

# Using Single-Use Connectors to Increase the Integrity of Closed Systems

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Considering the inherent complexity of biologic development and manufacturing and the added business pressures of biopharma's challenging landscape, the margin for error in today's industry is small. That is why minimizing the threat of contamination using a closed system during drug development and manufacturing is critical. Yet, the traditional method for connecting each step in a closed process may present other risks to the integrity of your product. Therefore, it is important you have confidence that the single-use sterile connectors you select meet the sterility and reliability needs of your particular application.

## INNOVATION IN DRUG MANUFACTURING OFFERS INCREASED RELIABILITY

The patent expiration of the industry's top-selling drugs, known as the patent cliff, that shifted the focus to smaller volume, multi-product manufacturing also enabled innovations in how drugs are developed and manufactured.

Traditional methods designed for large-scale manufacturing that typically include stainless steel and reusable equipment are being replaced with new technologies and methods that enable flexibility and process optimization using single-use technology (SUT). These approaches



Laminar Flow Hood

also focus on reducing microbial contamination, which is a major concern for drug manufacturers as well as regulatory authorities. When introduced into a biologic drug product during upstream or downstream processing, microbes can attack the cells, preventing them from growing as well as creating variability and other issues with safety and efficacy of the drug product. Preventing the introduction of particulates is also important, as they are the reason for most recalls of injectable drugs.<sup>1</sup>

Most often, microbial contamination and/or particulates are introduced by operators or the surrounding manufacturing environment. There is always a higher risk of this if connections are made in an open fashion, even in aseptic handling under a laminar flow

hood. Many SUT solutions have been developed to reduce these risks via closed systems, which are assemblies that protect the flow path of the equipment from the environment before, during, and after connection of various single-use processing equipment.

In the early days of connecting single-use process equipment together in a closed fashion, one would traditionally do so using tube welding, which is considered by the FDA to be a sterile connection. In this process, a portion of tubing from each process equipment is placed into a machine from both sides. Next, a hot blade cuts the tubes and then rotates them so that each end of the tubing bonds with the other. The connection is then given time to cool. However, tube welding presents several risks to the drug

product as well as your bottom line. The inherent process of cutting and heating tubing can degrade the tubing ends during welding, potentially introducing harmful extractables, leachables, and particulates into the flow path.

In addition to potential contaminants, there are also operational limitations to the welding process as well. One of which is the material considerations for tube welding is limited to only thermoplastic elastomer (TPE) tubing, which is popular in the biopharma industry but not compatible with silicone tubing. Not only does welding work only with TPE tubing, it typically functions best when each tube set is made of the exact same grade of TPE tubing. Also, users need to specify longer lengths of tubing than is usually necessary in order to reach into the welder and avoid undesired tension. This not only increases material costs but also provides more waste.

In addition, the equipment used for welding requires a significant investment in capital equipment, especially when you consider the need for multiple backup machines in case the primary ones break. If this happens, it must be sent back to the manufacturer, which can take months to resolve, causing costly delays to your manufacturing timeline. In cases where welding needs to occur in hard to reach areas of a facility, such as elevated positions, you must be able to lift the welder and extend tubing to those locations, which not only adds additional expenses but also safety concerns for the operator.

The welding process itself is also very time consuming due to the effort required for setting the tubing up the machine, welding the tubing, and then the time needed for the weld to set, which totals several minutes from beginning to end. This is not an issue when only a few welds must be completed, but in situations where dozens

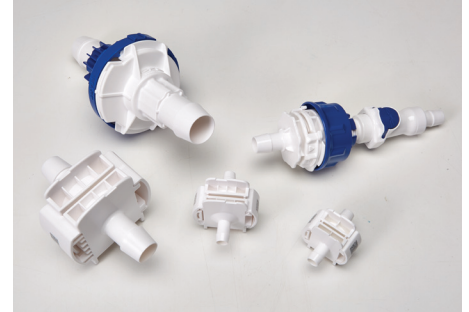


**MPX and MPC - Open connectors**

or hundreds of connections are needed, a significant portion of the day must be set aside to complete all of the welds, delaying production. Finally, the success of tube welding is operator dependent. If it is not done correctly, such as the tubing is not properly aligned prior to welding or the operator pulls on the tubing too soon (post weld) to test the connection, that tension (as well as any presented later during manufacturing) creates opportunities for leaks. The new standard for closed systems has quickly moved away from tube welding to single-use sterile connectors, which offer a quick and easy-to-use method for maintaining flow path sterility and integrity while enabling the protection needed to avoid costly failures from contamination and leaks.

