishing and informing standards development/review efforts for manufacturing cleanroom requirements, product quality and purity, cryopreservation methods, transportation methods, and definitions (e.g., media composition and reagents)
- Generating electronic batch records and developing raw material control for numerous processes in parallel to facilitate the tailoring of existing systems
- Developing simulation models for predicting supply chain logistics and manufacturing disruption on product availability and access

2030 Targets

Improved Biopreservation Stability

Non-cryogenic alternatives, such as room-temperature shipping to reduce cost and improve access

Consistent Product Potency

100% maintenance of product potency

Improved Patient Fulfillment

Reduced chain-of-custody errors

10X reduction in needle-to-needle time

100% patient fulfillment

Core Challenges

Difficulty estimating the cost and managing the complex logistics of distribution

- Distribution logistics and shipping schedules of cells, both fresh and frozen, are costly and difficult to manage due to the short shelf lives of cells and specific environmental requirements.
- Tracking large quantities of allogeneic cell products is challenging, yet critical to product safety and timely product delivery.

Difficulty scaling storage processes

- Current cell storage processes rely on cryopreservation and cold-chain-management equipment. Scaling up these processes could increase incidents of transient warming.
- Scaling cell storage to warehouse levels will be a significant cost driver.

Maintaining trust and integrity in cell sourcing

- Inconsistent cell collection practices both across and within centers can lead to unpredictable cell quality.
- Different manufacturers often have varied cell collection requirements, potentially leading to errors in recordkeeping or the loss of usable starting material.

High cost, limited supply, and inconsistency of raw and ancillary materials

- The high cost, as well as the limited supply and shelf life of some raw and ancillary materials—including growth factors, nutrients, and reagents—may prevent existing culture platforms from meeting increased cell manufacturing demand.
- Batch-to-batch media variability also reduces the consistency of cell properties and can pose contamination risks.
- The dependency on sole-source vendors for raw materials and equipment increases the risk of supply interruptions and could limit manufacturing throughput and scale.

Difficulty maintaining cell characteristics and potency during freezing and thawing

- During biopreservation, cell metabolic activity decreases and extracellular ice forms. During this process, initiation of molecular stress responses and intracellular ice formation can also cause mechanical breakdown, membrane rupture, or other stresses that interfere with cell survival and recovery.
- The community has limited understanding of cell viability and the functionality of cell types following preservation and thawing, making it difficult to preserve cells effectively and consistently.

