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
Standards provider drivers

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

Services
- RUO
- cGMP/GLP
- ISO

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

Assay Quality

Products

Services
# Certification and accreditation

<table>
<thead>
<tr>
<th>ISO 9001:2008 Certification for quality management system</th>
<th>ISO 13485:2003 Certification for the design, development, production, testing, and distribution of medical devices</th>
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<tbody>
<tr>
<td>▪ Demonstrates commitment to quality products, customer service, and continued improvement</td>
<td>▪ Applies to synthetic molecular standards, the HIV surveillance kit, and other diagnostic and research kits</td>
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<tr>
<td>▪ Applies to Certified Reference Materials (CRMs)</td>
<td>▪ Applies to all ATCC cultures, derivatives, and bioproducts tested in our laboratories</td>
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Benefits of standards

The Case for Standards in Life Science Research
Global Biological Standards Institute®
December 2013

Academic Labs & Institutions
- Ensure best practices incorporated into research process
- Produce more reproducible results
- Decrease misinformation
- Protect reputation
- Enhance collaboration with industry

Industry & Investors
- Reduce target validation and development failures
- Improve translatability and commercialization of discoveries
  - Enhance collaboration with academia
  - Improve return on investment
  - Optimize use of funds

Government & Non-Profit Funders
- Facilitate grant review process
- Optimize use of financial resources
- Protect reputation
- Improve public perception of life science research

Journals & Professional Societies
- Facilitate peer review process
- Protect reputation
- Decrease misinformation
- Improve public perception of life science research

More Efficient Use of Resources and Time
Protection of Reputation
More Favorable Public Opinion of Research
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

Using standards can help reduce unintentional differences between laboratories

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

Irreproducibility impacts reputation, public opinion of research, and the use of time and resources
Importance of using reference materials

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

- Test development
  - New technologies
  - Assay definition and optimization

- Test validation
  - Sensitivity, specificity, robustness, and reproducibility
  - Variants

- Quality Management
  - Quality control
  - Proficiency testing

Sample characterization requirement
Using reliable biomaterials as controls

Types of materials

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

- Fully authenticated
- Characterized genetic alterations
- Stable molecular profiles
- Avoid contamination or misidentification
- Reproducible results
Examples of standards/reference materials

Genomic DNAs are currently used by researchers and testing laboratories.

- Genomic DNAs extracted from patient samples or cell lines that contain biomarkers that have been quantified by validated methods for each product lot, and supplied with certificates providing measurement results with associated uncertainties.
- Genomic DNAs extracted from patient samples or cell lines that contain biomarkers that have been quantified once.
- Genomic DNAs extracted from patient samples or cell lines that contain biomarkers.
- Genomic DNAs extracted from patient samples or cell lines.
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

- 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

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

No single method of identification is sufficient
ATCC Certified Reference Materials (CRMs)

- 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

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

- 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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Learn more about our standards program at www.atcc.org/standards

Please email additional questions to: tech@atcc.org