

# Developing a Strategy to Optimize Clinical Trial Supplies

# Developing a Strategy to Optimize Clinical Trial Supplies

---

Given the global nature of today's clinical trials, effectively managing clinical supplies has become more complex than ever. Efficient supply planning is critical to the overall success and cost structure of clinical research and development (R&D). The annual expenditures for clinical supplies can account for 40 percent or more of a company's entire R&D budget.<sup>1</sup> Therefore, an effective supply chain management strategy is paramount.

The optimal supply management plan is one that strikes a balance between trial demand, trial budget and available stock. Optimizing the clinical supply strategy will decrease the amount of wasted supplies, drive down costs and ensure supplies reach the sites on time and in the correct quantities—helping to accelerate time to market.

The purpose of this article is to:

1. Outline the most common factors that influence trial supply and portray the influence they have on the decisions that determine the proper strategy.
2. Demonstrate how changes in the factors alter the plan and why one supply plan will not always translate to the next trial.
3. Briefly discuss what to do once the decisions for the supply strategy have been formulated and some methods of managing the plan during the live trial.

It is important to note that each company has different requirements for which line items are included in a clinical supply budget. For the purpose of this article, all supply and supply-related activities such as manufacturing, procurement, packaging and shipping will be considered part of the supply budget. Although destruction is typically part of the overall supply budget, it will not be a discussion point.

The first step in developing a balanced clinical supply strategy is to determine which factors most influence the supply chain.

- **Therapeutic Area (TA) Trends:** TA trends are key factors and guidelines to subject behavior expectations. TAs will shape trends such as:

- Enrollment (will it take days, months or years?)
- Compliance and retention rates (are there a lot of drop outs and will replacements need to be made?)
- Mortality rate (should additional packaging runs and replacement supply be planned if the mortality rate is taken into account?)

\*Note\*: A trial studying the pharmacodynamics of biologics in malignant cells requiring a certain number of completers may take into account the mortality rate of subjects to determine supply.

- **Regional demographics:** Regional demographics (where the trial is being conducted) provide significant insight that drive depot plotting and resupply strategy for a specific region rather than the general trial. Proper planning for importing/exporting supplies, including applying for the most efficient licenses and estimating tariff and broker fees, will diminish unexpected costs in global trials.

Knowledge of regional recruitment potential determines not only the initial shipment to local depots but also the resupply strategy for sites in a given region. For example, sites enrolling in New Delhi, India will most likely require a higher resupply type than those in Juno, Alaska due to New Delhi's larger population size.

- **Supply Cost:** The cost of the investigational product as well as the placebo, comparator, control supply and any supplied concomitant medications must be obtainable to make a practical decision regarding supply strategy. Cost and availability are the deciding factors in determining which is more beneficial: to have a greater number of shipments with less waste or combine several shipments into one.
- **Supply Availability:** As stated above, the amount of supply available for the trial and cost of the supplies are the deciding factors for the shipping strategy. If the trial is limited by existing inventory with only a small probability of a future manufacturing run, a just-in-time resupply may be the only supply strategy that will succeed. Conversely, if there is an abundance of supply, bolus shipping may be a more viable cost solution, such as trigger points and resupply amounts.
- **Technology:** Unless a trial is very small (consisting of few sites and treatment arms), an interactive response system (IXRS) should be employed. Ensure the system is intuitive and offers plenty of control and transparency into supply inventory, as well as a robust resupply algorithm.
- **In-Use Time:** Use this number in the supply packaging plan as the guide for the total number of dosing units per finished goods or dispensing unit. To ascertain this number, consider the total time required from one supply dispensing visit to the next and add the largest window (e.g., if the trial calls for a subject to come to the clinic every two weeks with a window of plus or minus two days, the in-use time for the unit allocated will be 18 days (14 days + four window days). If the trial calls for dynamic titration, this method is still applicable; however, additional calculations are needed to determine the optimal dispensing unit.

\*Helpful Hint\* Plan the visit schedule with the protocol writer to uniform the dispensing visits every two weeks, four weeks, eight weeks, etc.

- **Shelf Life:** Supply shelf life refers to the length of time trial supplies will be viable from the time dosing commences until it is no longer usable. If the supply usually expires six months from manufacturing and repackaging requires six–eight weeks, the shelf life will only be four months (three if the policy does not allow for dispensing to subjects 30 days prior to expiration). A supply with this short of a shelf life will require several manufacturing and packaging runs to fulfill a one–three year trial demand. The packaging intervals and quantities can be controlled and planned for with a proper forecast.

With an understanding of these factors in hand, the details of the clinical supply strategy can be put in place. The following sections list the major aspects of a supply plan.

- **Packaging Plan:** Labeling requirements and blinding techniques aside, the packaging plan should be devised using the enrollment expectations, supply availability, in-use time and shelf life factors. If customize packaging cannot be realized, then (whenever possible) there should be negotiations with the protocol writer for an appropriate dispensing schedule that limits the number of wasted dosing units. Packaging for pooled supplies across multiple trials is an excellent method to reduce the budget; however, an advanced IXRS capable of managing this scheme must be established. An inferior IXRS can belabor the efforts, resulting in an increase in overhead.
- **Distribution Logistics:** It is possible to determine the most strategic location of a depot to service an entire region without having a depot in every country by investigating local laws for both the customs bureau and the established departments of health.

\*Helpful Hint\* Using a regional label book instead of individual country label groups reduces the risk of lost supply as several countries can utilize the same supply.