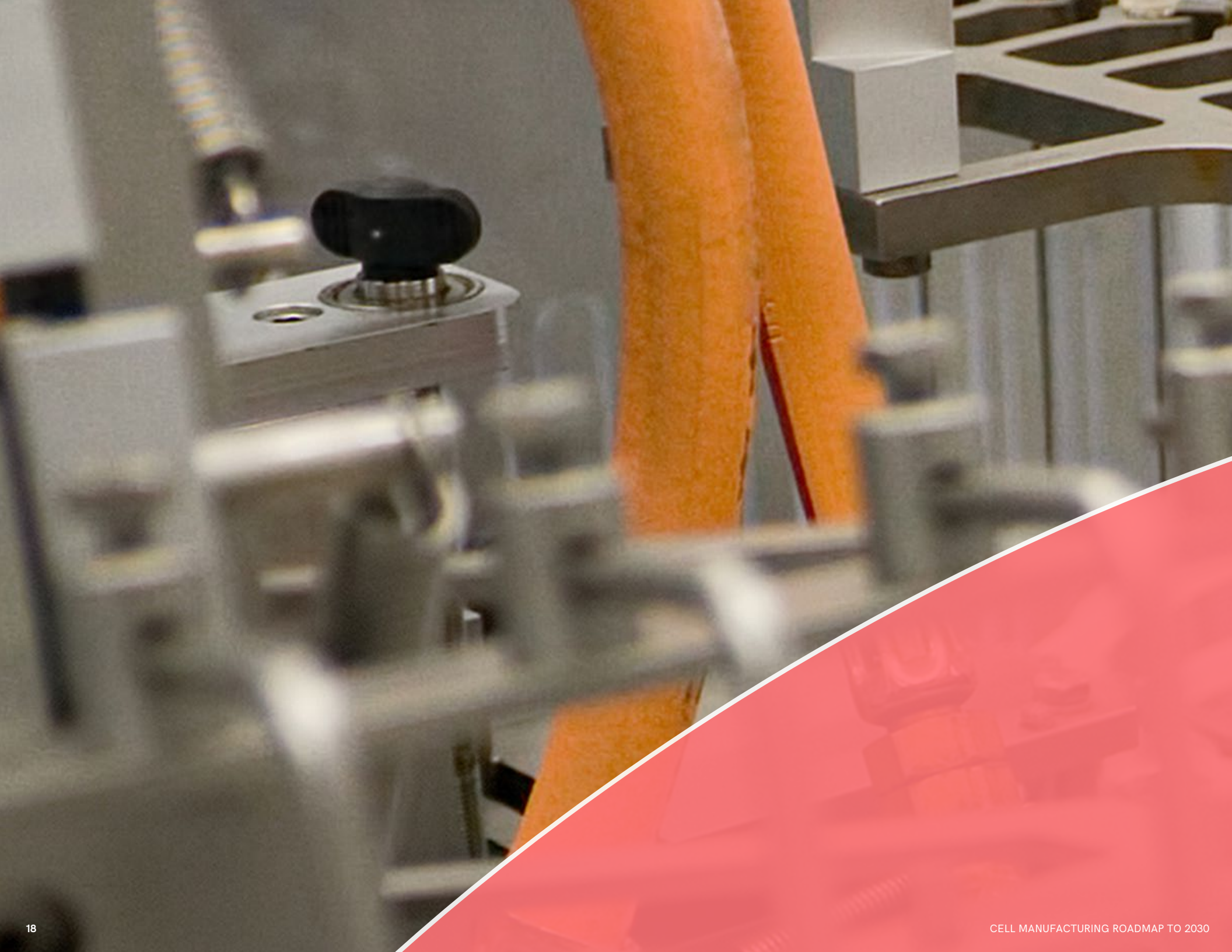
Activities

Bold = high-priority activity
✶= new activity

	Timeline to Complete		
	2019-2021	2022-2025	2026-2030
Preservation Technologies and Methods			
Improve understanding of cell responses to cryopreservation and thawing interactions	→		
Engineer end-user-friendly formulation that allows for higher-temperature storage alternatives to cryopreservation	→		
Develop processes for large-scale (i.e., number of units, unit volume) cell cryopreservation that improve cell quality, functionality, and batch homogeneity	→		
Conduct a study to identify biopreservation materials and methods (e.g., liquid nitrogen, ultradeep freezers, warmer-temperature cell bank storage, and small-batch controlled-rate freezing) to reduce potential risks from transient warming	→		
Develop technology for nitrogen- and dimethyl-sulfoxide-free transport and storage	→		
Develop clinically usable containers (e.g., smart or reusable packaging) that are effective both when cryopreserved and thawed to decrease shipping costs (cell packaging vs. shipping container)	→		
Develop technology to make cells “hibernate” and enable room-temperature transport		→	
Develop an automated storage process that includes cell harvest, vialing, transfer to controlled-rate freezers, and transfer to liquid nitrogen tanks for cryopreservation		→	
✶Develop tools for processing and packaging small volumes of highly potent cells		→	
Supply Chain Modeling and Design			
Integrate adaptive, real-time machine learning approaches into supply-chain modeling	→		
Assess Amazon’s approach (and other best practices) for fast fulfillment and economies of scale and identify aspects of this approach that could be applied to allogeneic cell manufacturing	→		
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	→		
Define and standardize the optimal supply chain design, defining data inputs, model types, and scenarios/ constraints for supply chain modeling of several transport designs	→		
Use modeling to identify bottlenecks associated with integration with electronic medical records and cloud-based enterprise		→	

