Discussion with VCAT on CETs: Biotechnology

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NATIONAL INSTITUTE OF STANDARDS AND TECHNOLOGY
U.S. DEPARTMENT OF COMMERCE

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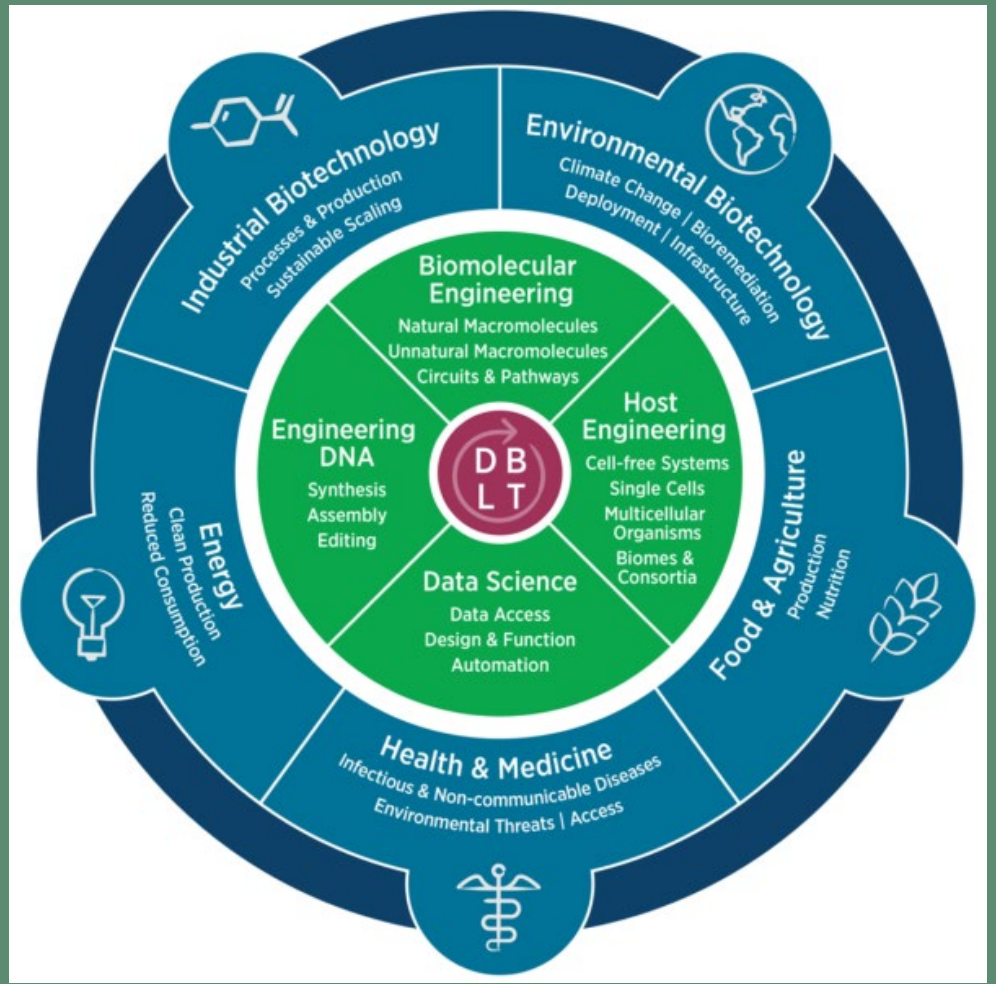
National Institute of Standards and Technology
U.S. Department of Commerce

Recent USG Biotechnology Policy and Actions

Why Now? What's Driving the Bioeconomy?



https://ebrc.org/focus-areas/roadmapping/engineering-biology-2019/

Recognition that **biotechnology** and **biomanufacturing** provide solutions to pressing societal issues related to human health, climate, food security, and others.

Biotechnology*: technology that applies to and/or is enabled by life sciences innovation or product development

Biomanufacturing*: the use of biological systems to produce goods and services at commercial scale

*https://www.nist.gov/bioscience/nist-bioeconomy-lexicon

Executive Order 14081 Signed Sept. 12, 2022

Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy

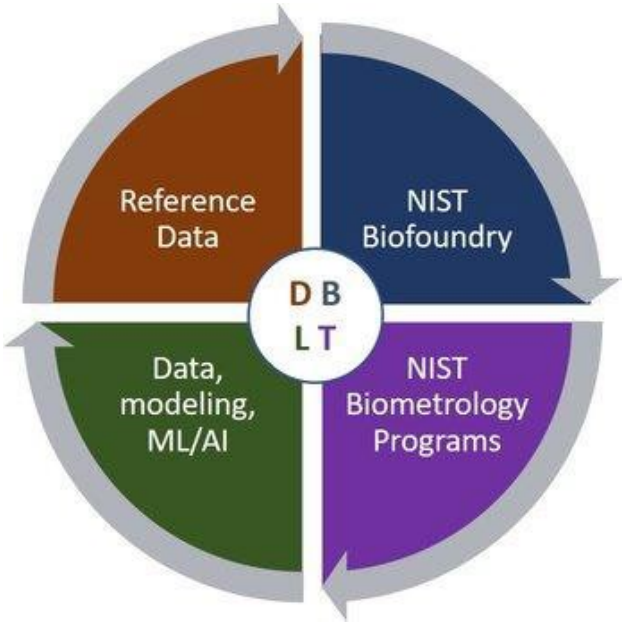
- National Security Council (NSC)-led effort across two Administrations intended to launch major National Biotechnology and Biomanufacturing Initiative
- Whole-of-government approach to advance biotechnology and biomanufacturing towards innovative solutions
- NIST “at the table” from the beginning, played a key role in its development, and continues to support its implementation

https://www.whitehouse.gov/briefing-room/presidential-actions/2022/09/12/executive-order-on-advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american-bioeconomy/

NIST technical strengths align with E.O. R&D focus

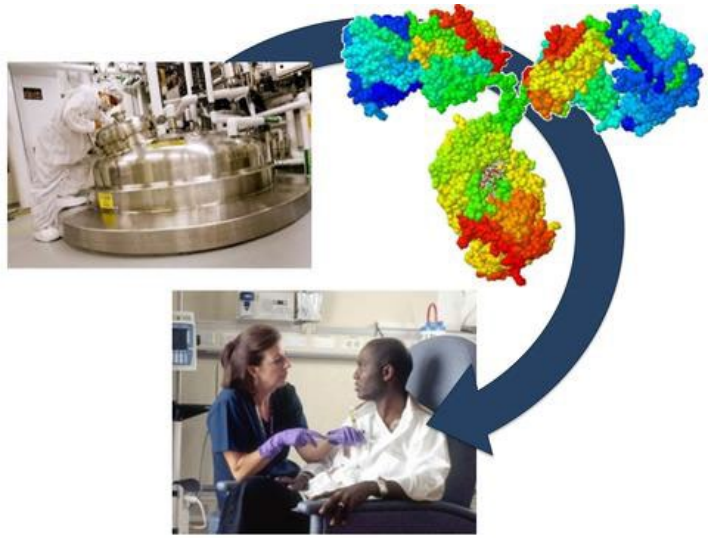
"Harness the power of biology to create services and products, provide opportunities to grow the U.S. economy/workforce, and improve the quality of our lives/environment."

