Steven Ng | AST

Cleanroom containment expert AST's CTO and VP of Customer Service, talks about the creation of the company's new isolator technology and how the industry trends and pain points were taken into account

Written by Sophie Bullimore

In the last year, US-based AST has launched a new isolator solution for fill-finish in pharmaceutical manufacturing. Speaking to cleanroom containment expert's Chief Technical Officer and VP of Customer Service, Steven Ng, there was a lot of time and expertise that went into the creation of this new product.

For Ng, his expertise comes from education and experience. The CTO trained in Microelectronics and Physics, so has a background grounded in a "scientific approach to challenges". The hands-on executive, who has worked around cleanrooms for over 25 years, even has a patent to his name for "Method and System for Vacuum Stoppering".

"This was a very exciting collaborative moment for myself and others at AST who are included on the patent," Ng says. "We identified early on in our aseptic processing work that while the conventional methods for stoppering were effective, specifically vacuum piston placement, there were issues with a stoppered product becoming gaseous over time, otherwise known as developing headspace."

Ng explained that this was often due to piston placement accuracy and that this can be particularly problematic for fragile, high-value products like ATMPs. "What we developed at AST was a mechanically assisted, multi-stage vacuum stoppering process that achieved a precise stopper depth without compromising the shape or structural integrity of the stopper (an issue common in mechanical insertion methods)."

This multistage process effectively eliminates the potential for headspace, maintains the hermetic seal and ensures product integrity, Ng adds.

And this sort of innovation is what Ng loves about his job. He spends his days talking to clients about projects, as well as overseeing R&D for new technologies. "There's nothing quite like seeing an idea identified, workshopped, refined and then designed and built, that results in a robust solution in the hands of our customer. That process is extremely gratifying."

Two heads are better than one

AST did not work alone on its most recent isolator design, however. At the end of 2023, the containment expert announced its collaboration with US-based cleanroom design and build expert Germfree on a new fill-finish isolator.

At Interphex 2024, the product of this collaboration was unveiled for the first time, following over a year of hard work from the two teams.

"Our engineering teams worked hand in hand throughout the process," Ng explains. "The overall construction of the isolator as well as the design of the tech housing were just a couple of areas where Germfree contributed their expertise."

At the end of the day, Ng explains that the overall momentum of pharmaceutical manufacturing is always trending towards greater sterility assurance. So this is what the two companies had to focus on.

AST also later worked with CURIS System on an automated decontamination solution for the isolator, which is a huge leap in technology.

> **The exterior of the isolator avoids protruding features such as hinged handles and large external mechanisms**

The design process

An aspect of design that was given a huge amount of consideration was the actual problems that manufacturers run into every day. "We have an ongoing conversation with our customers to understand where they're at," Ng says. "This isolator is a direct result of cataloguing their feedback about what they would like to see out of a barrier technology solution and some of the biggest pain points they face in day-to-day operations."

Ng says that the team innovated from a place of "why not" instead of "why". They asked themselves questions like: "Could maintenance processes like HEPA filter change out be simplified; could more efficient, shorter decontamination protocols be implemented; and could lead times be improved?"

Once these questions were considered, Ng and his team then looked at the other priorities of efficiency, environment, and usability.

"Annex 1 spotlights and encourages a quality-by-design approach," Ng reminds. "This takes into account quality management and contamination control strategies, with a specific emphasis on automation where both those categories can be improved.

To make sure that the new isolator took care of both these new Annex 1 concerns, as well as the customers' pain points, Ng and his team used modern methods to create an elegant solutions. "We employed extensive design approaches, including CFD analysis, to troubleshoot common issues inherent to isolator design," he says.

"A clear, comprehensive solution began to materialise!" he says.

First Air

So what did all of this planning create? Ng explains the main changes surrounded a small footprint, semi-automated maintenance and operations functions, as well as leak monitoring and a new glove testing platform.

He explains that one of the main technical specification that was prioritised was First Air and sterility assurance from the onset. "This was even down to small, intentional details like our side-hinged doors designed to not block laminar airflow," he explains.

Ng adds that other design advancements like this included a new glove tester which is interlocked and tied to start-of-batch procedures and RTP ports that require no gloved/ergonomically-challenged ingress and can be completely open and closed from the outside of the isolator.

Cleanability

With sterility assurance as the main priority, cleanability was essential to design in. Ng says that the design priorities both and accessibility to aid it.

"We've avoided incorporating bulky, difficult-to-clean elements, which can be found in other designs," he explains. "The exterior of the isolator avoids protruding features such as hinged handles and large external mechanisms. The isolator doors have magnetically latched handles that can be easily cleaned and the mousehole doors are completely removable, with no external mechanisms or tubing."

He then explains that this commitment was carried over to the interior of the isolator, which has ample space for the operator to move around, avoiding hard-to-reach areas. "In our minds, these were clear, practical improvements that needed to be made," Ng says.

