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WHITEPAPER

# Cold chain fully automated assembly and labeling of pre-filled syringes for clinical trials

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# Abstract

Through 2022, and in the future, we'll continue to see significant growth in the sale of cold-chain drugs. Most will be injectables[1], generating an increased demand for pre-filled syringes. The need for refrigeration tops the list of fulfillment challenges; the TOE (time out of environment) for these costly biologics is limited and for some, non-existent.

Sponsors are seeking supply chain providers that can provide automated assembly in the proper—and critical—ambient environment. This whitepaper provides comprehensive information on cold-chain drugs, processes, and a robust list of questions to be posed to prospective providers.

In 2017, Thermo Fisher Scientific became the industry's first supply chain provider to make fully automated assembly and labeling of pre-filled syringes under cold conditions. Its newest innovation, the ProSyries℠ Pre-Filled Syringe Assembly and Labeling System 2°C to 25°C, is available exclusively at the Basel, Switzerland's dedicated cold-room facility. This facility also offers a full range of options that include storage, and temperature-controlled truck-to-dock distribution.

# Introduction

Cold is undeniably the new normal for the biopharmaceutical industry. Through 2022, sales of cold-chain drugs and biologics will outpace overall industry growth, representing nearly a third of the global biopharma sales. Most of these drugs will be injectables[1].

With sponsors devoting much of their resources to developing these large molecule products, the demand for pre-filled syringes is escalating rapidly. Many large biopharma companies have their own dedicated automated facilities for assembling and labeling pre-filled syringes for commercial products. However, some lack sufficient capacity to meet both commercial requirements and the growing demands of global clinical trials. Efforts to address both needs can lead to time-consuming bottlenecks as commercial and clinical operations compete for finite internal resources.

In an effort to forestall bottlenecks and conflicts, sponsors are turning to outsourcing partners for help. The process of assembling and labeling prefilled syringes is considerably more challenging than that of inserting tablets into blister packs, due to the special handling requirements of biologics.

Thermo Fisher Scientific has has become the first supply chain provider in the industry to make fully automated assembly and labeling of pre-filled syringes under cold (2°C to 25°C) or ambient conditions available.

To protect the shelf life of costly biologics, these products require refrigeration, with time out of the cold chain—also known as time out of environment or TOE—sharply limited. In fact, as many as 40% of biological products in development today are permitted zero time out of environment, meaning that the entire process of assembly, labeling and packaging of pre-filled syringes must take place in cold rooms. The proportion of these biologics requiring 24/7 refrigeration is projected to rise.

To address this growing market need, Thermo Fisher Scientific has has become the first supply chain provider in the industry to make fully automated assembly and labeling of pre-filled syringes under cold (2°C to 25°C) or ambient conditions available. Introduced in 2017, this service is exclusively available at the Basel, Switzerland facility, where a dedicated cold facility maintains cold-room conditions from truck to dock, through assembly, storage and distribution.

This whitepaper discusses the range of options available for the assembly and labeling of pre-filled syringes, including our latest innovation: the ProSyries℠ Pre-Filled Syringe Assembly and Labeling System 2°C to 25°C.

# Automated vs. manual

Inserting tablets into blister packaging is a simple process compared with that of assembling and labeling pre-filled syringes.

As little as five years ago, help from a supply chain partner in assembling and labeling pre-filled syringes for a clinical trial always meant a painstakingly time-consuming manual process. This limited the use of prefilled syringes to relatively small trials or production runs. Thankfully, times have changed and so have available options.

To illustrate the difference between then and now, imagine a production suite containing 10 trained operators who spend a day manually assembling and labeling pre-filled syringes. At the end of the shift day, the yield would be 1,000 to 1,200 syringes.

Today, using precision automated equipment in the same production suite, the yield at the end of the shift day is about 13,000 syringes. This huge increase in productivity has made it both practical and cost-effective to use pre-filled syringes instead of higher-priced vials and needles for global studies involving thousands of subjects.

