A number of challenges can arise when conducting clinical trials in the APAC region, with little margin for error. To effectively manage the supply chain, a cohesive strategy and a suitable partner are essential.
To manage and support the clinical supply chain, sponsors have long relied on multiple outsourcing partners. Conducting biopharmaceutical clinical trials in the Asia-Pacific region is becoming increasingly commonplace. Yet the area is so vast, diverse, and dynamic that multinational companies face logistical challenges in managing the supply of drugs needed for trials. To achieve efficiencies, they are turning to advanced technology, improved processes, and flexible outsourcing models. In this article we will outline best practices in creating a cohesive strategy for managing the supply chain, including the use of partners that can support any or all stages of the drug inventory and distribution process in Asia.

The Yin and Yang of Conducting Trials in APAC

The East Asia and Southeast Asia and Pacific (APAC) region features prominently in most major pharma companies’ strategic plans. Consequently, according to clinicaltrials.gov, the number of clinical trials conducted in the area is steadily increasing – from 11.6 per cent of all trials in 2011 to 16 per cent in 2013 – and with good reason. The area offers a multitude of treatment-naïve patients; India and China’s populations alone are sufficient to sustain virtually any trial, and overall trial costs are generally lower.

Even so, managing the drug supply for a clinical trial in APAC is more challenging than elsewhere. As in other regions, supply chain managers must cope with complex protocols, short timelines for patient enrollment, tight regulations, and cross-vendor alignment. In addition, they must contend with multiple languages, the need for round-the-clock support, country-specific regulations, a lack of trend data on which to forecast demand, and logistical challenges in transporting and distributing investigational products. Unless sponsors are able to find new ways of working, these difficulties can pile on costs, lengthen timelines, and strain resources; cancelling out many of the inherent benefits of running trials in the region.

A New Outsourcing Model

To manage and support the clinical supply chain, sponsors have long relied on multiple outsourcing partners – each offering expertise in one aspect of the process or one local market. However, that practice tends to replace one type of complexity with another. In such situations, trial managers are forced to become ringleaders, devoting considerable time to developing separate service agreements and financial terms with each contracting party, facilitating communication between partners and ensuring smooth hand-offs between entities.

Recently, leading companies have realized that in order to meet their goals for global studies, they need a different level of support from their supply chain partners. This is particularly the case in Asia where sponsor staff may lack the requisite experience to operate effectively across so many divergent countries.
Today, the best practice in clinical supply chain management is to adopt a more comprehensive approach that encompasses:

- A globally-consistent strategy that accommodates country-specific situations
- Sound information on which to base forecasts of product demand
- Clear channels of communication that support efficient study startup and management
- A robust distribution system that eliminates the risk of products not reaching their intended destination according to the required specifications
- Visibility to real-time supply and demand metrics across the supply chain
- Dynamic inventory and distribution tactics that can be adjusted to meet current trial conditions.

Achieving such consistency, insight, and agility dictates reliance on a single trusted partner that can offer a holistic solution across the entire supply chain and that has the technology to integrate information and processes seamlessly from one end of the process to the other. When a company’s outsourcing partner has sufficient breadth of expertise and the right technology framework, the sponsor can realize greater efficiencies, reduced costs, and improved trial outcomes.

**CLEAR CHANNELS OF COMMUNICATION THAT SUPPORT EFFICIENT STUDY STARTUP AND MANAGEMENT**

**FORECASTING DRUG SUPPLY IN APAC**

Developing and maintaining an accurate forecast of product demand over the course of a clinical trial is essential to being able to satisfy the demand cost effectively. The first step is to create a data collection plan that outlines which study variables will drive product demand. A baseline forecast is thus established to inform manufacturing and distribution plans.

In theory, the forecasting process works the same in APAC countries as elsewhere. However, the difficulty is that there is less historical data on which to base demand assumptions than in markets which have a long history of running clinical trials. The risk is that the initial forecast could be wildly off – causing a company to either overproduce a product or fall short, jeopardizing patient safety and study integrity.
WITH **REAL-TIME UPDATES**
**OF WHAT IS HAPPENING THROUGHOUT THE SUPPLY CHAIN, SUPPLY MANAGERS CAN BE ALERTED TO VARIANCES FROM THE FORECAST.**

The best insurance against this is to work with a supply chain manager that has experience in Asian markets and can draw upon institutional knowledge to improve the accuracy of the initial forecast. Even so, it may be necessary to create forecasts for different scenarios and to develop contingency plans.

