

CLINICAL TRIAL PACKAGING

**SMART CHOICES
CAN TRIM TIMELINES**

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Introduction

Getting a potential new therapy through the clinical trial process takes more time than ever before. Protocols are growing increasingly complex. Plus, many trials have trouble enrolling enough patients, and those who do enroll may have difficulty following the protocol and drop out. Complicating matters further, many drugs being developed are expensive biologic agents, leaving little margin for error in the clinical trial strategy.



Delays in getting a therapy approved mean less time to secure commercial success and recoup investments before generic forms are available. Most importantly, it delays getting potentially lifesaving drugs to patients. As a result, sponsoring companies look for ways to trim development timelines.

Establishing an efficient drug packaging strategy for a clinical trial is not often recognized as a potential timesaver, but it should be. A well-thought-out packaging strategy can significantly cut your clinical trial timelines and increase the likelihood of a successful trial.

There are several critical factors that sponsors need to consider about packaging: the drug's form requirements (injection, oral solid dose, etc.), the volume needed for the trial (lot size, trial duration), temperature requirements (freeze/thaw cycles, handling requirements), and whether the drug needs to be protected from light.

Taking those and other factors into account, experts at Thermo Fisher Scientific outline four key considerations that sponsors should evaluate when developing a packaging strategy:

- 1. What do your patients and healthcare providers need?**
- 2. What packaging options meet the needs of your drug?**
- 3. Can your packaging process be automated?**
- 4. Do you have in-house expertise?**

How your product will be used by patients and healthcare providers

The first thing to consider is how your product will be used by patients and healthcare providers involved in your clinical trial. If your packaging meets their day-to-day needs, they will find it easier to follow the trial protocol.

Drug distribution

How and where will the drug be administered to patients? There are many nuances to this issue that can affect packaging decisions.

For example, does the patient also need supporting materials? If the patient will get the drug at a doctor's office, packaging the drug and supporting materials in one container might work. In many cases, however, the drug needs to be delivered to a pharmacy and other materials to the doctor's office. "If it is all packaged together, you're making the package unnecessarily large, plus you're sending it to the wrong place," says Helen Underwood, Director of Strategic Client Relationships. That can cause significant delays in getting doses to patients.

What about drugs that are given to patients only once? For example, consider a vaccine that doctors will be delivering to large numbers of people in a rural setting. "You want something that the doctor can handle quickly, treat many patients when speed is of the essence, and then dispose of efficiently," says Underwood. "You don't want them to spend time assembling a syringe."

If patients or providers find it difficult to follow your clinical trial protocol because of packaging details, they are less likely to follow the protocol correctly, and you may need to enroll even more patients.

Drug dosing

How often is the patient expected to take the medication? Once a day? Several times a day? If the latter, the drug might need to be in

a small package the patient can bring to work, such as a blister pack that holds just a few pills. On the other hand, if the patient needs to take the medication just once in the morning, a less portable package might work fine.

If your medication must be injected, will your patients want to visit a healthcare provider regularly for injections? Or would they find that cumbersome, and perhaps be comfortable with administering it themselves with a prefilled syringe or auto-injector?

Patient demographics

What age are your patients? Children might object to daily injections. Seniors can find it difficult to inject themselves. What other demographic or lifestyle factors might influence your patients' packaging preferences?

Regardless of who your target enrollees are, if patients or providers find it difficult to follow your clinical trial protocol because of packaging details, they are less likely to follow the protocol correctly, and you may need to enroll even more patients.

A packaging expert can help sponsors to consider these and many other patient and provider usage considerations.

How packaging and production options meet emerging biopharma trends

Healthcare and the pharmaceutical industry are changing rapidly. Several recent trends should be taken into account when thinking about clinical trial packaging options: the rise of precision medicine, the popularity of biological therapies and prefilled syringes, and cold-chain processing.

PRECISION MEDICINE IS ON THE RISE

Precision medicine—the use of therapies tailored to subsets of patients based on their unique molecular and genetic profiles—is on the rise. These drugs, by definition, are intended for relatively small numbers of patients. A clinical trial sponsor may need only small quantities of their therapy, which means a smaller production run and potentially higher costs. In addition to exploring packaging that can be produced at a reasonable cost, sponsors need to consider whether the packager can scale up production in the future. Moving your packaging operation to a new vendor can mean costly delays when launching later-phase clinical trials.

Automated processes fill the syringes more precisely than humans, cutting down on product waste.

BIOLOGICAL THERAPIES AND PREFILLED SYRINGES ARE ON THE RISE

Rising alongside precision medicine are biological therapies, a relatively new class of drugs that are produced from biological materials.

Most biologics are large-molecule products in liquid form. Many are delivered by injection. In today's healthcare climate, more patients are comfortable with injecting medications on their own, especially if they have a chronic disease such as diabetes that requires frequent dosing.

This has led to an increase in use of prefilled syringes, a disposable drug delivery system that is filled with a precise dose of medication, as a packaging option.

Producing prefilled syringes used to be a time-consuming process that was done by hand. These days, however, some packagers can use automated processes to fill syringes, significantly cutting production time. For example, 10 people manually assembling prefilled syringes could produce about 400 units per day. Using automated processes, it's now possible to produce 13,000 units per day.