Bold = high-priority activity
✶= new activity

	Timeline to Complete		
	2019-2021	2022-2025	2026-2030
Supply Chain Modeling and Design, continued			
Achieve fast fulfillment connectivity from point-of-care to manufacturing pathway through a distributed supply chain		→	
Develop or leverage distributed models for case management that can integrate clinical data (e.g., trial, quality control in-process, final product release, post-marketing)			→
✶Develop an app for ordering in-house diagnostics and delivery of therapeutics that allows for real-time visibility into relevant scheduling queues as well as data correlations to clinical outcome			→
Product Tracking, Transport, and Administration			
Develop fool-proof packaging to reduce variability in administration	→		
Establish best practices and consensus metrics for coordinated distribution process	→		
Train hospital staff in the collection of cells/tissues and administration of cell therapies	→		
Educate customs agencies to facilitate international transport of cells	→		
Disseminate methods to segregate and securely track products and patient information in a multiproduct manufacturing facility	→		
Gather data from FedEx, UPS, Amazon, and grocery shopping services on what products are held in transport and rules for biologics in each country	→		
Leverage reusable distribution solutions such as easy-to-sterilize capsules that transmit location and record critical environmental encounters		→	
Generate global passport or standard for international transport of cell therapies		→	
Deliver cells via drones or self-driving vehicles, and establish related logistics standards		→	
Supply Chain Standards			
Inform standards that ensure consistency of quality and purity of raw materials (e.g., serums) from different suppliers, reducing dependency on sole source providers	→		
Develop standards for collection of starting materials for comparing tissue and blood processing practices across manufacturers and companies	→		



Standardization, Regulatory Support, and Cost Reimbursement

The complex and constantly evolving nature of the cell manufacturing industry makes it difficult to assess the consistency, safety, and efficacy of cells and cell-based products. Establishing standards and regulations—including for raw materials, testing procedures, manufacturing processes, and cell product handling—and reimbursement models is critical to drive the development of innovative cell products and efficiently move them to commercialization and clinical use.

Recent Progress

- Maintaining *The Regenerative Medicine Standards Landscape* report with existing and in-development standards relevant to cell therapy, gene therapy, and tissue engineering products to improve awareness and use of standards (Standards Coordinating Body for Gene, Cell, Regenerative Medicines and Cell-Based Drug Discovery [SCB])
- Engaging with the U.S. Food and Drug Administration (FDA) Office of Tissue and Advanced Therapies (OTAT) on cell therapy policy issues
- Advancing a variety of documentary standards, including for ancillary materials, cell collection, cell transportation, and cryopreservation
- Developing 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
- Determining cost reimbursement potential for regenerative medicine products based on existing commercial products

2030 Targets

Appropriate number of useful standards for advanced therapy

Improved cell manufacturing community knowledge of standards, regulations, and reimbursement

Increased number of companies engaged with Centers for Medicare and Medicaid Services (CMS) in early product development

Core Challenges

Insufficient knowledge about standards and regulations

- The cell manufacturing community lacks awareness of relevant standards and understanding of the relationship between and oversight of standards and regulations.
- Research activities are often removed from standardized assays and methods. Implementing best practices and standards into research laboratories could improve reproducibility, translation, and time to market.

Reluctance to share manufacturing and product data

- Cell manufacturing companies are protective of intellectual property, limiting the ability to compare data across facilities, companies, and products that could inform development of relevant standards and regulations.

Difficulty coordinating regulatory and reimbursement requirements

- The FDA's regulatory requirements for approving therapies do not always align with CMS requirements for cost reimbursement.
- This discrepancy makes it difficult for therapy developers to understand how their product will be approved and reimbursed, and it raises costs for patients.

Difficulty defining the products of biological processes

- It is challenging to develop useful standards and regulations in part because cells can be either the end product or a vehicle to the synthesis of other products, including exosomes, antibodies, vaccines, and cytokines.
- The complexity of combination therapies and products that include both regular cells and genetically modified cells makes it challenging to develop useful standards and regulations with specific parameters for a given cell type or product that still allow for further innovation.

Lack of available, robust durability data needed for reimbursement

- The cell manufacturing industry currently lacks durability data on safety and efficacy of personalized therapy products needed to help define cost reimbursement models.
- Larger sample sizes and data sets would help the community develop high-value propositions that could bring costs down for patients.

