

The path to genderless connectors: How genderless sterile connectors lead to more flexibility, faster changeovers and reduced costs.

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Genderless sterile connectors — with their ability to interconnect with each other without male/female limitations — can enhance the flexibility of single-use systems in a wide range of bioprocessing applications. Genderless connectors reduce system complexity, which in turn lowers requirements for inventory management, simplifies operator training and reduces misconnections in the manufacturing suite. In fact, it's possible this new connector design will drive industry change similar to the transition from stainless, reusable systems to single-use. How can something as small as a tubing connector have this impact? The answer starts with a bit of history.

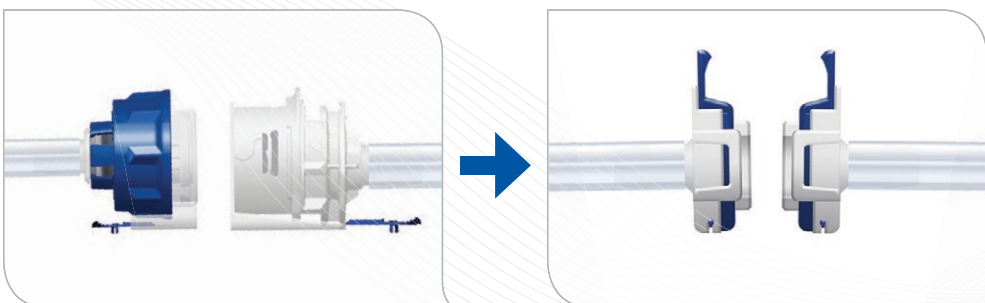
Bioprocessing began with reusable stainless steel systems, purpose-built processing plant schemes with steel vessels and permanent connecting piping. This plant approach offered large-scale biopharmaceutical manufacturers the ability to process larger quantities of product, but the downside was twofold: the cost and time associated with building these processing plants and the difficulty of making process changes once the plants were constructed.

As the industry grew, so did the pressures on biopharmaceutical manufacturers to develop more and different drugs, to bring them to market faster and to reduce costs. Something had to change to facilitate shorter production runs with more changeovers. Single-use systems, consisting of bags, tubing, connectors and filters, delivered the operational flexibility needed to meet

industry demands. One of the benefits of single-use connectors is that design manufacturers can purchase them clean and presterilized, effectively “outsourcing” the cleaning and sterilization activities required in a traditional stainless steel operation. This not only reduces validation and operations expenses, it also improves the speed and safety of drug development and delivery.

Single-use initially gained acceptance in sterile cell culture media and process buffer storage applications, where the first sterile media bags were used. Following this, engineers developed single-use bioreactors that have quickly moved from research and development labs into pilot plants and production facilities. To illustrate, a recent online survey reported that 50% of respondents agreed stainless steel pilot-scale 50L to 500L bioreactors/fermenters are increasingly obsolete due to the emergence of single-use pilot-scale solutions (*Aspen Alert*, April 23, 2015).

For many research and small- to medium-scale operations, single-use systems are the way to go. These facilities need the ability to easily add new products to the mix, rapidly convert processes and quickly make process adjustments as needed. Large operations are also seeing the benefits of incorporating single-use systems, and hybrid systems (a mixture of stainless steel components with single-use components) are popular alternatives for manufacturers with existing



stainless steel equipment. Regardless of size, all bioprocessors need to be able to adapt processes and execute changeovers while meeting required time-to-market and efficiency goals. There are also a number of drug and contract manufacturers focusing on internal projects to standardize single-use designs across their processes and facilities to reduce the complexity of single-use systems manufacturing.

This brings us to tubing connectors, an often overlooked but critical component in single-use and hybrid bioprocessing systems. Single-use systems need secure, reliable, leak-free connections between various components and processes. These connections are used in conjunction with the silicone or thermoplastic tubing that serves as inlets and outlets throughout a processing system. Single-use connectors can be the first and last line of defense in a single-use system. Even with the best bag, the best filter and the best tubing, it is all pointless without a reliable and robust connector.

