



# Korea Path

**Karen Politis Virk at Language Connections looks at the challenges and benefits of outsourcing clinical trials to South Korea**

The pharmaceutical industry has turned to outsourcing clinical research to emerging markets in an attempt to reduce drug development costs. Several new Asian markets have emerged as promising clinical trial locations because they do not have the problems associated with clinical research in more established regions. Among emerging Asian countries that have exhibited growth in clinical research, South Korea has shown a significant increase in clinical trial activity over the last decade – between 2002 and 2006 the annual growth rate for the number of clinical trials in the country was 18 per cent, comparable to India's 20 per cent annual growth rate (1). Moreover, South Korea has more multinational trial sites than Japan and China (2).

Several factors have facilitated growth in the country's clinical research sector, including successful patient recruitment, quality research, and an improved regulatory system. Furthermore, South Korea has sophisticated hospitals and a westernised healthcare system, but still maintains low costs for conducting clinical research. South Korea has also experienced a market growth that is second only to Japan among Asian countries, and has the highest healthcare expenditure of all emerging Asian markets due to its rapidly ageing population (3). Along with greater market opportunity, South Korea's strong infrastructure, highly trained clinical research personnel, and increased collaboration with the west have played a significant role in the country's growth in outsourced clinical trials.

Despite the advantages, several hurdles for non-Korean sponsors remain. The Korean regulatory system is fairly new, including the adoption of GCP guidelines and the establishment of IRBs, and there are multiple

regulatory requirements for clinical trial approval. Although the regulatory process is becoming more streamlined, government policies are often complicated. While patient recruitment rates are higher than in the US and western Europe, South Korea's relatively small population, especially when compared to China and India, may impose some limitations on its growth rate. In addition, as with all international trials, there are language and cultural barriers that must be addressed. First, foreign sponsors must be aware of differences in cultural attitudes and medical practices. Also, patient materials must be culturally adapted, and expert translators must be employed in order to ensure the accuracy and quality of translation. Finally, language and cultural barriers must be resolved when dealing with regulatory authorities in order to avoid potential misunderstandings. As a result, successful outsourcing of clinical research in the country requires knowledge of the factors that affect clinical research, and the methods that can be used to overcome them.



## THERAPEUTIC AREAS

Sixty per cent of all clinical trials conducted in South Korea are Phase III trials (2), the majority of which are in leading therapeutic areas such as oncology, cardiology, CNS, endocrinology, infectious and respiratory diseases. Several types of cancer are prevalent in the Korean patient population – stomach and lung cancers are especially common in men, and stomach, breast and cervical cancers in women. As a result of the high incidence of cancer, 29 per cent of all multinational trials are in oncology (4). In addition, South Koreans have increasingly adopted western lifestyle habits, which have led to a higher incidence of so-called ‘western diseases’ like diabetes. As a consequence, this has increased the number of clinical studies conducted in these therapeutic areas.

## DEMOGRAPHICS & DIVERSITY

Most Korean clinical trial sites are located in major urban centres where a large portion of the population resides – half of South Korea’s 46 million people live in and around the city of Seoul. Moreover, Seoul is one of the most populated cities in the world, which partly accounts for South Korea’s success with patient recruitment (5). Although the population size cannot be compared to China or India, recruitment rates in South Korea are comparable to other major countries in the region.

There is growing pressure on the pharmaceutical industry to increase patient diversity in clinical research, due to evidence that racial and ethnic differences are associated with an individual’s response to medication. For example, differences in drug metabolism and absorption have been linked to race and ethnicity. The Korean population is fairly homogenous, with the exception of a minority of Chinese origin. Many Koreans have migrated to various parts of the world, where they have established large communities, although they have settled all over the world, Koreans outside of Korea live mainly in China, Japan and the US. In the US, Koreans comprise a sizeable portion of the ethnic Asian community.

Despite the fact that Asian Americans form the third largest ethnic minority in the US, they are very poorly represented in US clinical trials. Korean American immigrants in particular,

are one of the most under-served and under-studied minority populations. Many suffer from treatable diseases such as diabetes, and cancers that are under-diagnosed. Among ethnic minorities living in the US, Korean Americans have the highest incidence of stomach cancer (6). These statistics have put greater pressure on the pharmaceutical industry to represent this growing ethnic minority more equally in clinical research.

## REGULATORY APPROVAL

In 1995, the South Korean regulatory environment improved significantly following the implementation of the Korean version of the GCP guidelines – later revised in 2002 to adhere with ICH-GCP guidelines. Internationally sponsored clinical research is fairly new, as South Korea did not conduct multinational clinical trials until a decade ago. However, with the implementation of ICH-GCP guidelines and other regulatory reforms, the number of outsourced clinical trials in South Korea has grown to make it one of the most popular in Asia. Although IRBs have only recently been instituted, more and more are being established in response to the growing number of trials being conducted in the country. However, there is some concern that they will not be able to adequately meet the demands imposed by the exponential growth in outsourced clinical research.

Federal agencies responsible for overseeing international clinical trial approval have also recently been established. The first agency, the Korean Food and Drug Safety Headquarters, was opened in 1996, and soon after it became the Korean Food and Drug Administration (KFDA) – which is the primary government agency responsible for clinical trial approval. The overall regulatory approval procedure in South Korea has recently been streamlined by the KFDA such that applications can be submitted in parallel to both the country’s ethics committees and government regulatory authorities. This has shortened the time necessary to obtain clinical trial approval to approximately 30 days, and made it comparable to timelines in North America, western Europe, and other Asian countries – with the exception of China where regulatory approval can take up to 10 months. Another regulatory agency, the Korea National Enterprise for Clinical Trials (KoNECT), was created in 2007 to support the development

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of the clinical trial centres in the country and promote Korea as a hub for multinational studies.

