

Advancing Standards for Clinical Diagnostics

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About ATCC

- Founded in 1925, ATCC is a non-profit organization with HQ in Manassas, VA and an R&D and Services center in Gaithersburg, MD
- World's premiere biological materials resource and standards development organization
 - ~4,000 cell lines
 - ~70,000 microbes
 - Genomic & synthetic nucleic acids
 - Media/Reagents
- ATCC collaborates with and supports the scientific community with industry-standard and innovative biological solutions
 - Growing portfolio of products and services
 - Sales and distribution in 150 countries, 12 International distributors
- Mission: To acquire, authenticate, preserve, develop, standardize, and distribute biological materials and information for the advancement and application of scientific knowledge



An innovative global partner for authentic biomaterials, standards, and services



Standards provider drivers

Products

- Fully authenticated, characterized, and purity tested
- Breadth and depth of content
 - Cell lines/microbes
 - Derivatives



Standards

- Globally available
- Globally recognized
- Collaboration with government regulatory and standards organizations
- Consensus standards

Services

- RUO
- cGMP/GLP
- ISO

Certification and accreditation

ISO 9001:2008 Certification for quality management system

- Demonstrates commitment to quality products, customer service, and continued improvement



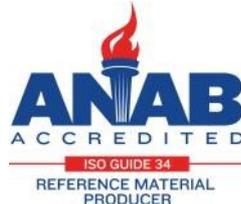
ISO 13485:2003 Certification for the design, development, production, testing, and distribution of medical devices

- Applies to synthetic molecular standards, the HIV surveillance kit, and other diagnostic and research kits



ISO Guide 34:2009 accreditation for production

- Applies to Certified Reference Materials (CRMs)



ISO/IEC 17025:2005 accreditation for testing

- Applies to all ATCC cultures, derivatives, and bioproducts tested in our laboratories

