SA25 aseptic filling workcell

ADVANCED AUTOMATION FOR THE RAPID DEPLOYMENT OF FLEXIBLE FILLING

Designed to address your needs for flexibility, contamination control, and speed to market, the SA25 aseptic filling workcell (Fig 1) is a standardized gloveless workcell in which specialized robots fill then close nests of vials, syringes, or cartridges.

Advanced automation combines every aspect of the aseptic process. Without human intervention—the greatest potential contamination source—processes are consistent, repeatable, and carry less risk to the product.

Our workcell technology provides:

- Built-in scalability, flexibility, and adaptability essential for companies looking for flexible production capacity, with the ability to scale up with additional workcells, or to switch the capacity to other products.
- A standard aseptic filling machine that provides consistency and repeatability without the risk of human operator intervention.
- Minimal human involvement and reduced operator requirements by integrating the process within a gloveless barrier.
- Simplified setup and process that reduces the operational complexity of traditional pharmaceutical production lines.
- Configurable environmental monitoring capabilities which integrate real-time monitoring systems that enable monitoring of viable and total particulate in real-time, providing risk reduction and increased process knowledge.
- Simplified material handling using industry-standard nested containers and closures, which results in less risk to product through particulate generation or human intervention.

Fig 1. SA25 aseptic filling workcell.

The SA25 aseptic filling workcell—a gloveless isolator—is a cutting-edge product for the fill/finish of injectable medicines. This workcell integrates several proven technologies including robotics, nested containers and closures, as well as automated environmental monitoring. When compared with conventional isolators or restricted access barrier system (RABS) production lines, you can achieve greater agility, allowing you to produce many products in different container formats.

The idea of the workcell comes from the semiconductor industry, where significant productivity and quality gains have been made using standard robotic workcells.

Gloveless means no human intervention

Our workcell is called 'gloveless' because it doesn't have glove ports through which operators can intervene in the production process. Conventional systems need glove ports because problems occur that can only be corrected by operators. Removing gloves addresses the number one source of microbial and nonviable particulate contamination: human operators.

Using robots that are fully integrated into the aseptic process for material handling (Fig 2) creates a unified process and makes it easier to configure systems for different filling formats. A holistic design entirely based on robotics means human intervention is removed – leading to greater aseptic assurance. Robotic precision and strong process control through automation creates a highly programmable system. When a fully integrated robotic filling system is designed and built to utilize all robotic capabilities, everything works together in a highly repeatable and controllable process.

Fig 2. Robotics in motion inside the SA25 aseptic filling workcell.

Standardization and speed to market

Our SA25 aseptic filling workcell is a standard product with the built-in flexibility to fill and close multiple container types including vials, syringes, and cartridges. As such, it can be built quickly and represents a scalable platform on which manufacturers can ramp up their operations to meet demand. It's possible for you to reach GMP production within 15 months after purchase.

By using presterilized, ready-to-use nested containers and closures, the SA25 aseptic filling workcell requires minimal part changes in order to switch between containers. Containers are handled, filled, and closed entirely within their nest. Robotic handling, a closed isolator, and new container/closure methods mean that the SA25 aseptic filling workcell doesn't have conveyors, mouse holes, vibratory bowls, or other sources of possible biological contamination and/or particle generation. Using nested containers and closures removes the need for several pieces of supporting equipment. There's no need for a washer or depyrogenation tunnel. This removes a capital expense, qualification and validation, as well as associated staffing and energy costs. With low downtime between batches, it can be effective for both clinical and commercial quantities. This helps speed to market by enabling manufacturing process development earlier in a product's lifecycle.

Furthermore, our standard workcell reduces the time and expense needed to add capacity for new products. You can scale out, not up, with additional workcells to reach capacity requirements. This reduces your capital expense by allowing you to scale out dynamically, increasing capacity when you need it (Fig 3).