**Suppliers must adapt to the changing needs of sponsors by continuously innovating new solutions.**

## Quality assurance: Ensuring consistency and control

Precision automation also offers quality assurance that is superior to that of manual assembly when conducting large runs, making the use of pre-filled syringes as risk-free an experience as possible for healthcare professionals and patients.

Variations in the manual assembly of pre-filled syringes are inevitable and can affect performance. For example, an under or over-turned plunger rod can lead to leakage that compromises syringe integrity, ruining the unit and wasting costly investigational medicinal products (IMP).

Similarly, an imprecisely applied Needle Safety Device (NSD) could result in a needle stick injury, an unnerving experience even for a healthcare professional who knows the syringe was unused.

Automated assembly and labeling de-risk the process through consistency and control. The best automated systems are highly precise and efficient, assembling and labeling pre-filled syringes in a single, fully-automatic process.

The systems employ a combination of customized equipment, sensors, torque control and camera systems that permit operators to maintain full control over the entire process from start to finish. For instance, a fully-automated compliance check uses a camera system to detect the position of the syringe where the assembly of the plunger rod occurs.

Sensors monitor every step of the assembly and labeling process, reading exactly how much force is being applied to a plunger, and thus eliminating the risk of under or over-turning. Using camera checks, a labeling platform ensures that the correct patient label is affixed to the corresponding syringe.

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While automated assembly and labeling of pre-filled syringes are increasingly preferred by most sponsors, manual assembly may remain the most flexible and cost-effective option for small trials or production runs. New options are now available that couple some elements of automation with manual assembly to deliver greater precision to smaller runs.

Sponsors can benefit by building flexibility into their planning and by exploring the assembly and labeling services that are most suited to their needs. Importantly, this includes engaging a supplier capable of meeting every need, be it automated, semi-automated or manual.

## Asking the right questions

Once a sponsor decides to outsource the assembly and labeling of pre-filled syringes, the next step is selecting an innovative and reliable supply chain service provider.

All service providers aren't equal. Consistency, quality and a proven track record are critical requirements in choosing a supplier. Asking the right questions about a potential provider's service offerings and experience provides the data necessary to make an informed choice. Here are many of the questions to pose:

- What options are available for syringe assembly and labeling? Manual? Semi-automated? Fully-automated? And where is each option available?
- Is it possible to assemble and label under cold room conditions? If so, can water for injection be done on the same equipment?
- Who are the members of the project team? What roles do they play? What is their industry experience with respect to pre-filled syringes?
- How much experience does the project team have with automated pre-filled syringe assembly and labeling?
- How long has automated service been available? To date, how many syringes have been assembled and labeled? For how many clients? How many of these are return clients?
- In the last year, how many syringes were assembled and labeled using the automated equipment? What types of medical formulation were used?
- Can you describe the automated assembly and labeling process in detail?
- At which global sites is automated service available? Is there redundancy at each site in the event of equipment problems? Is the process for assembly and labeling consistent across all global facilities? How is the automated equipment qualified and validated? Is it possible to adapt and implement a sponsor's quality assurance (QA) requirements?
- How are precision, safety and consistency guaranteed? What safeguards are in place? What is the rejection rate?
- Are the automated equipment and processes capable of accommodating all sizes, types and design of syringes and other elements, such as backstops? In both glass and plastic?
- What are the limits of the equipment? In other words, what is the equipment incapable of handling?
- How much lead time is necessary for automated assembly and labeling?
- Can a decision to change syringes or other parts, such as a plunger or back stop, during the course of the trial be accommodated? How quickly?
- What special handling provisions are in place for cold-chain products? Can automated assembly and labeling be performed entirely in the cold-chain, for example?
- What is the capacity? Can all assembly and labeling be performed in cold rooms? How do you minimize time out of environment?
- What kind of back-up systems for equipment and processes are in place? How often have you had to use them? Under what circumstances?
- Are semi-automated services available? At which sites? What is the capacity?
- What are the quantity recommendations for manual assembly vs. automated assembly of pre-filled syringes?
- Is manual assembly an option for small studies or campaigns?
- Can you describe the labeling options and process?
- Are assembly and labeling discrete processes?
- What safeguards are in place to ensure that labeling is precise? Should there be a problem, how quickly can it be detected?

