Understanding the True Cost of Aseptic Tube Welding in Biopharma: Finding a Better Way

SUMMARY

Historically, biopharmaceutical manufacturers have had to rely on tube welders to unite small-diameter tubes (<3.2mm or <1/8") in their bioprocesses—simply because no other option existed for closed aseptic processing. As a result, biomanufacturers have traditionally assumed tube-welding associated costs and operational challenges out of necessity. With the recent introduction of the MicroCNX® Series Connectors, biomanufacturers now have a new option of a trusted and user-friendly single-use technology. This piece discusses survey data comparing the comprehensive operational costs of tube welding against small-volume, sterile, single-use connectors to help bioprocess teams make informed decisions about the best solution for creating their closed aseptic systems.

INTRODUCTION

Biopharmaceutical manufacturers routinely depend on closed aseptic systems to ensure the sterility of the therapeutics they produce.[1,2] To build closed aseptic bioprocesses, biomanufacturers and process engineers must routinely join individual tubes, forming sterile connections using either single-use connectors or tube welders.

Single-use technologies (SUTs), like single-use sterile connectors, have long played a vital role in the closed processes found in biopharmaceutical product manufacturing. Single-use technologies offer several well-documented benefits for commercial operations, including reduced manufacturing costs, time and labor savings, the elimination of batch cross-contamination risks, and more.[3,4,5] Even with single-use connector advantages, biomanufacturers also use sterile tube welding systems for creating a closed aseptic system using smaller diameter tubing (<3.2mm or <1/8").

MicroCNX sterile connectors are available in three convenient termination sizes: 1/16", 3/32", and 1/8", making it easy to connect to many common tubing sizes and materials.

As precision medicine gains greater momentum and new candidates enter clinical trials, the demand for smaller batch aseptic manufacturing will grow further. This is especially true for new modalities such as cell and gene therapies and other small-batch biotherapeutics, including those needed for clinical research. However, until recently, small-volume sterile single-use connectors have not been commercially available.[6] This means that sterile tube welding has been the industry's only solution for building closed aseptic systems with small-diameter tubes. As a result, biologic, cell, and gene therapy manufacturers have assumed the costs and risks associated with tube welders.

To increase the options available to biomanufacturers and solve for the challenges associated with tube welding, CPC recently launched MicroCNX® Series Connectors. MicroCNX connectors are aseptic single-use connectors that provide a simple and efficient method of connecting smaller tubing. CPC designed MicroCNX connectors specifically to quickly and seamlessly connect 1.6mm (1/16"), 2.4mm (3/32"), and 3.2mm (1/8") tube sizes. Importantly, MicroCNX connectors also easily connect tubes of different sizes and materials, whereas tube welding requires adaptors.

Now that there is an alternative to tube welding for small tubing connections, biomanufacturers can evaluate the actual costs associated with tube welding to make informed decisions regarding their closed system connection needs. To support this effort, CPC worked with an affiliated Dover Consulting team to perform an industry-wide survey that asked 63 international industry experts about their real-world tube welding costs. In particular, the survey collected tube welding user data on:

- Instrument and consumables costs
- Operator training and labor costs
- Tube welding-associated risks

In this whitepaper, we discuss some of the critical findings of this survey while also briefly discussing MicroCNX connectors as they relate to biomanufacturing processes.

TUBE WELDING INSTRUMENTATION AND COSUMABLE COSTS

Naturally, the purchase of tube welders and their consumables represent a core user cost. Generally speaking, a typical tube welder can easily cost $15,000 or more. Users reported often purchasing more than one welder for parallel use and as a backup. To create sterile tubing connections that are compliant with regulations, welding equipment requires annual validation and ongoing inspection and certification (IQ/OQ). As part of this, welders require ongoing maintenance to ensure proper function. The survey results indicated that welder maintenance could cost up to $5,000 per year per welder.

Additionally, each weld is supposed to use a new blade and include excess tubing. Plus, any connections needed between two different tube sizes will require adaptors. Though not individually expensive (Table 1), these consumables costs quickly add up as weld use increases.