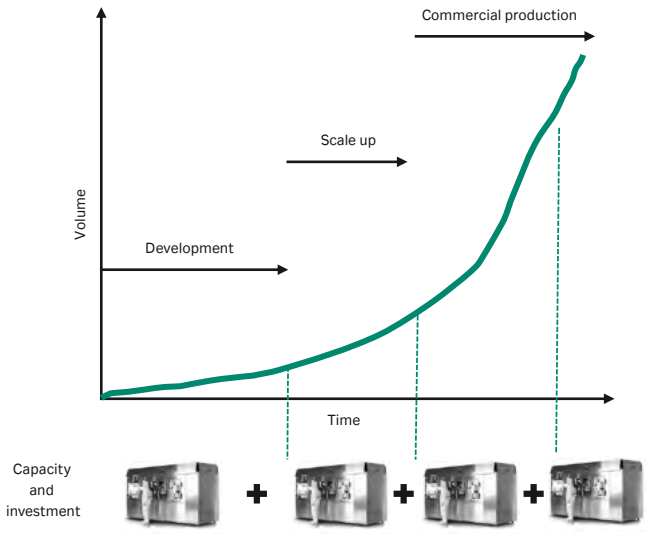

Fig 3. Scale-out is achieved by adding standardized workcells as demand requires.

Simplifying fill/finish facility design

The workcell simplifies facility design in several areas:

- The workcell is a standard product with short production lead times (32 weeks from purchase order [PO] to factory acceptance test [FAT]).
- Our workcells integrate the filler and isolator and are purchased from a single company.
- The SA25 aseptic filling workcell is compactly designed to minimize cleanroom space.
- Washer, depyrogenation tunnel, vibratory bowls, and other sortation and conveyance mechanisms have been designed out.
- The space in which the SA25 aseptic filling workcell is installed is ISO 8/grade C, which has less complex and less costly requirements than Grade A.
- Compared to alternative aseptic filling lines, the SA25 requires fewer process utilities, using less space and reducing energy costs.

The future of environmental monitoring

Biofluorescent particle counters offer continuous viable air monitoring in aseptic environments. Unlike more traditional methods, these particle counters don't pose a risk to the manufacturing process and offer you the ability to achieve improved control over operations. Our SA25 aseptic filling workcell can be configured with several biofluorescent particle counters (for example, BioTrak™ Real-Time Viable Particle Counter by TSI Incorporated) enabling real time monitoring of the state of control of the aseptic environment (Fig 4).

Continuous monitoring of total and biofluorescent counts offers higher sensitivity than traditional methods. This continuous and data-rich source of information can be used to increase process understanding and control while allowing the operator to react in real time to ensure product safety.

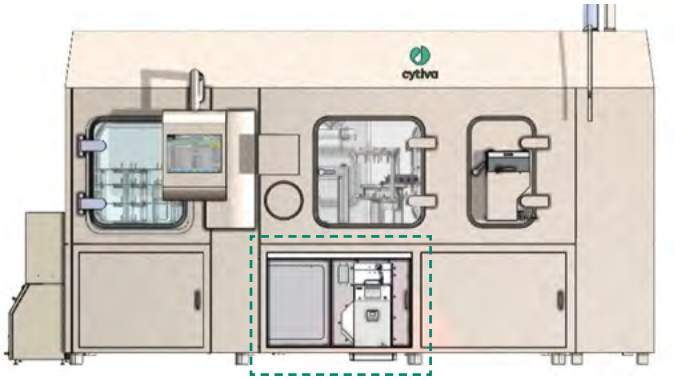

Fig 4. BioTrak Real-Time Viable Particle Counter installed under the machine.

Configurability of environmental monitoring

We make gloveless barrier systems, but we don't create barriers for you. The ability to support multiple technologies and configurations for environmental monitoring, thereby aligning with end-user preferences, is a key feature of our technology. You're not limited to biofluorescent particle counters. Many alternative configurations are possible, including the use of a passive monitoring approach and traditional active monitoring methods. It all depends on your needs and risk assessments.

No matter which strategy is being used, the operator can't access the chamber during critical filling and stoppering activities, thus eliminating the inherent risk associated with traditional, gloved aseptic processing lines.