Enable unprecedented innovation through predictive engineering of biological systems and parts



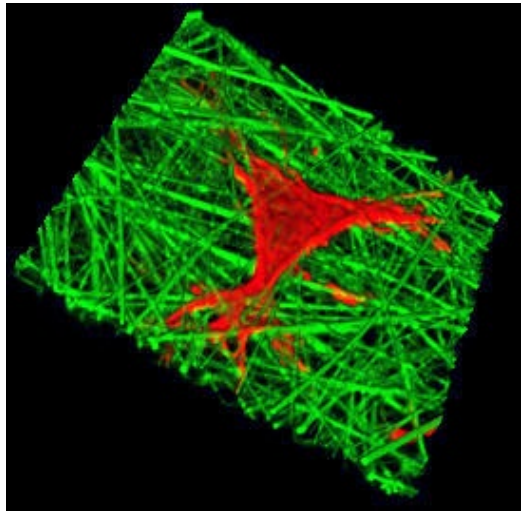
Engineering Biology

Advance technologies to enable *at scale* production of bioproducts



Biomanufacturing

Unlock the power of biological data through innovation; enhance data privacy and security



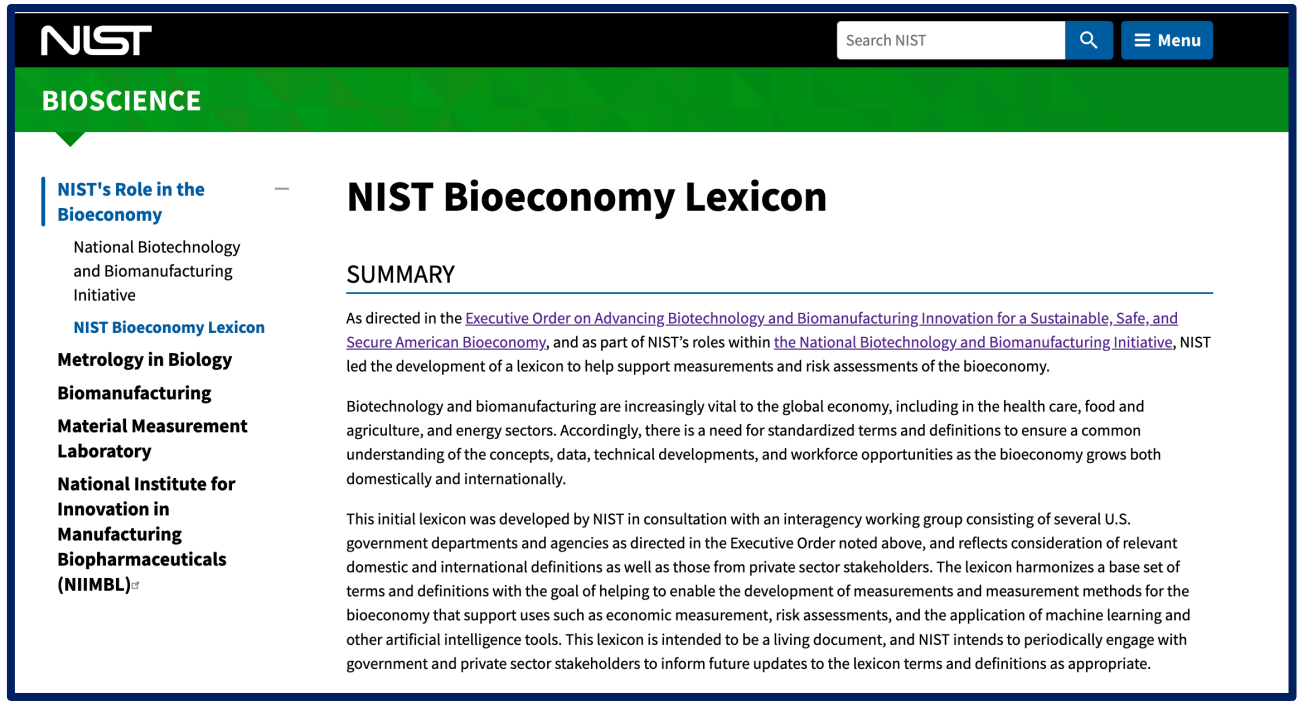
Biological data + AI

E.O. 14081: Key Sections

- **Harnessing Biotech. & Biomfg. R&D**
- **Data for the Bioeconomy**
- **Build Domestic Biomanufacturing**
- Encourage Biobased Products
- **Strengthen Biotech. Workforce**
- Clarify Biotech. Regulation
- **Advance Biosafety/Biosecurity**
- **Measure the Bioeconomy**
- **Assess Threats to Bioeconomy**
- **International Engagement**

Areas with NIST involvement in bold

NIST Lead Role: Develop a Bioeconomy Lexicon



Developed a process for delivering a lexicon within the interagency group

Conducted an inventory of existing terms and definitions; identified additional needed terms

Terms and definitions reviewed and harmonized through discussions with D/As to be broadly applicable

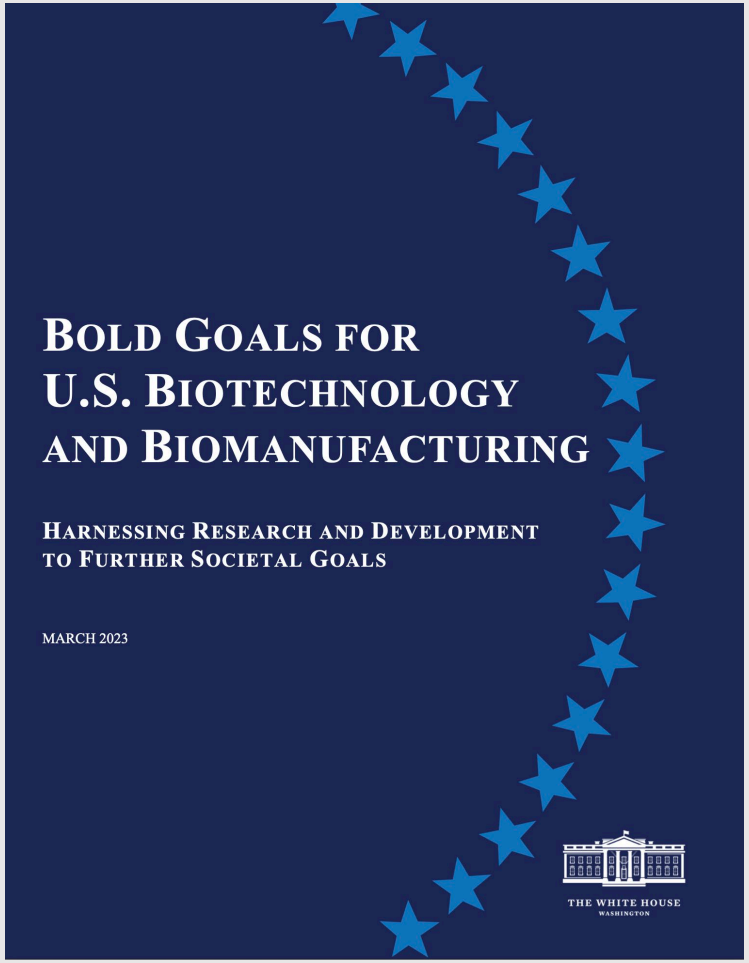
List of terms and definition released to the public within 90 days (Sept to Dec 2022)

