Balancing Quality, Risk and Commercial Viability in Scalable Cell Therapy Design

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About me

- PhD in embryo patterning & developmental biology
  University College London
- Research background in:
  - Aging & cancer biology
  - Next-generation sequencing (NGS)
  - DNA mutation analysis
- Career path from R&D → Regulatory affairs
  - Focused on ensuring high-quality, compliant, and scalable materials for CGT manufacturing

My Role at FUJIFILM Biosciences Inc.

- Lead regulatory strategy for CGT-relevant materials
- Support developers with:
  - Quality frameworks
  - Risk assessments
  - Documentation for regulatory submissions
- Advocate for harmonized, practical expectations for raw materials and SUS
- Passionate about bridging innovation, compliance, and commercial scalability

Today's focus

- How early integration of quality, risk management, and commercial viability supports:
  - Scalable cell therapy workflows
  - Robust CGT manufacturing
  - Efficient regulatory readiness
- Practical considerations to help teams avoid over-engineering while still meeting global quality expectations

Please scan the QR code to download the full paper associated with this presentation. It includes supplementary information and full access to all tables referenced throughout. Thank you.

Topics to be covered

Introduction

Early-stage innovations in Cell & Gene Therapy often come straight from the bench:

- Frequently designed without sufficient consideration for what comes next.

Key questions may be considered too late to influence critical design decisions

- “Is this product financially viable at scale?”
- “What would it take to manufacture it for broader clinical or commercial use?”

This document aims to bridge that gap.

- Intended for researchers and early-phase developers
- Offers practical insights and considerations that, if integrated early, can significantly ease the path to commercialisation and improve the overall lifecycle of these transformative therapies.

Challenges in CGT Manufacturing: Challenges from Complexity & Innovation

Single-Use Materials

- Rapid innovation outpaces standardization.
- Qualification complexity due to bespoke designs.
- Supply chain fragility and limited redundancy.

Ancillary Materials (Biologically Derived)

- High variability in source and composition.
- Regulatory ambiguity around grade and traceability.
- Risk of contamination and inconsistent performance.

Sterility

- Diverse interpretations of “sterile” across suppliers.
- Raw material sterility impacts final product safety.
- Lack of harmonized standards for aseptic vs sterile claims.

Industry Best Practices & Regulatory Frameworks

- Fragmented guidance across regions and agencies.
- Need for harmonized definitions and expectations.
- Limited clarity on material grades and documentation requirements.

Material scope in CGT manufacturing

Regulatory and quality framework: Summary & Gaps

By establishing clear definitions and quality grades for raw materials, the framework supports:

- Regulatory efficiency through reduced filing times and improved documentation.
- Quality assurance by minimizing risk and enhancing supplier transparency.
- Operational agility via early material qualification and reduced rework.
- Industry alignment through shared vocabulary and best practices.

Guideline/article title	Supports	Provides challenge
General guidelines for AM suppliers and users		
USP-NF <1043>[1] Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	• Development of the appropriate material qualification programs for CGT products • Identification of AM supplier and user responsibilities • Risk tier matrix of the AM so the user can identify additional risk mitigation steps • SUS and consumables	• Reference to risk assessment items for which there are no clear standards for the CGT AM industry, e.g. animal-free definitions, validation requirements
ISO 20399:2022[13] Biotechnology—Ancillary materials present during the production of cellular therapeutic products and gene therapy products	• Responsibility matrix for the supplier and user • List of quality parameters the user should assess for AMs and relevant GMPs	• AM storage and stability • Excludes SUS and consumables
USP <92>[23] Growth Factors and Cytokines used in Cell Therapy Manufacturing	• Recombinant human interleukin 4 as an example and lists typical quality attributes	• No general requirements for growth factors and cytokines used in CT manufacturing
Guidelines for AMs of biological origin		
EP 9.0 5.2.12[11]. Raw Materials of Biological Origin for the Production of Cell-Based and Gene Therapy Medicinal Products	• Identification of responsibilities of suppliers and users of AMs • Identification of risks of animal-origin materials • Quality attributes for the AM and the AM manufacturer	• Only applies to raw materials of biological origin • Does not cover medical devices, plastics, chemically synthesized raw materials, synthetic peptides, or synthetic polynucleotides
ICH Guideline Q5A(R2)[12] on viral safety evaluation of biotechnology products derived from cell lines of human or animal origin	• Risk-based approach to viral safety of products made from animal-derived cells, e.g. recombinant proteins, including testing, inactivation, and method validation	• No delineation in risk for animal cell-derived products intended for direct human use, and those for use as AMs
FDA Draft Guidance: Considerations for the Use of Human-and Animal-Derived Materials in the Manufacture of Cell and Gene Therapy and Tissue Engineered Medical Products[24]	• Identification of considerations for using animal-derived components across different species, including recombinant materials • Risk considerations and how to disclose human- or animal-derived materials used in products, including the source of materials • Adventitious agent testing considerations for both human-derived and animal-derived materials per source type	• Traceability disclosures from the 'birth' of material throughout the supply chain can be difficult depending on supplier definitions of animal-origin/animal-derived components
Guidelines for FDA-regulated human tissue culture media		
Tissue Culture Media for Human *ex vivo* Tissue and Cell Culture Processing Applications—Final Class II Special Controls Guidance Document for Industry and FDA Reviewers[25]	• Lists risks to health associated with use of the device • Special controls identified to address the risks (in 510k)	• Media or supplements containing biologic or cellular components are out of scope
Guidelines on particulates		
USP-NF <1790> Visual Inspection of Injections[26]	• Explanation of intrinsic, extrinsic and inherent particulates • Understanding some inherent (e.g. proteinaceous) particulates may be acceptable • Understanding unique challenges to CGT products	• Although specific challenges are noted for CT, guidance on addressing them is limited

