Maintaining Sterility in Cell & Gene Therapy Processes

And the use of sterile connectors during cryopreservation

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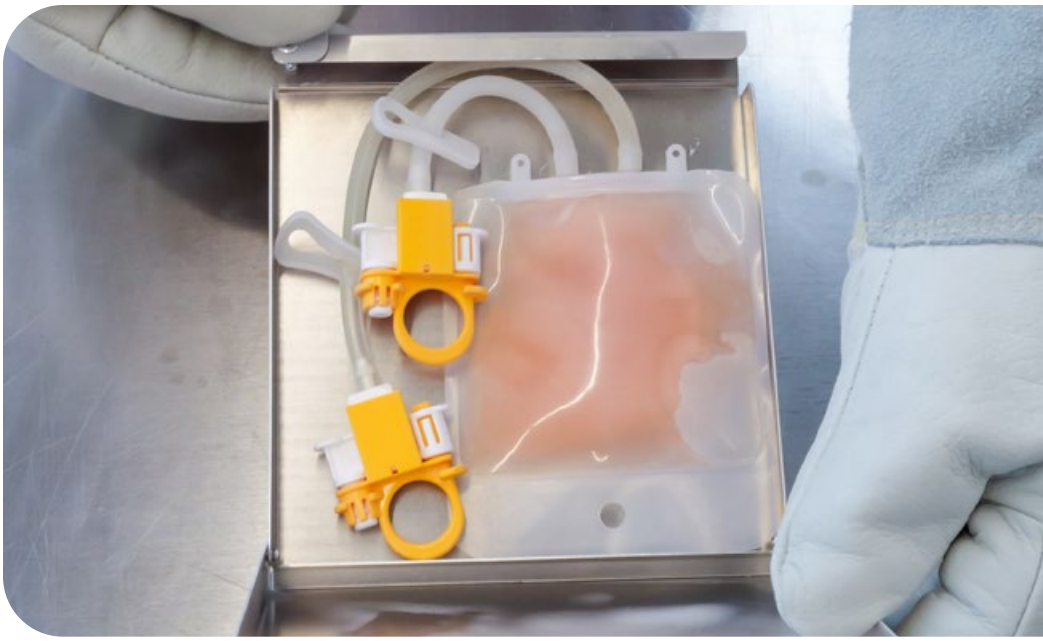


The cell and gene therapy (CGT) approval pipeline continues to grow at a rapid pace. In 2023, cell and gene therapies comprised of 10% of all U.S. Food and Drug Administration novel approvals, up from 7% in 2022 and 6% in 2021.[1]

Increased demand in the CGT space translates into more pressure to develop and deploy approved therapies as quickly and efficiently as possible. This is true for small biotechnology start-ups and major pharmaceutical companies, which are relying on their extensive capacity and capabilities to accelerate time to market for these high-value therapies.

In all cases, the key to success is the fundamental requirement to maintain sterility throughout cell and gene therapy processes. To that end, CGT players large and small are looking for ways to ensure product viability while streamlining processes, reducing risks, and protecting yield.

This paper examines ways to incorporate aseptic connectors into CGT processes and cryopreservation, which is essential in the manufacture and delivery of these innovative therapies.

STERILE CONNECTORS

Sterile connectors are devices connecting two fluid paths of tubing, while maintaining sterility of both. The sterile barrier on each connector half (usually a membrane) is used to prevent bacteria and contaminants from entering fluid pathways while the barrier is in place. Sterile connectors facilitate CGT processes outside of the biosafety cabinet (BSC) and replace the need for tube welding.

From a productivity standpoint, an experienced operator using a sterile connector can make an aseptic connection in less than 10 seconds vs. the estimated 3-7 minutes required for creating a tube weld.

Figure 1: This simple process helps reduce operator error and allows sterile connections to be made quickly and reliably with just a few steps.