E.O. 14081 R&D Bold Goals

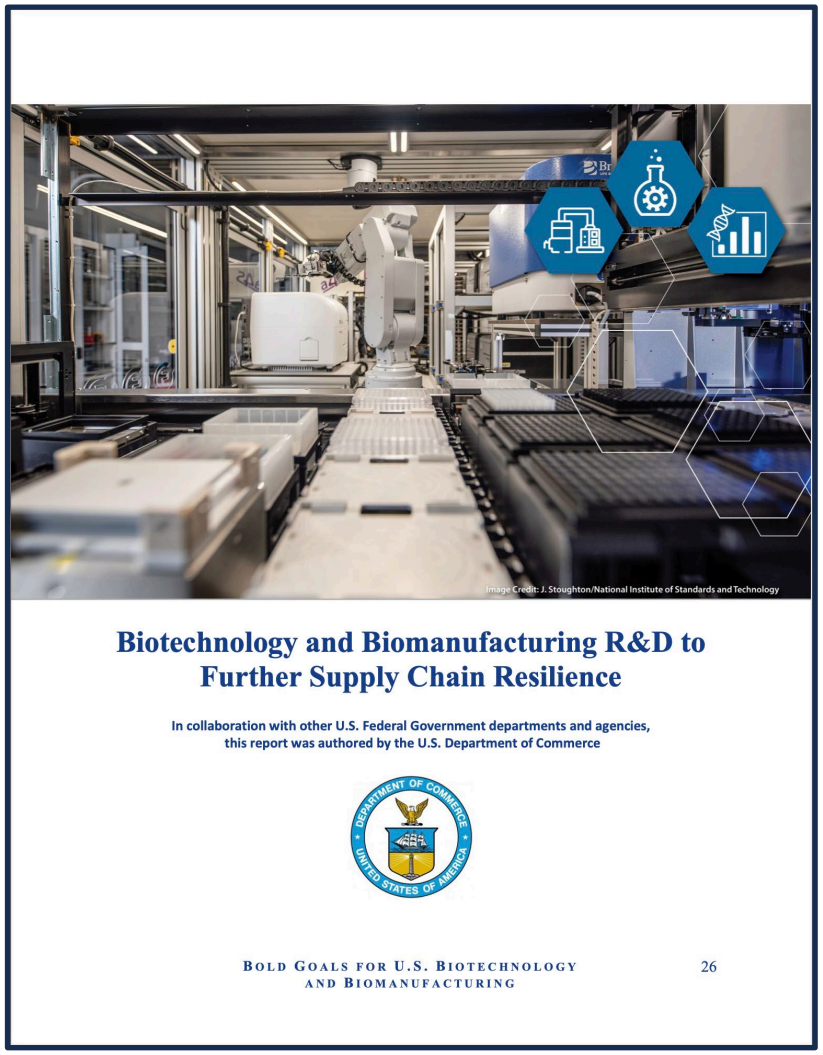
Multiple Departments:

- Medical breakthroughs (HHS)
- Mitigating effects of climate Change (DOE)
- **Supply chain resilience (DOC)**
- Food and ag. innovation (USDA)
- Crosscutting science (NSF)

Feedback from industry and private sector entities, WH roundtables, RFI



NIST and DOC/OPSP Lead Role for Supply Chain Resilience, with Inputs from ITA, BIS, EDA, BEA



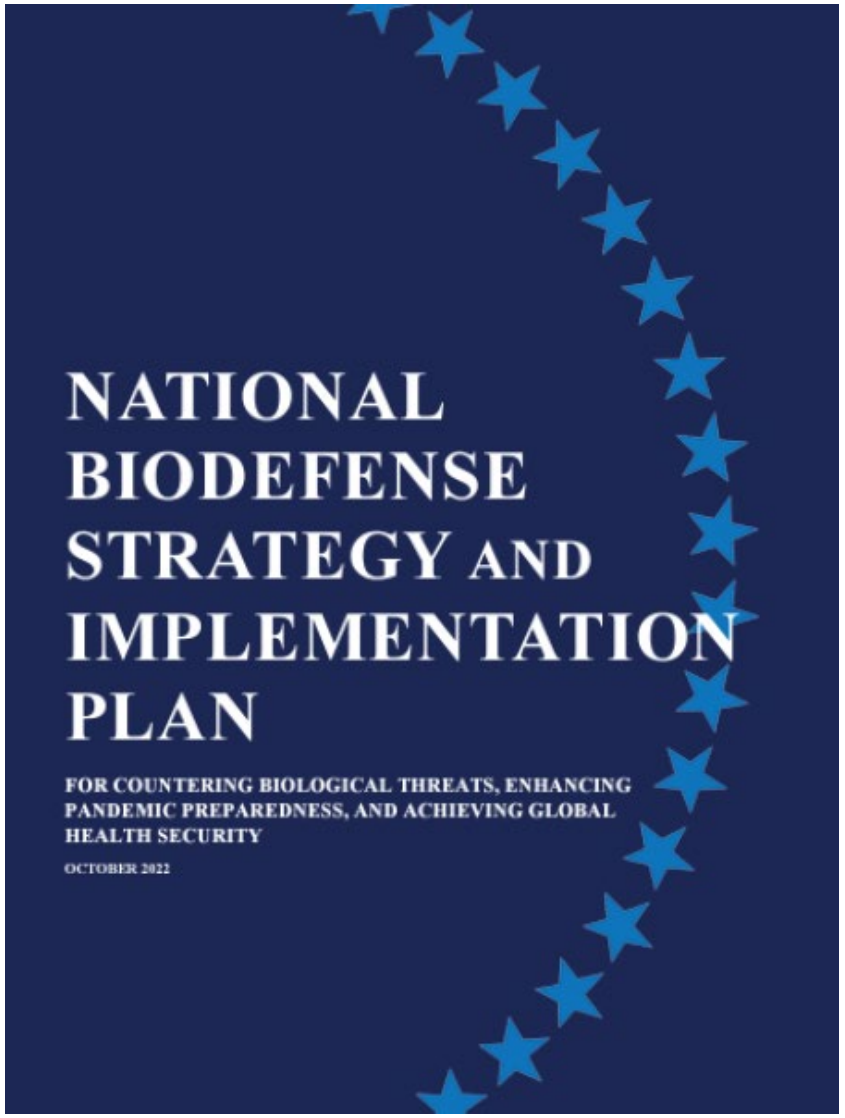
- **Alternative supply chain pathways**
  - Critical drug supply
  - Sustainable chemical production
  - Accelerating development of biomanufactured products
- **Supply chain resilience**
  - Predictive capabilities
  - Real-time biomanufacturing adjustments
  - Adaptive supply chains
  - Supply chain flexibility
- **Standards and data infrastructure**

Example Bold Goals and NIST Equities

Supply Chain Resilience

- Develop innovative in-line, at-line, and in-process measurement technologies, including engineered reporter cell lines and living measurement systems, to enable real-time evaluation of and adjustments to quality attributes. **(Goal 2.2)**
- Develop datasets, standards, and predictive capabilities (including use of AI, machine learning, and digital twins) to enable real-time feedback loops and analysis of process control and supply chain data with appropriate access controls and data security. **(Goal 2.2)**
- Advance smart biomanufacturing that can seamlessly integrate automation, software, equipment, and people to increase process speed, reliability, and efficiency. **(Goals 2.2, 2.3)**
- Develop platform technologies and standards to accelerate the development, production, and interoperability of biomanufacturing equipment, components, and consumables and improve the characterization and testing of biomanufacturing processes and products. **(Goals 2.3, 2.4)**
- Develop standard sets of microbial strains, cell free systems, key reagents, sequences of known function and performance, and supply chain precursor molecules and compounds that can be rapidly produced, distributed, and scaled up on demand. **(Goals 2.3, 2.4)**
- Develop standardized quality metrics for raw materials and reagents to enable interoperability from multiple vendors, and advanced algorithms to enable adaptive stockpiling capable of using alternative feedstocks or processes when supply chains are limited or disrupted. **(Goals 2.3, 2.4)**
- Develop innovative design, robust quality management systems, and standards to enable more

