APPLIED CLINICAL TRIALS

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Strengthening the Links in the Clinical Supply Chain: Aim for Transparency throughout the Process

By Michelle Foust

Most business leaders acknowledge the pitfalls of organizational silos: they breed inefficiency and signal systemic malfunctioning. They impede the flow of information, prevent alignment, inhibit innovation, and cause friction. But, what about the external silos between multiple vendors assigned to different parts of the clinical trial supply chain? Do they cause the same difficulties?

Provided that someone—normally the trial manager—is willing and able to serve as the "ringleader" and facilitate communication and transfers across entities, trials involving multiple vendors in the supply chain generally proceed without major setbacks. However, that is not to say that they run optimally, with all the systems, methodologies, and steps involved harmonized and coordinated. So, aside from creating more work for the manager serving as the point person between parties, companies that rely on multiple outsourcing partners miss an opportunity to drive efficiencies, reduce costs, and improve outcomes.

Some leading life sciences companies have realized that in order to meet their goals for ever more efficient clinical studies, they need a different level of support from their supply chain partners. They are seeking a strategic partner who can apply what Virginia Anderson and Lauren Johnson have described as "systems thinking[1]"—the ability to take into account the interconnections across a broad system. With such a comprehensive view, the supply management vendor can integrate information and processes to manage all trial supply needs cohesively … and can take advantage of those opportunities to work better, faster, and smarter.

The following outlines the benefits of adopting a comprehensive, end-to-end solution with the help of a strategic partner to manage the supply chain, and it shares best practices for each step along the way.

A Comprehensive Approach in Action

What, exactly, does a "holistic solution" applied across the supply chain entail? The hallmarks are:

- A globally-consistent strategy that accommodates country-specific situations
- An advanced technology platform that serves all touch points in the supply chain
- Sound information on which to base forecasts of product demand
- Clear channels of communication that support efficient study start up and management
- A robust distribution system that eliminates the risk of products not reaching their intended destination according to the required specifications
- Visibility into real-time supply and demand metrics across the supply chain
- Dynamic inventory and distribution tactics that can be adjusted to meet current trial conditions
- Reporting drawn from a single view of the drug lifecycle

The benefits that sponsors derive from working with a strategic partner capable of providing such wrap-around service are significant and include:

- A holistic view of the entire supply chain, supporting full lot genealogy
- Increased agility and resilience in meeting trial goals
- Faster, more accurate demand forecasts
- Efficiencies that translate into less drug wastage, the most cost-effective transportation solutions and improved study timelines
- Improved compliance
- Reduced oversight of vendors (owing to fewer hand offs and potential disconnects)

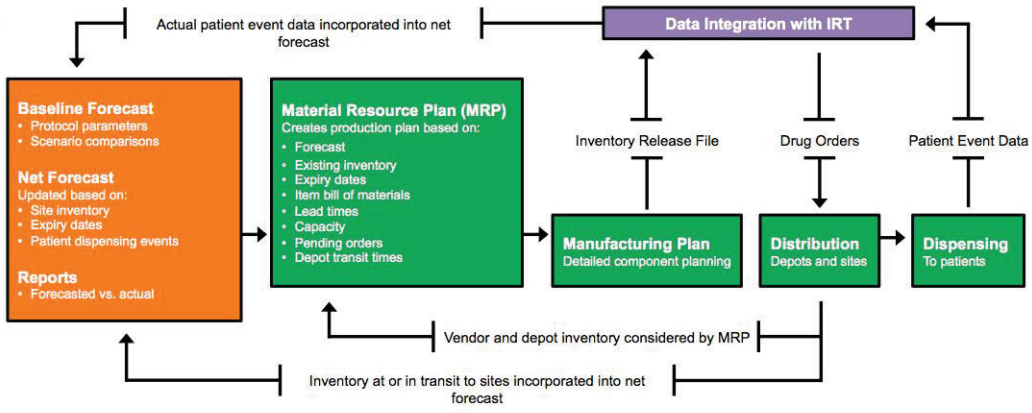
Technology that Creates a Closed Information Loop

There's a significant interdependency between clinical supply management services and the interactive response technologies (IRTs) that are used to connect those clinical supplies with sites and patients. This is most pronounced during the study start-up process with activities such as forecasting supplies, blinded labeling, pooling products, selecting resupply models, and defining the workflow for managing drug returns.