A production environment making 100 connections or more in a week will require about 5 to 11 hours of operator time. Time varies based on the tube welder, operator skill level, replacing blades and other potential delays. In contrast, an operator using sterile connectors could make 100 sterile connections in less than 17 minutes.[2]

THE NEED FOR SMALL FORMAT CONNECTIONS

Research involving industry representatives across biopharma, cell and gene therapy identified a gap in aseptic connector technologies for small-volume (<10L) aseptic processes, such as early-stage drug development or small-batch autologous therapies.

Responding to this need, newer aseptic micro-connectors have been introduced specifically for use with small-bore tubing in small-volume work. This includes applications such as sampling, seed train expansion, analytical processing, buffer/media transfers, and early cell-culture processes involving shaker flasks and rocker tables.

Importantly, incorporating aseptic connectors early in product development helps streamline scalability – the same validated materials and procedures can be applied as production outputs increase.

WITHSTANDING CRYOPRESERVATION AND FREEZE-THAW CYCLES

Cryopreservation is essential to the development, manufacture and delivery of innovative cell and gene therapies. Biological materials can be preserved at ultra-low temperatures, offering flexibility between drug production and delivery to a patient.

Freezing the cells in single-use assemblies makes transportation easier and ensures materials can be both shipped and stored for long periods of time while maintaining cell viability. Both primary containment systems such as bags, tubing and connectors, and secondary containment storage shells and cassettes must be able to withstand extreme temperature changes from freezing to thawing, while protecting product.

Long used in single-use biopharmaceutical processing, CPC aseptic connectors are built to withstand freeze-thaw cycles, typically being tested down to -80°C on the low end. However, now drug manufacturers are increasingly moving to ultralow temperatures (ULT) using vaporized liquid nitrogen of -130°C or lower for improved results, particularly in cell and gene therapy production.

To reduce cryopreservation-induced damage, cryoprotective agents (CPAs) like dimethyl sulfoxide (DMSO) and glycerol are widely used in both research and clinical applications, so primary containment system components must be chemically compatible with these CPAs.[3]

To meet the evolving needs of cell and gene therapy, the innovative MicroCNX® ULT Series from CPC is designed to withstand temperatures down to -190°C and chemically compatible with cryoprotectants, such as DMSO. The MicroCNX ULT series are the only aseptic micro-connectors and can be frozen with cryopreservation bags placed directly into protective freeze cassettes, streamlining materials handling (See Figure 2).

CPC connectors are also available for use with all established single-use subassembly manufacturers. For example, the MicroCNX ULT can be specified for biomaterial bags and tubing assemblies, or any assembly that includes polyvinyl chloride (PVC), silicone and thermoplastic elastomer (TPE).

SINGLE-USE BENEFITS IN FREEZE-THAW APPLICATIONS

- Lower cross-contamination risk
- Increase process flexibility
- Improve efficiency (reduce manual intervention complexity during freezing, thawing, handling and shipping)
- Reduce maintenance and eliminate cleaning or sterilization steps (by using pre-sterilized single use systems)
- Shorten validation times
- Simplify staff training requirements

Figure 2: MicroCNX® ULT connector in freeze cassette

AS CGT ADVANCES, SO MUST SINGLE-USE TECHNOLOGY

In the rapidly evolving world of CGT, drug developers want to maintain product quality while optimizing processing times and reducing costs.

Newer sterile connector technologies support robust, closed and sterile CGT processing. They also help protect cell and gene therapy products during freezing, transportation, storage and thawing.

Aseptic connectors designed specifically for CGT applications provide fast, easy and reliable methods for maintaining sterility from the earliest development stages to commercial production.