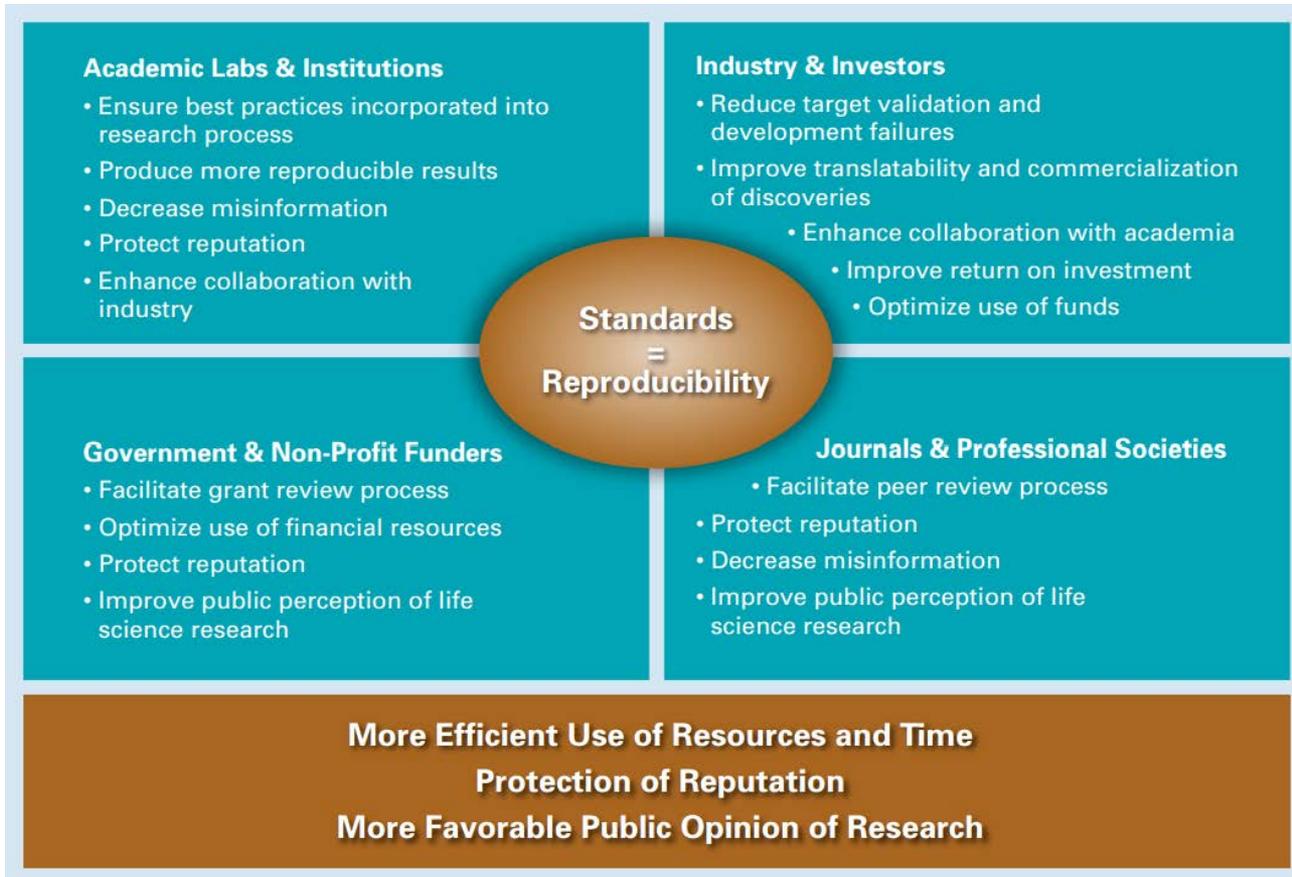


Benefits of standards

The Case for Standards in Life Science Research

Global Biological Standards Institute®

December 2013



Standards in life science research

What is a reference material?

A material or substance, one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of a measuring system, the assessment of a measurement procedure, or for assigning values to materials (ISO 15195:2003)

A variety of reference materials, including:

- Certified reference materials
- Standard reference materials
- Calibrators
- Characterized genomic nucleic acids

Reference material properties

- Qualitative
- Quantitative

Importance of using reference materials



Irreproducibility impacts reputation, public opinion of research, and the use of time and resources

Using standards can help reduce unintentional differences between laboratories

- Reagent consistency
- Consistency of laboratory processes
- Experimental design and analysis
- Data reporting and sharing

Importance of using reference materials

Recognized need for established, fully characterized, globally accepted reference materials



