

WHITE PAPER

OPTIMIZING THE CLINICAL TRIAL SUPPLY CHAIN

Ensuring the right items arrive in the right place, in
the right quantity, at the right time... and within budget.

Testing out new medicines around the world is becoming more complex due to a range of issues, from changing import/export regulations to temperature deviations to planning uncertainties. The complexity will only increase as sponsors look to add new sites in new regions, implement adaptive trials or provide direct-to-patient delivery.

These challenges are forcing a new view of clinical trial supply chain management. This paper will examine how an integrated solution for technology, services and facilities can help to produce optimal results. Implementing the right clinical trial supply chain solution can eliminate the concern that a patient might be turned away at the clinic because a drug wasn't available. Achieving that goal requires a complex set of actions that begin at the earliest planning stage of a trial. This enables you to implement technology-enabled processes that provide greater visibility into each critical supply chain stage to mitigate risk.

You will likely need to involve critical outside experts, where necessary, to assist in regulatory and import/export issues. A single source for these expert services and technology is more likely to ensure all processes are well integrated and produce the desired results. Finally, data and analytics about every supply chain stage should be readily accessible at all times, ensuring that key members of the clinical trial staff can easily access this intelligence, assess needs and make informed decisions. The adoption of this approach should help you mitigate risk and reduce supply chain costs.

INTRODUCTION

The pressure is on. As sponsors run increasingly complex trials while seeking to reach faster go/no-go decisions on their treatments, clinical trial supplies and logistics are vital cogs in the clinical development works. In order to find the best way to ensure that the correct study drug is available on time, sponsors need to have the right people, processes, facilities and technology in place. Success will mean that the clinical trial supply chain is efficient, effective and compliant with the necessary regulations so that you can assess results as soon as possible while maintaining the highest levels of patient safety.

Achieving this goal in a worldwide trial involving hundreds of sites and thousands of patients means coordinating a variety of functions including manufacturing, packaging, temperature management, storage and distribution. Technology used by study teams, supply depots and sites must not only be able to maintain supplies records but also be able to interact seamlessly with other systems and be visible both to local site managers as well as senior study leaders. To complicate matters, the clinical trial supply chain needs to be efficient and cost-effective.

Finally, the system must be in place in time to begin the study as soon as possible. That includes ensuring that the system is capable of modifications, should there be a need to switch dosing or randomization strategies as early stage results prompt changes.

In short, you need a supply chain strategy to manage each and every trial ensuring that the complex elements in every trial and at every site work seamlessly.



Figure 1. Interlocking elements of a clinical trial supply chain

CHALLENGES

In an era of increased regulation to ensure patient safety, supply chain managers don't need to be reminded of the myriad things that can go wrong in their efforts to deliver products to hundreds of remote sites around the world in a typical clinical trial. Like dominoes, if any of the pieces fail, the effect can ripple throughout the clinical trial supply chain. Potential points of failure are illustrated in the following graphic.