In the past, inadequate data protection measures, excessive requirements for clinical trial approval, and the favouring of domestic products created transparency issues for foreign pharmaceutical companies outsourcing clinical research to the country (7). As South Korea establishes itself as a significant global economy, however, efforts have been made to help improve this situation both in the form of regulatory initiatives and increased cooperation from the country's pharmaceutical industry. The Korean Fair Trade Commission is also playing an active role in establishing ethical business practices. Thus, South Korea's regulatory system is quickly improving and shows strong potential to meet growing demands.

### **LANGUAGE, CULTURAL CONTEXT AND TRANSLATION**

The Korean language has many dialects, each of which is related to a specific geographic region. The official language of South Korea is based on the dialect primarily spoken around Seoul. Despite regional variations, Korean is a homogenous language, and most Koreans can understand each other without much difficulty. Therefore there is a single translation requirement for regulatory documents, unlike other countries in the region, such as India, that have multiple translation requirements. In addition, South Korea has a high literacy rate of 98 per cent that facilitates the informed consent process and places the focus on accurate, high quality translation.

The majority of Korean documents, including regulatory documents, are written in Hangul script. The use of a second script, Hanja, has declined in popularity, and is now mainly used by scholars to study historical documents. Because translation into Korean represents the only translation requirement for South Korea, the regulatory process is somewhat simplified. However, one must still keep in mind several important elements which are crucial for successful translation of regulatory documents. In order to ensure accurate and high-quality translation, it is important that documents are translated by an expert who is a native speaker and has a background in clinical research. Translating into the host language, however, is only one

aspect of translation. Regulatory documents, especially patient materials, must also take into account the culture of the target population. Cultural context is necessary in order to ensure effective and clear communication between the sponsor, investigator and patient.

Experts in the field use localisation strategies in order to ensure that translations take these cultural aspects into account rather than directly translating from the original text into the target language. This is an essential component in the translation of patient-informed consent forms, as well as all other patient-related information including recruitment materials, investigator brochures and patient reported outcomes. Cultural context is also important when dealing with IRBs and regulatory authorities in a host country. Failure to incorporate cultural factors may result in delays or misunderstandings. Finally, back translations must be performed in order to ensure that the original meaning has not been lost in translation. Text is translated back into the original source language to see that it still makes sense. High quality translation has been shown to help overcome patient recruitment barriers, ensure quality clinical data, and improve the overall success of international clinical trials. For this reason, most companies conducting multinational trials rely on CROs or language service providers with experience in a particular region to help them overcome language and cultural barriers.

### **CULTURAL FACTORS AND MEDICAL PRACTICES**

Foreign sponsors must also address cultural attitudes that can affect clinical practices, and thus play a role in clinical research. For example, there are important cultural differences between South Korea and many Western countries. Professional position, age and gender largely determine social status in Korean society. Furthermore, traditional values in Korean society emphasise the importance of family in decision making. Unlike some Western countries where the decision to receive medical treatment is primarily made by the patient, Korean patients often allow their family to make medical decisions for them. Also, because physicians are highly respected in Korean society, patient enrolment is largely a consequence of a physician's recommendation to participate in clinical trials. These factors must be considered for their effect on the

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informed consent process. On the other hand, as a result of the strong relationship between physicians and patients, patient enrolment, compliance and retention is higher in South Korean clinical trials than in clinical trials conducted in most western countries.

In Korean society, bad news is thought to dispel hope. As a result, Korean patients are often protected from any bad news in order to assure the best possible outcome of their treatment (8). Such partial disclosure practices are particularly common in terminally ill patients. In what is considered to be in the best interest of the patient, physicians often may not reveal all of the risks associated with participation in a clinical study. According to Western practices, however, all risks associated with clinical trial participation must be fully explained to a patient prior to enrolment. Foreign sponsors must therefore take measures to address these issues when outsourcing clinical trials to Korea.

Sponsors should also be aware of the cultural factors that affect patients' perceptions, such as the reporting of symptoms or side effects. The perception and acceptance of pain, for example, is greatly dependent on cultural attitudes. Studies involving cancer patients have shown that Asians living in the US rarely complain about pain (9), and in many Asian countries such as South Korea, pain has been reported to be underestimated. This can mainly be attributed to the cultural belief that pain is natural and should be accepted as part of one's illness, and should be taken into account in the interpretation of clinical data. In addition, the use of traditional Korean therapies must be taken into account, as they are often used in conjunction with Western therapies. This has been observed especially among elderly Korean American patients (10). Red Ginseng, for example, is commonly used in Korea to control or alleviate symptoms caused by rheumatoid arthritis, and acupuncture may be administered for pain management. Although they are well accepted in Korean society, and may be beneficial to the patient, such traditional medical practices should be reported for their effects on study results.

## CONCLUSION

South Korea is emerging as a key outsourcing location for conducting clinical trials, offering quality research, highly skilled clinical investigators, and a large patient population. The country's patient recruitment, retention and compliance rates are higher than in most western countries and are comparable to other emerging Asian countries.

However, foreign sponsors must recognise that Korea's regulatory system is relatively new. Quality, accuracy and localisation are all key factors in the successful translation of international clinical trial documents. Identifying these issues, locating a language service provider with experience in the country, and partnering with a clinical investigator in an established site, are all important factors in ensuring success.

## About the author



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