Product flowpath

Only presterilized, single-use flowpaths are used to support a high level of aseptic sterility and containment (Fig 5). The product flowpath doesn't rely on aseptic assembly as part of the process. This practice removes the risk of an operator using an incorrect aseptic technique, which would compromise the sterility of the fill needle and flowpath. The only product contact surface inside the SA25 aseptic filling workcell is the interior of the flowpath. The flowpath is terminated with a sealed, single-use needle assembly, and the entire flowpath is sterilized via ionizingirradiation. The filling needle assembly uses a needle-sheath component to protect the sterility of the needle during the nonaseptic installation inside the filling isolator and enables the fully closed, robotic operation. Opening and closing of the flowpath is fully integrated into the automated process and is performed by robotics.

Fig 5. Flowpath installed on the SA25 aseptic filling workcell.

Sanitization and decontamination

Adding to the improved aseptic sterility and flexibility of an automated system, the simplification of the internal environment with robotics also shortens decontamination cycles and, in addition, simplifies the cleaning process. The decontamination cycle uses rapid injection of hydrogen peroxide in smaller volumes than conventional vapor-phase hydrogen peroxide (VPHP) systems, enabling shorter dwell times and faster aeration.

Design controls

The SA25 aseptic filling workcell offers a highly simplified aseptic process through the use of preassembled and presterilized nested components and single-use flowpaths. Activities with the potential to compromise the cleanliness of the critical zone, such as operator intervention, are removed and appropriate detection methods as well as design controls are in operation.

Airflow is one such control. The movement of air around an aseptic filling process is a critical consideration when evaluating the contamination risk. Visualization of the airflow allows us to understand some of the protection offered. When coupled with particle dynamics it provides valuable knowledge on the process and product protection.

The SA25 aseptic filling workcell is equipped with horizontal unidirectional airflow protection for exposed products during processing. At configurable speeds of 0.36 to 0.54 m/s, the airflow safeguards the product from settling of particles. Figure 6 shows computational fluid dynamics (CFD) of airflow patterns.

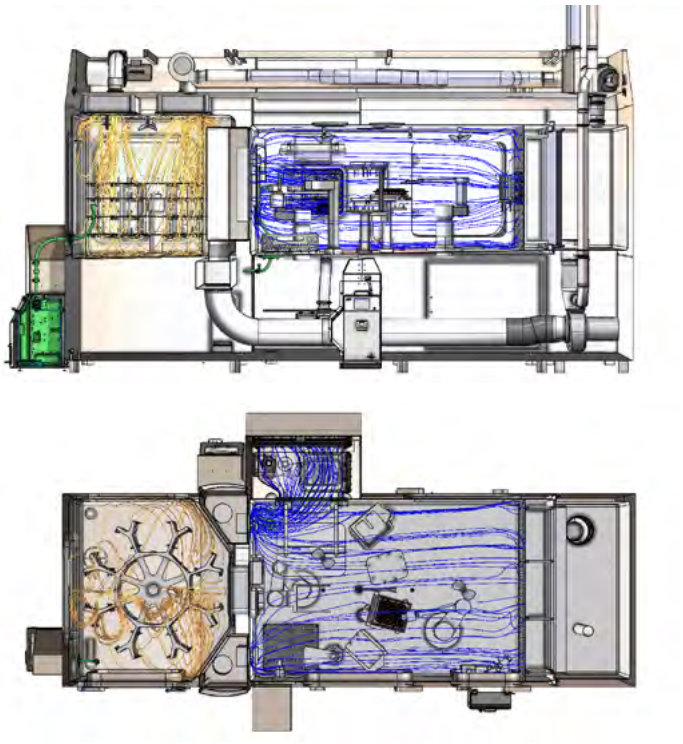

Fig 6. CFD of airflow patterns in our SA25 aseptic filling workcell.