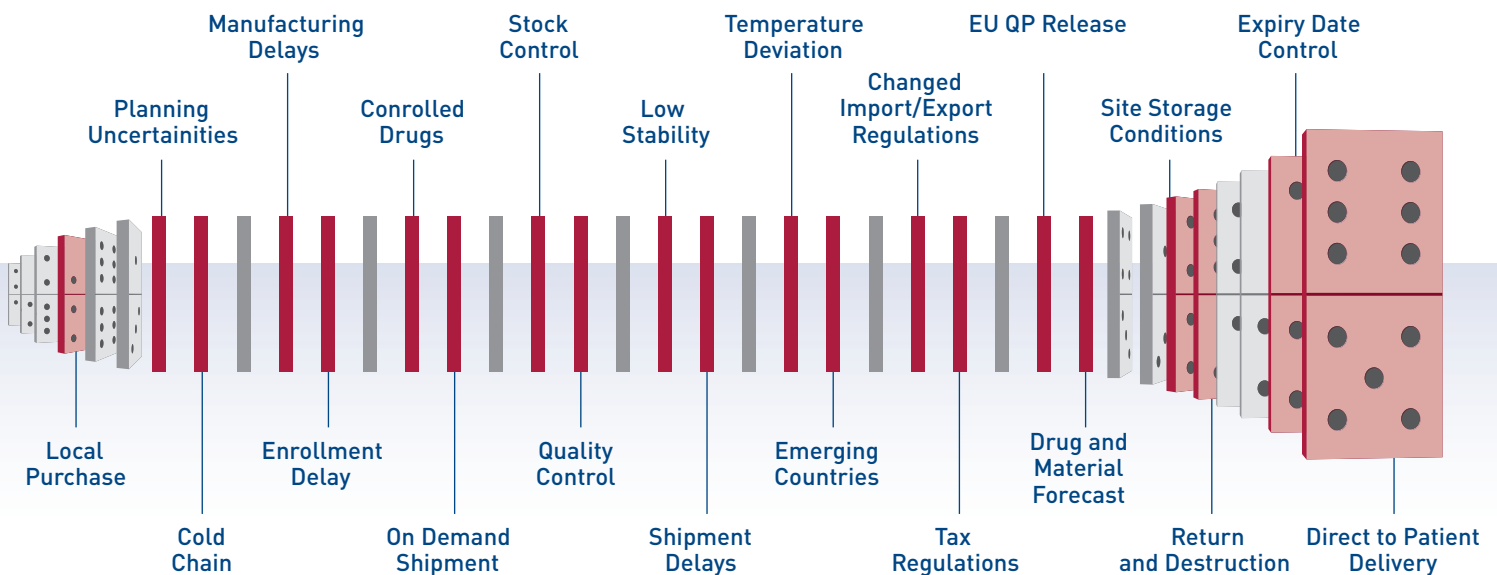


Figure 2. Challenges in the clinical supply chain

Keeping all the pieces in place requires a clinical trial supply chain system with three key parts:

- 1) Delivery of clinical trial supplies including investigational as well as non-investigational medical products
- 2) Ancillary supplies, including all necessary medical devices, equipment, and documents
- 3) Laboratory logistics, including sample tracking, preparation of forms and manuals, lab kit assembly, and laboratory and data management

This system requires expert, proactive project management that ensures quality procedures and deals with complications, changes and any unexpected issues that arise during the conduct of the trial; a storage and distribution network; and technology that connects the clinical trial supply chain stages and facilities, providing intelligence throughout the process.

THE SOLUTION

A holistic strategy combined with the people, processes and technology to execute.

A SUPPLY STRATEGY

Getting the clinical trial supply chain right begins with early involvement of logistics experts in the clinical trial planning process. This is especially true, given the expansion of trials into emerging countries and growing export challenges. Addressing the future challenges requires being aware of what risks exist so that the appropriate clinical trial supply strategy can be developed. Various elements must be engaged including coordination with manufacturing and the development of a global storage and distribution system that may include global drug product purchase. Building and testing a clinical trial supplies and logistics strategy for each study means that sponsors can minimize overage and avoid shortages, optimize production and packaging campaigns, optimize global clinical trial supply chains and balance shipment and supply costs.

To ensure that supplies arrive on time, the sponsor should engage experts with knowledge of local regulatory and distribution issues in each country, including local regulatory updates. That may require using local regulatory experts as well as local or global specialized custom brokers. That's because some countries change regulations frequently, and sponsors must be aware of local regulatory updates. Increasingly, consideration must be given to temperature needs and monitoring during transit.

In this critical planning phase, clinical trial supply chain strategy experts can assist in forecasting and simulation of the clinical trial supply chain. The strategy should also include consideration of lab logistics services including sample tracking to patients, the preparation of forms and manuals, kit assembly, lab and lab data management. The plan should also include sample return and destruction as well as study closure and data transfer.

Last, the strategy should take into account ancillary supplies including consolidated shipment planning and depot configuration, import/export management, warehousing and distribution of non-drug clinical supplies, acquisition and coordination of any medical devices and technical equipment as well as the purchase, printing coordination and distribution of study-related paper documents. Careful planning involving ancillary supplies can achieve transportation and delivery efficiencies.

The clinical trial supply strategy should be supported by automated systems that facilitate processes at the sites and depots and provide more visibility across the supply chain, leading to better quality control. By connecting these services, guided by holistic project management, sponsors can reduce risks and surprises while enabling responsiveness and flexibility to adapt to real-time events during the study. Building a strong strategy upfront that anticipates risks should give sponsors confidence in a system that delivers seamless integration between manufacturing, logistics and technology, offering real-time data processing, smart storage and fulfillment and increased supply chain visibility.

PACKAGING AND LABELING

Packaging and labeling should be considered early in the planning process because many aspects of the design process can have a significant impact on the quality and efficiency of the logistics of the trial.