Then, over the course of the study, with the right Interactive Response Technology (IRT) in place, the baseline forecast can be continuously refreshed based upon how demand actually unfolds. With real-time updates of what is happening throughout the supply chain, supply managers can be alerted to variances from the forecast. They can optimize production planning and shipping/distribution, avoiding stockouts and emergency planning, as well as stockpiling supplies that incur storage costs and lead to waste.

**DISTRIBUTING SUPPLIES**

When distribution is optimized during a clinical trial, just enough investigational product is on hand at sites, having arrived in an acceptable condition and with minimal cost. Achieving this ideal requires careful planning that begins when the protocol is still under development. Creating a distribution strategy entails identifying the study milestones (such as first patient in) that will affect product demand, and understanding all of the regulatory and logistical details (ranging from sourcing comparator products to transportation and customs lead times) that will impact delivery. 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 initial stock levels at each site.

As the trial progresses, the product supply 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.
The cost of shipping products to and from clinical trial sites is estimated to be 70 percent of the total logistical cost of a clinical trial. Clearly, the physical placement of inventory and the number and mode of product shipments to sites is an important consideration. In some trials, all sites are supplied directly from a central location; in others, fixed central depots supply country-specific depots run by local partners in a ‘hub and spoke’ fashion.

What will work best in any given study within APAC depends upon the study design, how widespread the sites are, and which countries are participating in the trial. In most APAC situations, the hub and spoke system works best, given the amount of territory to be covered. It is possible, for example, to ship a product very economically from a central hub in Singapore to a number of APAC countries, all within a six-hour radius, by air.

Meeting Import/Export Regulations

Unlike in the EU where member countries all subscribe to the same set of import and export regulations, APAC countries do not necessarily abide by the same customs requirements. While some countries have efficient systems and well-documented standards, others (such as Vietnam and the Philippines) are still developing their customs regulations, and having to work through them can add significant delays to the distribution process. Regardless, each nuanced difference must be understood and then accounted for in the supply plan so that investigational products end up where and when they are needed.

Some, but not all, Asian countries are members of the Pharmaceutical Inspection Co-operation Scheme (PICS), which aims to harmonise inspection methods under Good Manufacturing Practices (GMPs). A country’s membership in PICS has a bearing on how well its customs officials adhere to specific handling requirements for products. In one country, for instance, controlling the temperature of a shipment may simply mean storing it in a particular building; in the absence of specific instructions, the officials will not know to conduct temperature mapping and validation procedures.

Another common issue is that customs officials are frequently rotated into different jobs, leaving staff unfamiliar with the requirements for pharmaceutical products. This adds to the turnaround time and risk of product damage.

Minimizing Transport Costs

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MAINTAINING TEMPERATURE STABILITY ACROSS CLIMATIC ZONES

Most of the APAC region enjoys year-round summer temperatures, with Australia, Japan, and South Korea being exceptions. As trials in many emerging economies will involve delivering products to remote regions where it is difficult to maintain a cold chain, these conditions must be considered when selecting shipping packs. If the product starts in a winter climate but is transported to a summer climate, the winter pack-out kit will start to lose energy when it is being staged for final delivery. Similarly, if a product starts in a summer climate and is shipped to a winter climate, the summer pack-out kit could permit cold shock. These climatic changes have been so problematic that some manufacturers elect to use active, rather than passive, shipper boxes, despite the five-fold cost increase.

To manage costs and ensure integrity of the investigational product, a robust process must be agreed upon between the partner and courier. In-country depots reduce transit time by removing the cross-border challenges and mitigate against extreme temperature fluctuations. This also allows the use of passive shippers between depots and sites.

