Local heroes

Using locally sourced materials for international clinical trials can lead to significant savings. Tibor Kovacs, key account manager at **Pharmaroad**, advocates considering the following factors when reviewing appropriate national markets and suppliers.

The cost structure of international clinical trials is extremely complex, with financial resources dedicated to the procurement of the required clinical trial supplies – such as comparators, rescue medicine or drugs for basic and complementary therapy – accounting for a major share of overall budgets. The sourcing process for these products is always a challenging task because within the realm of clinical trial supplies numerous factors – such as lead time, cost-efficiency, product documentation and batch or expiry date requirements – must be carefully weighted.

Procurement specialists can consider multiple approaches to tackling the daunting mission of purchasing supplies for large-scale, multicountry clinical trials; experts frequently discuss the merits and perils of central, local and hybrid sourcing methods. All three of these procurement strategies represent different sets of advantages and disadvantages, as well as different levels of complexity with regard to logistic, commercial, and quality control processes.

In addition, the task becomes substantially more complex when it concerns not only the procurement of products but also related services, such as storage, packaging, labelling, contract manufacturing or distribution of clinical trial supplies.

Options to choose from

Historically, central sourcing has been the favoured procurement strategy among sponsors and contract research organisations (CROs). This method involves purchasing every relevant commercial drug and related service needed for a multicountry clinical trial from a single nation; typically from a larger market with the greatest availability of products, or from the country where the central depots of the sponsors initiating and CROs coordinating the trials are located.

Central sourcing allows the highest level of control over all the involved processes; products are procured from a single market via the minimum number of suppliers, manufacturing steps are carried out in-house and logistic processes are coordinated from one central depot.

The financial resources needed to procure clinical trial supplies account for a major share of overall budgets.

As costs associated with the procurement of clinical trial supplies have been gradually increasing (particularly in trials where higher-value reference drugs are used), local sourcing as a cost-effective method has become a more widely accepted solution by sponsors and CROs.

In these cases, procurement of clinical trial supplies and related services is not controlled from a central depot, but is organised locally by qualified vendors in each country in which investigator sites are located.

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A successful local sourcing strategy requires the presence of reliable partners in the markets involved, and the selection of these partners, as well as their coordination, represent extra tasks and responsibilities, as well as additional risks.

Mixed or hybrid methods also exist. These might be employed when, for example, in a multicountry trial, some local markets are capable of offering domestic service providers while others should be supplied from central depots. Combining the two strategies is common. In certain markets, import restrictions determine that clinical trial supplies are to be sourced locally, while in other markets products are available domestically, but the required additional manufacturing processes are rather performed in central depots (export for re-import).

Benefits to enjoy

In general, cost-efficiency regarding the procurement of products has driven the proliferation of local sourcing strategies. Markets typically considered for local sourcing (Southern and Eastern Europe) enjoy a substantial price advantage over Germany, Ireland or the UK, where central depots of sponsors and CROs are usually located. Such differences in prices are particularly relevant where trial requirements include high-value comparators that can be as much as 30–40% cheaper in these markets than in other EU member states.

Cost-efficiency regarding the procurement of services is also a significant factor to consider. Classical local sourcing markets – through lower costs of rent, infrastructure or wages – tend to offer lower prices in terms of related manufacturing

or logistic processes as well, let them be tasks related to relabelling, repacking, storage or distribution. Transportation is the classic example; delivering trial supplies to investigatory sites from a local vendor's warehousing facility is considerably more cost-effective than from a central depot located in another country. This is particularly so if the required products need temperature-controlled transportation or if they include narcotic substances that can only be transported in separate and dedicated vehicles.

The past decade has seen an increased collaboration among manufacturers with regard to the supply of comparators to each other in case of clinical trials. Such efforts have been supported by multiple initiatives, such as the establishment of the TransCelerate's Comparator Network with the participation of several major pharmaceutical companies.

However, situations still prevail when manufacturers afraid of losing future markets to new innovations are hesitant to provide comparators for international clinical trials sponsored by their competitors. In these scenarios, the availability of products in a domestic market can easily tilt the scale of procurement strategies towards local sourcing.

> "Opting for a local sourcing strategy presents an extra amount of work, as finding the suitable markets and suppliers involves a lot of analytical and organisational tasks to be performed."

While forecasting plays a significant role in the work of procurement experts, it is almost never possible to provide an exact calculation for the quantities of products to be used during a multicountry clinical trial. Given that a shortage situation of a specific commercial product during a trial is a highly feared scenario, purchasers tend to rather err on the side of caution and secure slightly larger volumes of comparators and related products than the initial estimates. This can lead to scenarios in which unused stock of substantial value is to be scraped at the end of trial. In these

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situations, local sourcing can also contribute to reducing overall costs by optimising waste management.