New technologies
Assay definition and optimization

Sensitivity, specificity, robustness, and reproducibility
Variants

Quality control
Proficiency testing



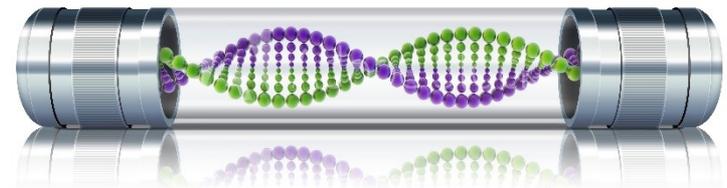
Using reliable biomaterials as controls

Types of materials

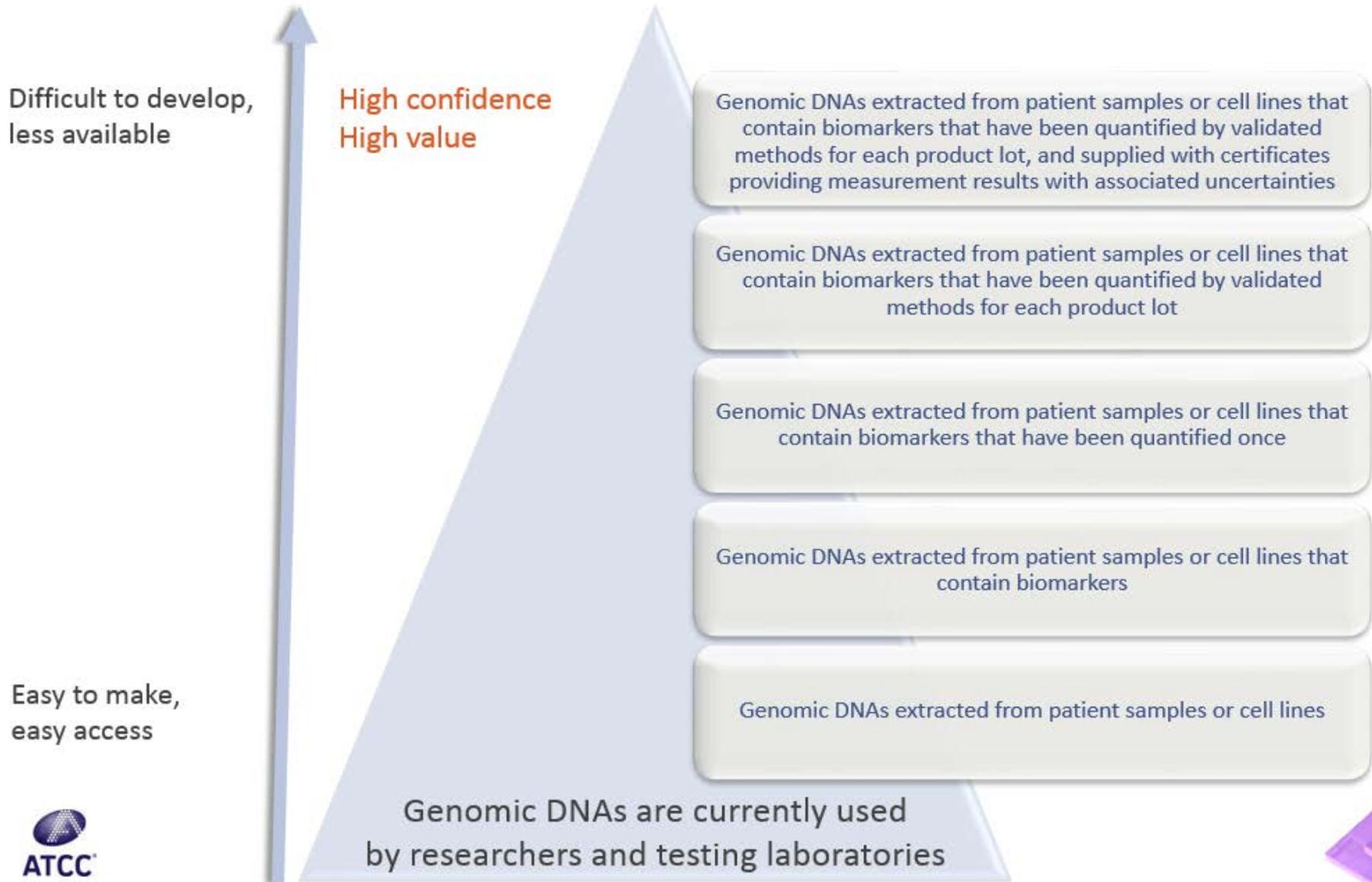
Reference Material	Benefit	Disadvantage
Synthetic oligonucleotides	Easy to design and synthesize	Do not resemble complexity of the whole genome
Whole cells and genomic DNA	Mimics complexity of the whole genome	Genetic stability; rare mutations are difficult to obtain
Patient samples	Representative	Not a sustainable source

Properties to consider

- Fully authenticated
- Characterized genetic alterations
- Stable molecular profiles
- Avoid contamination or misidentification
- Reproducible results



