Clinical Trial Logistics – Meeting the Needs of an Evolving Pharmaceutical Industry

The pharmaceutical industry, and its approach to outsourcing clinical supply chain activities, has evolved rapidly over the past two decades. Early outsourcing by major pharma was typically a tactical exercise, aimed at alleviating short-term peaks in demand on internal resources. Outsourcing was often prescriptive and aimed at specific tasks – for example packaging and labelling of clinical supplies. Big pharma generally possessed internal capacity and expertise, and service providers simply delivered services based on specific instructions provided by these clients. Conversely, the emerging biotech sector took a different approach. These companies mostly operated under virtual models, with the majority of development services outsourced. Biotech companies typically did not have large clinical supply departments or experience internally, and largely relied on input from service providers to help design and implement clinical supply strategies.

Over the past 20 years, these two approaches have moved closer together. As a result of downsizing, many big pharma companies have shed their internal capacity, and a focus on core competencies has resulted in a reduction in experienced in-house clinical supply managers. While there are specific exceptions, it is reasonable to conclude that both types of company are seeking true strategic partnership with their service providers, with the latter having greater input not only into execution of tasks, but also into the planning process.

This is especially true in the management of clinical trial logistics, which has changed dramatically over the years. This paper will discuss where we have come from, how this service has developed, and drivers for some of this change.

Clinical Trial Distribution – Origins

Two decades ago, shipments of clinical trial supplies typically shared the same supply chain as commercial product. Clinical supplies would be packaged centrally (either in-house or by a vendor) and shipped to the company’s own in-country distribution facilities in territories where the trial was taking place. In-country depots would then ship to clinical trial sites within each country. With the exception of couriers, most of the tasks in the supply chain were performed by each company’s own assets.

Based on the design of the clinical supply chain at that time, this strategy made sense.

- Costs were minimised, as companies were using existing infrastructure and import/export expertise.
- Clinical supplies were often supplied to study sites as a statistical ‘block’ of medication for several patients (block = minimum number of randomised kits required for each site to have an equal number of kits for each treatment arm without unblinding a study). Sites were also supplied with all potential doses for each patient for the entire duration of the study, so additional shipments were not required even if a patient titrated from a low to a high dose. Since the size of the block often exceeded the number of patients enrolled at a clinical trial site, repeat shipments were limited. As a result, the additional clinical trial workload did not over-burden the commercial supply chain.
- Shipping a single large international shipment, followed by multiple short-distance local shipments is more cost-effective than multiple international shipments.

This model had some advantages:

- Lower freight costs than shipping direct-to-site from a single central depot.
- Consistent processes and visibility (one company, one IT system).
- Under block-based clinical supply strategy, low burden as few shipments/site.

However, it also had disadvantages, which would grow as clinical supply strategies evolved:

- Higher overage requirements increasing drug costs – safety stock at each depot, an issue that increased with the growth of biopharmaceuticals and associated increases in drug values/dose.
- Lack of scalability. Can this model be maintained without increasing fixed costs if there is a significant uplift in shipping frequency? What investment would need to be made if additional storage conditions are required across the entire network?

The above approach is used by very few companies today. Changes in clinical supply strategy as a result of technologies such as IRT, globalisation of clinical trials, an increase in the number of temperature-sensitive products in development, an increase in product value, downsizing, increased regulation, and the need for more improved cost control, have led...
to the development of new distribution management models.

**The Impact of Interactive Response Technology (IRT) on Distribution Strategy**

As mentioned above, clinical supplies were traditionally delivered to study sites as blocks of medication, including every possible dose a patient could need. This is potentially very wasteful – supplying a site with eight patients’ medication if they subsequently enrol only one patient would waste seven patients’ supply of drug. Similarly, if a patient discontinued in the trial, the patient-specific nature of clinical packaging at that time meant that their drug was wasted – it could not be re-assigned. Finally, providing all possible doses to a patient was also wasteful.

IRT systems removed the need for ‘patient kits’ and patient-specific labelling of packs. Instead of providing the site with a full block of medication to cover every patient for the entire trial duration, sites could be provided with a small quantity of visit kits covering each dose level for each treatment arm. Since drug was assigned by the IRT system during dispensing visits, there was no longer any need to use patient-specific labelling – if a patient withdrew from the trial or changed dose, medication could simply be assigned to other patients. As sites dispensed drug to patients and inventory was used up, resupplies were automatically ordered by the IRT system once pre-determined trigger levels were hit. As a result of this, inventory could be stored centrally, labelled for multiple countries, and only shipped to site in small quantities as and when required.

While this has a dramatic effect on reducing drug overages and the costs associated with this, switching from supplying each site with multiple smaller resupplies rather than a single ‘full study’ supply dramatically increased the volume of drug shipments required to support each trial. This, in turn, impacted on the costs and workload associated with the clinical supply chain. While some companies persevered with the model of shipping through their commercial local depot network, many companies sought alternatives.

As a result of the increased burden on the commercial supply chain, many companies centralised distribution at a regional level where possible, and contracted all, or surplus, storage and distribution to clinical supply specialists. The EU single market allows shipments to be made easily to other member states from a single EU depot. Also, the EU Clinical Trials Directive made it mandatory for clinical supplies imported from outside of the EU to be released by an EU Qualified Person. Importing through a single EU hub and shipping directly to clinical sites from there reduced the burden of multiple EU imports and releases associated with shipping to multiple EU sites.