This is also where the AST's cooperation with CURIS System comes in. "Our new low concentration hydrogen peroxide solution (from our partners at CURIS System) will be integral," Ng says.

This new automated technology not only offers one-touch automation, but fully integrates across systems. "This equates to a turnkey aseptic processing solution where the barrier, fill line and decontamination technology all are run and monitored through a single, centralized HMI, a significant operational improvement," Ng adds.

Lead times

Lead times is a buzzword in pharmaceutical manufacturing in all aspects. The status quo lead time for fill-finish isolator manufacturing and delivery can average anywhere from 1-2 years.

So it was a main goal of Ng's to reduce this.

Domestic design and production in the US was a key part of this. "That type of value and benefit hasn't been accessible to the fill-finish isolator market in recent years," Ng says.

This localised model for supply and service not only reduces lead times, but allows "an elevated level of responsiveness throughout the life of the technology," Ng points out.

Maintenance

One of the biggest point pain points for isolator manufacturers was HEPA filter changeouts.

Ng explains that changing out air filters typically is time-consuming, requiring at least

two operators, and must be installed by manually tightening bolts. "Filters are also known to be large and awkward to handle," he adds.

With the installation being that difficult and involved, Ng explains that there's also a prevalent risk of tearing the filter during the process. "To address this, we're implementing a new approach that leverages custom-made bag-in bag-out filters with automated sealing that makes this common maintenance process significantly easier."

As such, a single operator can simply set the filter in the corresponding grooves, and the seal will be initiated pneumatically once prompted through the HMI. Ng states proudly that the removal and installation of a filter can be executed in just over five minutes by a trained operator.

Ng and his team have also improved the diffuser membrane placement and installation. "Operators simply place an air distribution membrane in corresponding brackets," he says. "Once placed, magnetic clips will support the air distribution membrane and prevent it from falling, as operators complete installation. This approach saves time and helps conserve fragile membrane fabric."

This approach saves time and helps protect the fragile membrane fabric by eliminating the manual use of tools.

Another new feature to avoid unnecessary maintenance workload is that the glove ports were specifically designed by the team for no-tear installation. "Beyond making that process more durable, we've improved the construction of glove ports as a whole with stainless steel fittings and designed them in concert with a comprehensive glove testing solution," Ng adds.

Is the industry excited?

Ng says the team and the industry are excited to see the isolator in action, as well as a sense from the sector that the new advancements are needed and long overdue in the industry.

And the industry can be excited for a long time, as sustainability was built into the design in durability. "Our commitment to quality isn't just about performance, it's about durability. We don't want to just build things that work, we want to build things that work for a long time," Ng says.

Ng also reveals that his team's momentum won't stop hear. "We have plans to make it more automated, include additional failsafes, implement even faster turnaround times, and continue to simplify user operations."

"Taken as a comprehensive solution, there's not a product like it currently in the marketplace," Ng enthuses. "When you consider both the manufacturing and supply realities of the past few years, and the current demands in the liquid pharmaceutical market, this isolator is designed to meet customers where they're at today and serve them well into the future." ■

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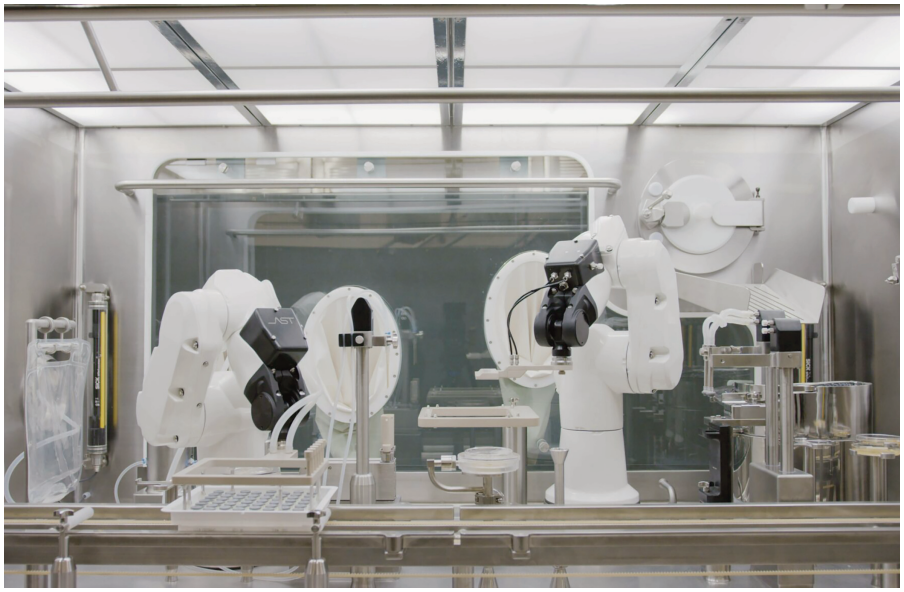

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