The Case for Modernizing Small-Volume Aseptic Processing

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Key Takeaways

- Eliminating tube welder costs (~$20-45K per welder) and associated consumables like blades and adapters (~$7-$20 per weld).[7]
- Avoiding costs for tube welding instrument validation, calibration, maintenance, and repair.
- Reducing the time required to make sterile connections. Making a sterile connection with MicroCNX Series Connectors is 4-7X faster than an operator using a tube welder.[8]
- MicroCNX connectors also can connect tubing of different materials and sizes without adapters, unlike welders.
- Reduces holdup volume - Connectors do not require the extra tubing that is involved in tube welding, which is a source of hold up volume.

Maintaining sterility for therapeutics that biopharmaceutical and cell and gene manufacturers produce is critical, particularly when unique, personalized samples are processed for precision medicine. As precision medicine grows, so does the demand for greater efficiencies in smaller batch aseptic manufacturing.

Historically, clinical laboratories and small-batch drug producers have used either biosafety cabinets (BSCs) or tube welding to achieve sterility in their processes. In part, drug makers have relied on these older methods of sterile processing simply because there were no viable options for connecting small-diameter tubes (e.g., <3.2mm or <1/8) using the types of aseptic connectors widely used in higher-volume biopharmaceutical manufacturing.

Single-use technologies (SUTs), like single-use sterile connectors, have long played a vital role in biopharmaceutical processes. SUTs offer several well-documented benefits for commercial operations, including reduced manufacturing costs through time and labor savings, a significant reduction in hazardous waste, the elimination of batch cross-contamination risks, and more.[1,2,3]

These same advantages are now available for smaller batch cell therapy

and gene therapy (CGT) manufacturers, with newer single-use solutions designed specifically for their sterile processing needs.

MOVING BEYOND BIOSAFETY CABINETS AND TUBE WELDING

Open system bioprocessing exposes both media and cells to the environment, so working within a biosafety cabinet (BSC) can help mitigate the risk of contamination. BSCs have long been used in research and development so people are familiar with how they function and the equipment is often readily available. However, biosafety cabinets present several challenges, particularly as processes move further down the development pathway.

In addition to their limited operating space, BSCs require strict setup and cleaning protocols before and after use as well as filter monitoring and maintenance. BSCs are also susceptible to airflow disruptions. Walking too close or moving too quickly within the BSC space can disrupt airflows leading to contaminated air entering or circulating within the cabinet.[4] BSCs are expensive as well, which can limit access for some organizations. Given the capital expense associated with BSCs, this solution is a major hurdle for start-ups – while also being a barrier for scale-out efforts when moving through to commercial production.

In contrast to open sterile processing with BSCs, closed aseptic systems help ensure the sterility of the therapeutics that biopharmaceutical and cell and gene manufacturers produce by closing off each unique process step from the external environment.[5,6]

Until recently, tube welding had been the industry's only option for closed aseptic processing with smaller-diameter tubes. Small-volume sterile single-use connectors were not commercially available until the early 2020s.

Even with the arrival of aseptic connectors designed specifically for smaller tubing, many biologic, cell, and gene therapy manufacturers continue to use tube welding because it is a familiar process for creating closed aseptic systems. Also, many organizations already have invested in tube welding equipment, so their processing protocols are based on using tube welders. However, as the need for greater speed and efficiency affect drug developers and manufacturers, it is time to examine the practicality of tube welding compared to using aseptic connectors.

TUBE WELDING COSTS: TIME, MONEY, EFFICIENCY

To evaluate the actual costs associated with tube welding, 63 experts from across the world participated in an industry survey.[7] They provided data regarding instrument and consumables costs; operator training and labor costs; and tube welding-associated risks.

Each weld is intended to consume a new copper wafer, and requires excess tubing on either side of the weld which is disposed. Connections between two different tube sizes also require adapters, making the consumables cost add up quickly.

