# Maintaining Aseptic Processing Through Effective Transfer Solutions

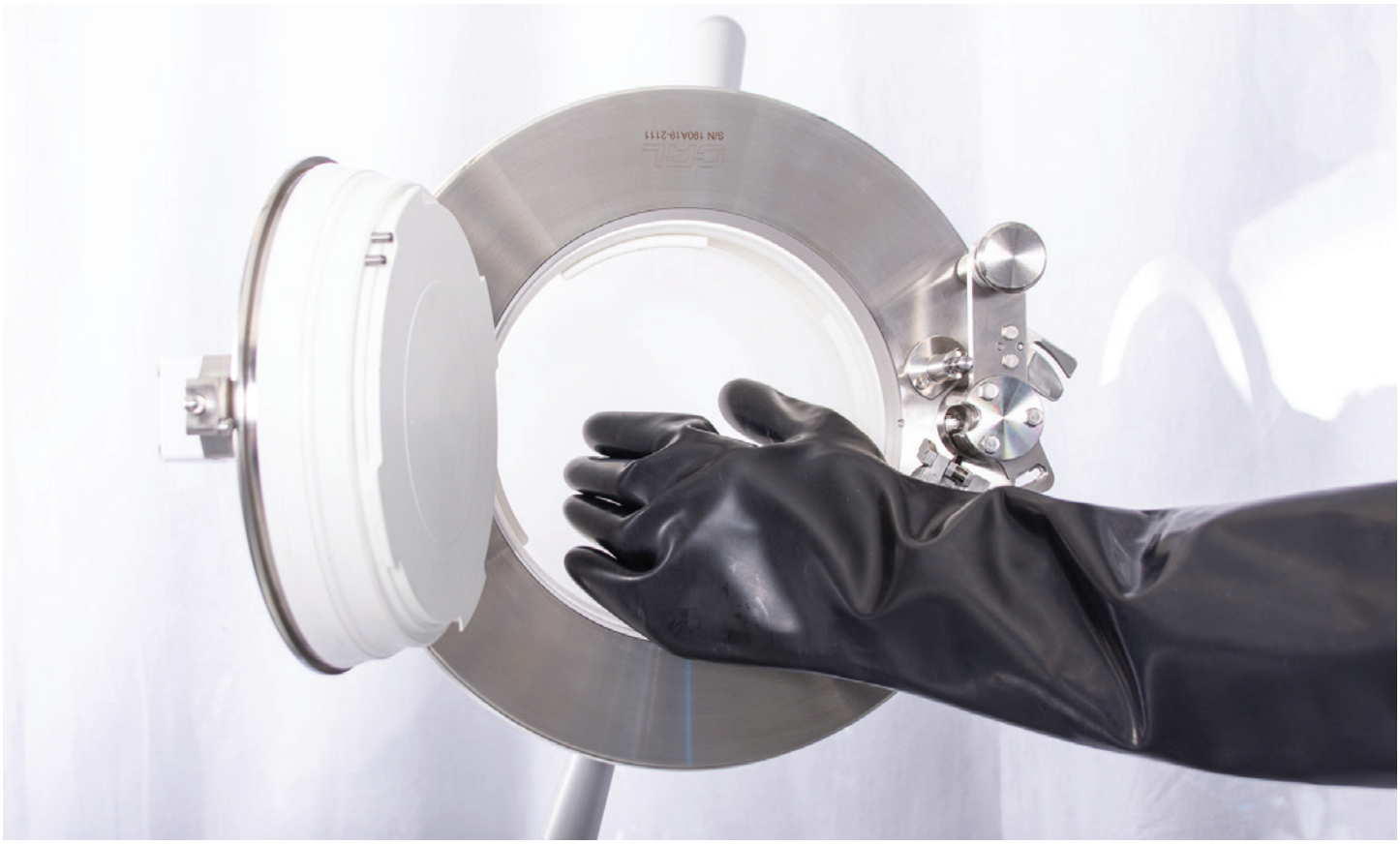
## AN ENHANCED FOCUS ON STERILE ENVIRONMENTS

Over the past several years, a wave of impressive novel medical therapies has launched into the market. These therapies have positively impacted the lives of patients suffering from rare and common conditions all over the world, and they have dramatically changed the approach to developing new treatments. For decades, drug development was dominated by pharmaceuticals derived from synthetic compounds. More recently, the industry has shifted toward biologics (i.e., therapies derived from living organisms). Developing and manufacturing biologics presents new challenges, including an enhanced focus on sterile materials and environments. Accordingly, more biotechnical, pharmaceutical, radiopharmaceutical, and contract manufacturing organizations (CMOs) rely upon the use of containment systems (i.e., isolators) for research and commercialization of therapies. This evolution has caught the eyes of regulatory entities like cGMP, FDA, and the U.S. Pharmacopeia (USP), to name a few. Nearly all of these bodies have revised (or will be revising) policies to provide additional clarity around best practices for the manufacture of sterile medicinal products. These updates reinforce the use of isolators and improved cleanrooms.