Promoting *and* Protecting the U.S. Bioeconomy



- Two sides of the same coin: platform measurements and technologies; standards
- NIST plays key role within the USG to address diagnostics, testing, among other needs
- Sequence screening -- NIST asked to develop standards, databases, and tools to help implementation of new guidance

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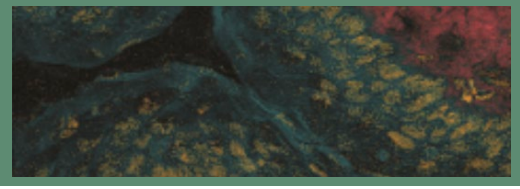
NIST Biotechnology and Biomanufacturing Research and Outreach

Example Capabilities and Platform Technologies



- Biomolecular measurements
- Genomics and multi-omics measurements
- Cell measurements
- Viral and non-viral vectors
- Multiple cellular systems

Biometrology

- Genome engineering & editing
- Protein engineering
- Cell line engineering
- Cell free systems engineering
- Microbial engineering
- Biofabrication

Engineering Biology

- Single cell engineering & msmts.
- Automation: P-CAMP, LMSF, library prep, microbial, Flow Prep
- End-to-end bioprocessing, NIST strain biorepository & cell lines
- Advanced data analytics, ML/AI, NASA/JPL IAA

Core Platforms

Building the Next Generation Biometrology and Engineering Biology Capabilities to support U.S. Biotechnology Enterprise and Bioeconomy

Living Measurement Systems Foundry

Advanced Biometrology

Unprecedented measurement capabilities to quantify complex *living* systems and processes

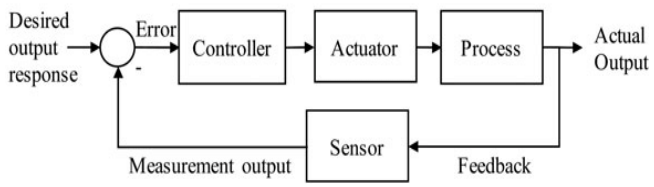
Design-Build-Test-Learn

Tools, platforms, and data/knowledge to predictively engineer biological systems to accelerate innovation in R&D and to advance biomanufacturing

Standards

Standards and related infrastructure to accelerate technology development and translation/clinical use

Engineering/Synthetic Biology via *Microbial Systems*

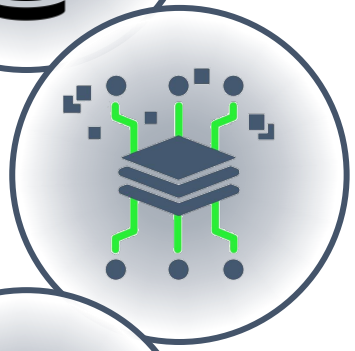


Measurements and standards to understand controlled evolution

Data integration for modeling and prediction

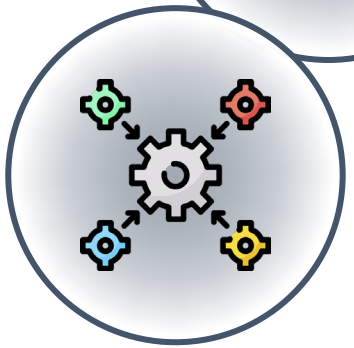
Synthetic biology for tissues, consortia, and multicellular organisms

Abstraction for design

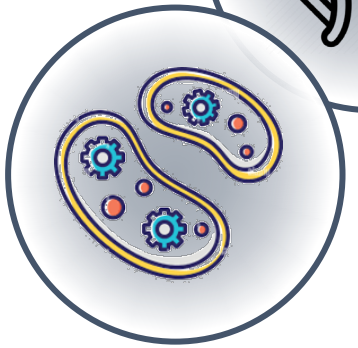


Dynamic, programmable whole genome remodeling

Integration of parts and systems



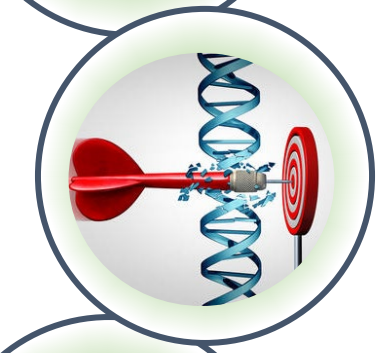
Synthetic and minimal cells



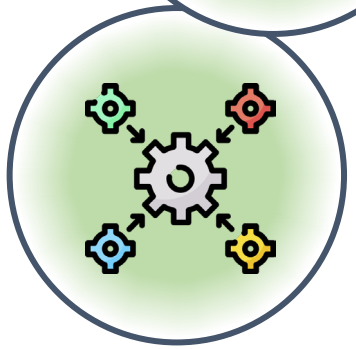
The Bioeconomy

Engineering/Synthetic Biology via *Mammalian Systems*

Data integration for modeling and prediction



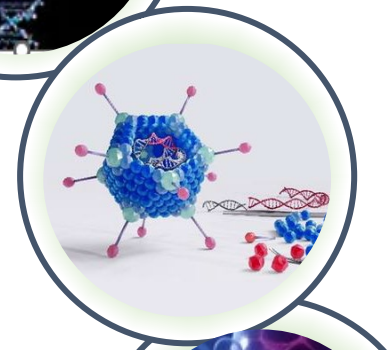
Predictive on target genome engineering



Fit for purpose application via engineered systems

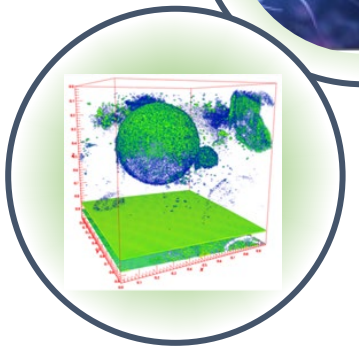
The Bioeconomy

Genome Editing



Engineering of viral and nonviral gene delivery systems

Engineering of cells and producer cells



Engineering of multicellular systems and tissues

Building a Measurement Infrastructure

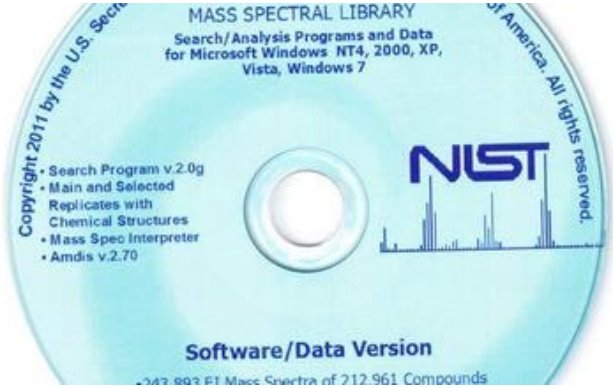
Reference Materials

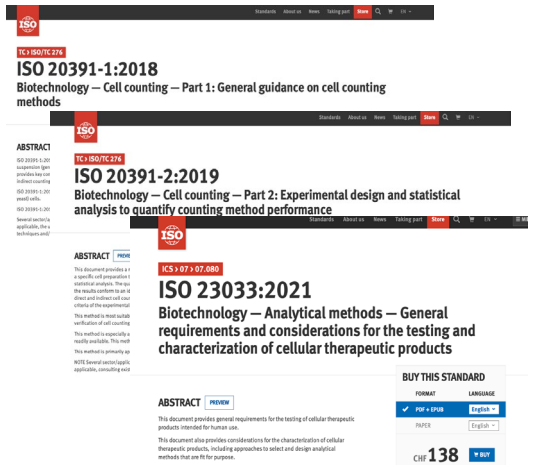
Reference Data

Measurement science & technology development

Documentary Standards

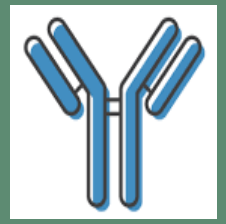
Calibration Services





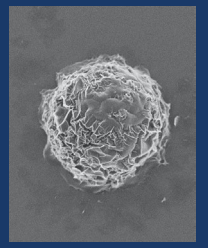
Advanced Biological Reference Materials (& More)