HOW GENDERED CONNECTORS LED TO THE ADVENT OF GENDERLESS

While gendered connectors have been a key building block in the implementation of single-use technology, using typical gendered connectors can lead to unintended consequences that genderless connectors eliminate. Here are some of the real-world problems behind the development of genderless connectors:

Mating issues

Many processors can relate to the frustration of getting different single-use systems from multiple suppliers with the same gender connections (one system comes in with a male half, and the other system also has a male half). The inability to connect system halves is particularly frustrating because the problem often goes unnoticed until the point of use. This means the user has to quickly create some sort of adapter piece to go between the two systems because the connection is needed *now*.

For instance, if a processor received the two systems as described above (each system with

a male connector half), he or she would need to obtain two female connectors, a short piece of tubing and something to secure the tubing to the connector (i.e., cable tie, barb retainer, etc.). Then the processor would need to assemble the two female halves to the tubing, secure the tubing, and autoclave the final assembly in-house. This time-of-use jerry-rigging leads to several negative impacts for the processor:

- Adds material and labor costs to create the adapter assembly
- Adds labor costs to assemble the adapter
- Adds costs for autoclaving the assembly in-house
- Delays the usage of the single-use systems until the adapter has been created and sterilized
- Introduces additional risk of leaks or contamination

Another way to deal with the same-gender issue is to use a connector adapter, such as the back-to-back adapters available from CPC (see figure 1). However, this solution requires anticipating the problem — and adapters are not presently available for gendered sterile connectors.

Inventory issues

Any time a component requires a specific mating component, finished-goods inventory needs can more than double, or even triple. As an example, consider an assembly as simple as a basic transfer line with sterile connectors on each end. There are three possible configurations depending on the application set-up: a female-to-male version, a male-to-male version and a female-to-female version (see figure 2).

Figure 1: MPC/MPX back-to-back adapters give end users the flexibility of connecting single-use systems that feature identical coupling connections at the end of their tubing.



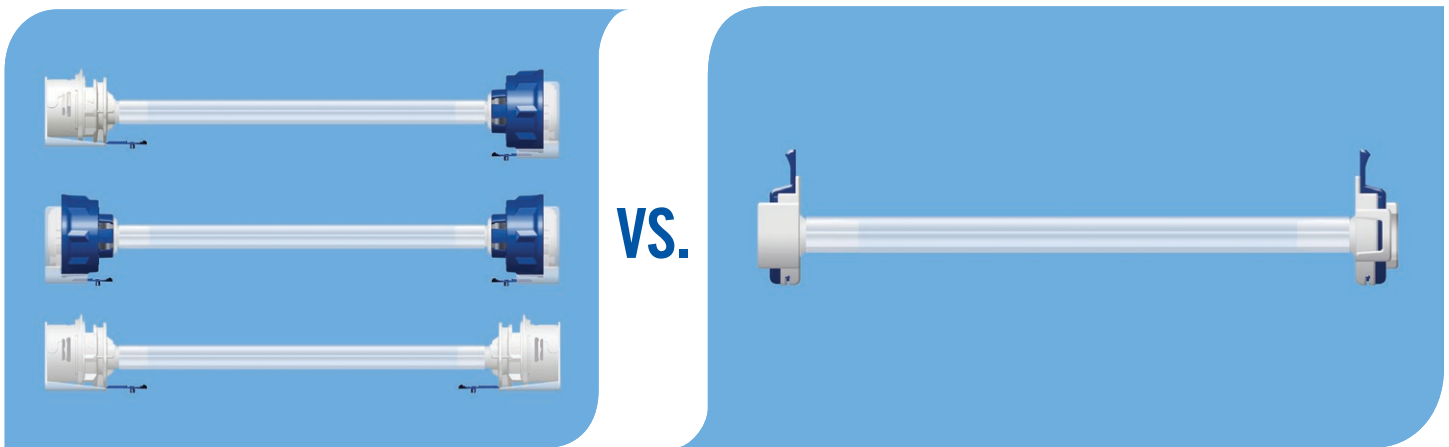


Figure 2: Female-male, male-male and female-female tube sets generate three times the SKUs as genderless tube sets, adding inventory costs and increasing complexity. In contrast, genderless connectors enable stocking just one tube set.