An increased focus on aseptic processing has resulted in an explosion of the types of isolators available on the market. In recent years these isolators have grown in complexity and specificity. Modular, pop-up, small-batch, custom, and automated isolators are all available today. By design, containment systems encourage sterility by restricting airflow and moisture while limiting human interaction. Sometimes, though, items must be moved into or out of the isolator. That's where transfer systems come in. These systems make it possible to aseptically transfer items like tools, waste, supplies, and byproducts or yields before, after, or mid-campaign.

## TRANSFER SOLUTIONS

One type of transfer system that is growing in use is the Rapid Transfer Port (also known as RTPs or Alpha-Beta transfer assemblies). RTPs are versatile, ease to use, and effective at maintaining sterility. Manufacturers like Getinge, Sartorious, Atec, and Central Research Laboratories (CRL) offer RTP-type solutions. Typically, RTP systems consist of two main components: the Alpha assembly and the Beta assembly. Each has a door,



seal, and, often, an interlock function. The Alpha assembly is mounted in an isolator wall, and the Beta assembly is mobile and used to transfer the materials. When the two assemblies are mated, materials can be rapidly transferred into and out of an isolated environment without breaking containment. The interlocks can provide an added measure of safety and sterility by helping protect against the Alpha door opening when a Beta assembly is not fully docked. RTPs come in several sizes, materials, and configurations; and serve various purposes from liquid transport to connecting one isolator to another. Common RTP sizes are 105mm, 190mm, 270mm, and 350mm.

One potential challenge with RTPs is the Area of Concern (or Ring of Concern), where the Alpha door and the Beta assembly meet. This area could potentially become contaminated after repeated use with insufficient cleaning by the user. There is also a chance that transferred items could graze the Area of Concern and bring contaminants into the isolator. Users should pay close attention to this area, and issues can be mitigated by employing proper procedures and equipment. Common methods of addressing the Area of Concern include: covering the sealing surfaces with contained transfer funnels or sleeves; Standard Operating Procedures (SOPs) developed by the user and that mandate periodic cleaning; and choosing an Alpha port, such as CRL's Sterilizable Rapid Transfer Port, that allows for heat sterilizing of the sealing surfaces.

Alpha ports have variable configurations that depend on the manufacturer and the specific application. Even more variability is seen in Beta assemblies. Beta containers are reusable, sturdy, come in several sizes, and make it possible to transfer a wide variety of items. Autoclavable Beta containers provide added convenience by allowing items to be autoclaved while inside of the container before it is docked. This helps ensure sterile components are transferred into the isolator. RTPs are also available to move sterile fluids into isolation. The CRL Sterile Liquid Transfer Port (SLTP) system was developed to connect a bulk product tank to a SLTP Beta Flange. That flange is first docked to a Steam-In-Place (SIP) docking plate for sterilization. The tubing and components needed inside of the isolator can be sterilized in an autoclavable Beta container and transferred into the isolator. The SLTP Beta flange can be docked to a CRTP Alpha with a liquid transfer door, isolator-side connections made, and product tank filled to transfer the sterile liquid. The result is end-to-end sterility without breaching containment.

Another development in the RTP space is the proliferation of single-use technology. Today, you can find single-use Beta bags in a myriad of sizes and configurations and that

Single-Use Beta Bag docked to
Clean Rapid Transfer Port (CRTP)

transfer just about anything. The previously mentioned manufacturers (among others) provide these bags. CRL manufactures a Single-Use Beta Bag composed of Tyvek and HPDE to transfer tools, components, or powders via Alpha ports. These specific bags are compatible with CRL and DPTE® XS Alpha Ports to provide additional product flexibility. Some single-use Beta bags are also designed to transfer fluids. These types of bags incorporate disposable tubing and connectors to move fluids from various areas of a cleanroom into isolation.

There is no universally correct choice when comparing reusable Beta assemblies with single-use Beta bags. Beta bags have grown in popularity because they reduce the risk of cross-contamination, startup costs, cleaning requirements, and can provide more campaign flexibility. That said, the difference in performance between a rigid vessel and a flexible bag may make one a more obvious choice for an application. The great thing about RTPs is that users have the flexibility to use both depending on their specific requirements.

Rapid Transfer Systems have become a popular method of transferring items in an era where containment systems are needed more than ever. As drug development and manufacturing continue to evolve, aseptic processing remains critical to the commercialization of new medical therapies. Rapid Transfer Ports can provide the flexibility needed for this critical work while helping maintain the sterility and containment required in isolator and cleanroom environments.

## ABOUT CRL

CRL is a leading provider of innovative remote handling, transfer, and containment solutions. We design and manufacture industry-leading technology to help you safely and efficiently handle sterile materials. With 75 years of product expertise, our flexibility and customization provide the best solutions and deliver high-quality technology you can count on, including Telemanipulators, Glove Ports, and Transfer Systems, including Rapid Transfer Ports and Single-Use Beta Bags. For additional information visit crlsolutions.com.

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