Early decisions should be made on packaging issues including:

- How the barcode and labeling will be used – such as for dispatch verification at sites, for reconciliation or other uses.
- How the interactive response technology (IRT) system will capture information from the barcode.
- Whether the size of the kit will fit into standard control temperature shipping systems.
- Whether the kit size will cause storage issues at the site or at the patient's home.
- Does the kit design protect against breakage and vibration during transfer? Does it affect temperature control?
- Does the label design and kit allow for multiple updates of expiry, if necessary?

If your study is considering e-labeling, you may need to consider ways in which that may be accomplished. For example, an RFID chip could be embedded in the patient pack or label, and the patient would use a smart phone app to read the label translated for their own country. The technology can be used to track patient compliance, either in a seal or barrier enclosing the dose or a chip that is actually ingested by the patient.

Other innovations impacting packaging and labeling include on-demand or just-in-time labeling as well as direct-to-patient delivery.

STORAGE AND DISTRIBUTION

To ensure clinical trial materials arrive on time, the entire system of storage and distribution needs to be a key part of a clinical trial strategy. Positioning the product closer to the patient can reduce delivery times. Fewer handoffs and reduced transit lane durations can also safeguard your product from possible damage in transit. Companies must be aware of site storage constraints so that deliveries are as close to a just-in-time model as possible, ensuring that excessive amounts are not kept on-site for a prolonged period of time. Managing shipping allocation expiry offsets is important so that you make sure that the drugs are not past expiry or that you are not ordering a drug that ceases to be useful relatively quickly after it arrives at a site.

Good systems minimize investigational product waste and shipping costs while getting the product to depot sites. Effective use of forecasting and simulation will mitigate unplanned repackaging of additional supplies. A well-constructed strategy uses a “study in the box” principle that combines ancillary supplies into one site shipment. Central material flow management leads to cost savings from time and process efficiencies as well as inventory transparency.



Figure 3.
“Study in a box” –
consolidation
of ancillary supplies

Temperature management is becoming a more important part of the storage and distribution chain as regulators require additional verification of conditions during transit. Managing a temperature excursion has placed significant burdens and costs on companies. Passive systems are now available using phase change materials in vacuum insulated panels. More sophisticated systems are available to provide both heating and cooling functionality to maintain the required temperature. Temperature monitors have also evolved. The majority of companies opt for USB monitors, which allow for rapid download of temperature data. The future lies in GPS systems, which allow real-time monitoring as well as track and trace capabilities.

The future of clinical trial supply chain optimization includes on-demand fulfillment strategies to increase flexibility and reduced waste. In addition, interactive response technology (IRT) allows postponing a commitment of product to a patient until the time of dispensing visits.

SITE AND PATIENT MANAGEMENT

At the heart of the clinical trial supply chain is the patient, and the sites that dispense medication to them. Randomization and Trial Supply Management (RTSM) services, enabled by IRT (also known as IVR/IWR), provide the connection between clinical trial supply management and clinical operations. In addition to managing treatment allocation according to randomization strategies to balance treatment groups, eliminating selection bias and limiting the predictability of medication allocation, RTSM services manage real-time subject enrollment at sites and automate inventory management and restocking at sites and depots. They can apply advanced methods to solve difficult clinical trial supply issues that include managing adaptive trial designs, titration regimens or medication pooling across multiple protocols, as well as temperature logging and deviation reporting.

RTSM systems should be rapidly adaptable to enable faster implementation at study start-up and quick response to changes to studies either pre or post go-live. The technology should be straightforward for study and site personnel to use, providing quick access to the functions and data they need. And they should be supported by experts in randomization and clinical trial supply chain strategies to minimize the risks to your studies, since a mistake in randomizing treatment allocations could lead to the entire cost of the trial being lost.