### REDUCING RISKS IN BIOPROCESSING USING SINGLE-USE CONNECTORS

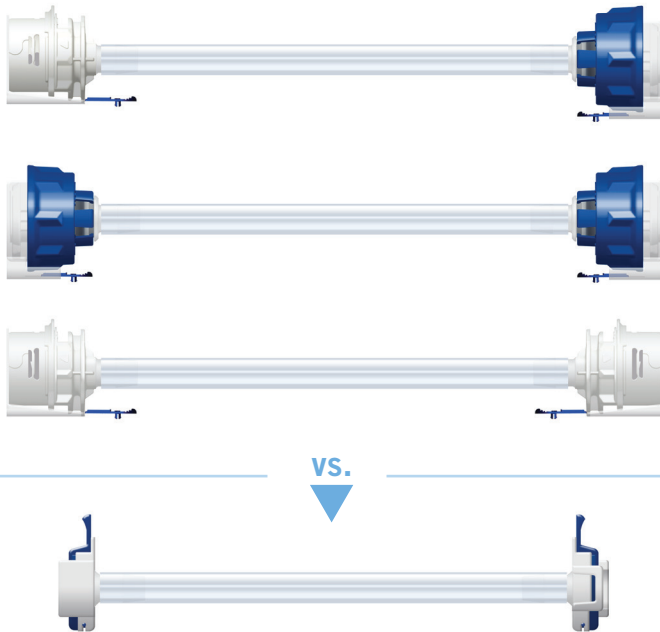
As speed and efficiency become essential in the race to market, single-use connectors can reduce many of the risks associated with tube welding by offering benefits that help drive effective closed system processing. Most importantly, they provide the reliability and sterility assurance necessary in today's highly regulated environment, giving you confidence in your drug product. Their ease of use and flexibility can reduce operator error, which can be one of the leading causes of leaks or contamination on the manufacturing floor.



**AseptiQuik family - Closed connectors**

For example, the simple, three-step “flip-click-pull” method of CPC’s AseptiQuik® genderless sterile connectors provides an easy and quick way to make a sterile connection between single-use equipment. This can be done without the need for clamps, fixtures, or assembly aids, and the robust performance is the same regardless of the size of the tubing. AseptiQuik connectors also feature an integrated pull tab cover that not only protects the connector pre-use but also assists with the proper removal of the sterile barrier membranes. This ease of use eliminates the time and labor commonly associated with tube welding by reducing time per connection from several minutes to a few seconds per connection, giving personnel the opportunity to use their time for more value-add activities.

The rising adoption of single-use technology (SUT) in downstream processing has led to further concern of potential extractables and leachables (E&L) contamination and, as a result, regulatory scrutiny about E&L testing. As part of quality assurance, the FDA requires E&L data in biological license applications. CPC’s AseptiQuik connectors were tested for extractables per the BPOG guidelines and presented an acceptable extractables profile, giving manufacturers information needed to assess the materials of construction for their process.<sup>3</sup> [Visit the CPC website to request a copy of the report.](#)



CPC connectors are also genderless (which means each half is identical and not unique), making them compatible with any single-use venter bag or tubing assembly design. This feature simplifies system integration, further reducing operator error and added costs due to time of installation or delays due to connection issues. It also offers flexibility when designing single-use configurations, facilitating the next wave of innovation of modularity of single-use systems. This modular design allows drug manufacturers to simplify SUT designs and add more flexibility to the process setup at the point of use, which could only be done with genderless connectors. CPC's AseptiQuik family of single-use connectors are offered in ranges from 1/8" ID to 1" ID (which is larger than welding can reliably go) and many connectors can mate different sizes and materials of tubing (something welding cannot do).

Some misconceptions about single-use connectors that have impeded adoption in the past are now being overcome by the reputation they have gained as single-use adoption has increased across the industry. For example, flaws in the reliability of early entrants that impacted manufacturer confidence have since been resolved through innovation by connector experts who focus only on connectors. Additionally, the perceived direct costs of tube welding may be lower than single-use connectors, but they are not reflective of the true cost of ownership when you consider other factors, such as the necessary capital investment, equipment maintenance, extra tubing, and extensive time to weld. Overall, the biopharmaceutical industry has traditionally been averse to change even at the expense of innovation; however, drug manufacturers should consider novel solutions that can give them the advantage they need to get ahead of their competitors.

## FIND A SUPPLIER FOR THE FUTURE

As you consider implementing single-use connectors, look for connector suppliers that specialize in connector technology and feature a market-neutral supply through the global single-use OEM network. This gives you the freedom to work across the entire network of single-use suppliers as well as take advantage of consistent pricing and lead times to secure a continuous supply of equipment for the lifetime of your product. Security of supply is critical, especially as unpredictable factors like natural disasters and the unknown impact of COVID-19 can potentially hinder your production. A supplier that invests in extra capacity and redundant manufacturing to ensure capacity before it is too late demonstrates they value your success as much as their own. Finally, suppliers with a concentration on connector technology know their success relies on the dependability of their technology. Those with a wide range of product offerings may not have the focus you need to make sure their connectors are keeping pace with the industry and its ever-changing needs.

### REFERENCES

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**Confidence at Every Point of Connection**