OPERATOR TRAINING AND LABOR COSTS

Though often overlooked, it is also critical to consider the operator-associated costs of learning and using tube welders. Manufacturers should factor in the time it takes to train operators to reach tube welding proficiency. According to survey respondents, most operators need to perform 11-30 welds before becoming proficient. To contextualize

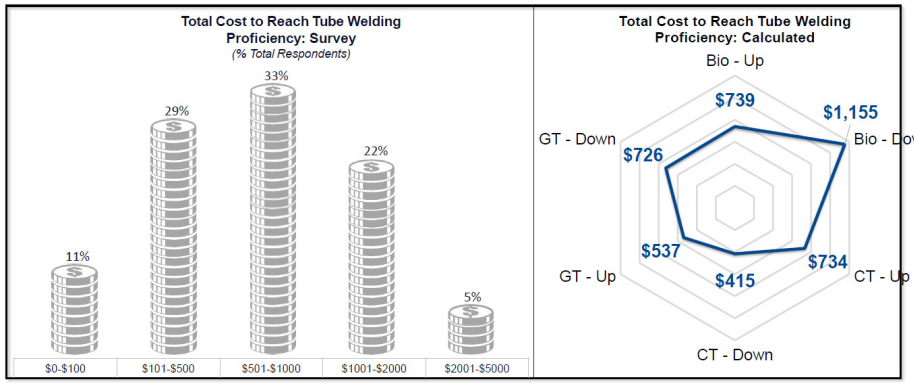

Figure 1: Operator training costs per year

this, respondents estimated training costs. One-third of respondents estimated training costs between $501 and $1,000 per trainee, with an additional 22% falling between $1,001 and $2,000, and 5% even reaching between $2,001 and $5,000 (Figure 1, above). Importantly, pharmaceutical manufacturing teams will likely need to train multiple operators and routinely train new hires in response to growth and turnover. With multiple operators and new staff, the cumulative costs of these trainings over the course of a year can be significant.

To put operator costs in full view, manufacturers must also consider labor costs and production efficiency associated with the many welds that occur over each bioprocess.

To better understand real-world tube welding times, the survey asked experts about the average time it takes to perform a single sterile weld (Figure 2).

Though users reported weld time differences depending on the application, the survey indicated that one weld takes an average of ~12 minutes (Figure 2). However, survey results indicate some subjectivity with respect to when exactly a weld starts and ends. To help further evaluate the time required to create a single weld, CPC conducted an internal time study defining a weld as including set-up, initiation, welding, curing and tear down. In our study, we observed that one weld takes ~4-6 minutes, costing about $5 to $20 per weld in labor alone (Table 1).[7] Using this figure, it is estimated that a trained operator could execute 10-15 welds per hour.

TUBE WELDER DOWNTIME COSTS

Like any instrument, tube welders can sometimes stop working correctly. Regular use of tube welders can lead to wear and tear, contributing to unscheduled downtime. In fact, 30% of respondents said they contend with

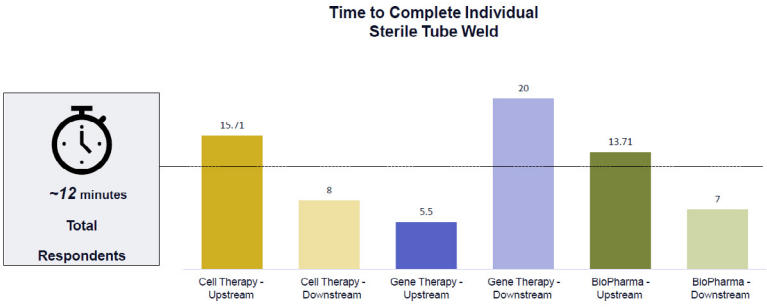

Figure 2: Time to complete individual sterile weld by biopharmaceutical application

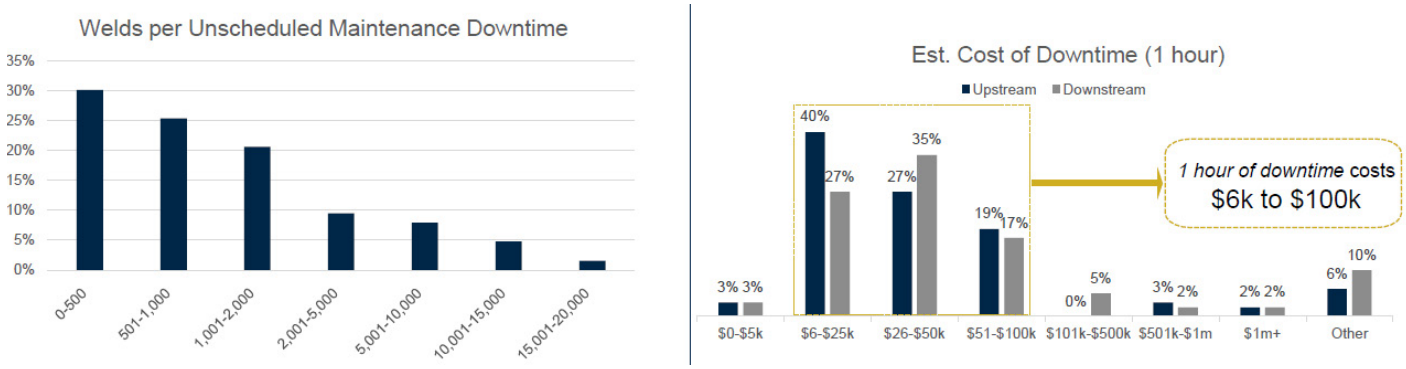

Figure 3: Unscheduled tube welder downtime results

unscheduled maintenance between 0 and 500 welds, with another 25% reported experiencing welder breakdowns between 501 and 1,000 welds (Figure 3, above left). Thus, welder maintenance can be quite frequent depending on the welds needed in a given bioprocess. Importantly, welder breakdown is costly not only because of repair costs but because of potential lost revenue. 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 3, above right).