In addition, automated processes fill the syringes more precisely than humans, cutting down on product waste. A more precise dose can also mean fewer protocol deviations, and fewer patients producing unusable data or dropping out.

“Biologics are incredibly expensive products,” says Underwood. “You want all of the product to get to the patient. You want a delivery system that’s going to perform the right level of dosing with the greatest ease. The prefilled syringe is an ideal way to do that.”

It's also important to know how syringe production is carried out at a facility. Not all systems are equally efficient or error-proof. For example, we have eliminated glass-to-glass and glass-to-steel contact, eliminating the possibility of cracked or scratched syringes, which can cause units to be rejected and slow down production.

How packaging and production options meet emerging biopharma trends (continued)

COLD-CHAIN PROCESSING

Most biologics require refrigeration. They degrade at ambient temperatures, and remain more stable if refrigerated. They must be assembled, labeled, and packaged in a temperature-controlled room, and shipped in special packaging with careful monitoring at every step to ensure that their time out of environment (TOE) is limited.

Such cold-chain processing can be complex. For example, manual labeling at very cold temperatures is challenging. Operators need personal protective equipment, but it's very difficult to apply labels to packages while wearing thick gloves. Our Thermo Fisher Scientific facilities have cold rooms with the ability to package and label drugs at minus 80 degrees, notes Shawn Regits, Process Engineering Manager.

It's vital to choose a vendor that can do cold-chain processing and has the capacity to meet your production needs in a timely manner. Choosing a vendor that has only limited cold-chain capacity could mean your packaging run gets delayed while other jobs are completed.

It's also important to make sure your packager can get your product shipped to clinical sites in a timely manner with minimal or zero TOE. Packers have advanced far beyond the old dry ice technologies. Today, some can pack the finished product in "smart boxes," containers that keep products cool when in transit but go into a resting state when they detect they are being stored in a refrigerator.

In addition, sophisticated temperature monitors on shipping packages can now make it easier for clinicians to see if a product has spent too much time out of its required temperature range, providing certainty that a product is still viable. Products that have not been properly cooled, or are even suspected of not having been properly cooled, may be disposed of by clinicians, leading to delays and increased costs.

Automated or manual production? Or both?

“Many people have the misconception that clinical trial packaging is all done manually,” says Underwood. “I want to dispel that myth.”

Underwood notes that Thermo Fisher Scientific has large-scale automated equipment for large trials, but also smaller-scale equipment that can handle smaller runs. “We just need to understand the type of trial and the trial phase to make an appropriate match.”

Automated assembly increases consistency and control, and lowers the risk of human error. The assembly equipment can also run for long periods of time, much longer than a human. But while automated assembly is fast, full automation can also mean longer lead times due to up-front engineering and design needs.

Manual assembly will be slower, but has the advantage of requiring less setup time.

“In many cases, the best option is a semi-automated solution,” says Regits. “For example, a machine would do the critical packaging step or inspection, and a human operator would load components into the machine.” A semi-automated solution can achieve a good balance of start-up time, flexibility, and labor.

Decisions on whether to automate or not depend primarily on the study design, volume, and timelines (including whether a study might run over several years), rather than technology, adds Underwood.



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Take full advantage of packaging experts

Working with outside packaging experts can speed up your clinical trial.

Not all trial sponsors have the resources of a large pharmaceutical company at their disposal. Many companies seeking to launch drugs are small and entrepreneurial. For them, partnering early on with packaging experts such as the Thermo Fisher Scientific team can reap major benefits. Experts can bring ingenuity and a sophisticated packaging plan to a project that will significantly cut timelines and increase patient compliance with your protocol.

“We work with clients to understand their true needs, what’s really important to their product,” says Regits. Sponsors are usually juggling many competing needs, such as volume requirements, refrigeration needs, clinical trial timelines, costs, possibly scaling up production for later phases, and more, he notes.

“Sometimes you have to distill it down, peel the onion and figure out what they really need,” he says. “And then find the right solution. There are a thousand different ways to solve a problem, but what is the right solution for that client?” Finding the best solution often requires brainstorming sessions involving experts in operations, engineering, and other areas.



“We do our best to error-proof the process, to design processes where errors are impossible, and then we standardize those processes and make them available to our clients,” he adds.

“When clients come to us with an open mind, we can ask probing 12 questions, find out more about their product and how it’s going to be used,” says Underwood. “We can make recommendations about how it might be used by a patient, lead into package design, automation options, and the production strategy we would deploy. We pull it all together into a holistic supply and packaging strategy.”

Indeed, partnering with packaging experts such as the the Thermo Fisher Scientific team can streamline processes and cut overall timelines. Our experts can help you to:

- **Fully explore** the needs and preferences of your patients and healthcare providers, and the packaging options that will work for them
- **Take** full advantage of innovative packaging options, such as small production runs and cold-chain processing, that meet the needs of your drug and clinical trial
- **Determine** the best processing options for your packaging, whether it’s fully automated, fully manual, or a combination of options
- **Take** full advantage of our years of experience working with a multitude of trials, therapies, and packaging design options

Most importantly, our experts can help you develop a more efficient clinical trial strategy and ensure that your patients and healthcare providers are fully engaged in your protocol.

