Analysing Trends in Global Comparator Sourcing and Distribution in 2015 – A Preview

Introduction
Activity in clinical trials continues to rise unabated, despite subdued dynamics in the world economy along with severe political tensions between Russia and the West, as well as infringements in some regulatory environments.

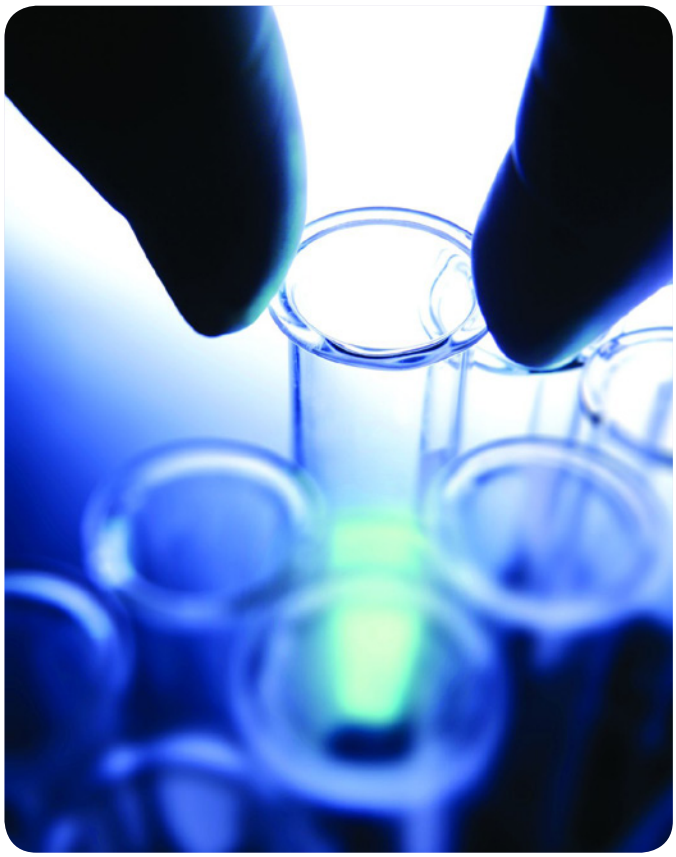
In developed countries the requirement to meet economic and clinical standards for a new drug entering the market seems to be increasing year after year. Local bodies in Europe such as the UK's National Institute for Health and Care Excellence (NICE) and Germany's Institute for Quality and Efficiency in Healthcare (IQWiG), to name a couple, have been shown to be tough in their assessment of new drugs. Thus, sponsor companies have to implement appropriate clinical trials to meet requirements as well as to aim for increased efficiency.

The search for potential benefits by sponsor companies has resulted in an expansion of multinational clinical trials to involve fast-growing countries in the Latin Americas, such as Brazil and Mexico, and Asian countries, such as India and China, in addition to developed western countries. These benefits include a reduction in the associated costs, access to large patient pools, and in some cases higher recruitment rates. However, looking at the global spread of clinical trials, it has become obvious that in a number of these countries, pharmaceutical companies face significant and in some cases rapidly changing challenges for clinical trial supply, and as such also for the sourcing and distribution of comparators.

A recent report published by the Institute for Healthcare Informatics, also forecasts that the surge in cancer drug innovation is projected to continue over the next five years, with oncology currently already making up 25 % of the global late-stage pipeline[1]. Underlining that, the need for secure and transparent sourcing of comparator drugs and non-investigational medicinal products (NIMPs) on a global scale is likely to rise significantly.

This article aims to identify some patterns in the sourcing and distribution of comparators in the coming 12 months within this environment.

Change in China
China is now the world's second-largest pharmaceutical market, behind the US[1]. As has been observed for some time, an aging population coupled with a steady increase in chronic diseases and rapidly growing city-based populations means that China seems to be an ideal location for pharmaceutical research and development. Unlike other emerging or fast-growing markets, the



number of clinical trials initiated in China looks to be increasing year after year[2]. As can be seen by numerous investments in China by pharmaceutical companies recently, this is unlikely to decrease. With Bayer having set up a research and development facility a few years ago, 2014 saw AstraZeneca partner with the Shanghai-based Pharmaron and a number of companies set up central research laboratories in the country.

Although a move to initiate clinical trials in locations such as China offers a number of benefits, such as rapid enrolment, companies face regulatory and bureaucratic hurdles that can often cause significant delays, as the regulatory landscape in China evolves and specifications become more stringent. Although quality and supply chain expectations are increasing, in markets such as China that are still developing reliable and consistent regulatory systems, it is advisable to monitor the supply chain closely to ensure the prevention of falsified medicines entering the chain remains high by all parties at all times. Particularly since recent trends in comparator sourcing show a preference towards sourcing locally registered commercial drugs in China, if these are available.

Looking at the overall picture, the number of trials taking place in China looks set to continue to expand in the next 12 months, as the supporting regulatory system and infrastructure develops into a sustainable foundation for future work in this area, thus giving confidence to investors.