Topics to be covered

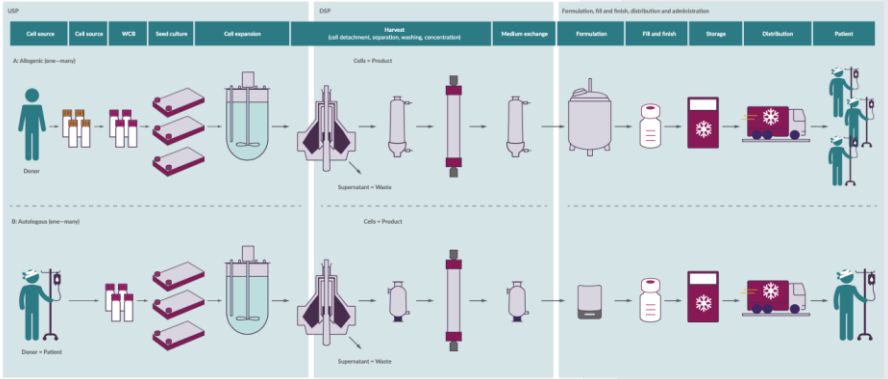
Single-use systems

Single-use systems are a cornerstone of modern cell and gene therapy (CGT) production. Their primary advantage lies in minimizing contamination risks while offering greater process flexibility. These systems typically include:

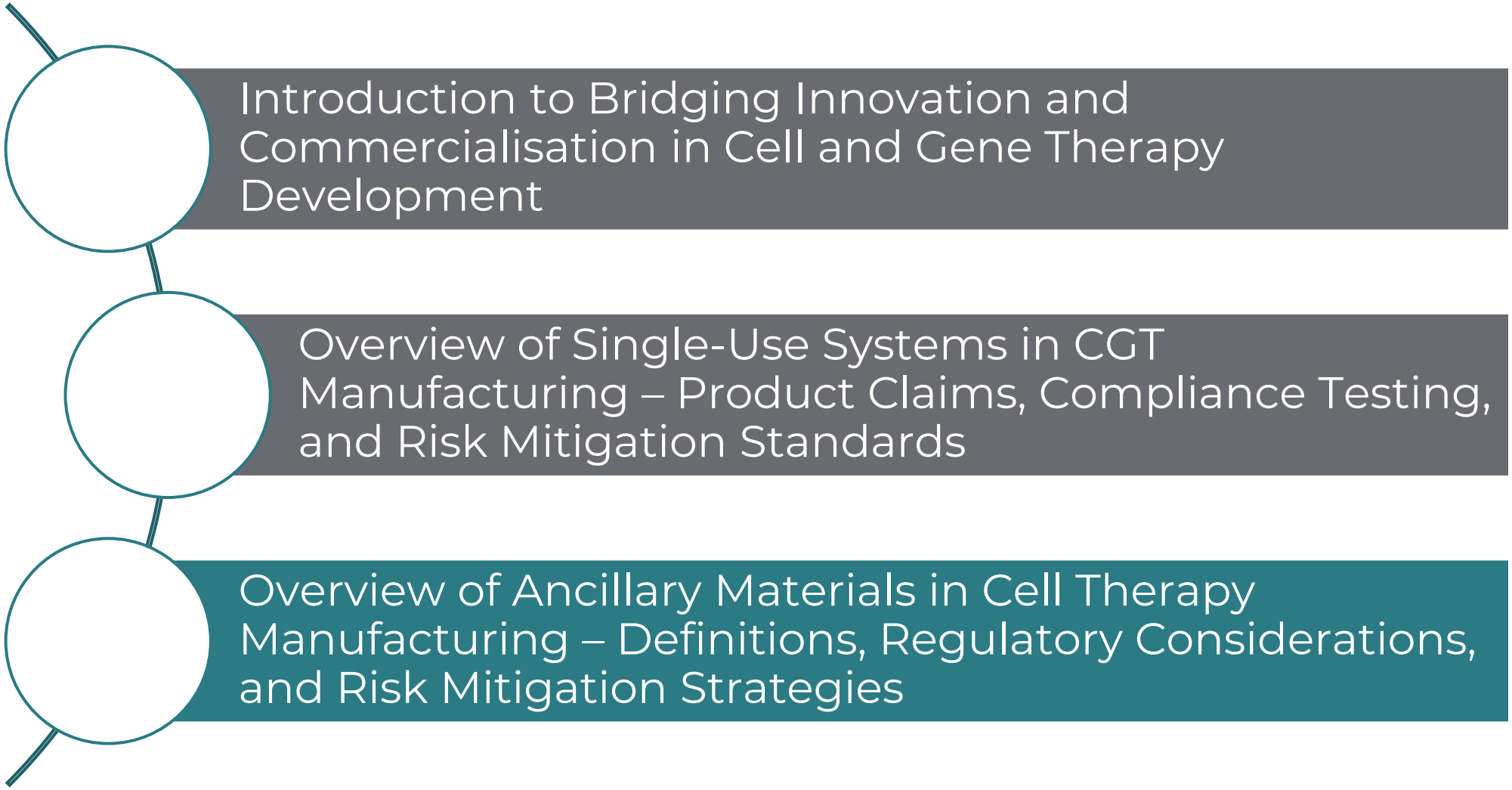
- Bags, Filters, Tubing, Electroporation cartridges