- **Shipping Strategy:** The shipping strategy includes the initial shipment, upper and lower buffer limits, and resupply levels.

1. **Initial Shipping Strategy** – A small initial shipment with just enough clinical supplies to enroll one subject to any treatment arm is a typical conservative initial shipment. For example: two treatment arms sending two finished goods to 100 sites with 10 non-performing sites will produce 20 wasted finished goods, whereas if a trial contains ten treatment arms this example yields 100 wasted finished goods. The following contains examples of alternate initial consignments.

- **If supply is expensive or limited:**

- » S. Hamilton and K. Fai<sup>2</sup> describe using forced randomization as a means to institute a dynamic approach to the shipping algorithm by fully utilizing the IXRS system. They state, “A dynamic approach to distribution strategy is to initiate each site with enough supplies to cover the first n number of subjects regardless of the number of treatment arms or stratum.” Using this method the randomization list is generated in blocks of x/n allowing for more evenly distributed subject population as well as significantly reducing waste. Using this method permitted the sponsor to reduce waste by ~25%.<sup>2</sup>

- » Another solution is to delay shipping seed supplies until a subject is screened at the site. Of course this is only practical if the screening period has a minimum of five days and expedited shipping costs should be expected.

- **If supplies are inexpensive, sites are proven, the study population is solid or the trial is very short:** It may be fiscally beneficial to ship large quantities of supplies to enrolling sites that will cover 50–75 percent of all subjects. Sites must have ample storage conditions. Note that this tactic will generally not work for temperature-controlled supplies due to lack of refrigerated storage capacity.

2. **Resupply algorithm** – Christopher Ellis stated, “The leading cause of waste is the excess caused by unnecessary supply shipments. This is in part due to the lack of planning when setting up trigger levels that send shipments to sites. Since most sponsor companies disallow site-to-site shipments this excess supply is unusable.”<sup>3</sup> Resupply consists of two levels: trigger-based and automatic resupply. Trigger methods are used to resupply sites during enrollment and should be discontinued or significantly decreased when site supply availability meets the demand for remaining subjects yet to be randomized. Waiting until enrollment is complete to discontinue trigger shipments can result in a surplus at sites. An advanced IXRS system will allow individual site resupply levels for high, medium and low enrolling sites and provide the ability to discontinue resupply for an individual site. The same principles used for determining initial supply can be applied to resupply shipments.

3. **Buffer** – When establishing an emergency resupply it is not typically necessary to allocate more than one additional kit of each supply type per site. Near the end of the trial, allow the buffer to deplete by changing the level to zero in the IXRS. If this is not done and the trial parameters include, say, 100 sites and three treatment arms, there will be up to 300 unused finished goods. If dispensing the emergency supply causes a medical risk to the subject and supplies are extremely limited, run a separate packaging scheme with fewer dosing units for the emergency finished goods kit.

Once the most effective supply and shipping strategies have been determined, the supply plan can be put into action. A forecast should be created to determine total trial supply demand. Although there are several tools that can assist with forecasting, it appears using a spreadsheet remains the industry standard. Although spreadsheets may have been quite functional in the past, they can no longer produce plausible outcomes capable of meeting the expectations of current budgetary constraints and complex adaptive randomization schemes. A good forecasting tool should consider the deterrent factors mentioned previously and calculate need based on the same algorithms used by the IXRS for resupply shipments. Once the packaging plan, distribution logistics, shipping strategy and forecast have been determined, the supply budget can be formulated.

Once the trial has gone live, inventory levels and supply activities must be monitored. Comparing the reports from the IXRS system to the forecast allows verification of congruent behaviors. Unexpected activities, such as slower enrollment, should be promptly controlled. If an overabundance of supplies is being sent to sites, it may be necessary to adjust the resupply levels.

Given the current economic climate, expenses are being tempered in every industry. The pharmaceutical industry is no different. Since the cost of clinical supplies is such a large portion of the overall R&D budget this is one area that can be improved upon. The most successful way to reduce costs is to diminish waste by developing an optimal clinical supply strategy. Determining the factors that pose as the drivers for trials is the first step toward creating that plan. Once the guides have been clarified, the strategy can be constructed, implemented and managed.

## About Medidata

Medidata Solutions is the leading global provider of cloud-based solutions for clinical research in life sciences, transforming clinical development through its advanced applications and intelligent data analytics. The Medidata Clinical Cloud™ brings new levels of productivity and quality to the clinical testing of promising medical treatments, from study design and planning through execution, management and reporting. We are committed to advancing the competitive and scientific goals of global customers, which include over 90% of the top 25 global pharmaceutical companies; innovative biotech, diagnostic and device firms; leading academic medical centers; and contract research organizations

[info@mdsol.com](mailto:info@mdsol.com) | [mdsol.com](http://mdsol.com) | +1 866 515 6044

### Medidata Clinical Cloud™

Cloud-based clinical research solutions | Innovative technology  
Data-driven analytics | Reduced costs | Improved time to market  
Faster decisions | Minimized risk

## Endnotes

1. A. Fleischhacker, Y. Zhao, "Planning for Demand Failure: A Dynamic Lot Size Model for Clinical Trial Supply Chains" 2008.
2. S. Hamilton, K. Ho "Efficient Supply Algorithms for Stratified Clinical Trials.," Applied Clinical Trials, February 1, 2004.
3. Christopher Ellis an Account Manager at Aptuit Inc., a major global supply distribution and destruction company, has over 10 years experience with designing supply distribution strategies.