Genome in a Bottle (GIAB) Human DNA, cells, engineering cells

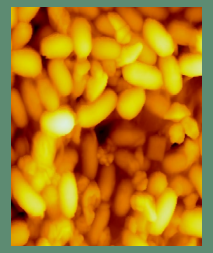


NIST mAb &

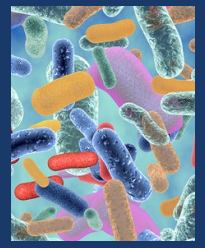
NIST CHO



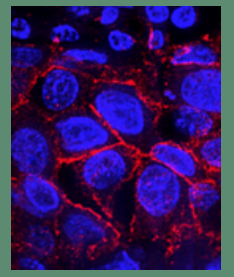
Viruses, Viral vectors & Jurkat cells with different VCNs



Genetically tagged strain of yeast



Microbial whole cell RMs & mixed DNA RMs



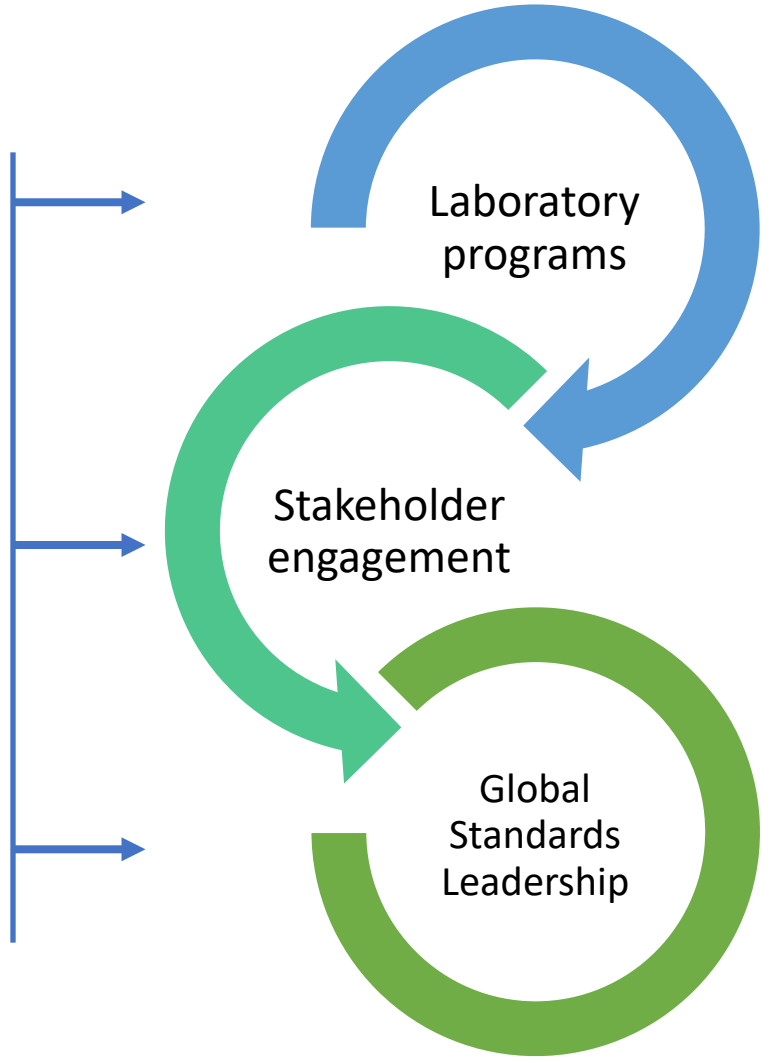
Fully consented matched cancer/ normal cells/DNA; engineered cell lines

From Laboratory Programs to Standards

NIST Core Laboratory Capabilities

NIST Consortia, Interagency coordination, NMIs, NGOs & other strategic partnerships

SDO: ISO, IEC, OECD, WHO, ASTM, PDA, etc.
SCB*: engage, coordinate, educate



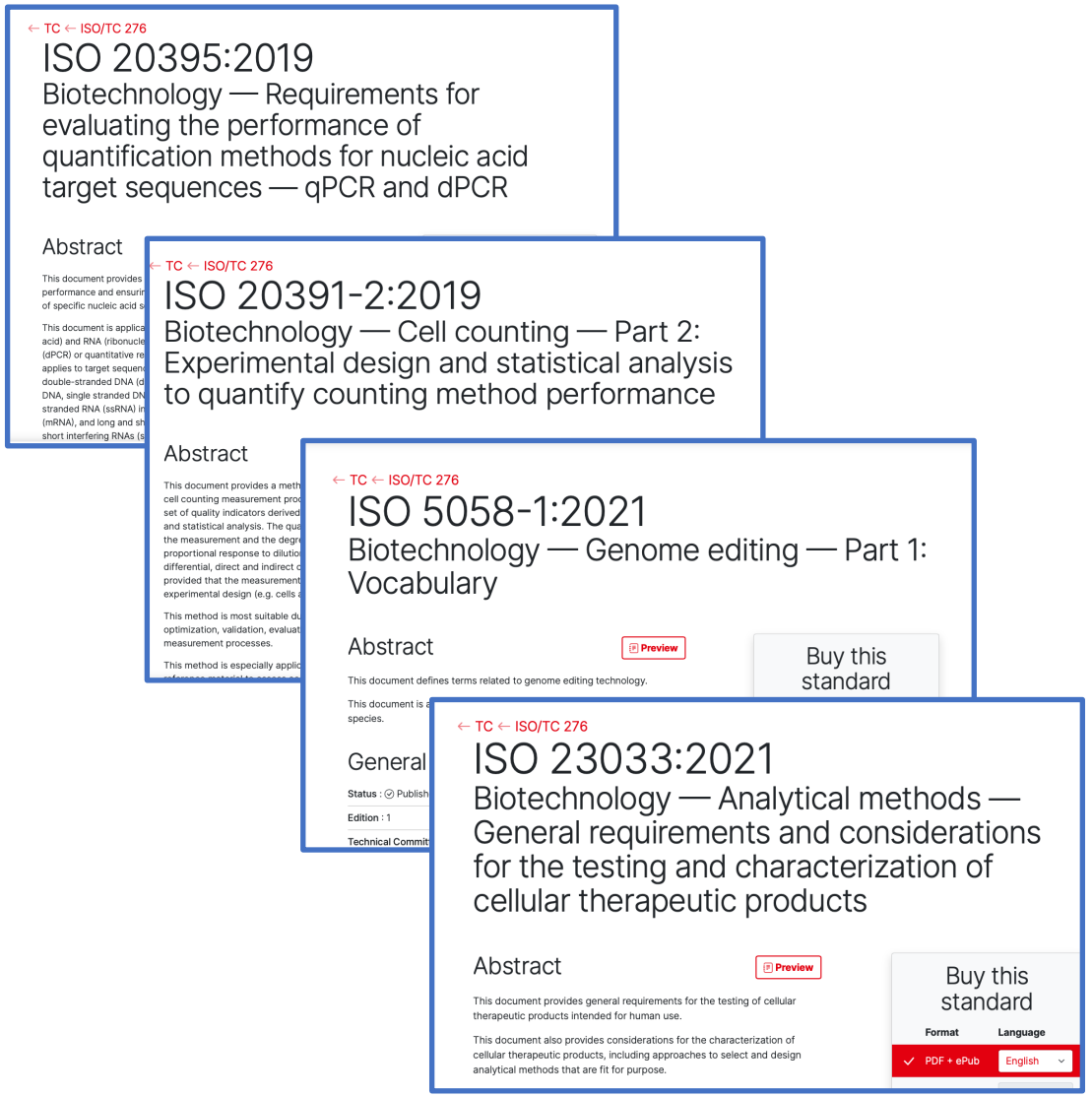
In house capabilities & expertise to support the rapidly evolving biotechnology

