ALMAC

Partnering to Advance Human Health

White Paper

The perfect remedy for clinical trial distribution

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The perfect remedy for clinical trial distribution

Over the past decade the distribution of Investigational Medicinal Products (IMPs) has become a complex part of the supply chain for companies involved in new drug development. In this article we will discuss why an effective distribution strategy is essential to a clinical trial's success.

Clinical studies are becoming increasingly globalised as more pharmaceutical and biotech companies look to reach new seams of treatment-naïve patients and lucrative potential markets for their products. The management of clinical trial logistics is a critical component to the successful development of any new drug or biological product. Entry into new markets means consideration of the specific customs, regulatory and logistical challenges of each country.

The revision to EU GDP guidelines has shown the development to a more generic line. Additionally, this revision has meant that development of an effective distribution strategy inside Europe, is essential to trial success and cost management. No single company can achieve this task on its own; the need to partner with experienced solution providers that have established and tested processes adhering to Good Manufacturing Practice (GMP), Good Distribution Practice (GDP) in multiple distribution routes and product categories is more critical than ever.

What is an optimised distribution strategy?

Success often means different things to different people and, for this reason, it is imperative that, as a Supply Chain Manager (SCM), you do not make assumptions. The first step therefore is to work with the sponsor to identify what "optimal" means to their trial or programme. In the beginning, to build a strategy, Almac will discuss the concept using this starting definition: "an optimised distribution strategy is one that places enough investigational medicinal products (IMPs) and ancillaries of the correct type, at the correct site, in an acceptable condition, and in time to meet patient need using the appropriate level of risk with a clear and reasonable cost adhering to applicable GDP". The SCM will then target each of the aspects in that definition to ensure all stakeholders agree on what optimal actually means.

Once this task is completed, the project team, and Supply Chain Manager, are now ready to move into the operational tasks that govern the clinical supply chain. The ultimate goal in planning any distribution strategy is to ensure that Almac provides the sponsor with the most cost-effective solution while ensuring patients receive an accurate and robust supply of IMPs.

The key to developing an effective distribution strategy

When distributing IMPs, Almac will ensure it adheres to GDP, which is the quality assurance that products are consistently stored, transported and handled under suitable conditions as required by the marketing authorisation or product specification. In order to be successful, an optimised distribution strategy requires upfront planning from the time a protocol is being drafted. The effective collaboration of an experienced, multidisciplinary team or partner with significant understanding of global markets and their various regulatory and logistical requirements offers a significant advantage.

The initial step when developing an optimised distribution strategy is to identify the key distribution milestones at a protocol level, and then put the relevant information sharing processes in place between various stakeholders such as the sponsor, Contract Research Organisation (CRO), Contract Manufacturing Organisation (CMO) and Interactive Response Technology (IRT) to be able to monitor shifts per country from the baseline. Typical milestones for consideration include:

- receipt of material at CMO for distribution
- receipt of Qualified Person (QP) release
- planned Interactive Response Technology (IRT) go live
- provision of Inventory Release File (IRF) to IRT
- planned date of first depot-to-site shipment per country
- planned date of first shipments per depot per country
- planned resupply campaigns
- planned last shipment date per country
- accountability complete and Certificate Of Destruction (COD) reports available.

The second step is to take what was agreed as optimal and apply that to the management of material integrity, timelines, service levels and ultimately budget, performing a thorough risk analysis during project initiation.

The physical placement of clinical trial material is core to successful supply management. The most conservative approach is to have all sites supplied directly from a central location. However, this may not provide adequate

timelines or flexibility, so the need to include a combination of direct-to-site and local depot models will be assessed. The current industry standard is a 'hub-and-spoke' approach that allows for a hybrid of fixed central depots, plus country-specific depots when these are required from a regulatory or strategic product placement perspective.

Design and set-up of the drug-ordering modules in the IRT will have a significant impact on distribution efficiency and cost. The SCM team must use a combination of art and science to build the supply strategy in terms of initial stock levels at site, trigger levels, resupply quantities and timings. Matching these to the stop-assign, stop-inventory and stop-ship within the system is a fundamental part of good distribution management.

Ultimately, the key to success lies not only in the set-up but, more importantly, in the monitoring and ongoing adaptation of the strategy to meet the needs and mitigate the risks to the trial until completion. Flexibility and agility based on clear, real time data sources are cornerstones of the emerging model for global clinical supply management best practice.

Benefits of a dedicated distribution partner

There are many benefits to working with experienced vendors or third-party logistic providers. Almac leverages its Supply Chain Managers' experience of working with a diverse range of clients, products and trial designs to benchmark and continually develop best practice in distribution management. All clients benefit from Almac's interaction across the pharma and biotech industries.

Using this knowledge, the company is able to provide solutions to the operational, supply and budget challenges faced by sponsors when moving their IMP to countries worldwide. The company has made a significant difference, not only during the study initiation phase, but also throughout the lifecycle of a trial using its expertise in trending.

In addition, with a complementary and integrated service portfolio extending into packaging design, QP release and IRT systems, their integrated business model has demonstrated its positive impact on distribution success. For example, during trial initiation, Almac's SCM team recommended that its client, a large pharma company, make changes to its patient pack design. This allowed the pack size to more effectively fit modular shippers, therefore maximising the return from each size of shipper and significantly reducing distribution costs. Add in the effect of matching the initial and resupply order quantities inside the IRT to the shipper size and you have a powerful driver towards optimised distribution.

