



# Gloveless or less gloves: Reframing the “hands-off” isolator debate

As fill-finish automation continues to make exciting progress, the question of how best to implement automated solutions in an isolator setting continues to be raised, specifically as it relates to gloved vs. gloveless applications

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**T**he topic of fill finish automation raises some important questions in modern pharmaceutical settings. Specifically how this relates to gloved vs. gloveless applications.

Broadly speaking, the benefits of aseptic operation within an isolator setting are clear. In many cases, it's economically prudent over the life of an operation to run fill-finish processing in an isolator as opposed to lesser barrier settings. From a sterility and compliance standpoint, isolator technology is the obvious choice; regulatory standards, such as the latest Annex 1, reflect this reality. The drive towards greater sterility is a foundational and guiding principle in the pharmaceutical industry, and

one trend that has remained consistent over the decades is that if there's a path towards greater sterility assurance, the industry will follow it as quickly as technological advancements allow.

This motivation is what makes the current moment in isolator technology so intriguing. It's well understood that whether through direct interventions or pre-handled equipment introduced into an aseptic setting, human beings are the single biggest threat to sterility in the fill-finish process. Without exception, any aspect of the fill-finish environment or process that can be successfully automated lessens the overall risk of loss in an operation and raises product quality standards. And while in a perfect world, a gloveless solution would be the ideal choice,



imperfect functions and unanticipated events will always exist and require that operator interventions, both planned and unplanned, be forecasted. The choice then between gloved and gloveless centres on the tension between what's possible and what's practical, and an honest conversation about how we get the most out of various automated solutions.

And if practical, real-world scenarios are taken into account with the wide array of circumstances and obstacles possible, perhaps it's not an either/or choice. What if the path forward isn't a matter of "gloveless" per se, but rather a matter of less gloves?

### Considerations for gloved isolators

Gloved isolators are designed to run without human interaction, but even the best machines will require intervention at some point. The logic of a gloved isolator design accounts for planned interventions like changes in the environmental monitoring system or introducing sterile equipment into the fill line. Glove ports are also useful in corrective actions and certain non-qualified machine emergencies. When a batch worth millions of dollars per vial stops due to an easily fixable problem, for example, you don't want to be George Costanza standing on the outside of the vending machine, yelling at the candy bar to "jump!" when you are entirely unable to do anything about it. These types of inevitable scenarios illustrate both the good sense of a gloved isolator for certain operations and an area where gloveless isolators have substantial room to further demonstrate proof of concept.

For a gloved isolator, having comfortable and easy ergonomics is key. Making your operators' jobs easier by having procedures in place to dictate when an intervention is allowed and what types of interventions are permissible is essential. A poorly designed glove port offers all the dexterity of a high school mascot costume, and that sort of inconvenience hampers operational productivity at best and, at worst, causes riskier interventions that require sterility protocols to be repeated. Having the ability to intervene or work ergonomically and aseptically—without introducing contamination or violating first air—should be a high priority on par with efficiency.

That being said, the limitations of gloved isolators are well understood. Any iteration of a gloved isolator comes with substantial cGMP protocols, as an ingress into isolator space can represent a potential pathway for contamination. Annex 1 specifies that inspection and maintenance of gloves and glove ports should be conducted at frequent intervals. In practical operational terms, this includes a thorough preventative maintenance program, routine performance of glove integrity tests, visual inspection of gloved areas with every use, and frequent glove replacement that makes sense

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## It's economically prudent over the life of an operation to run fill-finish processing in an isolator as opposed to lesser barrier settings

within the scope of the operation. A successful QMS approach depends on the accuracy of these procedures and the diligence of the operator. Many of the recent advancements, whether it be material use or quality control measures like glove testing technology, have only improved sterility and validation protocols.

### Hands-off interventions: Gloveless aspirations vs operational realities

Gloveless solutions have been a focal point of the latest developments in isolator technology as the industry looks for viable, accessible advancements towards greater sterility assurance and product quality. The crux of the discussion is what a gloveless solution actually can and cannot accomplish in an operational setting. A gloveless isolator may reduce human interventions, but can it eliminate them completely? They may reduce risk in some areas, but if we eliminated every glove port from an isolator, would that equate to the low-risk solution some thought it to be?

The most important questions to consider in any fill-finish setting include how precisely you will handle planned and unplanned interventions. Automating in such a way that you can optimize the most sensitive of routine operations and anticipate the best interventional solutions to maintain operational uptime is paramount. This is one essential area where the practical application of a gloveless isolator runs into limitations, but the overall push toward automation has been a clear net positive. It's one thing to say you have a gloveless solution—it's another thing entirely for robotic tools to have demonstrated competence in the full breadth of possible interventions needed in an operational context. A gloveless isolator is only as good as the quality and scope of the automation it offers, and even the best automation has a risk of failure, however small. And if any sort of failure is possible, then the actual choice isn't between "glove and gloveless" but between a glove port and a door. The question then becomes in what sterile setting is it appropriate

# containment pharmaceutical

to open a door? The answer is never. In a manufacturing context, sacrificing a batch in the name of gloveless convenience is simply not an option.

## Regulatory trends towards automated solutions

It's been said the perfect intervention is the one you don't have to perform. This attitude is the impetus behind our industry's push to reach more stringent quality standards and is always the goal of an aseptic processing operation. A point of emphasis in the new Annex 1 is utilising better barrier systems and advancements like robotics and automation where feasible to improve overall sterility assurance and reduce instances of human intervention. Much like the regulatory push towards the use of isolators, as technological advancements provide a path towards new possibilities in product quality and reliability, regulatory standards will be reevaluated. As automation is a clear prerequisite to effective isolator arrangement, Annex 1's highlighting of robotics, automation, and rapid solutions should be noted. As technologies like telemanipulation continue to improve in the application of routine and non-routine interventions, it stands to reason that regulatory emphasis on automation will continue.

## Automation strengthened by gloved redundancies

How then should we proceed if our goal is to offer fill-finish professionals the best, most effective solutions that are regulatorily robust?

What operators are looking for, and what regulations like Annex 1 are speaking to, is a

focused quality-by-design approach that leverages solutions, automated or otherwise, to design out risk and design in quality. This means innovating for the sake of effectiveness and not getting lost in the realm of ideas. We don't want our automated solutions becoming the proverbial knife slicing the soda can in half—that's the wrong type of cutting-edge. The goal should be advancements that can be implemented seamlessly into an improved containment control strategy while prioritising the safety and viability of whatever sterile parenteral product is being produced. This approach includes the use of precisely engineered robotics and automation, simplified designs that minimise the likelihood of mechanical failures, and using appropriate troubleshooting tools and failsafes for unplanned interventions. In this respect, there are a myriad of situations where a well-placed, well-designed glove port is a key to strengthening automated solutions and sterility practices rather than a hindrance.

That's why at AST, our mission is to provide robotic and automated solutions designed and optimised to meet the real-world operational realities of fill-finish manufacturing while envisioning a future where greater sterility and product quality are possible.

As we push towards innovative ways to strengthen aseptic processing, and as advancements continue to unveil new possibilities, the considerations laid out here on the most effective ways to integrate automation and isolator technology are ones that fill-finish professionals industry-wide must continue to revisit.

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