**Globalisation of Clinical Trials**

Two decades ago, clinical trials typically enrolled patients in the industry’s main markets of Europe and the US. However, competitive enrolment rates and large treatment-naïve populations have encouraged the industry to broaden the global clinical trial footprint to include new territories in Eastern Europe, Asia, Latin America, the Middle East and Africa.

Many new clinical trial destinations were not served by companies’ existing commercial distribution networks. Local import regulations made it difficult to supply directly to patient sites from outside of each country, and the costs and distances involved in shipping from a central global hub made this an expensive option. As a result of this, pharma companies set up relationships with local distribution depots. Initially this was done independently by local study teams in each country. This approach created some difficulties – separate contracts meant that pharma companies could not maximise volume discounts on service pricing. Also, a decentralised...
approach to depot management led to inconsistent service delivery in each country. As each depot provider operated different IT systems, getting real-time visibility of global inventory and distribution activities was impossible.

This model has the following advantages:

- Allows access to emerging clinical trial territories.
- Hybrid of hubs covering multiple countries, local depots where necessary provides a balance of lower inventory requirements, and lower distribution fees.
- Use of depots in countries with complex import requirements helps reduce administrative burden of shipping to these countries (import licence application) and the number of times the supply chain is impacted by customs delays.
- Use of local depot providers gives local knowledge, which central HQ may not possess.

However, there are some disadvantages:

- Multiple providers of depot services reduce the potential for volume discounts.
- Multiple providers with inconsistent processes can introduce quality risks into the supply chain.
- It can be difficult to get a full ‘global’ picture of inventory.

Setting up global teams and owned facilities to improve this situation was contrary to the industry’s strategy to reduce fixed costs and focus on core competencies. Pharma instead turned to their clinical supplies and logistics outsourcing partners to help determine global distribution strategy, and to manage global depot networks on their behalf.

Changes in the Nature of Pipeline Products and Regulations

Biopharmaceuticals are making up an increasing proportion of the industry’s development pipeline. Global sales of biopharmaceuticals have risen 353% to $163bn between 2001 and 2012. Similar growth has been seen in the development pipeline, with the number of biopharmaceuticals in development increasing from 355 in 2001, to 907 in 2012. Biopharmaceuticals are sensitive to changes in temperature, and as a result are typically shipped under refrigerated conditions in insulated shipping systems. The large cost and weight of these systems compared with standard uncontrolled ambient shipments has vastly increased shipping costs. Also, the expertise required to manage these shipments has increased the skill set required in distribution teams, again driving increased outsourcing to specialist service providers. Storage facilities for temperature-sensitive products require major capital investments and running costs. The growth in temperature-controlled shipping costs looks set to continue to increase as older biopharmaceutical patents expire and generic versions of these (biosimilars) enter development.

New GDP regulations, and the need to demonstrate adequate temperature control even for products traditionally shipped under lower-cost ambient conditions, look set to further increase distribution costs in the future. Industry forecasts estimate that clinical trial logistics spend will reach $2.99 billion in 2014, rising to $3.16 billion in 2018.

Finally, as pharma companies increase their focus on rare diseases, and the number of orphan drugs entering pipelines increase, further increases in...
logistics costs are expected. For example, if a rare disease only affects a few thousand patients globally, recruiting sufficient patients in a short timeframe to support a global clinical trial is likely to require patient enrolment from a wide range of countries, further adding to pharma’s rising logistics bill. It has been estimated that the cost per patient for an orphan drug trial can be more than 25-times greater than that for a more common condition.

Industry Response
None of the above factors look likely to change in the coming years. Pharma will still use IRT technology to control overages and waste in clinical studies, which is becoming more critical as unit dose costs for new drugs continues to rise. In fact, the advent of mobile technology and lower-cost fully-configurable IRT systems is likely to increase the number of trials employing this technology. There is no sign that biopharmaceutical development will slow down – new biosimilar regulations in key markets are likely to continue to increase the growth of these compounds. Clinical trials will continue to globalise – especially as markets such as China become increasingly important to the global industry, necessitating trials on local populations.

To control increased costs and risks associated with these developments, pharma needs to choose between investing in expertise and assets internally, or working strategically with external partners to ensure the supply chain is efficiently maintained. While a handful of companies continue to work in-house and outsource tactically when required, the majority have now chosen to work with a small number of external global partners to benefit from their expertise, asset investments, and volume-based pricing.

The model below illustrates the direction most large pharma companies seem to be taking, in which 1-2 partners are contracted to manage the depot network. It is important to highlight the word manage and point out that it is not necessary for the partners to own their own facilities. No clinical supply company has a depot in every country. Similarly, performance varies geographically even for large global couriers. A multiple provider model managed by a single partner can be very successful – provided partners take responsibility for the quality and performance of any depots they manage. The partner managing the network should also work to ensure that, even if multiple depots are used, the sponsor is able to access supply chain information (e.g. global inventory) from a single source by integrating subcontractor systems and reports with their own, either by rolling a single IT system out across the entire network, or by integrating third-party IT systems with their own.

The management of clinical trial distribution has changed over the past two decades, very much as a result of changes in the wider pharmaceutical industry. While management of the clinical supply chain is a critical part of drug development, it can be viewed as a high-cost (technology, assets and headcount), low-value-adding component of drug development for a pharma company to take on single-handed. External clinical supply specialists, by spreading this cost over multiple sponsors, have been able to invest in improving distribution models to provide a truly global clinical trial supply chain.

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References

Figure 4: Entire Distribution Network Managed by 1-2 Clinical Supply Partners

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