There are few clearer illustrations of the rapid changes impacting the pharmaceutical sector than the clinical trials industry. Clinical trials were once undertaken largely in the West. However, the associated costs combined with intense pressures on pharmaceutical revenues and general financial upheavals in the US and European economies and financial markets have resulted in a major relocation in recent years. Estimates¹ have suggested that 100,000 trials are now being carried out in over 100 countries at any one time.

Along with the change in location, the outsourcing of clinical trial activities to clinical research organizations (CROs), particularly in emerging economies, has become a highly effective way for major pharmaceutical companies to streamline operations and concentrate on core activities. This has seen the dynamics of outsourcing change dramatically in just a few years, with CROs emerging as strategic drug development partners rather than transactional headcount providers facilitating recruitment, site management or data analysis tasks.

Asia, in particular, has risen to the forefront as a top clinical trial destination and, with service providers maturing, this region now offers an alternative to traditional emerging regions, for example, Eastern Europe or Latin America. Such changes are paving the way for a new strategic relationship between CROs and clinical supply chain service providers such as Zuellig Pharma Specialty Solutions Group.

Increasing focus on Asia
There are numerous reasons why Asia has become the fastest-growing pharmaceutical market globally. The region is home to 60% of the world’s population, offering tremendous market potential. There is a growing educated middle class interested in health issues and/or aging populations, and an increasing pool of talented human resources. As economic prosperity impacts on the way people live, chronic and lifestyle diseases such as diabetes and heart disease are beginning to affect more of the population in the region. These factors, together with people’s growing ability to spend more on healthcare have all helped to attract pharmaceutical research and development and CROs in growing numbers to Asia.

In addition to consumption of marketed drugs, Asia facilitates clinical trial operations in several ways. High population densities in metropolitan areas, coupled with large hospital infrastructure, allow individual study sites to recruit more patients more cost effectively while keeping study timelines on target.

Although evolving regulations in Asia continue to be a challenge, the greater number of studies in the region also helps regulatory authorities to understand more about practices in other leading regions such as the United States and European Union. Such involvement and exposure should continue to positively influence the review of local regulations, with the aim of providing each community with the most affordable healthcare products.

¹ Cited in Loke, W.C., “There are no winners in the clinical trials race in Asia”
Industry drivers
Faced with stagnating sales, an array of upcoming patent losses, and rising research and development costs, concerns have arisen about research and development productivity at leading pharmaceutical companies in recent years. This has resulted in major bids to reduce research and development expenditure. It is widely expected that such resources will further contract.

The industry overall has also been downsizing. In 2010, approximately 80,000 job cuts in the pharmaceutical and healthcare sector were announced in the US alone, according to one recent article. The trend for outsourcing key activities is compounding these losses. Meanwhile, strategic business planning, bio-statistical analysis, laboratory services, and clinical operations have been growing business sectors for CROs. Many of these jobs are being created across the Asia-Pacific region.2

Transformation of CROs
As the involvement of CROs has risen, the industry has enjoyed growth in recent years, increasing from US$14 billion in 2006 to US$24 billion in 2010. The expectation is that this will continue on an upward track. However, outsourcing clinical research is highly complex and if pharmaceutical companies want to see a true productivity increase then efficiency in managing CROs also needs to be considered. This has led more sponsors to transition from traditional multiple transaction-based relationships to fewer strategic drug development partnerships. Such partners need to have global coverage and expertise in many therapeutic areas while covering all functional disciplines.

In line with this, mergers, acquisitions and alliances have become a trend in the CRO industry, including the Indian and Chinese markets. Many global and local CROs have merged or formed alliances with small to medium-sized companies to enhance capabilities and improve local therapeutic expertise, allowing them to better compete for global clinical development programs. Companies possessing complete geographical coverage, diverse therapeutic competence, and the ability to provide comprehensive services covering the various stages of drug development will be among the most promising contenders for strategic deals that could be valued in excess of US$100 million. Such services range from project management and medical affairs to regulatory matters, quality assurance, and data analysis. The consolidation trend among the current 1,000-plus CROs is hence expected to continue.

Pressure to succeed
As opportunities increase for CROs so do new pressures, including the need to find an accelerated development process for faster returns. CROs are also increasingly being asked to share more of the risks. To handle such developments, greater collaboration between CROs and sponsors is necessary in the early phase of the drug development process. In addition, improved patient recruitment performance could shorten timelines. Commentators note the significance of CROs getting their market access and site-development strategy right for success, especially in the fast-changing evolving environment of Asia. The approach to site development is also an important determinant of whether a study is completed on time and to acceptable, internationally recognized quality standards.