Activities

Bold = high-priority activity
✶= new activity

	Timeline to Complete		
	2019-2021	2022-2025	2026-2030
Standards and Regulatory Convergence			
Engage with the FDA (i.e., Center for Devices and Radiological Health [CDRH], Center for Biologics Evaluation and Research [CBER]) on issues of single-patient personalized medicine and regulatory requirements, potentially through existing liaison meetings, including with the International Society for Cellular Therapy (ISCT) and Alliance for Regenerative Medicine (ARM)	→		
Work with regulatory authorities to identify ways to redesign Good Manufacturing Practice (GMP) facilities to better accommodate highly individualized therapies and products	→		
Develop a general project plan outline and task list for navigating pre-IND and IND filing	→		
Broaden participation with standards advancement efforts of SCB, the National Institute of Standards and Technology (NIST), and ARM, including addressing Section 3036: Standards for Regenerative Medicine and Regenerative Advanced Therapies of the *21st Century Cures Act*	→		
Establish a working group to define the regulatory pathway for cellular products through the FDA—addressing their unique challenges and requirements—and develop regulatory education tools (e.g., templates, checklists, and limited population studies)	→		
Identify differences between smaller-scale autologous and larger-scale allogeneic manufacturing processes that would affect FDA regulatory interactions		→	
Standardized Technologies and Tools			
✶**Define and regulate tests for common assays in cell manufacturing (e.g., counting, viability, flow cytometry)**	→		
Work with SCB and NIST on establishing reference materials for in-process and release assays to contribute to the testing of candidate materials	→		
Establish industry standards and specifications for consistently gathering and recording data (from donor, through process, to delivery), engaging SCB and NIST to establish the standards along with tools and technology providers to integrate them	→		
Develop guidelines for cell genetic stability and chromosomal aberrations (i.e., pass/fail)	→		
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	→		

Bold = high-priority activity
✶ = new activity

	Timeline to Complete		
	2019-2021	2022-2025	2026-2030
Standardized Technologies and Tools, continued			
Work with SCB on establishing quality-by-design principles for cell product manufacturing	→		
Assess how to standardize validated, automated processes in a de-centralized setting		→	
Develop high-throughput, low-cost tools and assays for reliable assessment of potency, including processing (i.e., form potency toolkits)		→	
✶Develop robust quality control standards and tools for each category of cell products		→	
Cost Reimbursement Models			
✶**Develop new payment models and coverage policies relevant to cell therapies**	→		
Continue to engage organizations—including FDA, CMS, professional societies, industry groups, and other clinical centers and organizations—to address third-party payer issues	→		
✶Develop ecosystem models that identify cost-saving measures for cell therapeutics delivery, including opportunities in the manufacturing process, supply chain and logistics, and patient treatment and delivery	→		

Workforce Development

Realizing and capitalizing on the benefits of advanced cell manufacturing technologies and techniques depends on a highly skilled, multidisciplinary cell manufacturing workforce—with expertise in areas such as biological science, engineering, computational modeling, physics, chemistry, mathematics, and statistics. To strengthen the current workforce, it is critical for the cell manufacturing community to facilitate communication between industry and academia to outline skill sets most needed in the industry and to align training programs with industry needs.

Recent Progress

- Early efforts to identify skill sets needed for various cell manufacturing industry jobs
- Small-scale efforts to engage local community colleges and technical colleges to help train the entry-level workforce

2030 Targets

Increased number of undergraduate and graduate students who enter and are retained in cell manufacturing education programs

Increased number of students (undergraduate, graduate, technical school, and community college) who enter cell manufacturing jobs

Increased number of students (across all levels) participating in cell manufacturing internships

Assessment demonstrating that all trainees are versed in data science and analysis, Good Manufacturing and Good Laboratory Practices (GMP/GLP), and basic regulatory frameworks

Core Challenges

Insufficient credentialed cell manufacturing-specific education programs

- The constantly evolving nature of the industry makes it challenging to design relevant and comprehensive undergraduate, graduate, and continuing education training programs.
- There are no clear mechanisms for integrating cell manufacturing-specific classes into existing programs.
- Because cell manufacturing is a relatively new multidisciplinary field, it is difficult to credential education programs.

