



Six Strategies to Stretch Your Limited Drug Supply for Clinical Studies



EXCELLENCE IN PHARMACEUTICAL OUTSOURCING FROM MOLECULE TO MARKET

Bringing a new drug to market can be a heavy financial burden on any pharmaceutical company. It has become even more burdensome over the last several years as the industry pushes the boundaries of innovation. This is because newer, often more-complex therapies not only increase risk in drug development but also drive costs even higher. A recent analysis of the investment needed to develop a new prescription medicine shows the total cost can be as high as \$2.6 billion.¹ That number becomes even more staggering when you consider the fact that only about 12 percent of drug candidates that make it to Phase I testing are eventually approved by the FDA.² The investment companies lose as a result may be too devastating to their bottom line to ever recover.

That is why it is important to have a clinical packaging strategy that can successfully manage the supply of your expensive drug product throughout the duration of clinical testing. To do this, sponsor companies must balance control of the drug supply with control of shipping costs. Achieving this requires maximizing the amount of drug available for distribution while minimizing overages across clinical trial sites.

The following six strategies can be used to find balance; nevertheless, they all require the support of a trusted clinical packager. Without this valuable insight, a company could experience a costly interruption or extended delay and, as a result, a devastating impact on its timeline to commercialization.



1. Employ a drug-sparing strategy

If there is a limited drug supply that can be manufactured only in small amounts infrequently, the sponsor company's

clinical group must design the study to be as drug-sparing as possible. Plan your patient enrollment timeline so supplies can be distributed when patients are enrolled — not prior to — and build in lead time to get the clinical supplies to the appropriate site on time. It then becomes up to the clinical supply group and clinical packager to determine the optimal balance between maintaining control of the drug supply and maintaining control of shipping costs. Shipping supplies out per patient helps maintain control of the drug supply, but it must then be determined if the sponsor company can afford the shipping costs associated with this strategy. An experienced clinical packager can identify the optimal balance between these two extremes.



2. Ensure rigorous patient screening and user-friendly packaging

Drug waste is never wanted in any clinical study, especially in one where the drug is

in limited supply. If drugs are going to be sent to clinical sites, the sponsor company should do everything it can to make sure they will actually be used. This starts with a rigorous screening process of potential patient candidates to ensure they meet the study's patient qualification standards. Some



of drug candidates that make it to Phase I testing are eventually approved by the FDA².



Quick tip

Understand that clinical groups plan studies with overall averages. This can lead to miscalculations of how much total supply is needed to initiate, support, and finish a clinical study. For example, while the clinical group may calculate supply needed based on an average of 0.75 patients enrolling per site per month, the clinical supply group needs to plan on supplying a full patient. Work with your packager on packaging and distribution strategies to overcome this.



studies are already challenged by the inherent characteristics of the target patient pool, such as with Alzheimer's or addiction patients. If a company does not carefully screen patients and, if necessary, evaluate compliance using a run-in study, drug is wasted when it is administered to patients who will ultimately not take it.

User-friendly packaging is another issue that needs to be addressed to minimize drug waste. An experienced clinical packager can identify packaging that will encourage compliance. For example, a blister pack is the preferred packaging over a bottle for complicated dosing schemes. This is because it can clearly indicate to the patient which pill should be taken when rather than relying on the patient to remember. While user compliance is not necessarily a clinical supply issue, it does create a risk of drug waste if a patient drops out of the study due to confusion. By putting thought into how the drugs should be packaged, drug waste can be minimized.



3. Identify accommodating kit design

Sponsor companies tend to design their kit contents around maximum drug dosage in an attempt to avoid additional shipments later and to cover extreme scenarios, such as the majority of patients needing higher drug dosages. With a limited supply of an expensive drug, kits should be designed for the dosage most likely to be used, and supplemental kits can be designed to cover extreme scenarios, such as the example mentioned above.

This is a good strategy to consider when dosage per patient varies. For example, for a drug dosed on a milligram per

kilogram basis twice a day over five days, you may need 10 doses. Therefore, a site would need a kit of 10 vials (assuming one dose per vial). However, what if each vial supports only patients up to 120 kilograms? How will patients over 120 kilograms be dosed? While instinct may be to increase the contents of the kit to accommodate patients of all weights, this would significantly increase the chance of drug waste. A practical alternative is to make an educated guess of how many patients will be over the 120 kilogram limit and create a number of supplemental kits with a smaller number of vials based on that guess. Or, to avoid the confusion of having to track the quantity of two types of kits, make all kits contain a smaller number of vials. Through educated decisions, a sponsor company gains better control by conserving its supply and also avoids the costs associated with wasted drugs.