Indeed, coordinating all the complex activities that go into distributing products to trial sites and mitigating the associated risks calls for a closed-loop technology solution that gives all functions visibility to the entire supply chain. This single system supports forecasting and all the downstream processes of manufacturing, packaging and labeling, drug ordering, inventory management, and product distribution with integrated information throughout the life of the study. As the trial progresses, data are gathered from each stage of the process and are used by supply chain managers to consider modifications to all activities upstream. This virtual cycle of information and adjustments allows companies to optimize their approach to meeting the actual demand for the investigational product—all in real time.

Adopting a closed-loop solution through IRT is perhaps the most significant step a company can take in improving supply efficiencies. The right system will remove information gaps that contribute to delays and added expense.

FIGURE 1: Closed Loop Technology for Supply Chain Management



The ability to optimize both production and distribution is tied to having a closed loop of information, with data collected from along the supply chain and integrated for coordinated oversight. The right system will remove information gaps that contribute to delays and added expenses.

Demand Forecasting

A good supply chain plan will begin with a carefully prepared forecast of material demand and incorporate iterative forecasting throughout the life of the trial. The first step is to create a data collection plan that outlines which study variables will drive material demand. From this, a baseline forecast is created to inform manufacturing and distribution plans.

Then, over the course of the study, this initial forecast should be continuously refreshed based upon how demand actually unfolds. The IRT system should provide real-time updates of what is happening with patient enrollment and product inventory throughout the supply chain. Supply chain managers, alerted to variances from the baseline forecast, can modify the forecast and know with great precision how much drug to produce and when. Such dynamic management aids with budget preparation, prevents the wastage that comes from stockpiling supplies, avoids the risk of stock-outs, and reduces emergency measures needed to replace expiring drugs.

The ability to optimize both production and distribution in this way is tied to having that closed loop of information, with data collected from along the supply chain and integrated for coordinated oversight.

Packaging and Labeling

The various options for product packaging and labeling should be evaluated while the protocol is still being developed so that the pros and cons of different formulations and kit designs can be taken into account. A vendor who brings experience across thousands of protocols and all therapeutic areas should be able to advise the sponsor on how to package and label kits most cost effectively and how to use the kit design to encourage site and patient compliance.

In a recent survey of clinical trial participants conducted by the International Society for Pharmaceutical Engineering (ISPE), 60 percent of respondents reported that the design and layout of the medicine kit actually helped them take their medicine on schedule.[2]

The vendor's expertise can also be tapped to find creative ways of "accommodating patients' differing needs and preferences within the confines of a study protocol,"[3] which the ISPE study recommended as a key finding for investigational medicinal product professionals.

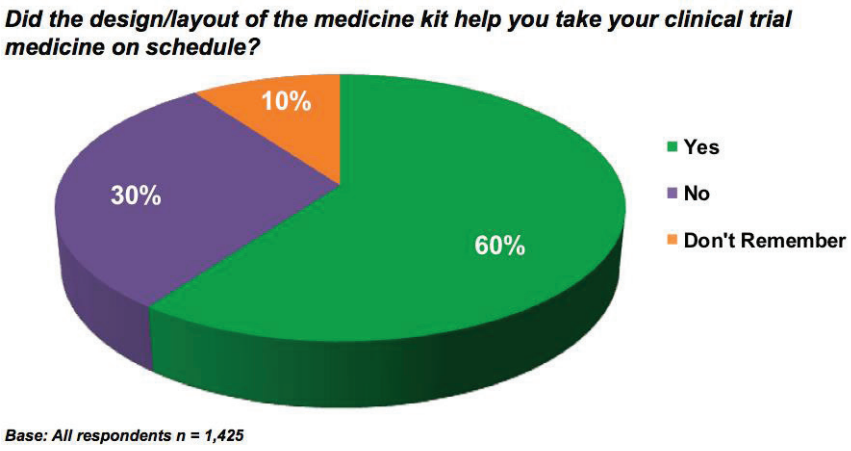
It is not at all uncommon for insights gathered from supply chain management professionals to impact the presentation of the commercial product in significant ways. In one case, for instance, a sponsor had planned to provide a compound in lyophilized powder form to hospital pharmacies. The hospital pharmacist needed to reconstitute the powder and prepare an IV infusion. In the early-phase trials, however, it became apparent that this approach was creating inconsistent dosing and incurring high administrative fees. The supply chain partner was able to help the sponsor develop a new formulation for the product (a pre-mixed solution) that guaranteed a consistent dose, rapid dispensing, and brought hospital charges down to a simple dispensing fee. This was an important advancement since the product was dosed in acute, life-threatening illnesses. Because the partner helped the sponsor through all phases of the drug development for this product, the subsequent transition to commercialization was quite smooth.

