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Tech Note

Fill & Finish Services – Supporting Complex Manufacturing for Liquid and Lyophilized Drug Products

Complex drug product manufacturing can involve several challenges, including the use of high-cost raw materials and APIs, the need for precise fill volume control, product sensitivities, and the demand for high-yield production. These complexities impact the manufacturing processes for many modalities, including mRNA-LNP drug products.

Our Fill & Finish services in Indianapolis address these challenges by providing reliable, high-quality GMP manufacturing as well as the versatility required to advance a variety of innovative therapeutics from the lab to the patient using the VarioSys® isolator filling line.

This modular filling line can be tailored to the unique demands of complex drug product manufacturing through several advanced features, including:

- Flexible recipe capabilities that can support small batches in early phase development through commercial GMP drug product manufacturing.
- Non-destructive, inline weight checks with recovery filling to eliminate waste and protect high-value drug product.
- Integrated lyophilization capabilities for enhanced stability and shelf life of the final drug product.
- Closed isolator technology for sterility assurance and consistent aseptic performance.
- Ready-to-use (RTU) components for reduced setup and cleaning time between batches.

Flexibility to Support Early Phase Clinical Manufacturing Through Commercial GMP Production

Indianapolis Fill & Finish services have the flexibility to support small-batch sizes and process sensitive products, a key requirement for clients in early-phase clinical manufacturing. With complete recipe control over several parameters, including filling speeds, needle movement, needle timing, pump speeds, and light and oxygen sensitivity, a wide variety of fill processes can be implemented and executed.

Our Fill & Finish line is also designed to support commercial GMP production by providing flexibility and efficiency while adhering to regulatory standards. The modular design is easily integrated and customized, accommodating different product formats and batch sizes. Advanced automation features help reduce manual intervention, minimizing the risk of contamination and supporting consistent product quality. Additionally, the system complies with stringent GMP regulations. The modular system can be configured for multiple vial sizes ranging from 2R to 20R vials, with expansion capabilities up to 100R vials. It also features distinct modules that can be integrated for syringe and cartridge filling.

Enhanced Filling Accuracy, Reduced Product Loss, Higher Batch Yields

The filling module performs precise dosing with 100% non-destructive, inline weight checks and real-time adjustment capabilities, ensuring dosing accuracy, product integrity, and maximum product yield.

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Unlike legacy filling lines that pull vials from the line for destructive testing, the platform performs weight checks in real time on every vial; if a vial is underfilled, the system automatically returns to that vial on the line to be filled to the desired level. This approach ensures consistent fill volumes while maintaining robust quality and batch integrity, eliminating product loss and reducing downtime associated with rework or investigation.

This feature is particularly critical for preclinical and early-phase programs, especially in mRNA-LNP drug products, where batch sizes are small, and API materials are extremely expensive. By eliminating destructive testing and recovering potentially lost volume, the line maximizes yield, delivering more doses per batch and greater efficiency from each production run.

Lyophilization Module – Ideal for Drug Products with Limited Stability in the Liquid Form

Our Fill & Finish services can integrate an automated lyophilization module capable of processing over 20,000 vials, depending on size. This module supports the production of lyophilized drug product, which is often essential for enhanced stability, storage, and transport, particularly for temperature-sensitive or long-shelf-life applications. With automated loading and unloading and the ability to continue liquid filling operations during lyophilization cycles, the system ensures maximum throughput without compromising flexibility.

Superior Sterility Assurance with Isolator Technology Reduces Risk During Manufacturing Operations

The Indianapolis isolator-based filling line is a modular, state-of-the-art platform designed for high-performance, aseptic fill & finish operations (**Figure 1**). The platform consists of several advanced technologies:

- Three closed isolators and two laminar flow units ensure robust sterility assurance throughout the entire filling process.
- A material transfer chamber enables the supply of items or materials through a standalone decontamination cycle without affecting the Grade A environment.
- Filling technology includes modules for debagging, de-lidding, de-nesting, precision filling, stoppering, nitrogen gas purging/flushing, capping, and UV printing. This flexible system supports both liquid and lyophilized vial formats, delivering precise, efficient, and highly reliable operation.
- The freeze dryer has five shelves totaling 4.7 m^2, offering scalable lyophilization capabilities over 20,000 vials, depending on vial size, which can range from 2R to 50R.

Figure 1.

The VarioSys® isolator line filling platform incorporates the latest technologies to ensure the highest standards of product quality and sterility.

To ensure the highest standards of product quality and sterility assurance, the isolator Fill & Finish line incorporates several critical best practices. Line set-up procedures and vaporized hydrogen peroxide (VHP) decontamination establish a validated decontaminated environment before any product enters the isolator. All components, materials, and consumables are placed into the isolator prior to VHP to ensure a thorough decontamination of all items within the Grade A environment.

Robotic modules automate de-lidding and de-nesting of the vials, eliminating manual intervention and further reducing contamination risk. Vials are transferred to the infeed table and accumulation table in preparation for filling. After filling and stoppering are completed, the system moves into automated capping and UV printing.

Faster Turnaround with Ready-to-Use Components

The filling process uses sterilized components, including vials, stoppers, and needle assembly, to streamline manufacturing timelines. These components are loaded directly into the isolator to reduce cleaning requirements and setup times and enable rapid batch execution.