Stoppering of nested materials

The SA25 aseptic filling workcell exclusively uses ready-to-use (RTU) nested materials and as such removes the stopper bowls and conveyance that are associated with traditional bulk filling and gloved isolators. Hazard pathways associated with indirect product contact surfaces are removed. Using a press-fit closure reduces manufacturing complexity. Applying the cap and stopper doesn't require separate operations, as the cap and stopper come preassembled, presterilized and are never removed from the nest. With the increased regulatory focus on maintaining Grade A conditions through the completion of the capping process, the elimination of a separate crimping work center offers substantial cost savings and quality benefits. Press-fit caps reduce the risk of losing revenue due to incomplete crimp formation or loss of container integrity due to excessive seal forces.

Syringes and cartridges are closed using a vacuum process without the need for flip-over bars/rods/tubes. Similar to vials, all syringes and cartridges are closed in a single closure step within the Grade A environment. A vacuum is drawn inside the entire chamber to stopper syringes and cartridges without any indirect product contact surfaces. See Figures 7 and 8 for images of nested vials and nested syringes, respectively, inside a workcell.

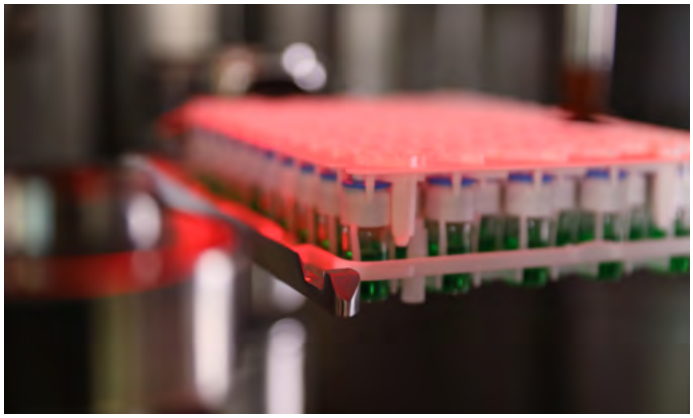

Fig 7. Fully sealed nested vials and press-fit caps.

Fig 8. Fully stoppered nested syringes.

Dynamic peristaltic pump

One of the biggest quality concerns is whether the right amount of drug product is filled into the container. Our experience told us that rotary piston pumps were accurate for low fill volume applications like ophthalmic prefilled syringes, but posed a risk for particle introduction. Peristaltic pumps are gentle and easy to use, but not as accurate as rotary pumps at low fill volumes below 1 mL. Our peristaltic pump is a dynamic rethink of the usual mechanical design, with software improvements that provide rotary piston accuracy. Figure 9 shows the dynamic accuracy.

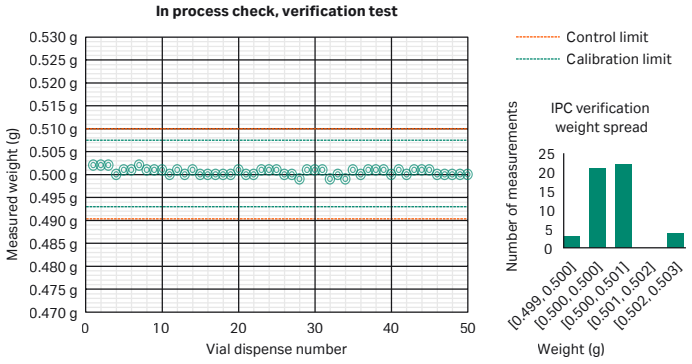

Fig 9. Dynamic peristaltic pump accuracy. IPC is in process check.