The right partner can also recommend methods that can save time and money, whether it be in creating kit designs that can take advantage of automation in the production line or in using just-in-time packaging and labeling to prevent wastage. The key, however, to realizing the benefits of a given package and labeling strategy is to align it with the IRT functionality so that every aspect of production, distribution, and drug assignment is coordinated.

Distribution of Supplies

When distribution is optimized during a clinical trial, enough investigational product is on hand at sites to ensure continuity of care, having arrived in acceptable condition and with minimal cost. Achieving this ideal requires careful planning that begins when the protocol is still under development. Developing a distribution strategy entails identifying the study milestones (such as first pa-

FIGURE 2: Packaging design influences patient compliance and is an important consideration in the supply planning process.



Source: "Patient Experiences with Clinical Trial Materials," International Society for Pharmaceutical Engineering (ISPE), November 2013.

tient in) that will affect product demand and understanding all of the regulatory and logistical details that will impact delivery. Just a short list of the considerations includes:

- Import/export regulations and associated lead times
- The number and mode of product shipments to sites and related costs for storage and transportation
- The need for maintaining temperature stability
- The availability of comparator products
- Regulations concerning product return and destruction

With that information in hand, it is then possible to perform a thorough risk analysis and design a system that delivers what was agreed upon as optimal, beginning with providing initial stock levels at each site. What will work best in any given study depends on the study design, how widespread the sites are, and which countries are participating.

As the study progresses, the product supply "engine" must conform to shifts in demand. When the proper ordering, tracking, and information-sharing processes are in place within the IRT, every function along the way can monitor supply and demand, working proactively to forestall potential issues.

Reporting

Technology should be leveraged to provide everyone involved in the supply chain visibility to the disposition of supplies and to study progress. Through ongoing reporting and analytics, supply chain managers can make informed decisions to ensure that the supply plan is executed properly and adjusted as needed to reflect changing trial conditions. Ideally, technology should provide:

- Insight into the current status of patient enrollment, with trends by site and country
- Comparisons of predicted vs. actual material forecasts
- Dashboard graphics on key indicators of the disposition of supplies.
- The flexibility to download data, manipulate it, and export it into other formats for distribution
- Alerts when conditions approach pre-defined thresholds

Product Tracking and Reconciliation

By working with a single partner that has the right technology in place, sponsors can access a single, comprehensive view of drug inventory across all stages of the study—ideally from receipt of bulk product through production, distribution, administration to the patient, and return of unused or damaged product.

Increasingly, it is important to be able to trace a product by its manufacturer lot number or, in the case of a biotech product, the cell line. Being able to trace the lot genealogy across the supply chain can be critical for inspection readiness, regulatory submissions, swiftly executing product recalls, and managing impending product expirations. When multiple vendors are used in packaging and distributing products, they all assign their own tracking codes to the product, and a full lot genealogy analysis can only be completed by piecing together information from disparate systems.

Regulations require that product inventories be reconciled, with all outstanding product accounted for. The ISPE survey found that 22 percent of respondents have kept trial medications for future use, 4 so it is clearly easy for kits to "fall through the cracks" of companies' tracking systems. Reconciling the amount of product shipped, vs. what was used by patients, vs. what went unused is made far less challenging when a common technology is used to track kits as they move through the process.

Conclusion

Clearly, firms capable of providing comprehensive supply chain management services must have a long list of competencies. And, most important, they must be systems thinkers, able to look at the overall trial plan and take into consideration every regulatory, logistical, and technological aspect involved in seeing that trial supplies are packaged, labeled, stored, shipped, tracked and even destroyed for best effect and least cost. To execute all of these steps, they must have experienced staff, the systems, tools, and procedures to work seamlessly across multiple functions. Transparency from one end of the process to the other is key.

Sponsors that are committed to working with such a provider in a strategic relationship will be able to move beyond simply running trials that progress without incident to achieving substantive process improvements that translate into a competitive advantage.

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1. Anderson, Virginia and Johnson, Lauren, Systems Thinking Basics: From Concepts to Causal Loops, 1997.
2. "Patient Experiences with Clinical Trial Materials," ISPE, November 2013.
3. "Patient Experiences with Clinical Trial Materials," ISPE, November 2013.
4. "Patient Experiences with Clinical Trial Materials," ISPE, November 2013.

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