Enable Your Drug Development with cGMP Cell Banking and Storage Services

Shalmica Jackson, PhD
Marketing Segment Manager, ATCC

Credible Leads to Incredible™
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 largest, most diverse biological materials and information resource for microbes – the “gold standard”
- Innovative R&D company featuring gene editing, microbiome, NGS, advanced models
- cGMP cell banking and biorepository services

- Partner with government, industry, and academia
- Leading global supplier of authenticated cell lines, viral and microbial standards
- Sales and distribution in 150 countries, 19 international distributors
- Talented team of 450+ employees, over one-third with advanced degrees
Overview

- The origin of GMP
- What is cGMP and why is it important?
- cGMP regulations and drug manufacturing
- Biologics manufacturing and cell banking
- ATCC’s cGMP cell banking and storage services
The Origin of Good Manufacturing Practices (GMP)

- **1903**: Upton Sinclair's book "The Jungle" exposes the poor conditions in US meatpacking plants, leading to the passage of the Pure Food and Drug Act.
- **1906**: The Pure Food and Drug Act is passed, requiring factories to clean up their production methods.
- **1937**: "New Drug Law!" by Dr. Wiley attacks the food industry for using harmful substances.
- **1957**: Federal Food, Drug & Cosmetic Act is passed, mandating GMP for pharmaceuticals.
- **1962**: ATCC Good Manufacturing Practice (GMP) is established for biological products.
What Are Current Good Manufacturing Practices (cGMP)?

- Requirements for methods, facilities, and controls used in manufacturing
- Ensures that products meet specifications and Quality/Regulatory standards
- Covers requirements for Quality Control and Production
Why Is cGMP important?

- Public and consumer safety
- Minimizes risks
- Ensures safety, efficacy, and quality
- Reduces health hazards
- Improves health care economics
cGMP Regulations

US FDA Title 21 Code of Federal Regulations (CFR) Parts:

- 11 – Establishes the US FDA regulations on electronic records and electronic signatures (ERES)
- 210/211 – cGMP for pharmaceuticals
- 600/610 – Covers biological products (e.g., mAbs, vaccines, and blood)
- 820 – Quality System Regulation (QSR) for medical devices
# Drug Manufacturing

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Small Molecule Drug</th>
<th>Large Molecule/ Biologic Drug</th>
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<tbody>
<tr>
<td>Example</td>
<td>Aspirin</td>
<td>IgG Antibody</td>
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<tr>
<td>Size</td>
<td>180 Da</td>
<td>150 kDa</td>
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<tr>
<td>Complexity Analogy</td>
<td>Bicycle ~ 20 lbs 150 parts</td>
<td>Private jet ~ 25,000 lbs 6,000,000 parts</td>
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### Process Flow Schematic

**Small Molecule Drug:**
1. From recovery unit
2. Feed tanks
3. Reactors
4. Solvent
5. Acetic acid
6. Acetylsalicylic acid
7. Filter
8. Crystallizer
9. Aspirin crystals
10. Solvent
11. To recovery unit

**Large Molecule/ Biologic Drug:**
1. Create the cell line (11 steps)
2. Cell expansion
3. Cell expansion (5 steps)
4. 5-11,000 cell biosecreter
5. Impurities
6. Purification
7. Purification (for each batch)
Challenges with Biologics Manufacturing

- Inherent biological variability
- Characterization of biological material
- Cell line development
- Process development

- Quality by Design (QbD)
- Robust Quality Management System (QMS)
- Validating processes
- Maintaining consistent product quality

- Raw material qualification
- Maintaining a clean hygienic manufacturing area
- Controlling environmental conditions
- Equipment maintenance
- Supply chain integrity

- Understanding guidelines
- Interpretation of guidelines
- Minimizing risks
Importance of Cell Banking & Storage

- Detailed descriptions of cell line history, production process, methods, reagents, in vitro cell age
- Reduces the cost of continuous cell culture processes
- Reduces the frequency of genetic drift in culture
- Foundation for building a biologic
- A 2-tiered cell bank system provides a common starting source for each manufactured lot of product
Global cell banking market is growing rapidly, but is challenged by regulatory climate and high costs

**Market Driver #1**
- Limited in-house storage and testing capabilities
- Full-service outsourcing

**Market Driver #2**
- Improved operating efficiency
- Increased pipeline productivity

**Market Driver #3**
- Increased expenditures on healthcare (biologics)
- Advancements in regenerative medicine, cell & gene therapy, and tissue engineering
- Novel cryopreservation technologies and surging research in cell line development

**Market Restraint #1**
- Increasing regulatory stringency regulatory requirements
- Clonality documentation requirements
- Host cell line history traceability