Risks and challenges in Asia
With the emergence of more CROs across many countries and higher clinical trial density per site in major agglomerations, recruitment and retention of research participants is often the most difficult deliverable in Asia. Reasons include:

- Only around 35% of patients in Asian countries live in metropolitan areas with sites that support clinical research
- Low awareness of enrolment opportunities into clinical trials
- Aging populations that take drugs for multiple chronic conditions, making them ineligible for most trial protocols

Besides recruitment, regulatory frameworks can be a challenge in Asia. Unlike North America or the European Union, Asia currently does not have a harmonized regulatory body and rules vary for each country in the region. Another major challenge is new drug registration regulations in some countries (for example, China and Korea) that require a local or regional population to be included in a clinical study if a sponsor ultimately wants to gain permission for local marketing.

Partnering with a clinical trial logistics supplier such as Zuellig Pharma, with its established presence in the region and knowledge of individual country regulations and their differences, can thus be beneficial for CROs.

2 Rebuck, A., "Outsourcing strategy for drug development in Asia"
Key clinical trial destinations

For more than a decade, the emerging markets of Asia-Pacific have held special promise for the global pharmaceutical industry. Driven by a combination of rapidly expanding economies, technological innovation and a talented workforce, the region has seen explosive growth in both economic and political power. Asia-Pacific's clinical trials market has been steadily growing with greater focus primarily on India and China, with South Korea, Singapore and Taiwan, among other favorite destinations. The following offers a snapshot for various key locations in the region.

Australia
Australia is the most mature clinical trial market in Asia-Pacific. Over the years, it has developed an effective regulatory system, led by the simple Clinical Trial Notification (CTN) scheme. With CTN, approvals can be obtained within weeks. Such rapid approvals, which save time and money, have helped Australia to become a popular destination for sponsors, especially those seeking early, reliable proof-of-concept data. Australia is commonly regarded as a costly country in which to conduct clinical trials. However, as one recent article pointed out, the relatively cash-strapped product development environment means the country is used to handling tight budgets and outsourcing to CROs. There is also a research and development tax credit scheme, which allows eligible applicants to receive a 45% reimbursement of research and development expenditure.

Malaysia
Current clinical trial activity is at a low level and this is unlikely to change rapidly. However, if the Ministry of Health follows through on its planned initiatives, Malaysia could be in for a turn-around. An announced revamp of 12 key national economic areas includes the development of a supportive environment for the growth of clinical research. Strategies include an increase in clinical research sites, streamlined regulatory processes, more CROs, and fostering of relevant human resources, among others.

Singapore
Singapore has attracted research and development to its shores for many years by providing incentive programs and being at the forefront of intellectual property protection. As a result, there are around two dozen CROs and pharmaceutical companies that manage regional clinical trial programs from Singapore. A robust economy has also enabled the government to pledge billions more Singapore dollars in research and development investment, while other economies are still recovering from downturns. The Lion City's sophisticated transportation and communication infrastructure, advanced regulatory framework and educated workforce not only support clinical operations but also the clinical supply chain. This has also attracted numerous logistics companies to set up depots in Singapore. Its inherent challenge is a small population of just over five million.

South Korea
The country has become a leading clinical development hub in Asia, helped by a government focus on healthcare. One illustration of such support is the Korea National Enterprise for Clinical Trials (KoNECT), which was set up in 2007 to boost the medical industry, human resources and core technologies in this area. KoNECT has been active in forging partnerships with industry heavyweights such as ICON and INC to advance standards and build a high-quality international clinical trial infrastructure. The Korea Drug Development Fund was established in September 2011 with assets of US$1 billion to develop at least 10 new drugs by 2019. The Fund has chosen PAREXEL as the first CRO to help Korean companies develop and commercialize healthcare products for the global market. With English still not widely spoken, the language barrier is probably the biggest challenge for South Korea.

Philippines
The country has yet to see its full potential optimized. While the country’s geography sometimes makes it tough to supply sites with the required drugs, the country boasts a highly educated healthcare infrastructure that is widely English-speaking. Importation of investigational products can be challenging for a clinical supply chain without a local depot. However, enhancements to the regulatory environment and in particular to investigational product import

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1 Pennisi, M., "Australia is the new hotspot for clinical research"
procedures would further the country’s appeal. In recent years, several CROs have furthered their presence to support a pick-up in activities. As a low-cost country, the Philippines may be well suited to provide regional services around patient compliance and data management through call centers.