Examples of standards/reference materials

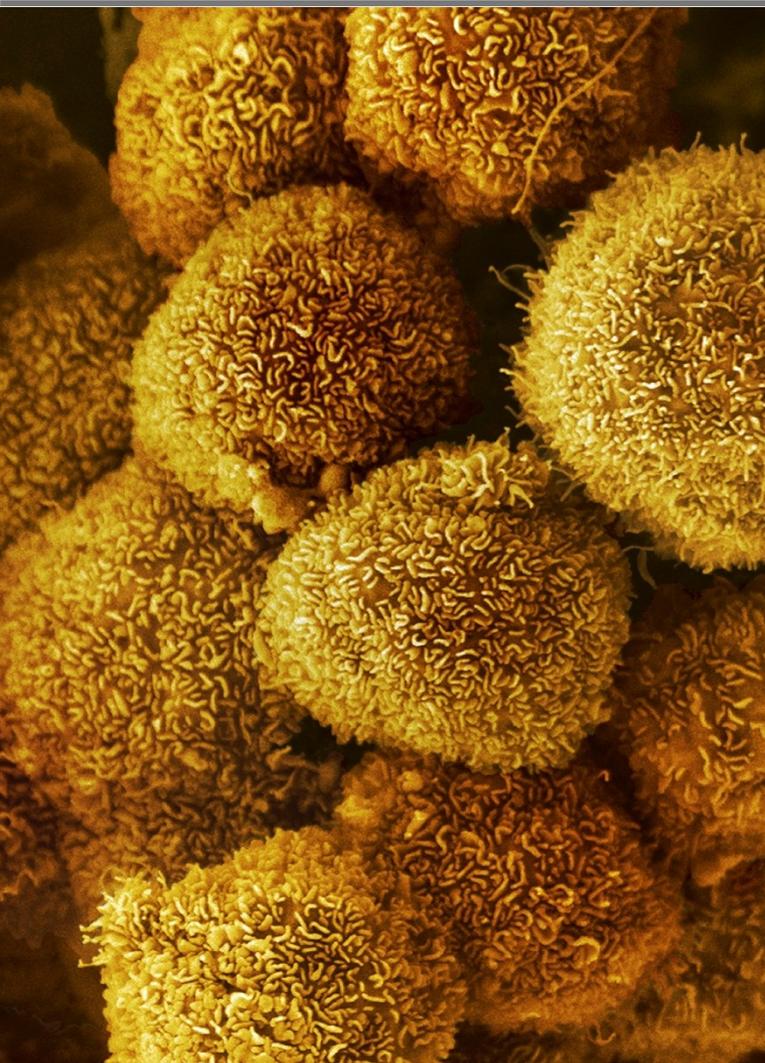


ATCC global standards recognition

- Over 475 ATCC products recognized by 30+ government and commercial organizations
- 10+ International Government organizations/agencies
- Ongoing collaborations with US agencies to develop reference material for new diseases, applications and technologies
 - FDA
 - NIH
 - NIST



Examples of standards/reference materials



Cancer

- Cell lines/tissue
- Tumor normal matched cell line pairs
 - Melanoma (COLO 829 / COLO 829BL)
 - First comprehensive catalog of somatic mutations from an individual cancer
- Cell line genomic DNAs for the molecular diagnosis of cancer
 - ISO Guide 34 Certified Reference Material
- Tumor cell panels
 - Annotated with gene mutation data and additional in-house testing
- Isogenic cell lines
 - Targeted variants created by CRISPR gene editing (NSCLC EML4-ALK fusion)
 - Intensively validated – genomic, transcript, and protein
 - New technology with promise for standards applications

Cancer cell line-based standards

NCI Selects ATCC To Distribute Cutting-Edge Cancer Models To Support The Human Cancer Models Initiative

July 2016

NATIONAL
CANCER
INSTITUTE



ATCC[®]

- HCMI is an international collaboration between the NCI, Cancer Institute UK, Wellcome Trust Sanger Institute, and the foundation Hubrecht Organoid Technology
- Goal – develop ~1,000 cancer cell models that better represent the hallmarks/diversity of human cancer
- ATCC will develop the infrastructure to support the intake, authentication, production, quality control, marketing, and distribution
- Variety of cancer types, including rare and pediatric cancers
- Complete genetic analysis and de-identified clinical information about the patients/tumors, including their response to treatment

Using authenticated cell lines as controls



- Fully authenticated
- COI and STR testing to avoid inter-species and intra-species contamination or misidentification
- Characterized tumor genetic alterations
- Stable molecular profiles
- Control FFPE process
- Control IF or IHC staining process

Examples of standards/reference materials



Infectious disease

- Highly characterized microbial strains for assay development
- Genomic nucleic acids
 - Quantitative
 - DNA from bacteria, fungi, protists, and viral strains
 - RNA from viral strains
- Synthetic nucleic acids
 - Genetic surrogates
- Zika – recent strains, genomic and synthetic RNA, inactivated strains

Microbial strain authentication



No single method of identification is sufficient

ATCC utilizes both classical and modern techniques

- **Phenotypic analysis** – Colony morphology, cell attributes, biochemical analysis
- **Genotypic analysis** – Sequencing, toxinotyping, ribotyping
- **Proteotypic analysis** – VITEK MS
- **Functional analysis** – Serotype, drug resistance, virulence

ATCC Certified Reference Materials (CRMs)



Certified Reference Materials from ATCC are accompanied by a Certificate of Analysis