The work delves into:

- Workflow of CGT product manufacturing use of SUSs
- Examples of typical product claims
- Examples of typical performance claims
- Selecting the right bags for CGT: materials, performance and risk
- Validation needs (bags, tubing and filters)



Topics to be covered



Ancillary Materials (AMs), definition and risk mitigation

Such as: Cell culture media, Recombinant proteins, Cryopreservation media, Dissociation regents, Sera, Supplements

Ancillary materials (AMs)

- Critical components that contact cellular therapeutic products during manufacturing but are not intended to be part of the final product
- Regulatory bodies like ISO, FDA, USP, and EMA define them with slight variations.
- These materials play essential roles in cell growth, differentiation, selection, and purification processes, requiring careful consideration for quality and safety while maintaining clear distinctions from excipients and starting materials to ensure regulatory compliance.

Risk mitigation when qualifying ancillary materials

- Advanced therapy manufacturing often requires using a variety of material grades due to the uniqueness of the finished product, necessitating comprehensive risk assessment including supply continuity, material suitability, traceability and testing strategies.
- When qualifying these materials, manufacturers should request quality documentation from suppliers, evaluate RUO materials thoroughly, follow USP <1043> risk tier guidance, and implement appropriate risk reduction measures such as vendor audits and safety testing for residuals

Ancillary materials – key requirements addressing safety and stability

Supplier and user Responsibilities

Several guidelines (USP-NF <1043>, ISO 20399-2022) establish responsibility matrices between suppliers and users of ancillary materials, with clear identification of quality attributes that must be assessed.

Traceability challenges

FDA Draft Guidance highlights that traceability throughout the supply chain can be difficult depending on supplier definitions of animal-origin/animal-derived components.

Limited standardization

There are noted gaps in standards for the CGT (Cell and Gene Therapy) industry, particularly regarding animal-free definitions and validation requirements for ancillary materials.

Critical testing framework

Identity verification, TSE/BSE risk mitigation, bioburden and endotoxin testing required across ALL ancillary material categories

Quality by Design approach

BioPhorum's QbD process recommended to identify Critical Material Attributes with material-specific controls tailored to each AM type

Universal safety controls

All AMs require mycoplasma testing, batch traceability, adventitious agent control, and REACH compliance (EU)

Stability requirements

Comprehensive shelf-life studies with storage temperature specifications critical across all material categories

Table 2: Requirements and considerations for AMs (not an inclusive list)

Requirement	Proposed testing	Cell culture media	Recombinant proteins	Cryopreservants	Dissociation reagents	Serum	Supplements
Identity verification	Identity testing for materials, the user should confirm with the manufacturer that they are prepared to disclose key information to	Must	Must	Must	Must	Must	Must

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Thank you for your time

If you would like any information on the subject discussed in today presentation, please feel free to reach out to:

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Legal and policy framework

Policy framework

- equitable contributions
- consensus driven
- end user led
- sales free
- safe and confidential

Legal framework

- competition compliance
- supplier interactions
- code of conduct
- privacy policy

Phorum user guide and privacy policy

To read BioPhorum's policies and procedures please see our Phorum user guide

To learn more about how we collect, keep, and process your private information, please view our privacy policy

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