Efficiency Gains and Enhanced Reproducibility

Our Fill & Finish services deliver significant efficiency improvements and enhanced reproducibility over traditional filling lines, a critical benefit for manufacturers of mRNA-LNP drug products as well as other modalities such as antibody-drug conjugates (ADCs), small molecules, and liposomes. By integrating enclosed isolator technology with advanced automation and non-destructive inline weight checks, the system ensures sterility and minimizes manual interventions that can slow processes and introduce variability.

As shown in **Figure 2**, filling performance achieved <2% variance of 6R vials at fill ranges from 3 mL to 8 mL. These capabilities demonstrate precise, repeatable performance and directly translate to higher throughput and maximized batch yield.

Conclusion

Our Fill & Finish services are a powerful solution for versatile, precise, and efficient aseptic filling of drug products, including mRNA-LNP therapeutics. With advanced recovery filling and lyophilization capabilities, combined with rapid turnaround times, the Indianapolis isolator Fill & Finish line is uniquely designed to support both small early-phase manufacturing and commercial GMP batches ensuring critical programs move smoothly from the lab to the patient.

Table 1.

Summarizes the VarioSys® platform features that ensure flexible and scalable fill and finish operations without compromising efficiency, precision and accuracy.

Feature	Description	
Environment	Isolator (Grade A) Outside Isolator (Grade C)	
Weight Check	100%, Non-Destructive, In-Line, Automated	
Vials	Pre-Sterilized, Ready-to-Use (RTU)	
Caps	Aluminum crimp seals with flip-off caps Lot ID printed on each with UV-ink	
Vial Size	2R, 6R, 10R, 20R, 30R, 50R*, 100R*	
Other Modules	Syringes* Cartridges*	
Max Vial Speeds	60 VPM, 2R Vials 48 VPM, 6R Vials 48 VPM, 10R Vials	
Stoppers	13 mm Serum, 20 mm Serum 13 mm Lyo, 20 mm Lyo	
Lyophilizer Capacity	20,035 Vials → 2R Vials	5,580 Vials → 20R Vials
	10,505 Vials → 6R Vials	5,580 Vials → 30R Vials
	8,800 Vials → 10R Vials	3,090 Vials → 50R Vials

*Expansion capabilities possible with the modular system.

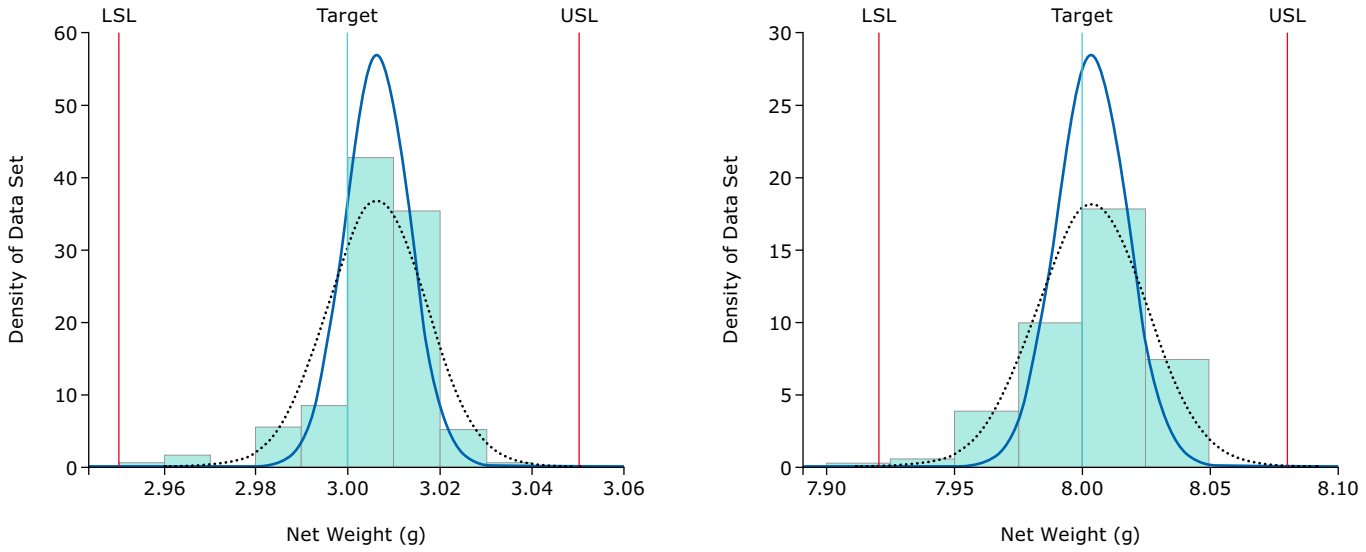

Figure 2.

Filling performance of 6R vials at fill ranges from 3 mL to 8 mL. All test cases demonstrated <2% variance, highlighting the VarioSys® platform's precision, reproducibility, and contribution to high product yield.

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Merck KGaA
Frankfurter Strasse 250
64293 Darmstadt, Germany

SigmaAldrich.com

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