Sometimes, clinical trials do not succeed because of incomplete planning and a lack of contingencies for when circumstances change. As 5 Critical Steps In Developing Your Clinical Supply Chain illustrated, proper planning is critical for the success of a clinical trial. But how do you plan for unanticipated obstacles that may affect the clinical supply chain and, ultimately, the outcome of your trial? This article will provide three strategies which can help build flexibility into your clinical supply chain plans and overcome unforeseen obstructions to your trial’s success.

One of the essential elements in running a successful clinical trial is to ensure that patients receive treatments on time, every time they need them. Losing patients due to a lack of supplies and/or treatments must be avoided at all costs as patient recruitment and retention can be a challenge, and it can prolong the overall timeline of a study. This can have two major adverse impacts. First, patient safety and treatment efficacy can be hindered. Secondly, the cost of the trial can also increase. A simple incident, even for an inexpensive product, can have massive repercussions down the road. Depending on what caused the delay and how long it lasts, correcting these issues can potentially add costs.

Having flexibility in a distribution plan means that you have created a plan that is not so rigid that it won't accommodate possible changes or delays. However, it can be challenging to predict the efficacy of distribution, where patients of the trial will enroll, how frequently they will enroll, and how quickly parts of the distribution plan will be executed. By drawing on the knowledge of subject matter experts, you can gather information to support realistic projections for distribution plan timelines and supply quantities. Your contract research organization (CRO) will be able to provide guidance using historical knowledge of recruitment and treatment timelines to aid in creating an achievable supply chain plan. Additionally, the following strategies can be used to further build flexibility into supply programs.
IxRS Systems
Interactive voice and web response systems (IxRS) are an excellent tool for building flexibility into a clinical supply chain. These web-based systems are highly customizable and are able to manage supply material, patients, randomization, and locations of materials within a trial across the globe. Each trial is unique and comes with its own set of variables and constraints. An IxRS system can be programmed to meet the needs of the specific trial and take into account what criteria may need to be changed and adjusted over time. Further, these systems are designed with each trial site’s country, anticipated patients, drug types and delivery, site and supply depot information, including inventory, and many other criteria and variables in mind. These systems are especially beneficial for large studies where manual tracking of data and materials would be virtually impossible. And as trials have evolved to become more complex, so have these systems and their capabilities.

Through predetermined patient demographics within the system, IxRS preserves unbiased trial results. Inventory management is also preprogrammed into the system based on the sponsor’s needs. During drug dispensing, the system determines the correct drug or placebo, dosage, and delivery frequency on the randomized patient list and site inventory. IxRS systems can constantly communicate with sites and depots to determine which products are needed at which sites.

Where these systems truly shine is in their built-in ability to add flexibility to the trial. With predetermined, customized criteria for each trial, IxRS is able to trigger drug shipment as needed and manage expiration dates for current inventory. For instance, if a trial has 10 sites, and materials are sent to each site in advance of the trial, some of the sites may not use the full quantity — essentially wasting them. IxRS significantly reduces waste by automatically sending the correct amount of supply as needed to its appropriate destination. Further, adaptive capabilities can also be built in; for example, there may be a trial site where patients are titrating, and doses are increasing to a maximum tolerated dose. Maximum tolerated dose can be very different from patient to patient, increasing the risk of wasted and/or not enough product. The system can help manage what you do know, and help predict unknown factors, so that you don’t have to send material in advance; you can wait and see if you need it before committing to sending it. Once materials are sent, they can be further managed at the depot level with the IxRS system. Additional adjustments can be made in real-time to add/remove sites, change threshold levels, and react to trial activities. This adds flexibility to the supply chain while minimizing risks and costs.

Investing in IxRS can be expensive, and the systems are designed for each unique trial, so in a sense, they are a “one-and-done technology.” The length of the study and how many patients, depots, and sites that will be used must be weighed while considering whether to manage supply chain activity manually versus digitally and automatically. That being said, the system’s capabilities and the benefits it provides in managing drug supply, and numerous other areas of a trial, can often significantly offset the cost of investment.
Packaging And Labeling Strategies

Flexibility can be built into the clinical supply chains through carefully planning and executing some packaging and labeling initiatives. One effective approach for flexibility is through **multi-language booklet labeling**. These labels are an all-encompassing approach and are applicable to studies occurring in multiple countries and allow for labeling compliance in each of them. By expanding the breadth of countries in the labeling booklet, delays in creating compliant labels mid-study can be avoided. For instance, you label a large amount of supplies, perhaps 3,000 bottles, for 15 countries. Now, that product can be used at any point, by any of those 15 countries. And if the study is utilizing IxRS, overages and shortages are easily accounted for and can be adjusted in real-time as needed. Creating labels for multiple countries is an added cost upfront, but this additional cost can be offset by eliminating the risk of non-compliant labeling, and the need to have new labels manufactured and applied later during the study.