- **Pre-competitive technology, measurement solutions, reference materials and ref. data, etc.**
- **Ongoing bilateral collaborations with LGC, NRC, INMETRO, AIST, KRISS, etc.**

- **Supports innovation and commerce**
- **Supports FDA's upcoming std recognition program**
- **Supports ICH, WHO, & global regulatory convergence**

*NIST and FDA funds SCB to jointly advance standards per 21st Century Cures Act
https://www.nist.gov/mml/bbd/standards-and-tools

Coordinated Standards Leadership in Biotechnologies



Catapulted NIST leadership in global biotechnology standards development, well recognized WH NSTC/OSTP, other agencies, and U.S. industry

Supported all sectors of bioeconomy via the creation of an inclusive and collaborative environment for consensus building and standards development

Exceptional productivity and impact (40+ ISO stds); numerous NIST-led standards underpinned by the biotechnology & biometrology laboratory programs

Global Standards for the Bioeconomy

- Supported by Schmidt Futures and co-organized by the Engineering Biology Research Consortium (EBRC), Imperial College London, NIST, and National University of Singapore
- Brought together global experts to produce community-driven standards and metrics to advanced global bioeconomy
- Findings will lay the groundwork for the establishment of open voluntary standards for engineering biology

NIST Consortia: Public-Private Partnerships to Address Pre-competitive Challenges

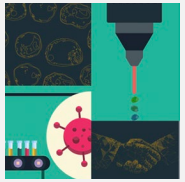
NIST GENOME IN A BOTTLE (GIAB) CONSORTIUM

Provides authoritative characterization of benchmark human genomes

NIST GENOME EDITING CONSORTIUM*

Develops measurement solutions and standards needed to increase confidence and reduce risk

Formal members: 40



NIST FLOW CYTOMETRY STANDARDS CONSORTIUM*

Accelerates the adoption of quantitative flow cytometry in biomanufacturing

Formal members: 29

NIST RAPID MICROBIAL TESTING METHODS CONSORTIUM

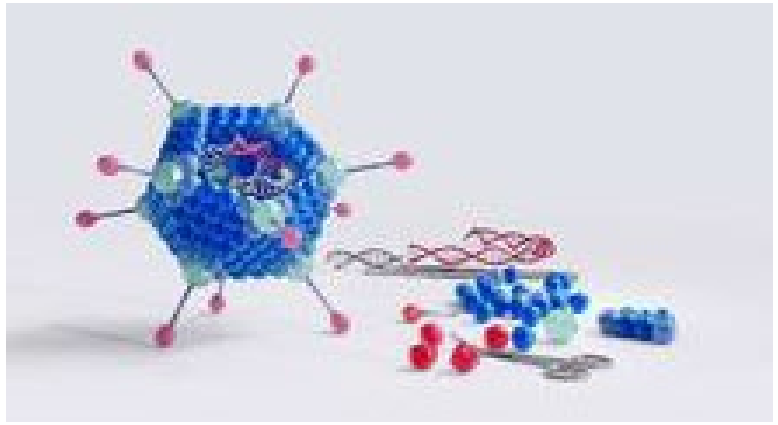
Addresses measurements and standards needed to increase confidence in the use of rapid testing

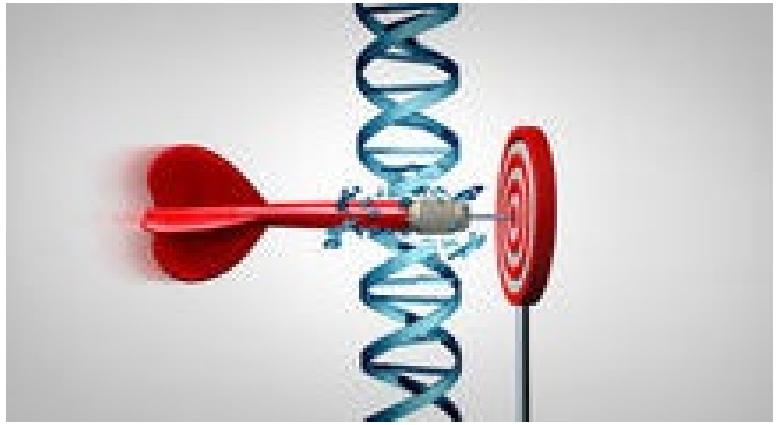
Formal members: 35

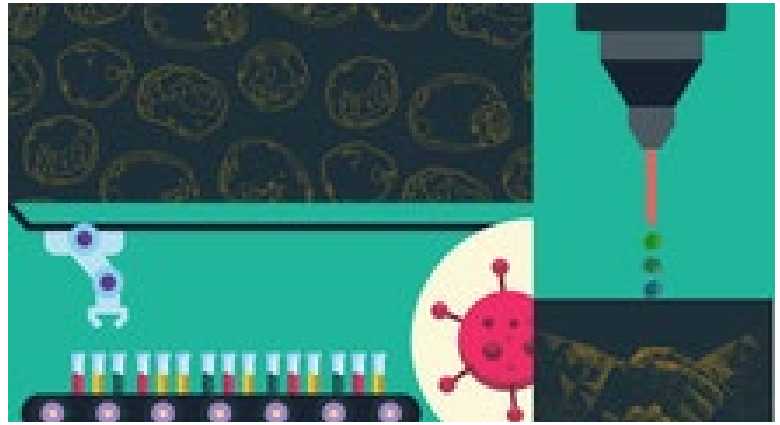
Working to expand and integrate into an Alliance