Taiwan
Among Taiwan’s benefits are its relative cost-effective environment compared with other neighbors such as Korea or Japan and its own biotechnology industry that creates domestic demand. With liberalization of certain regulations in Japan, Taiwan has seen a surge in demand initiated by Japanese manufacturers extending more trial activities to neighboring countries (China, Taiwan, Korea). Communication can create obstacles as English is not widely spoken in Taiwan. In addition, the fact that investigational products cannot be destroyed or exported immediately upon discontinuation of study activities in a particular hospital site pose additional logistics challenges that sponsors or CROs will have to overcome. However, use of a local depot offers an effective solution to address this concern.

China
Significant progress has been made in China in allowing more trials to be conducted. The attraction remains the huge, treatment-naïve population representing different ethnic groups and low-cost environment. Every major research institution has a presence. The CRO market is expected to grow to US$750 million by 2015 (CAGR of 15%). Chinese government plans to invest some US$1.5 billion in new drug development between 2011 and 2016 have also been cited as evidence of a solid commitment. More than 400 sites have been accredited.

CROs continue to invest in China to enhance their ability to meet the growing demand for clinical drug development programs by adding more professional staff and locations. For global drug development to continue successfully, the need to access patients at high-quality International Conference on Harmonization/Good Clinical Practice (ICH/GCP) sites is critical. There are several obstacles in conducting clinical trials in China. English is not widely spoken. Ethics are still challenged and regulations, outside of Hong Kong, could be clearer and processes more efficient. Approvals are not yet as expedient as Korea, Singapore or Australia. China requires clinical trials with Chinese patients before a new drug can obtain permission to be marketed. To gain approval for drug imports, marketing authorization from a reference country other than China must be available. In addition, China has to wait until the compound has been tested in Phase II elsewhere, before the study can commence in China. This creates a time lag and means the country cannot participate in simultaneous global drug development.

India
India has not yet enjoyed the same appeal as China and the clinical trial industry has not risen as fast. Of nearly 500 clinical trials conducted in 2010, 75 were from multinationals. However, the number of clinical trials is expected to grow at a CAGR of 17.4% to reach more than 1,200 trials in 2016. The country’s main attractions are its low-cost environment, a population with a large patient pool and a broad spectrum of diseases, and the increasing prevalence of chronic lifestyle diseases as a result of a growing and affluent middle class. Challenges include the country’s evolving regulatory system, which has led to intermittent cycles of long approval times. Doubts over quality and data authenticity, and persistent ethical concerns due to the number of illegal trials, are also serious difficulties that plague the Indian clinical trials industry.

The role of clinical trial logistics
In the past decade, clinical trials have started to take a global or regional approach. Trials today commonly involve multiple countries and ventures in new and expanding markets, and CROs are expected to lead the way in creating market access, especially in Asia with its promise of a vast patient population. CROs have also been tasked with managing clinical supply chains, which could lead to a new strategic relationship between CROs and clinical supply chain service providers. For example, ongoing changes to clinical trial designs will continue to be something that all stakeholders will have to work out collectively. More than half of the trials do not recruit as planned. As a result of poor enrollment, a clinical trial may have to add additional sites or further expand into more countries to reach the desired patient population. These changes can negatively impact supply stocks. Therefore, clinical supply chains must be set up in such a manner that they can adapt to major design changes. In addition, all variables in a trial must be constantly monitored in order to ensure that demand can effectively be met throughout the trial.

Since CROs are instrumental in demand forecasting and demand creation, a newly emerging collaborative model between such organizations and clinical supply chain providers such as Zuellig Pharma Specialty Solutions Group could bring a more efficient clinical supply chain given data exchange for better planning purposes. Recently announced collaboration intentions between Parexel and Catalent seem to support this direction.

About Clinical Reach
Zuellig Pharma Specialty Solutions Group (ZPSSG) operates the most comprehensive proprietary clinical trial depot network in Asia, comprising 17 depots across 15 countries and regions. The network allows clients to route their investigational products and ancillary supplies in the most effective way to clinical sites across the region. The choice of three distinct supply chain models (central, local or hybrid depot) offered by ZPSSG allows the tailoring of a solution that addresses the uniqueness of each study design, takes full advantage of opportunities and addresses the study specific challenges of each country.

ZPSSG’s Clinical Reach solutions suite provides complete clinical trial logistics services, aimed at sponsors, CROs and contract manufacturing organizations who wish to benefit from a single source opportunity. Services encompass importation, drug storage, labeling, comparator drug sourcing, distribution to sites and returns & destruction of investigational products, lab kit building and specimen logistics.

For more information or enquiries about Zuellig Pharma Specialty Solutions Group’s Clinical Reach, please email enquiry@zuelligpharma.com

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