**Just-in-time labeling** is nearly the antithesis of multi-language booklet labeling but is also an effective strategy for building clinical supply chain flexibility. In this approach, only small quantities of supplies are labeled and shipped on an as-needed basis. This builds in flexibility because large amounts of products aren’t being pre-dedicated to a specific country or protocol in advance. This reduces waste, which is especially important when labeling and shipping very expensive material. The overall cost of just-in-time labeling and shipping can potentially end up costing more than if you prepared a large supply upfront; however, this amount may still be significantly less than the cost of producing extra drug product that will ultimately be wasted. For example, manufacturing of an additional 100 bottles of a drug that costs $1,000 per bottle will cost $100,000 overall. However, by moving forward with the just-in-time strategy, this may only cost $50,000 in labelling and shipping costs, resulting in an overall savings of $50,000.

In regard to packaging specifications, **single bottles vs. product kits** is an important consideration for building flexibility into clinical supply chain plans. In trials years ago, before the widespread use of IxRS systems, clinical supplies were often shipped in kits. For example, if a patient was going to be on a drug for an extended period, that patient would receive one bottle for each month. For a six-month trial, a six-bottle, uniquely numbered kit would be sent — Kit #1,000, bottle one, bottle two, etc. Patients would be assigned a kit and receive treatment from only that kit and its contents. Now with IxRS systems, the ease of having to only manage one number per subject is replaced by a system that can manage multiple numbers per subject on a global scale. Bottles can now be kept loose at sites; a patient may receive treatment for bottle 1,000 at one visit, and bottle 6,548 the next. The IxRS system tracks all of this automatically, negating the need for manual tracking with kits. If a patient drops out, no drug is wasted due to pre-allocation; it simply goes to another patient.
Supply And Drug Depots
Depots are another excellent tool for building flexibility into clinical supply chain plans. Rather than shipping given quantities of supplies to individual sites, utilizing depots allows you to send larger quantities of supplies to a geographical region at once. From there, the depot can ship the required supplies to each trial site as needed. When planning your supply chain strategy, it is a good practice to consider any products shipped to sites as used — whether it was ever dispensed to a patient or not. Site to site transfers and returns for re-use may be possible in some situations but should generally be avoided. Depots allow you to reduce the number of international shipments being made, which ultimately may reduce cost and provide a more predictable transit time as customs delays are not always foreseeable. Once in country, the depots can respond to site demand for materials within a few days, allowing you to reduce the amount of product to send to the site initially.

Depot-to-depot transfers further supply chain flexibility. For example, if a trial is running simultaneously in the U.S. and Europe, half of the trial’s supplies can be sent to each continent’s depot. If European enrollment isn’t as high as the U.S., the European supplies can be easily sent back to the U.S. via a depot-to-depot transfer. Keep in mind that export requirements from some countries are more extensive and possibly not permitted, so shipping supplies back from a depot that was originally only intended to import materials may not be possible in every situation. Due diligence of knowing exportation and importation requirements, and any other catalysts of possible delays, is a must.

Clinical trials will continue to grow in complexity and so will their supply chains. While it is impossible to create a plan so flexible that it will eliminate every possible delay, there are strategies to proactively plan for unforeseen disruptions. Creating supply chain plans based on good, historical data will lead to reliable forecasts for clinical supply planning. Adding contingencies into those plans for obstacles allows for today’s trial needs to be met and lays a solid foundation for meeting tomorrow’s needs.
About the Author
Tracy Chase is Manager of Proposals and Training for Bellwyck Pharma Services which supports clinical and commercial packaging and distribution. She has almost 20 years of experience managing small to global size clinical trials in the pharmaceutical industry.

Tracy Chase, Manager, Proposals & Training, Bellwyck Pharma Services
enquire@bellwyck.com