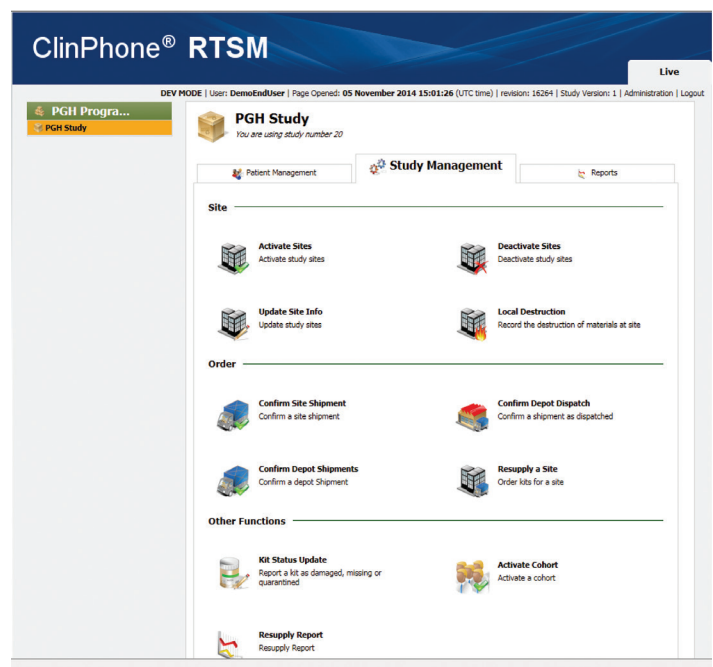


Figure 4. Study management screen from RTSM system

RTSM systems should not live on an island. In addition to connecting to other clinical trial supply chain systems, RTSM should be easily integrated with Electronic Data Capture (EDC) to enable dispensing transactions to be seamlessly performed when recording a patient visit in the EDC system. RTSM should also integrate closely with eClinical Outcome Assessment (eCOA) technologies to close the loop between dispensing of medication and patient reported outcomes.

In order to be tailored to meet the needs of any study, regardless of size, complexity, phase, region or type (drug, device or combined), the RTSM technology should be flexible and scalable, with functionality selectable based on the specific requirements of a company and protocol.

REGULATORY COMPLEXITY

As regulators increase scrutiny to ensure patient safety, many issues arise involving the transport, storage and distribution of medical products. Companies need to ensure that the product remains safe and accountable during transportation and storage, while evaluating product handling requirements, transportation lanes to be used, container availability and cost.

Bringing on board the right partners is key. Those partners should not only have the ability to expand as trials grow, but they should also have detailed knowledge of regulatory issues in each jurisdiction. That means they should have local regulatory experts and local or specialized customs brokers. They should be especially sensitive to countries where regulations change constantly, and companies need to be aware of local regulatory updates and global trade laws so that drugs are not caught in customs delays.

RETURN AND DESTRUCTION

A good clinical trial supply chain management system includes tracking for not just allocation and dosing, but also management of returns, reconciliation and destruction. The return and destruction process should be defined in the beginning of the study with the integration of technical solutions. Best practice takes advantage of interactive response systems to manage the supply chain, reduce storage and dosing errors, manage multiple expiry dates, and account for final reconciliation, recycling and destruction.

This phase should also include the elements that involve study closure and data transfer. A good system that provides dispensing and inventory logs should also provide query resolution functionality and full audit trailing ensuring the integrity and transparency of drug accountability data. When the trial is completed, returns depot personnel should be able to provide the link to destruction certification, meaning that the site, monitor, depot and destruction facility information is completely integrated into comprehensive drug accountability requirements.

PARTNERING FOR INTEGRATED SERVICES, FACILITIES AND TECHNOLOGY

In the best of all possible worlds, you want to identify an expert clinical trial supplies and logistics partner to provide an efficient, safe and economical clinical supply chain for your studies. As you know, the supply chain is rarely linear. Supplying a worldwide trial can produce rocky developments and uncertainties that can escalate down the entire clinical trial supply chain. With the focus on efficiency and patient safety, you cannot afford errors or omissions in managing this complex global supply network.

Your partner should be able to advise you on the best technology to ensure that your electronic systems work efficiently and speak to each other. Engaged early on, they should be able not just to advise on set-up, but to solve problems, identify opportunities and implement actions that will make sure that the trial begins on time and that the new medication is available at the appropriate sites for the patients. That includes making sure that shipments negotiate the regulatory and trade barriers and export/import challenges to arrive at your depots or sites safely and on time. By optimizing the clinical trial supply chain, your partner should be able to help you reduce costs. And, an outsourcing partner should operate under a governance structure that incorporates strong direction, accountability and team orientation. Because change will occur during most trials, trust and transparency allow the ability to anticipate and plan for those changes and also allows continuous improvements.

In addition, your partner should have the sophistication to assist you, should the needs change within the study, or as demands come for better methods to reach patients such as direct to patient delivery. For example, a site enrollment delay can impact timelines, country start, depot set-up, drug expiry dates and re-supply. Your partner needs the experience and sophistication to help you navigate these challenges. Holistic supply chain project management reduces risks and surprises, enables responsiveness and flexibility, and facilitates cooperation and strong partnership between technology, logistics and manufacturing.