The survey experts were also asked to estimate the time required to create a single sterile weld. The average was found to be ~12 minutes from the start of tube welder setup to the first weld being finalized, which is an important efficiency consideration with the many welds that occur throughout each bioprocessing step (Figure 1).

The survey found that **a typical tube welder costs approximately $25,000 - $40,000.** Users also reported often purchasing more than one welder for parallel use and as a backup.[7]

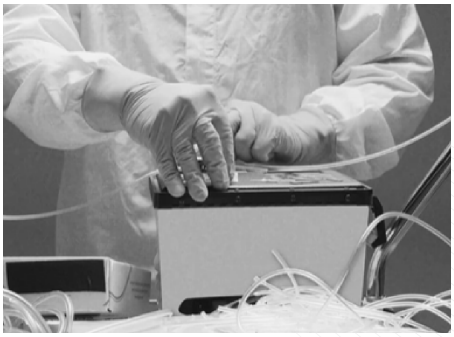
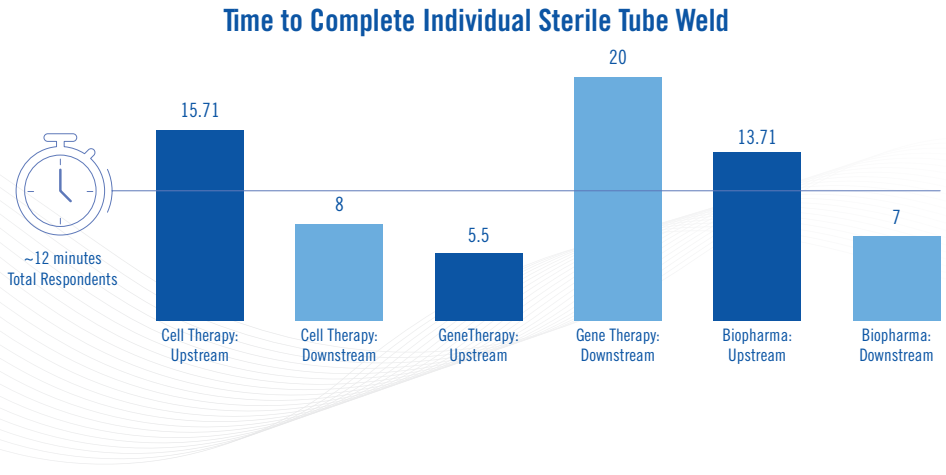


Figure 1: Time to complete individual sterile tube weld



Welding equipment requires regular maintenance as well as annual validation and ongoing inspection and certification (IQ/OQ) to ensure compliance with applicable regulations. Respondents indicated **welder maintenance costs at an average of $5,000 per year per welder.**[7]

Successful tube welding requires good technique. One-third of the survey respondents estimated **training costs between $501 and $1,000 per trainee.**[7] An additional 22% of respondents estimated these costs between $1,000 and $2,000, while 5% said between $2,000 and $5,000.[7] It is easy to see how training multiple operators and new hires in response to growth and turnover presents significant costs.

Welder downtime also impacts productivity and efficiency. Though responses varied widely, most indicated that one hour of welder downtime could cost between $6,000 and $100,000 in lost revenue, with some even reaching well beyond (Figure 2).

Though the higher losses are likely associated with larger operations, even smaller organizations may invest in more than one tube welder as backups, which then increases equipment and maintenance costs accordingly.