For companies that need extreme control of the drug supply, work with your clinical packager to design a flexible kit that accommodates a varying number of vials or packaged drugs. This packaging strategy — combined with a reasonable patient enrollment lead time that has been agreed to by the sponsor company, clinical site, and clinical packager — allows for varying quantities of drugs to be shipped on an as-needed basis. A word of caution when shipping on an as-needed basis: the minimum supply each clinical site has needs to take into account the amount of supply necessary to avoid randomization failures. For example, for a blinded one-to-one randomized study, a clinical site needs to have, at minimum, two drug and two placebo kits to ensure blinding is not inadvertently undone. This is another area where the sponsor company must weigh the costs of shipping against the benefits of having more control of its supply.



4. Centralize clinical supply storage

As the number of global clinical studies increase, clinical supply groups must take international factors into account to make

certain all clinical sites are adequately supplied. If possible, for studies held in multiple countries, find a depot in a country that allows clinical supply to be delivered conveniently to all countries in the study. This helps maintain maximum control of your drug supply.

The following considerations should be made for these specific countries:

- Europe As of the date of this article's publication (Oct, 2017), the U.K. is in negotiations to leave the European Union (EU). The European Medicines Agency (EMA) has indicated the U.K. will be treated as a third country. This means moving clinical supply between the U.K. and mainland Europe may have additional import/export implications that are not yet known. At least until March 2019 when the U.K. will officially leave the EU, consider centralizing clinical supply for European studies at a depot in only Europe to ensure the clinical supply chain is not interrupted.
- Asia Consider using a packager whose global depot network includes Singapore. Their laws offer favorable trade advantages, even though some import licenses must be processed.
- Latin America Centralizing the clinical supply to cover multiple countries in this region is not a realistic option as each country is governed by its own set of import regulations and moving supply between Latin American countries has import/export hurdles. To maintain control of supply, a local depot within each country is needed or shipments sent from the U.S. must be sent on an as-needed basis.



5. Select countries with flexibility in mind

Different countries have different import and export laws. Therefore, choose the countries hosting your clinical trials

carefully, as flexibility to move drug supply between clinical sites may be necessary to stretch a limited drug supply. While moving drug supply between clinical sites should be minimized, sometimes the sponsor company has no choice if the drug supply is limited and clinical sites do not enroll patients at the expected rates. Also, be wary of one-way deposit countries, where exporting previously imported drugs is practically impossible. By having a clinical site in a country where it is difficult to export drugs, the sponsor company would not have the option to move drugs from a low-patient-enrolling clinical site in one country to a high-patient-enrolling clinical site in another, resulting in avoidable drug waste. If a country with complex import and export rules cannot be avoided, you must minimize the number of times drugs need to be imported. Market research should be conducted to determine where and when patients are likely to show up. This ensures clinical sites with high patient enrollment in a complex import country are selected to mitigate the risk of drug waste.



6. Use Just-In-Time strategies

A just-in-time (JIT) strategy should be executed when there is a single drug product committed to multiple studies, which is often the norm. The drug is

packaged, labeled, and dedicated to the studies as needed, rather than sending materials already pre-dedicated. This helps avoid situations where a low-patient-enrolling site receives too much supply or a high-patient-enrolling site does not receive enough. As previously mentioned, some sponsors will try to move drug products from a low-en-rolling site to a high-en-rolling site in situations when patients do not enroll at the expected rate. This is not recommended for temperature-

sensitive drugs as the distribution back and forth increases the chances of a temperature excursion. Regardless of the strategy used, temperature-sensitive drugs require a chain of custody report, temperature records, and verification that the kits have not been compromised.

From the point of view of the clinical site, receiving identical vials that are meant for several studies can be extremely confusing and make the study more prone to human error. It ultimately leads to an increased chance for error during reconciliation at the end of the study. By partnering with a clinical packager that has experience implementing JIT methods for one drug across several studies, the chances for these errors can be minimized.