As the use of pre-filled syringes continues to grow, flexibility and careful planning in clinical settings will benefit sponsors during development and beyond by establishing a strong foundation for building a commercial plan. Meanwhile, suppliers must adapt to the changing needs of sponsors by continuously innovating new solutions.

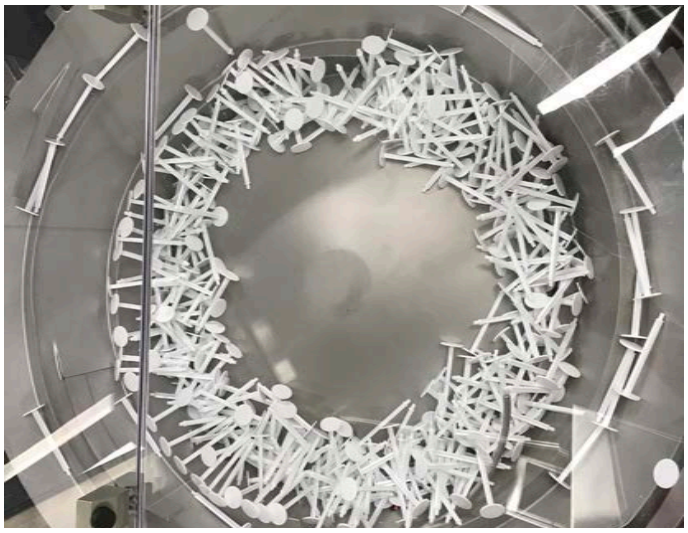
## Leading innovation in pre-filled syringe assembly and labeling services

Six years ago, a customer approached the Thermo Fisher team with a proposition: Could the organization build a pre-filled syringe assembly machine in the United States for one of the firm's drugs? The sponsor explained that it wanted to de-risk its supply chain by assembling and shipping the product from our US-based facility in addition to the European facility already in use.

As they say, the rest is history. The automated pre-filled syringe assembly and labeling services established at the request of a single forward-thinking customer has grown as the biopharma industry shifted its attention and resources to biological drugs.

In the five years since initiating the automated service, the Thermo Fisher Scientific team has assembled and labeled more than five million syringes. It has also managed campaigns of many sizes, from 500 to 50,000 syringes, with one of the largest campaigns numbering a quarter-million units.

So rapidly has demand grown that the organization now offers precision pre-filled syringe assembly and labeling at three of its facilities—in Allentown, Pennsylvania, U.S; in Basel, Switzerland, and in Horsham, UK. All three facilities employ a consistent global process. This and the expansion of services underscore the innovation and flexibility that have become the hallmarks of Thermo Fisher's offerings.



Consistency, quality and a proven track record are critical requirements in choosing a supplier.

Innovations include eliminating glass-to-glass and glass-to-steel contact in equipment. Glass-to-glass contact can cause syringes to crack, causing safety issues, compromising product sterility and resulting in waste. Glass-to-steel contact can scratch syringes, a cosmetic effect that can nonetheless cause units to be rejected.

## Introducing: The new ProSyries℠ pre-filled syringe assembly & labeling system 2°C to 25°C

This latest Thermo Fisher innovation includes the labeling and secondary packaging of pre-filled syringes by fully automated, quality-driven, proprietary processes and technology under both cold (2°C to 25°C) and ambient conditions. Capacity is 1,800 pre-filled syringes per hour for a maximum yield of 15,000 per shift day.

Introduced in 2017, the fully-automated cold-chain services are available at the Basel facility, while both the Allentown and Basel facilities support fully-automated operations. Semi-automated services continue to be performed at Horsham.