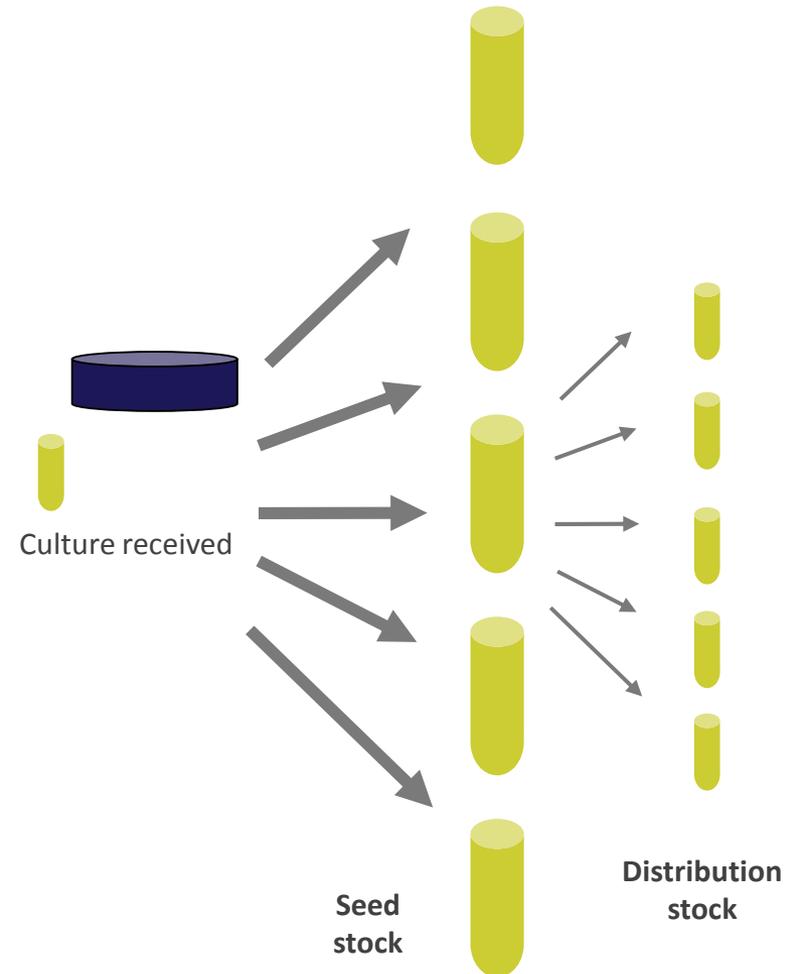
- Challenge assay performance
- Validate or compare test methods
- Establish sensitivity, linearity, and specificity during assay validation or implementation
- Benchmark critical assay performance during development/validation for regulatory submissions and production lot release
- Testing and calibration in ISO 17025:2005 accredited laboratories

ATCC® Proficiency Standard Program®



- Dedicated highly characterized stocks
- PT testing panels - consistent, safe, reliable and traceable to their source.
- Test relevant, actionable targets
 - Representatives of contemporary strains
 - Genetic variations/mutations
 - New emerging strain variants
- New technology developments
 - NGS, MALDI-TOF, multiplex

Production



- Preserved cultures remain as close as possible to the original culture
- Seed stock is archived for future replenishment
- Distribution stock are used for distribution
- Authentication compares the seed, distribution, and initial cultures

Working Cell Banks (WCB) are essential for reproducibility and minimizing passage

ATCC Standards Development Organization

ATCC Standards Development Organization (SDO) is accredited by the American National Standards Institute (ANSI)

- Convenes and manages an international consensus group to produce written standards
- Develop best practices (standards) in life science laboratory testing and promote their use globally, using a consensus-driven process that balances the viewpoints of industry, government, academic, and clinical professions
- Ensures the reliability and reproducibility of biological materials
- Establishes institutional and lab systems that ensure research quality



Critical benchmarks for development, validation, and implementation

ATCC Standards Development Organization

ANSI/ATCC ASN-0001.1-2015

Standardization of *in vitro* Assays to Determine Anthrax Toxin Activities

ANSI/ATCC ASN-0002-2011

Authentication of Human Cell Lines:
Standardization of STR Profiling

ANSI/ATCC ASN-0003-2015

Species-Level Identification of Animal Cells
through Mitochondrial Cytochrome c Oxidase
Subunit 1 (CO1) DNA Barcodes



ATCC SDO consensus standards are available electronically through the ANSI eStandards Store

Summary



Quality standards.
Reproducible results.
Better science.

- An innovative global partner for high-quality authentic biomaterials, standards, and services
- Collaborates with industry and academia to support scientific research and breakthroughs through the continual development of new standards and reference materials
- Scientific expertise internally and through extended global partners to reach more than 150 countries

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