System specifications

Instrument operation occupied area (WxDxH)	4538 x 2723 x 2350 mm
Instrument service doors open area (WxDxH)	4538 x 3524 x 2350 mm
Isolator assembly weight	5500 kg
Isolator electrical cabinet weight	550 kg
Power input	208 to 240 ± 10% VAC (188 to 264 VAC)
AC voltage frequency	50/60 Hz
Max. power consumption	≤7 kVA (30A, 208V)[1]
Airflow in critical filling area	Unidirectional flow 0 to 700 CFM (0 to 330 L/sec) 0 to 0.5 m/s (0 to 100 ft/min)
Airflow in stoppering area	Unidirectional flow 0 to 150 CFM (0 to 70 L/sec) 0 to 0.5 m/s (0 to 100 ft/min)
Airflow in DSI (decon staging isolator)	Turbulent flow ~ 100 CFM (50 L/sec) 120 air-changes/hour (ACH)
Ingress protection	ISO 14644-1 class 5 isolator Positive pressure vessel (0 to 100 Pa) Interior and exterior cleanable
Clean compressed air input	6 to 8 bar(g), (72 to 116 psi[g]) Minimum flowrate of 285 LPM (10 CFM) ISO 8753-1 class 2 or better Oil - and particle-free
Water for cleaning (WFI), *optional*	Flowrate of up to 50 LPM (1.75 CFM) Pressure of up to 3 bar(g) (45 psi[g]) Temperatures between 10°C to 40°C
Inert gas supply, *optional*	Minimum flowrate of 285 LPM (10 CFM) Pressure of 1.4 to 10 bar(g) (20-145 psi[g])
Human machine interface (HMI)	AVEVA™ system platform
Machine communication	HMI interface Ethernet/IP

Codes and standards

Guidance	OSHA 21 CFR 210/211/Part 11/600 NEMA 250-2003 GAMP 5 NEC (NFPA 70) ISA 5.1
Designed	CSA, NE and CE UL/ULC, NEC/NFPA SA Z432, C22.2 and NFPA79 ASME BPE[1] (optional CIP)
Noise level	< 75 dBA (at 1.5 m)

[1] Uninterruptible power supply (UPS) recommended.
[2] New formats added as required, inquire for details.
ASME BPE = American Society of Mechanical Engineers: Bioprocessing Equipment
CFM = cubic feet per minute
EPDM = ethylene-propylene diene monomer
LPM = liters per minute
OSHA = Occupational Safety and Health Administration
PVC = polyvinyl chloride
RTP = rapid transport port

Recommended operating conditions

Ambient temperature	18°C to 24°C
Ambient relative humidity	40% to 60%
Maximum supported fluid viscosity	40 cP
Cleanroom area	ISO class 8 or class 7 cleanroom. (grade C or grade D)
Ambient relative humidity	40% to 60%

Decontamination system

Type	Integrated vapor-phase hydrogen peroxide (VPHP) decontamination system.
VPHP-cycle capability	6-log inactivation
Decontamination and aeration	≤ 1 h to ≤ 1.0 ppm ≤ 2 h to ≤ 0.5 ppm ≤ 5 h to ≤ 0.1 ppm

Filling throughput

Type	Vials, syringes, cartridges Nested components (RTU)[2]
Capacity per load	32 tub positions (8 closure + 24 container tubs)
Loads per batch	1 to 6 (< 3 recommended)
Fill volume	0.2 to 100 mL by weight
In process check Process capability	Up to 100% ≥ 1 .33 CpK ± 1.5% capability < 2 mL ± 1.0% capability ≥ 2 to < 6 mL ± 0.5% capability ≥ 6 mL
Throughput	Varies per configuration Typically ~ 4 min tub
Change tooling	Installed in less than 60 min Two operators

Isolator construction

Materials	316/316 L stainless steel, PEEK, polyethylene, fluorocarbon, polycarbonate, viton, silicone, EPDM or PVC
Surface finish	Ra ≤ 1.0 µm or better on stainless
Air filtration	Minimum H14 HEPA intake and exhaust

Environmental monitoring

Particle monitoring (options) Growth-based media (options)	CI-3100 or BioTrak Real-Time Viable Particle Counter BioCapt: Microbial Impactor or SettleShell
Particle probes, available locations (3x)	1x near filling pedestal in fill isolator (FI) 1x near stopper vacuum chamber (SVC) 1x near loading activity in decontamination staging isolator (DSI)
Growth-based media locations	BioCapt: Microbial Impactor at RTP location SettleShell at two locations

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