To make JIT successful, a clinical packager must be able to assure quick turnaround when a sudden request for more kits and shipments is made. If the packager is overburdened, unresponsive, and/or does not have experienced project managers and standard operating procedures, the sponsor company could miss its first patient in-date. This is the first date a patient is expected to start taking a drug, and it is

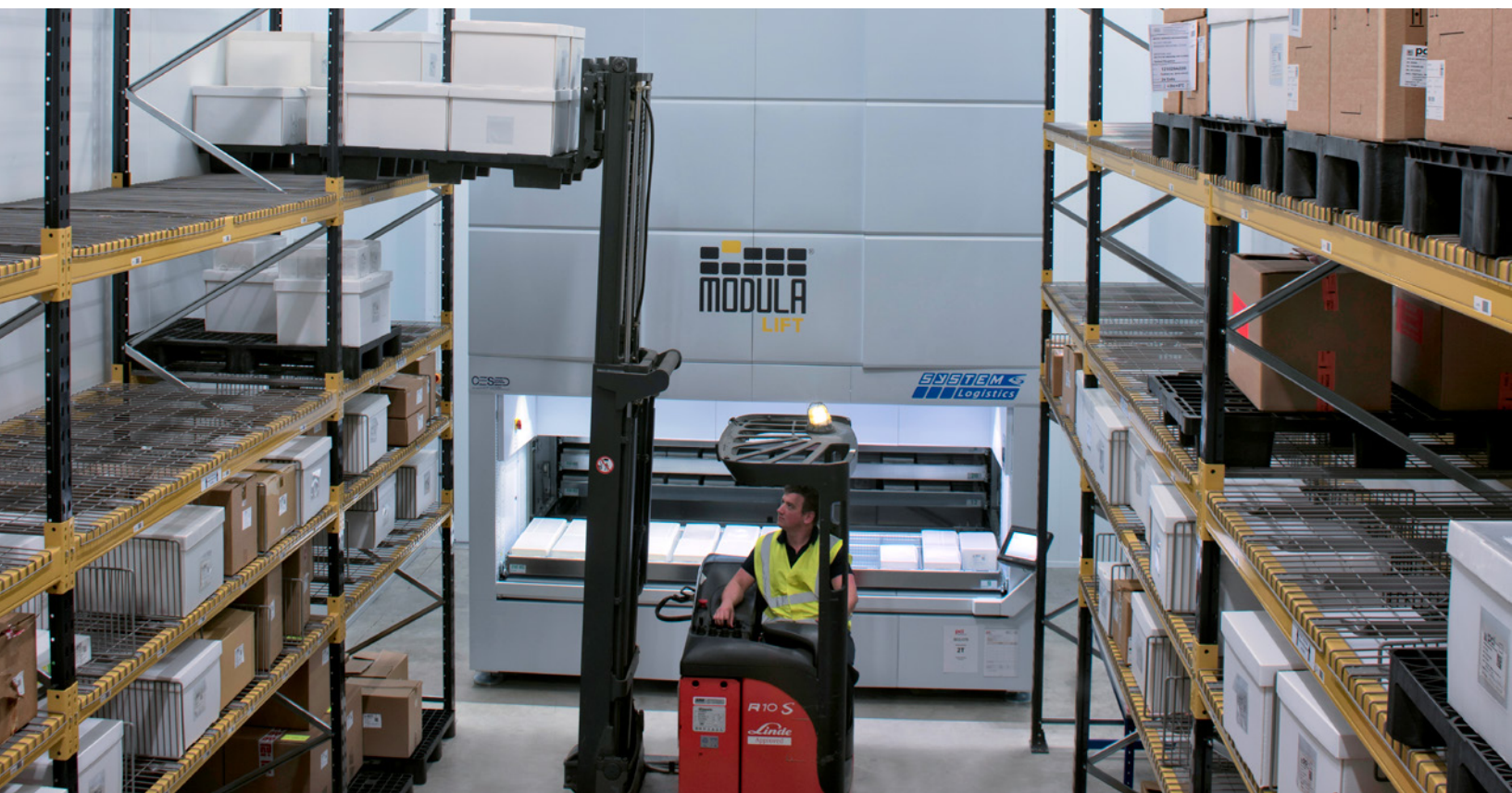
a critical factor when executing a clinical trial. To increase the likelihood that this strategy is successful, partner with a packager that has a dedicated team for studies utilizing JIT.

Regardless of which strategy is used, there must be protocols between the clinical packager and the sponsor company that make sure the distribution of drug supply is managed smoothly and efficiently. Doing so ensures the drug arrives on time and the study is completed as intended. The clinical packager a company partners with must be knowledgeable enough to walk through each available option and help weigh the pros and cons. In addition, it is imperative that for every potential challenge identified, your partner has the expertise, flexibility, and resources to overcome it.

References

¹ Tufts Center for the Study of Drug Development, Tufts CSDD Assessment of Cost to Develop and Win Marketing Approval for a New Drug Now Published — http://csdd.tufts.edu/news/complete_story/tufts_csdd_rd_cost_study_now_published

² PhRMA, 2015 Profile, Biopharmaceutical Research Industry — http://www.phrma.org/sites/default/files/pdf/2015_phrma_profile.pdf





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