Indications for India

Continued change can also be viewed as a key feature of India's complex regulatory system, making it important for sponsor companies and other clinical trial stakeholders to monitor developments to enable them to adapt to changes in a timely manner. Furthermore, positive change, such as the creation of the Indian Clinical Trials Registry, shows a shift towards greater transparency. Coupled with more robust quality overall, and thus increased safety, it appears that the gap to western developed country quality systems is shrinking. As 2014 showed, there arguably remain some uncertainties with regard to patent infringements, which may mean that some pharmaceutical sponsor organisations choose to be cautious with regard to carrying out clinical trials in India in the coming months, instead opting to observe and await stabilisation of the regulatory landscape.

Preview of Russia

The implementation of Russia's strategy of development of the pharmaceutical industry saw a move towards increased innovation in Russia in the last few years and it looks as if the regulatory landscape is opening up more to pharmaceutical research and development. Furthermore, overall increased quality, including closer GMP alignment with European standards, shows a positive shift. Yet, like in other countries that have been prominent for some time now, Russia is also going through significant change. In Russia's case this includes restructuring of its healthcare system, but also improvements in pharmaceutical conditions including import / export and the removal of certain bureaucratic barriers. As these factors have the potential to cause long delays, they should be considered at an early planning stage when assessing the complexity of a trial's supply chain. From a comparator perspective it is also essential to consider suitable distribution strategies early on, particularly in a vast country like Russia.

Overall it can be said that Russia's market looks to be on the rise, but it is very likely to be constrained by the political turmoil recently affecting western relations with Russia.

Other Countries

Like the above-mentioned countries, clinical trials moving to Brazil and even countries such as Mexico, which has seen some social unrest, look to be increasing. Access to population-dense urban areas and the prospect of high patient enrolment and retention continue to make Brazil especially an attractive country, particularly with presumably more political stability after the recent presidential election. However, as in other countries with less well-established regulatory systems, it should be noted that approvals, as well as processes such as local sourcing of commercial drugs for comparator use, can be slow.

Sourcing Strategies in a Global Setting

Since the sponsor organisation is arguably further away

at times when a multi-centre trial is spread globally, the risks can increase. One example is quality within the clinical supply chain, which can become significantly more complex in the global setting. This can also be said when looking specifically at the comparator sourcing and distribution process. It is advisable to qualify any supply chain to be used for proper and safe delivery of the clinical supplies. With this in mind, it may be beneficial to work with an experienced partner that can provide a company with access to an already qualified global supply and distribution network. Furthermore, there are hurdles such as local language barriers, working in different time zones, and potential cultural differences, that can be navigated together.

When sourcing comparator drugs as well as auxiliary products, often for late-phase, multinational, multi-centre trials, there are a range of sourcing strategies for a sponsor company to consider. A sponsor may choose to source themselves, e.g. via a local affiliate, outsource completely, or use a combination of the two strategies. If a team decides to outsource the comparator sourcing component of a trial, thorough research should be conducted to confirm capabilities of an external provider. Furthermore, it is recommended that in-place quality systems are audited and it may be advantageous to request to review case-study examples. This way it should be possible to find an organisation that best matches the needs of the clinical trial. It is worth bearing in mind that working with a sourcing partner, who has a presence in developed western countries as well as an emerging markets footprint, may be advantageous. They can offer access to reliable local market intelligence on commercial products, including product availability and information on product presentations. Working with a partner that has access to commercial drugs direct from manufacturers or their authorised distributors, can lower the risk by ensuring authenticity, with the appropriate paper trail. Furthermore, having access to flexible procurement options via a global network can enable sponsor companies to consider both local and central sourcing strategies for different products within the same trial.

Looking at both small and large molecule drug development, the focus on biologics looks set to continue. With biologics making up 36 % of the late-stage pipeline and 45 % of the late-stage oncology pipeline in October 2014[1] it is important to consider areas of particular risk in a supply chain, such as transport routes when handling such temperature-sensitive products. One such factor is the range of natural temperature differences between clinical trial locations globally, as well as factoring in potential delays in import and export processes. Furthermore, in some instances, export of samples can be very straightforward yet import of a comparator drug may be much more complex, and it may be advisable to work with an experienced partner, who can offer guidance on important factors such as documentation, in such instances.

Conclusion

Pressures to reduce the costs of clinical trials remain high in established markets. Many pharmaceutical sponsor companies continue to opt to include fast-growing countries, in their trials, where the potential for cost-cutting is significant, but where numerous regulatory barriers must successfully be navigated. The pattern of distribution of clinical trials that has emerged is likely to continue to govern future activities, with activities in China particularly leading the way. It thus becomes more important to monitor the regulations across all applicable markets or have access to such information through third-party providers. Furthermore, it is recommended to benefit from working with companies that have strength and experience in comparator sourcing in a particular country. At a time when the process of securing clinical trial supplies has become increasingly difficult and complex worldwide, working with a knowledgeable partner may enable a sponsor to more easily realise the benefits of working across a range of countries.

References

1. IMS Institute for Healthcare Informatics. Global Outlook for Medicines Through 2018. November 2014.
2. Beth Nuskey. Overcoming Clinical Challenges in BRIC Markets: A White Paper. Thomson Reuters. April 2014.

Ann-Marie Huss is the Managing Director of Multipharma Clinical Supplies Ltd, UK, which is part of the Multipharma Group. She is focused on clinical trial supply, namely sourcing of comparators and local NIMPs. She obtained her BSc (Hons) in Biological Sciences (Pharmacology) from the University of Edinburgh.
Email: ann-marie.huss@multipharma.com