When comparators are sourced through a local wholesaler – one that is well integrated into the domestic supply chain, regularly provides goods for pharmacies and hospitals, and is committed to a just-in-time delivery approach towards clinical trial supplies – unused, but not manipulated stock need not necessarily be destroyed. When forecasts have been exaggerated or a trial ends prematurely, products already acquired and not yet manipulated can be diverted back to the domestic distribution cycle.

Products in local languages offer multiple benefits when it comes to clinical trial supplies. They can guarantee more patient-friendly protocols as trial participants and medical personnel welcome products in local languages that enable better communication and provision of information through the original product documentation (SPC, PIL and LAB), as opposed to translated labels or booklets. Also, in many product categories (including rescue medicine, standard care, complementary therapy) local supplies might not need to be labelled or repacked at all, further reducing manufacturing costs.

In addition, when products in local languages require no manipulation of the packaging, they can also contribute to an increased speed of supply and resupply from the local market. What is more, the inclusion of local products in the protocol might even guarantee an easier administration and approval of the submitted trial documentation on behalf of the regulatory agencies.

Challenges to consider

Overall, the challenges presented by successfully implementing a local sourcing strategy can be grouped into two larger categories: risks associated with local markets and risks associated with potential suppliers. Even though these two factors can be mitigated by conducting thorough planning, it should be noted that local sourcing will always represent a certain level of additional risk, as well as an extra layer of complexity in the procurement system.

In terms of minimising country risks, a few determinants must be considered. The most important factor should be the

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security of the supply chain in the given local market. Procurement experts should consider local markets where the risk of potentially falsified medicine entering the legitimate supply chain is minimal. Regulatory agencies in local markets might maintain officially published lists that include all registered cases of falsification that could be reviewed to draw some general conclusions.

Markets with a well-established pharmaceutical industry and manufacturing base are better suited for a local sourcing strategy. These markets tend to have already developed a strong support service sector, including organisations specialised in contract manufacturing, temperature-controlled transportation, packaging and labelling, and analytical and laboratory services to name a few, which could be relevant within the domain of clinical trial supplies.

Obviously, the higher the number of the trials being conducted at investigatory sites in a given country, the better the chances are that the local market will include experienced – and even specialised – service providers.

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Sourcing specialists should look for markets in which goods procured for clinical study purposes pass through the shortest possible supply chains without myriad intermediaries.

Ideally, local sourcing suppliers should acquire stock from manufacturers and marketing authorisation holders on the basis of direct-supply contracts. The latter should enable wholesalers to request products for clinical trial purposes directly from manufacturers, in bigger quantities, with confirmed resupplying capabilities and according to specific expiry dates or batch requirements.

Procurement experts should identify suppliers whose close cooperation with manufacturers yields the result that preliminary product documentation (certificates of analysis and conformance, for example) is always available for clinical trial supply purposes. In addition, wholesalers working directly with manufacturers and participating in local sourcing strategies should be in a position to meet additional documentary requirements – a bovine spongiform encephalopathy or transmissible spongiform encephalopathy statement, or pedigree certificate for example – or acquiring otherwise difficult-to-obtain documents, such as a medical safety data sheet, or equivalency statement.

Ideal suppliers in local markets should have a portfolio that includes the widest range of potentially required services with regard to trial to be conducted. One-stop-shop service providers should be able to offer such relevant capabilities as product procurement, regulatory assistance, warehousing, distribution, labelling and packaging.

It is of paramount importance to work with local partners that are not only knowledgeable about the guidelines on good distribution and manufacturing practice (GDP and GMP) but are also well versed in industry-specific regulatory, quality control and operational requirements as detailed in the good clinical practice (GCP).

Returns on investment

There is no 'one-size-fits-all' way to provide goods and services to international clinical trials in a professional and cost-effective manner. There is no magic wand that can eliminate every difficulty associated with the procurement challenges of ensuring that investigatory sites in all participating markets are adequately provided with the fullest range of properly manufactured, packaged and distributed supplies.

Not every national market is suitable for local sourcing. In some markets, products are only available through secondary and tertiary suppliers; product documentation cannot always be acquired; and the risk of falsified products is considerable. The consensus is that local sourcing can serve as a useful tool for procurement managers – but only among the appropriate market conditions, and with suitable and carefully vetted vendors.

Opting for a local sourcing strategy presents an extra amount of work, as finding the suitable markets and suppliers involves a lot of analytical and organisational tasks to be performed. Potential local suppliers should be verified thoroughly through all the necessary documentary steps as well as through proper personal audits. Such supplier verification processes can be tedious, but, given the advantages local sourcing presents, they are well worth the investment of time and effort.

Several of the industry's largest CROs and manufacturers for which cost-efficiency and more patient-centric approaches towards trials are priorities are already engaged in establishing relations with trusted local partners. Those that are still to venture into local sourcing should be encouraged, as the benefits with regard to decreased costs and improved quality of service far outweigh the risks and additional workload. ■

Further information
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