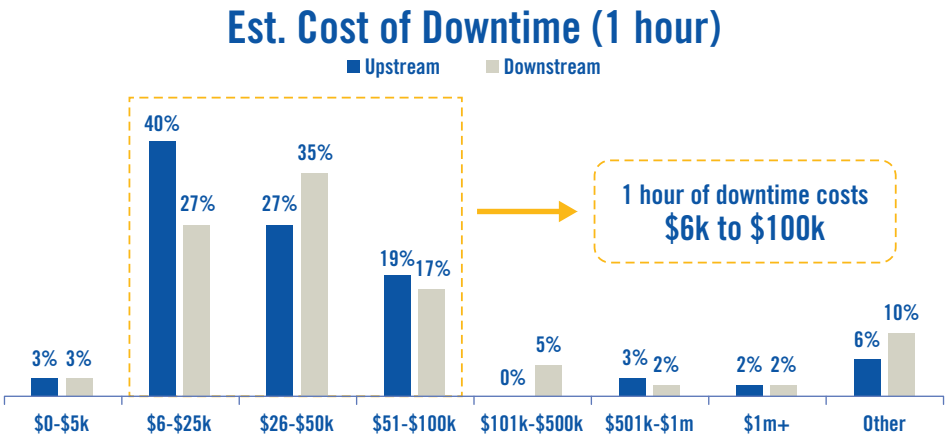


Figure 2: Estimated cost of downtime

SOLVING CHALLENGES FOR SMALL-TUBING ASEPTIC PROCESSING

Until recently, tube welding had been the industry's only option for closed aseptic processing with smaller-diameter tubes. Even with the arrival of small volume aseptic connectors in the early 2020s, many biologic, cell, and gene therapy manufacturers continue to use tube welding because it is a familiar. That changed with the introduction of the MicroCNX® Series connectors in 2021.

MicroCNX connectors provide a simple, efficient method of sterile connection of tubing used for small-format cell and gene therapy assemblies. They also are the only alternative to tube welding for creating closed sterile connections at small volumes.

Designed to quickly connect 1.6mm (1/16"), 2.4mm (3/32"), and 3.2mm (1/8") tube sizes, users simply click together the connector halves to create a sterile flow path. CGT manufacturers rely on 1/8" and 1/16" flow paths to move cells efficiently, with minimal turbulence, and to help reduce holdup volume, so the connection method needs to contribute to these goals.

Tube welding requires extra tubing on either side of the weld and can be a source of unnecessary hold-up volume if appropriate preparations aren't taken. Welding 1/16-inch tubes together also requires time-consuming precision to prevent tubing occlusion after clamping and heat application. Any offset of the tubing at the weld point can also lead to leakage and/or contamination risk.

MicroCNX connectors eliminate the need to add extra tubing into the process, helping reduce the amount of associated product hold-up or product loss. Until recently, tube welding had been the industry's only option for closed aseptic processing with smaller-diameter tubes. Even with the arrival of small volume aseptic connectors in the early 2020s, many biologic, cell, and gene therapy manufacturers continue to use tube welding because it is a familiar.

The MicroCNX product line was expanded in 2024 to include the MicroCNX® ULT Series and again in 2025 with the MicroCNX® Nano Series. These ultra-compact sterile connectors are the first to fit directly into the freeze cassettes used in cell and gene therapy processing. They can be frozen with vaporized liquid

nitrogen to -190°C, which is important as many cell therapy processes are dropping into -150°C or lower temperature ranges to maintain cell efficacy during storage and transport.

MicroCNX connectors also offer options for 1/8", 3/32" or 1/16" hose barb terminations to support the use of a wide variety of tubing sizes and materials, such as PVC, silicone and thermoplastic elastomer (TPE).

Now that there are alternatives to tube welding and biosafety cabinets for connecting small tubes, biomanufacturers can make informed decisions regarding the right approach for their closed system connection needs.

Learn more about MicroCNX® Sterile Connectors

About CPC

CPC (Colder Products Company), the leader in single-use connection technology, offers a wide variety of bioprocessing connection solutions. Our innovative designs offer flexibility to easily combine multiple components and systems including process containers, tubing manifolds, transfer lines, bioreactors and other bioprocess equipment. AseptiQuik® Connectors provide quick and easy sterile connections even in non-sterile environments—a critical capability for biopharmaceutical and bioprocessing manufacturers. Featuring a wide range of options including 1/8- to 1-1/2-inch sizes and genderless and gendered connections, AseptiQuik connection technology delivers sterile, high-quality single-use connections and easy media transfer with less error risk. For additional information visit cpcworldwide.com or call +1-800-444-2474.

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We inspire confidence at every point of connection.

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