https://www.nist.gov/mml/bbd

NIST-FDA Workshops on Measurements and Standards for Advanced Therapy







November 1, 2023

NIST Gene Delivery Systems Public Workshop

November 2, 2023

NIST Genome Editing Consortium Public Workshop

November 3, 2023

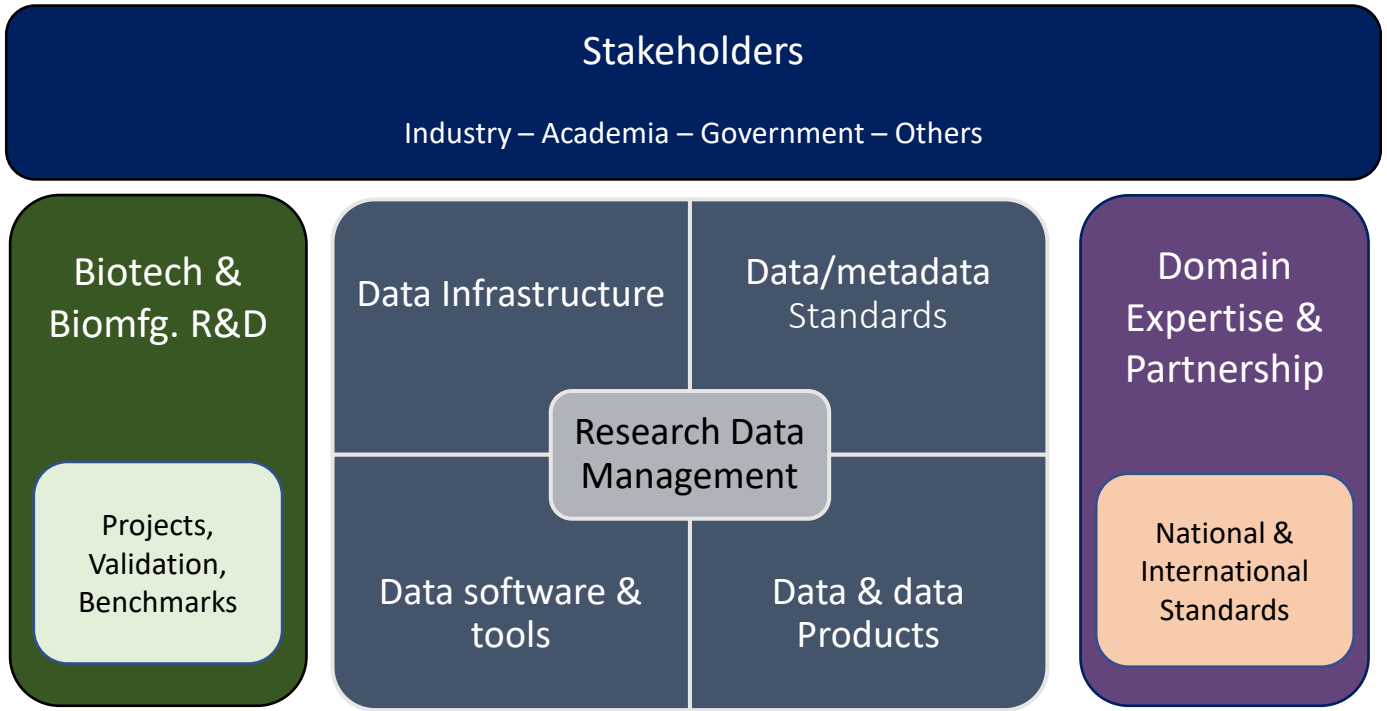
NIST Flow Cytometry Standards Consortium Public Workshop

https://www.nist.gov/news-events/events/2023/11/nist-workshops-measurements-and-standards-advanced-therapy

Data for the Bioeconomy

Research Data Management (RDM) vision and goals

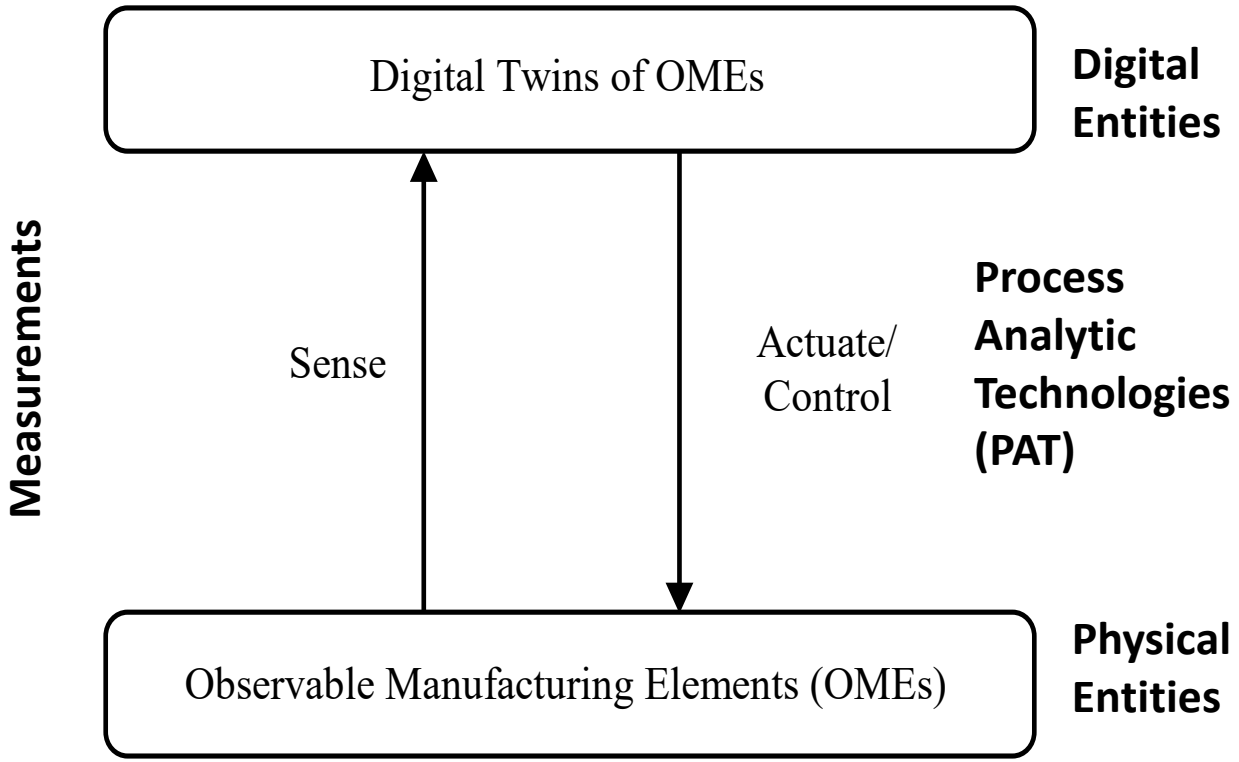
- Optimize outputs by integrating RDM across measurement space
- Strengthen data reuse and interoperability
- Enable data driven discovery and access
- Enable custom and/or shared laboratory workflows towards end-to-end automation
- Enable the development and realization of digital twin



Digital Twins for Biomanufacturing

Emphasis on synchronization between physical and digital entities

- Two-way synchronization is a key feature in digital twins, compared to conventional modeling and simulation
- Synchronization can be event-based or time-based
  - Event-based: updates occur in response to an event
  - Time-based: updates occur from a time-stamped data stream



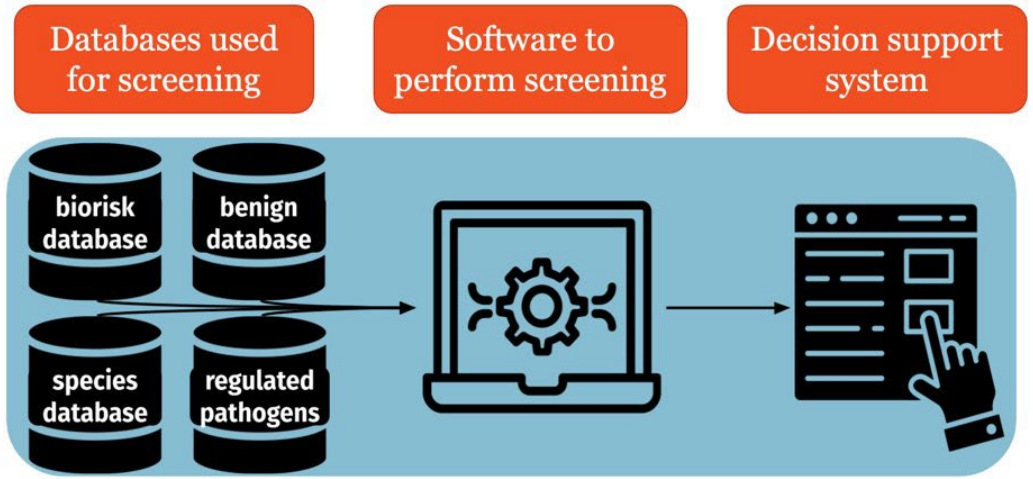
Derived from NIST contributions to

ISO 23247 series of standards on 'Digital Twin Framework for Manufacturing'