Like all of Thermo Fisher's offerings, solutions for assembling and labeling pre-filled syringes, the cold-chain system in Basel, is designed to meet the specific, unique requirements of clinical trials. Here are the key benefits:

- **Reduces IMP wastage.** This fully-automated system can detect +/-1MM stopper movement, ensuring that exact trial standards are met and reducing the potential for IMP wastage and syringe rejects. Global automated processes and equipment eliminate human error and variance, thus keeping reject rates low.
- **Mitigates time out of environment (TOE) via Cold Room assembly.** Cold-room assembly and labeling of pre-filled syringes can reduce or eliminate TOE for high-value biologics. Our dedicated cold facility in Basel—the first of its kind in the industry—maintains cold-room temperatures all the way from truck to dock, through the entire process of assembly, storage and distribution of pre-filled syringes. This facility features the fully-automated ProSyries System, including plunger rod and backstop assembly, label printing with optical character recognition and verification (OCR/OCV) and application in temperatures from 2°C to 25°C. Additional capabilities: The cold room can be modified to permit auditing of only one line for both biologics and other ambient syringe assembly requirements, such as water for injection.

All three facilities employ a consistent global process. This and the expansion of services underscore the innovation and flexibility that have become the hallmarks of Thermo Fisher's offerings.

- **Maximizes flexibility to meet the needs of every trial and every syringe.** Built with flexibility in mind, our quality-driven, fully automated pre-filled syringe and labeling services processes can meet the exacting requirements of any trial. Regardless of syringe shape, fill size or required packaging conditions, our systems can handle the dynamic and unique requirements of any trial, all while maintaining precision in meeting the quality standards set for stopper movement. No matter the fill level in the syringe, the plunger can be precisely inserted to mitigate stopper movement in accordance with trial standards. Besides the ability to package under 2°C to 25°C or ambient conditions, we offer multiple label and blinding options. High-precision syringe labeling, within an accuracy range of +/-0.5MM, is available when dosing graduation needs to be printed on the label.

**In the five years since initiating the automated service, the Thermo Fisher Scientific team has assembled and labeled more than five million syringes.**

- **Ensures accuracy and legibility of fixed and variable text.** The combination of OCR-OCV controls and built-in quality processes ensures 100 percent inspected variable and fixed text for accuracy and legibility when using labels supplied by our Clinical Label Services team.
- **Safeguards patients and medical staff.** A high level of precision in syringe assembly prevents breakage, protecting patients and medical staff. Needle safety devices can be assembled on any syringe to prevent accidental punctures of patients or medical staff.

- **Mitigates risk through global processes and quality.** A fully-automated, continuous process includes syringe assembly to label application and electronic verification of label text. The combination of global quality processes, systems and like equipment positioned at all major facilities ensures consistency and eliminates variability in syringe assembly or operational performance. For trials in which air transit of syringes and the corresponding air differential causing plunger movement are concerns, our proprietary, patented secondary packaging option is available.

- The Prosyries℠ Pre-filled Syringe Air Transit Packaging prevents stopper movement during flight, thus maintaining sterility and container integrity. In addition to electronic verification of all printed text when using our Clinical Label Services, OCR-OCV controls and built-in quality processes ensure 100 percent inspection of variable and fixed text for accuracy and legibility. Of course, we can also apply labels supplied by clients.

- **Delivers efficiencies and eliminates costly bottlenecks.** Clinical supplies held up waiting for manual assembly or for commercial lines to open up can impact the timely delivery of drug to sites and patients.Our automated equipment and processes not only deliver precision and reduce variability, but also allow for fast change-over and setup timelines that eliminate costly bottlenecks and reduce TOE for critical biologics. Kit assembly takes place in the same room where syringes are assembled and labeled, for one continuous, efficient process. Most importantly: Kits reach investigator sites and patients quicker.

## References

1. “Biopharma cold-chain market forecast.” Pharmaceutical Commerce. 3 September 2018

## About us

Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 65 locations around the world, we provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, formulation, clinical trials solutions, logistics services and commercial manufacturing and packaging. We give pharma and biotech companies of all sizes instant access to a global network of facilities and technical experts across the Americas, Europe, Asia and Australia. Our global leadership is built on a reputation for scientific and technical excellence. We offer integrated drug development and clinical services tailored to fit your drug development journey through our Quick to Care™ program. As a leading pharma services provider, we deliver unrivaled quality, reliability and compliance. Together with our customers, we’re rapidly turning pharmaceutical possibilities into realities.

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Published 08/21

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