CONCLUSION

The goal of an optimal clinical trial supply chain is ensuring that the right systems and personnel are in place, so that the right quantity of investigational product arrives at the right time, in the right place, and within budget.

To achieve that goal, you need the right people, the right processes, the right facilities and the right technology, managed by experienced partners with the foresight to adapt the unexpected events, changes or adaptations in the trial.

The underpinning technology should not just be flexible and equipped with an array of options to manage any upcoming needs; it should also be easy to use by site personnel and by patients. Great partners can ensure that the technologies incorporated are leveraged through the clinical trial supply chain to drive efficiencies, decrease cycle times and incorporate temperature management

adjudication. By providing accelerated decision-making through high visibility to data, you can also eliminate duplicative and reconciliation efforts. The technology should also enforce data quality through the automation of data collection.

When all the pieces come together, you have a successful, comprehensive end-to-end solution that saves time, saves money and gets supplies to the site at the right time. After all, the goal is to get investigational product to the patient, ensure their safety and find out if you have a compound that can be efficacious.

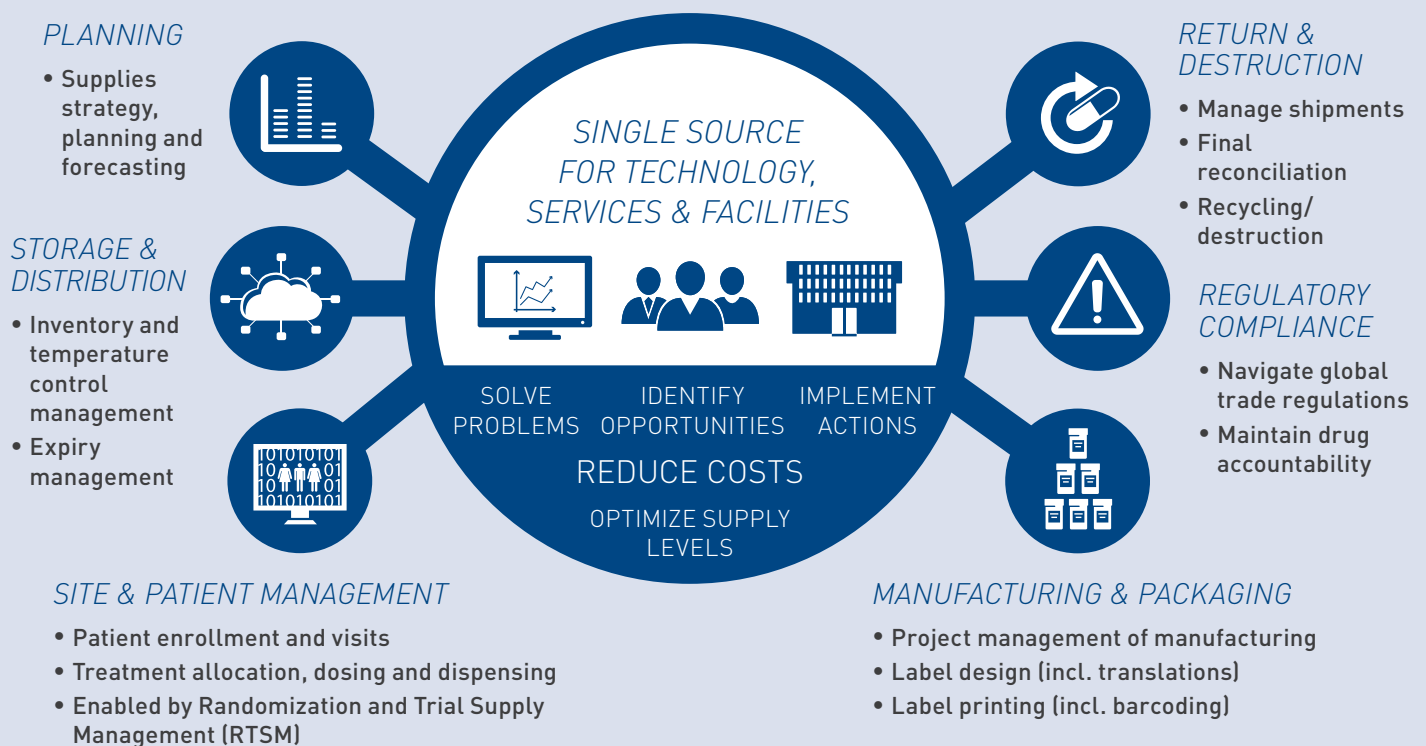


Figure 5. An integrated clinical trial supply chain solution

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