Industrial Ontologies Foundry specification from Open Applications Group Inc

Oligonucleotide Sequence Screening: A New Pilot

- Expand its work to develop global standards requiring & supporting screening practices.
- Engage with industry to identify appropriate features of Sequence of Concern (SOC) databases and engage with industry to develop clear expectations for screening tools
- Demonstrate performance of screening tools
- Develop enduring capabilities to evolving screening; support HHS Guidance and NBS Goals



Additional Biomanufacturing Partnerships

- NIST and UMD partnership through the Institute for Bioscience & Biotechnology Research (IBBR)
- Manufacturing USA
  - Sponsorship of NIIMBL
  - Engagement with BioFabUSA and BioMADE (DoD-funded)

Labs/MFG USA Biomanufacturing Collaborations

Manufacturing USA: Each institute is a public-private partnership that focuses on promoting robust and sustainable advanced manufacturing R&D; providing workforce training and education; **each has a standards emphasis**

NIMBL

***DOC-funded Institute**:* accelerate biopharmaceutical manufacturing innovation

***Technical Scope**:* Product focus areas include cell and gene therapy as well as existing biopharmaceutical products

biofabusa
Manufacturing the Future of Biofabrication

***DoD-funded Institute**:* make practical the large-scale manufacturing of engineered tissues and tissue-related technologies

***Technical Scope:** engineered* tissue-based products

BioMADE

***DoD-funded Institute**:* build a sustainable, domestic end-to-end bioindustrial manufacturing ecosystem

Technical Scope: enable domestic bioindustrial manufacturing at all scales

https://www.manufacturingusa.com/institutes

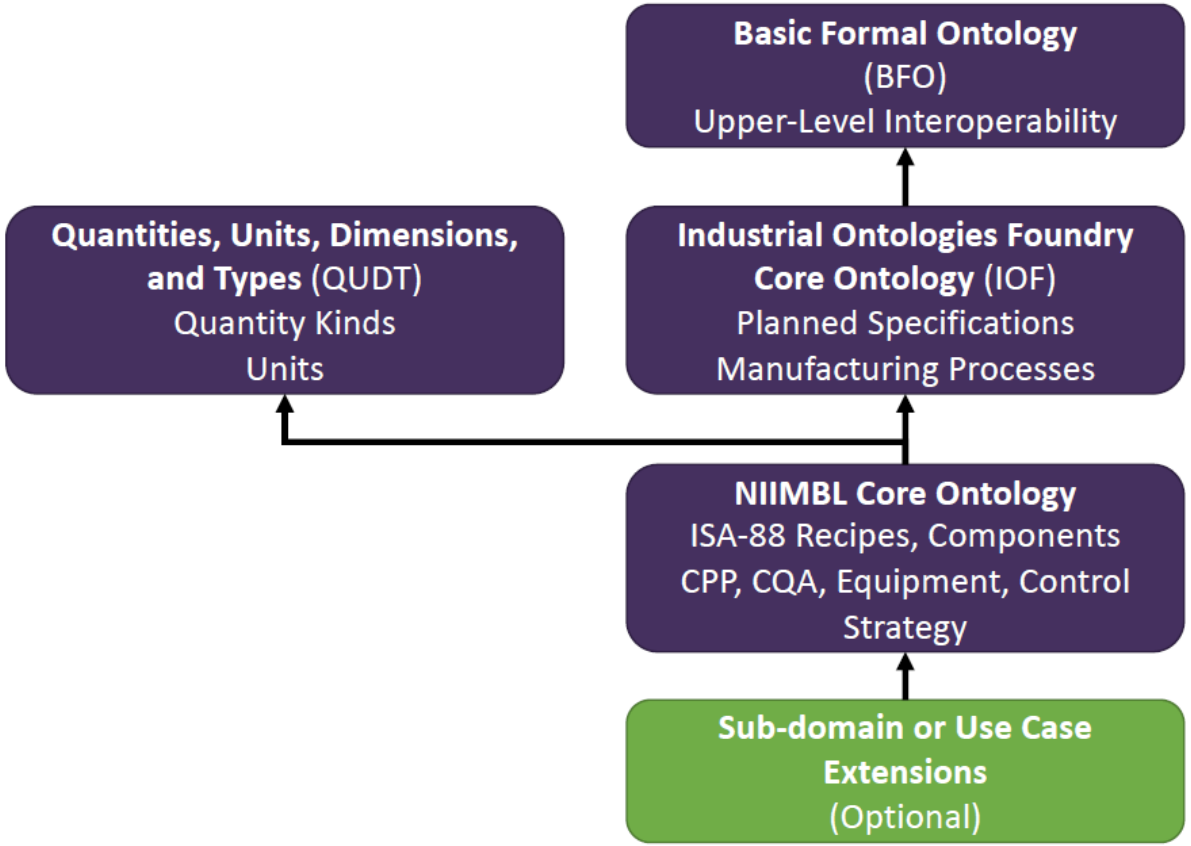
Big Data Project with NIIMBL

Standards to address data interoperability problems in biomanufacturing industry

NIIMBL Ontology Provides:

- A core modeling framework
- Initial terms for end-to-end processes
- A framework for future use case extensions

The NIIMBL Biopharma Ontology Architecture



Future of NIST Biotechnology/Biomanufacturing

- NIST continuing to play a key role in E.O. 14081 and NBS implementation now and in the future
  - ➢Maintain focus on measurement science and standards including emerging biomanufacturing technologies and convergence with AI/data security
  - ➢Expand NIST biotechnology and biomanufacturing programs to advance key societal goals outlined by the E.O. (health + climate, food/ag, energy, supply chains)

- **Biotechnology will be a *key growth area* across NIST and DOC**
  - ➢Balance of U.S. economic opportunities and risks similar to CETs, semiconductors

https://www.whitehouse.gov/briefing-room/statements-releases/2022/09/14/fact-sheet-the-united-states-announces-new-investments-and-resources-to-advance-president-bidens-national-biotechnology-and-biomanufacturing-initiative/

Proposed New Center for Biomeasurement and Biomanufacturing Innovation at the Institute for Bioscience and Biotechnology Research

Vision:
To become a nationally recognized research center for advancing measurements, standards, and data to accelerate development and biomanufacturing of biotechnology products

Positions NIST and IBBR to respond to E.O. 14081 by:

- **Leveraging Federal and State investment in state-of-the-art biological measurement science and standards** to stimulate advances in biotechnology and biomanufacturing
- **Actively engaging the local and national biotechnology ecosystem** to catalyze innovation and promote the growth of the National bioeconomy
- **Educating & training a skilled workforce and next-gen biotech leaders** from underrepresented and diverse groups

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Thank you