To mitigate this fact, manufacturers often invest in multiple welders, so they can have backups when one or more welders fail. Though this protects from lost revenue, it increases equipment and maintenance costs proportionally.

MICROCNX® SERIES CONNECTORS: A NEW WAY TO SAVE COSTS AND MAKE CONSISTENT CLOSED ASEPTIC SYSTEMS

While biomanufacturers have traditionally assumed the small diameter sterile tube welding costs discussed above, MicroCNX Series Connectors now offer a new and cost-effective alternative to traditional tube welding for these sizes. To support decision-making, the total costs associated with tube welding are directly compared to single-use MicroCNX connectors (Table 1).

With this new SUT, users can eliminate the costs associated with tube welding instruments ($15,000 or more per tube welder) and consumables (~$7-$20 per weld) used in tube welding, while only spending ~$15-$20 per MicroCNX connector. Additionally, users save instrument validation, calibration, maintenance, and repair costs.

MicroCNX connectors also significantly reduce the training and operation time. With MicroCNX connectors' simple three-step process, users become proficient more quickly. Our studies indicate that making a sterile connection with MicroCNX Series Connectors is between four and six times faster than an operator using a tube welder, saving ~80-90% in labor costs per weld (Table 1).

Importantly, MicroCNX connectors simplify the sterile connection process, reducing technique-dependent risks and helping to avoid challenges associated with faulty welds, welder breakdowns, or production delays due to instrument downtime.

MicroCNX connectors also can connect tubing of different materials and sizes without adaptors, unlike welders.[4]

MICROCNX® CONNECTORS ASSEMBLY PROCEDURE

PINCH

Remove the protective cover on each half.

CLICK

Join halves and click together.

PULL

Pull membrane strips directly away from the connector.

Table 1: Tube Welding and MicroCNX® Connectors: Total Cost of Ownership

COST	TUBE WELDING	MICROCNX® CONNECTORS
Instrumentation	$15,000 or more	N/A
Blades / Wafers	$5 to $10 / weld	N/A
Extra Tubing	$2 to $10 / weld	N/A
Labor	$5 to $20 per weld (Pre-weld + weld + post-weld)	$1 to $2 per connection
Servicing Plan	Up to $5,000 per welder / per year	N/A
Connectors	N/A	$15 to $20 per connector
Repair / PM costs	$5,000 to $$$$	N/A
Downtime Costs	$5,000 to $$$$	N/A
Operator Error	$$$$	$$$$*

Table 2: Tube Welding and MicroCNX® Connectors: Form and Function

ACTIVITY	TUBE WELDING	MICROCNX®
Training	+++	+
Time	Approximately 4-6 minutes (Set-up, Initiation, Weld, Cure, Tear Down) ~10-15 welds per hour	Less than a minute (3-Steps: Pinch, Click, Pull) ~60 connections per hour
Validation	Annual	One time
Maintenance	Continuous	N/A
Raw Materials	Extra Tubing, Blades/Wafers	Connectors
Difficulty	+++	+
Other Required Tools	Cutting Tool, Carts	None
Tubing	PVC (Terumo Welders), TPE	TPE, Silicone
Tubing connections of different sizes and materials?	Yes, but only with adaptors (Each adaptor requires 2 + additional welds)	Yes
Floor Space	6-10 ft^2	N/A

Conclusion:

MicroCNX Series Connectors are a single-use technology that offers a simple, quick, and seamless solution for connecting small-diameter tubing in closed aseptic systems. Though tube welding has long been the only option, the introduction of MicroCNX connectors into the biopharma market provides biomanufacturers and process engineers with the means to reduce costs and procedural complexity (Table 2). Small-batch biologic manufacturers—like those producing cell and gene therapies, precision medicines, and clinical trial drugs—stand to gain the most from MicroCNX connectors due to the high dependence on small tube connections.

To learn more about the MicroCNX Series Connectors and how they suit your manufacturing needs, **visit us online.** Otherwise, if you have any questions or want to speak with our experts, **contact us** today.

MicroCNX sterile connectors provide a smaller, smarter, and simpler alternative to tube welding to make sterile connections.

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