**Market Restraint #2**
- MCB & WCB quality control
- Increasing cell line testing demands
- Long-term continuity of production processes

**Market Restraint #3**
- High barrier to entry due to operational costs
- Significant investment in infrastructure and QMS
- Complex multi-step processes
ATCC – The Partner of Choice

- A pioneer in cell banking and storage
- Use of the most reliable and standardized procedures and equipment
- Provide critical starting materials for pharmaceuticals and biologics
- Trusted global source for cell authentication and uncompromised quality
- Avoid time and labor-intensive in-house production and eliminate associated risks and costs
ATCC Quality Overview

ATCC Quality Management Systems

- Maintain ISO 9001 certification across the broad organization
- ISO 13485 certification for synthetic standards, IVD test kits, and selected standards, controls and reagents
- Accredited for ISO 17025 and ISO 17034
Gaithersburg MD cGMP Facility

- Newly commissioned in 2021
- FDA 21 CFR part 11 compliant automated record keeping
- Our new purpose-built facility is the first to hold the distinction of being 21 CFR 600 and 610 compliant
- Examples of cGMP projects:
  - Expansion of mesenchymal stem cells, and production of exosomes (Pharma application)
  - MCB/WCB cell banks genetically modified CHO-K1 cell (Pharma application)
  - MCB/WCB KG-1A cells (Pharma application)
Expert cGMP Manufacture

**Highlights**

- Focus on Mammalian cells and stem cells
- Over 5,000 cell lines available from ATCC’s fully authenticated collection -or- use your own proprietary cells
- Healthy cells, as well as cells derived from diseased tissues
- cGMP master and working cell banks (MCB and WCB)
## Our Capabilities

<table>
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<th>Compliance Standard</th>
<th>cGMP</th>
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<td>21 CFR 600, 610</td>
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<table>
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<tr>
<th>Customers</th>
<th>Biologics manufacturers</th>
<th>Assay developers (potency &amp; toxicology)</th>
<th>Human cells, tissues, and cellular and tissue-based product manufacturers (HCT/Ps)</th>
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<table>
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<tr>
<th>Cell Types</th>
<th>Mammalian cells</th>
<th>Stem cells</th>
<th>Primary cells</th>
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<tbody>
<tr>
<td>Cell Bank Types</td>
<td>Production banks – cells will be used to make a “product” – produced in campaign “mode”</td>
<td>Non-production banks - typically, bioassay banks – non-campaign – strict acceptance criteria</td>
<td>Expansion of cells (CDU)</td>
</tr>
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<th>QC Release Testing</th>
<th>Mycoplasma testing (Direct/indirect &amp; PCR)</th>
<th>Endotoxin testing</th>
<th>Adventitious agents testing</th>
<th>CO1 assay (interspecies testing)</th>
<th>Sterility testing</th>
<th>Virus panel</th>
<th>Other tests as requested by customer and/or recommended for cell type</th>
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Seed Stock Sources
- Over 5K ATCC cell lines
- Customer’s proprietary cells
cGMP Biorepository

- Dedicated and validated units, with access restricted to cGMP-trained staff with QC and QA oversight.
- Tracking labels are supplied to ensure the proper segregation immediately upon receipt at ATCC.
- Separate storage boxes for each cell bank or multiple banks in one box (customer’s option). Only one customer per storage box.
- In addition to cGMP-compliant storage we also offer ISO 9001:2008
- We have storage at LN₂, -80°C, -20°C, and 2-8°C available
- Cell, microbe, protein, and nucleic acid storage options too
- Safe segregation of biological materials
- Cold-chain support and management
- On-call, after-hours personnel; 24/7 temperature monitoring
- Direct quality oversight of all unit entry and retrieval activities
Summary

- GMP is important for consumer safety
- Ensures that products meet specifications and quality/regulatory standards
- Biologics manufacturing is complex and requires additional considerations
- Use authenticated cell lines with established pedigrees under validated cGMP cell banking procedures
- Preserve the integrity of biologics cell banks long-term with ATCC cGMP biorepository services
- For more information please visit: [www.atcc.org/cGMP](http://www.atcc.org/cGMP)
References

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- ICH Quality Guidelines (Q5A - Q5E Quality of Biotechnological Products)
hTERT-immortalized Primary Epidermal Cells: Key Components in Complex Toxicological Models
July 28 at 12:00 PM EST
Kevin Grady, BS

Skin Microbiome: Considerations, Applications, and Future Directions
August 11 at 12:00 PM EST
Tasha Santiago-Rodriguez, PhD

Proteomic Studies Using Tumor-derived Organoids (Title TBA)
September 22 at 12:00 PM EST
Chia-Fang Tsai, PhD

For more information about ATCC cGMP services:

www.atcc.org/cGMP