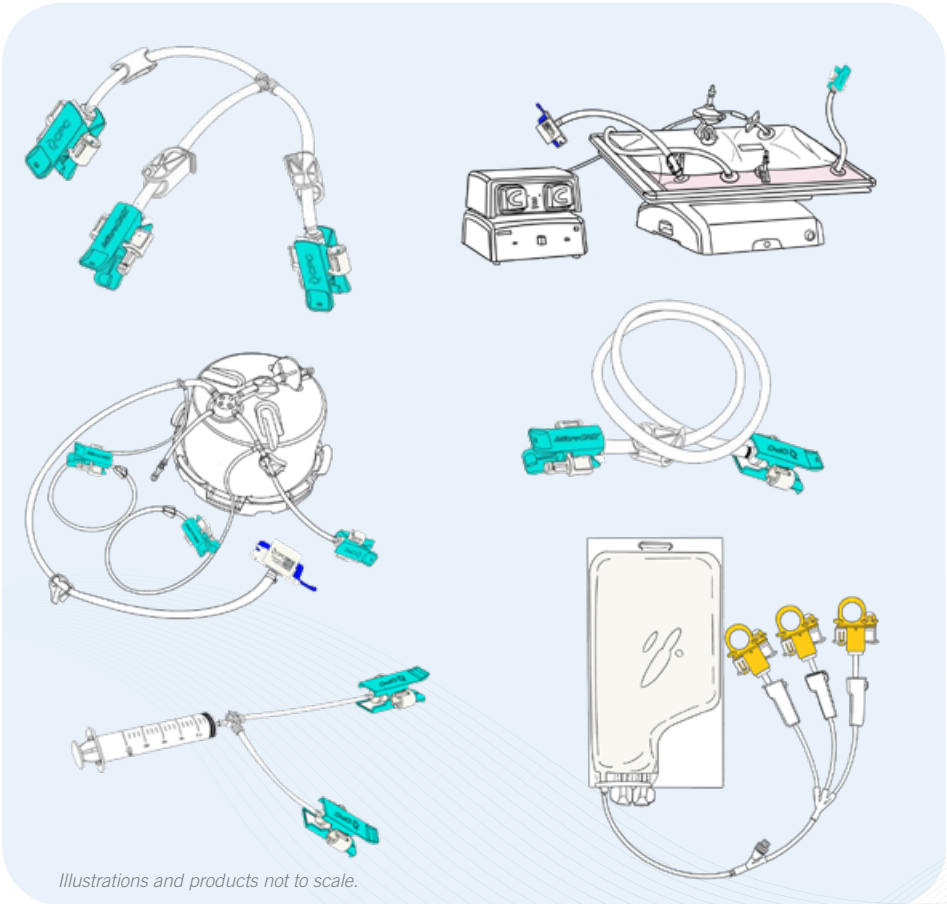
With the many benefits reviewed in this article on single-use, sterile connectors, CPC's broad portfolio of innovative aseptic connectors can support flexibility and compatibility while offering a long, proven history of making sterile connections easier.

The world's leading biopharmaceutical manufacturers rely on CPC's single-use AseptiQuik® sterile connectors to maximize productivity and speed-to-market, while helping reduce costs and contamination risks.

About CPC Biopharma

CPC (Colder Products Company) is a global leader in single-use connection technology, offering a wide variety of connectors for biopharmaceutical manufacturing, cell therapy and gene therapy. Innovative, flexible designs easily combine multiple components and systems including process containers, tubing manifolds, transfer lines, bioreactors and other bioprocess equipment. Robust single-use connectors maintain media sterility and integrity while improving production yields, decreasing time to market and reducing costs. The company's well-known AseptiQuik® connectors provide quick and easy sterile connections even in non-sterile environments. Learn more about our entire portfolio at cpcworldwide.com/bio. Connect with confidence with CPC, an operating company within Dover Corporation.

THE FUTURE OF ASEPTIC CONNECTIONS IN CELL & GENE THERAPY



Illustrations and products not to scale.

References:

1. https://www.cellandgene.com/doc/2024-market-outlook-for-cell-gene-therapies-0001

2. Gene Therapies: A Guide to Aseptic Single-Use Connectors Transferable Lessons From the Bioprocessing Industry

3. https://doi.org/10.1038/s41570-022-00407-4

"Where feasible, the use of newer technologies should be considered to mitigate or reduce risks to product quality identified in manufacturing processes and operations."

Source: Parenteral Drug Association "Points to Consider No. 1 Aseptic Processing" (Revised 2023)

We inspire confidence at every point of connection.

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