In another recent example, the company was engaged after the trial go-live date, with a small biotech sponsor company. Trending conducted by the SCM demonstrated that the original IRT design led to increased wastage of high-value kits due to a limitation in stop-assign management across differing visit windows. A solution that modified the IRT system has led to a sponsor saving of over 30 times the cost to change the IRT to date, with further savings every time an expiry event occurs; more importantly it has freed up kits that were of scarce supply in the trial.

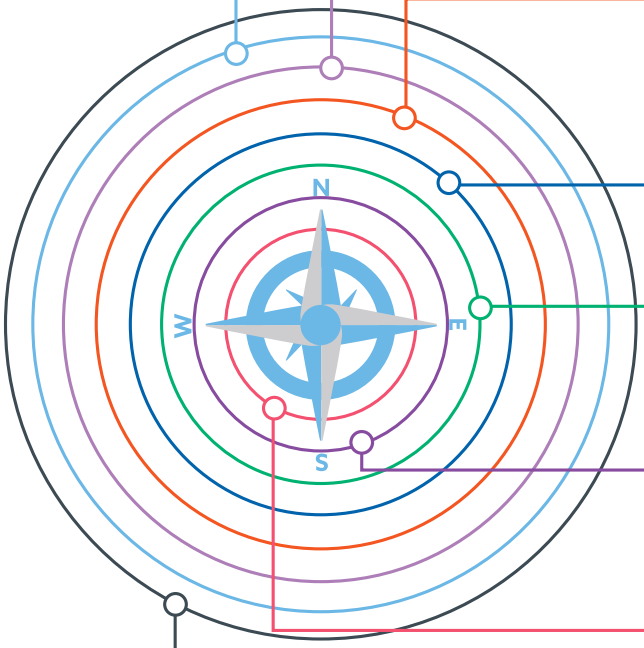
Problems will inevitably occur inside a well-managed supply chain so effective crisis management is needed. The flexibility to be able to respond to changes in times of a supply shortage means the SCM can react immediately. We liaise with our Clinical Technologies Business Unit to adjust the parameters within the IRT resupply strategies to ensure the most efficient distribution of kits and reduced rate of unnecessary stock-outs at depots or sites.

With a global network of couriers and depot partners using Almac-generated harmonised procedures, the company has a robust and flexible presence in all core geographical areas. The company's ability to match the correct courier, broker and route combination per shipment is central to its service level and ensuring the company remains fully compliant with all country regulations.

Summary

The global distribution of clinical trial materials is becoming more challenging and diverse at a time when budgets and timelines to market are also contracting. The implementation of a good distribution strategy can ultimately minimise waste and maximise efficiency in the supply chains of companies involved in new drug development. Almac is one of the market leaders in clinical research support, through its packaging and labelling, distribution, QP and IRT design operations. The Supply Chain Management Team further differentiates the company within today's marketplace by effectively integrating their knowledge and experience of the big picture with these key service offerings.

Identifying the optimum strategy, and key milestones per trial, linking these to real life operational tasks during set-up and constantly reviewing actual against projected progress. This ensures that Almac's Supply Chain Managers develop and adapt each distribution strategy to produce the best outcome possible for your global clinical supply.



Forecast and Simulation
Clinical material forecasting, forecast management and simulation tools along with SCM expertise, matches clinical supply to patient demand, ensuring optimised strategies to meet your trial needs.

Inventory Management
Almac SCMs continually monitor trial supply globally, trending study activities and adjusting future campaigns and material transfers to ensure that the right IMP is at the right place at the right time to meet study demand.

IRT Medication Management
Almac SCMs consult on the medication management IRT design to meet study needs. They set, monitor and adjust inventory management levels and system expiry strategies to ensure optimisation of IMP while reducing distribution costs where possible.

Label Development and Regulatory Vetting
Almac can oversee label text development, regulatory review, translation and artwork, ensuring that IMP labels meet clinical, regulatory, drug product and country specific requirements.

Temperature Services
Almac's innovative software program, TempEZ™, supports the full suite of Almac Temperature Services offerings, providing clients with a single central database to store temperature data while ensuring compliance to GxP and GDP regulations.

Bulk Drug Management
SCMs convert finished good demand into upstream manufacturing and API requirements, working with capacity and lead time limitations to avoid downstream supply interruptions and reduce over production and bulk waste.

Investigator Initiated Trials and Specialised Clinical Programs
Almac SCMs can provide full end-to-end planning, design and management of the clinical supply chain for Investigator Initiated Trials, Expanded Access and Named Patient Programs, designing flexible supply solutions and working directly with clinical sites where necessary to ensure continuous supply.

Pharmacy Services
Almac SCMs can serve as unblinded contacts for drug management and reconciliation, eliminating the need for additional unblinded site monitoring staff. We also have licensed pharmacists who can write pharmacy manuals, dose cards, patient and investigator educational materials; as well as provide input to clinical materials sections of trial protocols. These pharmacists can provide site personnel training at investigator meetings and can be on-call for dosing and drug compatibility questions throughout the trial.

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