Lack of multidisciplinary skills across cell manufacturing workforce

- The current cell manufacturing workforce does not have sufficiently broad expertise in fields outside of cell biology.
- The industry has a limited number of specialists with proficiency in quality assurance, regulatory affairs, and infrastructure protection needed to move cell manufacturing to commercialization and clinical application.

Inadequate communication about cell manufacturing career opportunities

- Lack of consensus on skill set needed for each level of workers.
- Lack of consolidated platform to post or learn about available positions.
- There is an unclear understanding of potential financial compensation for cell manufacturing careers, which is critical for drawing young talent.

Inadequate coordination and communication between industry and academia to develop and implement programs

- Currently, there is no clear mechanism for industry to communicate workforce needs. As a result, industry is dissatisfied with the skills of recent graduates, and academics lack clarity of industry's most critical needs.
- The cell manufacturing community will need leaders in industry and academia to work together to design and implement adequate curricula for students to learn industry-relevant skills.

Lack of consensus on industry diversity and inclusion goals and mechanisms to achieve them

- Diversity and inclusion initiatives are becoming an organizational focus for both the public and private sector.
- The cell manufacturing field has not yet set agreed-upon diversity and inclusion goals for their workforce or pathways for achieving these goals.

Activities

Bold = high-priority activity
✶= new activity

	Timeline to Complete		
	2019-2021	2022-2025	2026-2030
Cross-Cutting Education Initiatives			
✶**Develop a detailed, periodically updated roadmap to collect data to delineate the necessary skill sets for various levels of the cell manufacturing workforce and to inform better collaboration across industry and education programs (i.e., K-12, 2-year, 4-year, Masters, Ph.D., post-doctorate students)**	→		
Assess industry workforce needs (regulatory, technical, and soft skills) and map these needs to the skill sets provided by currently available training	→		
Assess reasons for current industry personnel turnover	→		
✶Hold a one-day meeting with industry partners, curriculum developers, and workforce and diversity experts to assess training needs and define how to address needs through existing (or new) educational programs	→		
✶Collate available educational resources related to cell manufacturing topics and post them in a centralized place		→	
Implement responsive educational 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)		→	
Monitor the current status of workforce diversity and target programs to address any deficiencies as the industry expands			→
Develop data handling and analysis curriculum for biomanufacturing to advance the field by equipping future cell therapy industrial analysts and engineers with software and analytical skills that extend beyond bioinformatics			→
Build global awareness of 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			→
Graduate Programs			
Develop 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)	→		

Bold = high-priority activity
✶= new activity

	Timeline to Complete		
	2019-2021	2022-2025	2026-2030
Graduate Programs, continued			
✶**Compile a description of different jobs and required skill sets that students with various education levels could aspire to in the cell manufacturing industry and post them in a centralized space**	→		
✶Develop Good Laboratory Practice (GLP), Good Manufacturing Practice (GMP), and Good Clinical Practice (GCP) courses or modules for undergraduate and graduate programs		→	
Integrate internships into credit-based courses at the graduate and Ph.D. level (e.g., professional development courses, clinical rotations, business school courses)		→	
Technical Colleges and Undergraduate Programs			
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	→		
Pilot and institutionalize internship or cooperative education program with preparatory courses for two- and four-year undergraduate programs	→		
Supplement current biological sciences and engineering curricula with areas of focus for cell manufacturing (e.g., specific technologies, GMPs, regulations, business management)		→	
Continuing Education Programs			
Develop flexible, rapid retraining programs, including certificates with stackable credentials, that leverage existing training networks (e.g., community colleges)		→	
Develop a career track for “cell manufacturing managers” with managerial internships focused on management skills such as decision-making			→
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			→
K–12 Education Programs			
✶Design apprenticeships for grades 9–12, including curriculum development and work study programs	→		
✶Encourage Research Experiences for Teachers (RET) trainees to develop modules/curricula that integrate with state education standards and distribute K–12 curricula—from a National Science Foundation (NSF) program designed to improve science educators by exposing them to research—through state education departments and boards		→	
✶Improve professional development for teachers by disseminating knowledge from RET trainees, and using a phased-development approach for curricula		→	

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