Other inventory issues include:

- Increased ordering complexity because the processor needs to define which tube set works with which part of the application
- Greater demands on single-use systems manufacturers because they need to be able to produce and stock three different assemblies
- Longer lead times because systems suppliers are making lower volumes of multiple SKUs as opposed to higher volumes of one SKU
- Increased stocking requirements for end users

In contrast, using genderless connectors on the same tube set results in only one possible tube set.

MOVING FROM GENDERED TO GENDERLESS STERILE CONNECTORS

The inherent simplicity of genderless sterile connectors is easy to grasp, but the idea of transitioning to genderless raises questions from systems designers and processors. Here are some frequently asked questions:

- *What obstacles might I encounter when transitioning to genderless connectors?* One obstacle can be the design of the genderless connector itself. It is critical to select a connector that is truly easy

to use, robust and does not require additional hardware to assemble. Some connectors are not easy to use because they require many assembly steps to make the final connection; the more steps there are for assembly, the higher the chance an operator will make an error. If the connector requires hardware not integral to the connector to secure the connection (e.g., tri-clover clamps), operators can misplace or forget to install the added components. A reliable connector should not need additional hardware, and an easy-to-use, robust connector has the greatest chance of being used correctly.

- *What needs to change in my facility to make genderless connectors work?* If a processor is already using another connector, the biggest obstacle is the change control process. Even though something can be significantly better and provide efficiency savings, the process of revalidating a new connector can be cumbersome and slow. Once validated, however, the change to genderless connectors usually results in process improvements, cost savings, reduced training requirements and fewer quality issues on the manufacturing floor.
- *Can I mate two genderless halves that have different hose barb sizes?* Yes, as long as the connectors are

from the same product family. CPC's genderless design allows this type of connection. For instance, one side with a $\frac{3}{4}$ " hose barb can mate with a $\frac{1}{4}$ " hose barb on the other side. This also includes mating a $\frac{3}{4}$ " sanitary to a $\frac{1}{2}$ " with a hose barb. This capability eliminates the need to install reducer fittings somewhere else in the system, an extra step that increases component and labor costs.

- *Are genderless connectors a step toward standardization?* It is next to impossible to attend a conference on single-use without hearing about standardization. While standardization can cover several topics, one of the most common discussion topics is connector compatibility (e.g., interchangeability). Research reported in "BioPlan Associates, Inc., April 2014, Biotechnology Industry Council™ Analysis of Single Use Connectivity" showed that 88% of respondents viewed standardizing connector compatibility as important. This same study reported a 73% preference for genderless connectors over gendered connectors. End users are identifying easy-to-use, robust genderless connectors as an answer for both standardizing single-use systems and eliminating many of the headaches experienced at facilities using single-use technology.

APPLICATIONS FOR GENDERLESS CONNECTORS

Genderless connectors can be utilized in all transfer applications where gendered sterile connectors are found, including suite-to-suite, seed train and formulation/final fill. The difference is that genderless connections significantly reduce system complexity in all of these processing applications. Because component configurations within transfer lines vary as much as the options for tubing, connectors and filters, viable connection technologies require flexibility. Multiple termination options provide the flexibility needed to meet today's mounting and flow requirements. For instance, a basic transfer line could be as simple as silicon tubing with two genderless sterile connectors, or it could be more sophisticated, incorporating tubing, SIP connectors, sterile connectors and sterile filters.

When changeovers need to occur, end users can pull stock and connect components and processes with genderless connectors, resulting in increased flexibility. No matter the processing stage, genderless connectors for maximum flexibility.

CONCLUSION

Just as single-use technology emerged in response to market demands, so too have genderless single-use connectors. Systems designers and processors have maximized the benefits of single-use and hybrid processes — those of increased flexibility, faster changeovers and reduced costs. Now the bioprocessing industry can also benefit from the reduced components complexity afforded by genderless connectors.



CPC's interchangeable AseptiQuik® genderless connectors enable tubing transitions between tubing of different sizes, from 1/4" to 3/4" flow.



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. Sterile fluid connections from CPC are available in a complete range of 1/8- up to 1-inch flow configurations.

Smart fluid handling to take you forward, faster.