COMPLYING WITH RETURN AND DESTRUCTION REGULATIONS

Just as import regulations are not harmonized across APAC countries, standards on the destruction or return of unused products differ by country. Some regions require unused or expired products to be returned to the source country, which incurs still more shipping costs; others require the product to be destroyed where it is currently held. Reconciling the amount of product shipped against what was used by patients and what went unused becomes challenging under these circumstances. Warehouses must be given specific standard operating procedures (SOPs) governing how packs are counted and handled.
TECHNOLOGICAL INTEGRATION

Coordinating all of 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 is a single system that supports forecasting and all of the downstream processes of manufacturing, packaging and labeling, drug ordering, inventory management, and product distribution with integrated information throughout the life of the study (see Figure 1). 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 actual demand for the investigational product – all in real-time.

FIGURE 1: CLOSED-LOOP TECHNOLOGY FOR SUPPLY CHAIN MANAGEMENT

Adopting a closed-loop solution 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 expenses.

TECHNOLOGICAL INTEGRATION

Companies are motivated to outsource their supply chain management to speed up timelines, reduce costs, tap specialised skillsets and knowledge, and access local facilities and infrastructures in study countries.

While the trend is towards outsourcing the management of the entire supply chain to one vendor that has end-to-end capabilities, companies may not be ready to relinquish so much responsibility to a partner. To test the relationship in a pilot, they may outsource every aspect of a low-risk program (such as investigator-initiated studies) or outsource only selected portions of the supply chain management responsibility.
Both approaches speak to the need to work with a vendor that has comprehensive capabilities, yet is flexible in the arrangements made for each clinical study.

Because the goals for each study are different, there are few generalizations that can be made as to how much time or money a company may save by relying on a supply chain partner. For example, the goal for one study may be to ensure that no patient ever runs out of the drug, no matter what the cost. In another, it may be to see that there is no more than a 10 per cent overage in the quantity of product manufactured. There are, however, ample examples demonstrating how study goals can be met through outsourcing.

During a recent multinational, double-blind Phase III trial involving 750 patients at 170 sites, dedicated oversight of supply chain management saved the sponsor over $1.5 million in investigational product and comparator procurement costs. Despite a number of obstacles – the investigational product and placebo were in short supply, the lead time for procuring the comparator was 16 weeks, and the product was expensive and had a short shelf-life – continuity of patient recruitment was maintained and all study timelines were met.

When establishing a contract with a partner, companies must develop detailed service level agreements and select key performance indicators that correspond to the study targets. They should also strive to enter into partnerships with an open mind toward recommendations and new best practices. The right partner brings to each trial the collective experience of studies across multiple sponsors, and should be offering a fresh perspective on what will work best.

CHOOSING A PARTNER

To select the best supply chain management partner for an APAC study, sponsor companies should consider the degree to which the prospective partner:

- Has systems and procedures designed to ensure quality, not merely to provide efficiencies. Look for the existence of SOPs that are created with input from local staff, regular procedural audits, and an investment in staff training.
- Maintains a global footprint. Obviously, supply chain management companies must have an extensive network to supply all destinations and encompass deep local knowledge.
- Has demonstrated stability and achieved maturity in the space. Succeeding in an area as vast and diverse as APAC requires substantial institutional knowledge that cannot be gleaned in a short time.
• Uses technology to support the process. Sophisticated- and proven-IRTs are the lynchpin of realizing efficiencies and mitigating risk throughout the supply chain

• Provides responsive service and proactive communications. The vendor should clarify how roles and responsibilities are defined, how issues will be addressed, and what the expectations are surrounding service and support

• Has a flexible offering that allows for choice in what functions or steps are outsourced. The ideal partner is willing to take on individual parts of the supply chain, study by study, as well as the capacity to ‘do it all’.

When companies take a more strategic, comprehensive, and end-to-end approach to managing the supply of a product in a clinical trial, they benefit from:

• Reduced oversight of vendors
• A holistic view of the entire supply chain
• Efficiencies that translate into less drug wastage, the most cost-effective transportation solutions, and improved study timelines
• Increased agility and resilience in meeting trial supply goals.

When running clinical trials in the APAC region, companies face increased complexity and little margin for error. By relying on partners with expertise, systems and procedures that span the supply chain, they can apply proven approaches to managing the supply of investigational products. Doing so effectively can directly affect the speed with which new products reach the market.

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