

GLOBAL CLINICAL TRIALS: THE CHALLENGE OF LANGUAGE

Pharmaceutical and biotech product development is an expensive and time consuming process. Approximately 30-50% of product development time involves clinical studies, with one-third of that time spent on patient recruitment. Due to the high cost of clinical research and time delays involved in recruiting clinical trial subjects in the U.S., many pharmaceutical and biotech companies are outsourcing abroad.

As the demand for larger patient pools grows, countries with less experience are quickly emerging as clinical trial sites.

The primary countries emerging as new clinical trial locations can be divided into three different regions: 1) countries in Central and Eastern Europe (CEE) such as Poland, Hungary, the Czech Republic, Romania, and Bulgaria, as well as countries of the former Soviet Union, particularly Russia and Ukraine, 2) Asian countries, especially India and China, and 3) Latin America and Mexico. Several factors make these emerging markets attractive for clinical studies. In addition to more rapid subject enrollment, these regions offer reduced costs for clinical research, large, drug-naïve populations, genetic diversity, high subject retention, and many Western-educated, highly-qualified investigators. It is not surprising, therefore, that recent expansion into these emerging markets now accounts for 20-30% of all clinical trials (Thomson CenterWatch, April 2007).

This globalization is introducing new challenges in conducting clinical research. Among these challenges, regulatory differences are gradually being overcome. However, the role that language and culture play in global clinical trials is typically underestimated. Even with new data collection methods such as Electronic Data Capture (EDC), the success and cost of clinical trials abroad depends to a great extent on accurate translation. In addition to that fact that many countries require translation of all regulatory documents, language and cultural differences can have a major effect on clinical trial data. Furthermore, the conversion to electronic data collection methods has been complicated by the introduction of several alphabets which differ significantly from the Latin. For example, the Japanese language, Kanji, contains more than 20,000 characters. Therefore, although translation in Japan is necessary only in one language, conversion to EDC has been quite challenging. Similarly, other languages such as Hindi, Mandarin, and Russian pose their own challenges to electronic data conversion.

Various subtle cultural differences can affect the way that clinical research is conducted. For example, many cultures do not believe in fully disclosing a patient's diagnosis; therefore, the potential risks of a clinical study may also be culturally filtered. This can negatively affect the process of informed consent. Another cultural difference which can interfere with patient informed consent involves the patient/physician relationship. More specifically, in many cultures patients are less likely to question a physician's recommendations.

In addition to influencing informed consent, literacy and language barriers are important considerations in developing nations as they significantly impact patient compliance, data accuracy, and reporting of adverse events. Although in most emerging regions educated populations speak English fluently, many patient populations may not. Thus, relevant study documents must be translated into different native languages, a process which requires great consistency and accuracy. Poor translation can result in delays, increased costs, litigations, and adversely affect safety and efficacy of the product being tested. For this reason good clinical trial management requires local translators who are well qualified to translate study documents and are aware of the particular language and cultural issues. Ensuring that language issues are properly addressed is key to maximizing the benefits of outsourcing clinical trials.

Central and Eastern Europe (CEE)

Over the past five years, clinical research in CEE has been growing steadily, with the number of new trials in the region more than doubling (Thomson CenterWatch, December 2007). This increase is due to several important factors specific to this region, including a reputation for solid clinical research, the presence of specialized investigational sites concentrating in one therapeutic area (a leftover from the previous medical system), and the availability of large, untreated populations centered around urban areas. In particular, Poland, Hungary, and the Czech Republic have become dominant locations for international clinical trials.

Recently, many CEE countries have joined the European Union (EU), including Estonia, the Czech Republic, Hungary, Latvia, Lithuania, Poland, Slovakia, and Slovenia in 2004, and Romania and Bulgaria as of 2007. As a result these countries are in the process of gradually implementing the European Clinical Trial Directive. This has greatly facilitated clinical research in CEE, where quality clinical research can be conducted at a significantly lower cost than in Western Europe. As in Western Europe, however, regulatory documents must be translated into each respective language. In the EU countries this means the ability to translate into at least twenty different official languages. In order to ensure a clear understanding by both investigators and study participants, most CEE countries require the translation of clinical study protocol summaries and patient-oriented information into their native language. In addition to overcoming language barriers in this region, differences in culture and medical practices must be taken into consideration. Thus, the use of high quality translation and localization strategy is clearly an important component of conducting clinical research in European countries.

Russia and Ukraine

Both Russia and Ukraine have recently experienced significant growth in clinical research. The number of approved clinical trials in Russia alone nearly doubled between 2000 and 2006, while the number of participants involved in clinical trials tripled from 2002 to 2006. This growth is due primarily to an increase in international, multi-center sites in this area. Many of the same factors which initiated growth in CEE exist in these countries of the former Soviet Union as well. However, in contrast to CEE, entire study protocols as well as all regulatory documents must be translated into Russian. In Ukraine there are two official languages, Russian and Ukrainian, further complicating the translation process. Both countries have adopted international regulatory guidelines for clinical research, despite the fact that they are not members of the EU. Cultural factors and differences in medical practices affecting clinical research should also be considered.

Asia

The number of clinical trials conducted in Asia has increased tremendously over the past several years. Between 2005 and 2006, Asian-Pacific clinical trials increased by 50% (Thomson CenterWatch, November 2007). With a genetically diverse population of more than 4 billion, many of whom have never been treated for their condition, Asia offers a prime patient pool and quick recruitment at a lower cost than in the West.

The cost of clinical trials in India, China, and Southeast Asia is significantly lower (less than two-thirds the cost of the West). For this reason, China and India in particular are becoming important locations for clinical trials. Although the greatest factor for India's role in clinical research is cost, an existing pharmaceutical base, improved government regulations, and the predominance of English play a role as well. English is the main language of communication in India (spoken by 100 million people out of a population of 1.2 billion), but several other languages are also prevalent. Hindi, the dominant second language, is spoken by one-fourth of the population. There are at least ten other languages spoken by more than 25 million people each. Thus, even in India language is a barrier for a significant portion of the population. Differences due to cultural attitudes in India, as well as medical practices such as the use of herbal medicine should also be noted.

China is also becoming increasingly popular as a site for clinical research. The number of clinical trials conducted in China increased by 25% between 2004 and 2005 alone. As in India, the largest advantage to conducting clinical trials in China is the ability to recruit subjects at a lower cost. This is partly due to the fact that large populations are concentrated in urban areas, specifically near formerly state-run hospitals. Presently all documentation must be submitted in Mandarin Chinese, the official language of China (850 million speakers). Other main languages spoken in China include Wu (90 million speakers), Min (70 million speakers), and Cantonese (70 million speakers). Thus, in addition to record keeping in Mandarin, the extent and complexity of these secondary languages are important factors for getting accurate results from clinical trials. Medical practices such as acupuncture and herbal medicine, as well as cultural differences that affect medical practice are also key factors in China. With such a diversity of cultures and languages in Asia, as in Europe, translation and localization must be well implemented at all stages of clinical research.

Latin America

Latin America is another expanding region for global clinical trials. Due to large numbers of drug-naïve subjects

near urban centers and rapid subject enrollment, clinical research costs in this region are substantially lower than in the U.S. and Western Europe. Mexico, Brazil, and Argentina, with more well-established regulations, have already emerged as clinical trial sites. Several other countries are in the process of improving their regulatory environments.

Another advantage to conducting clinical research in Latin America is the region's common language. With the exception of Brazil, where the official language is Portuguese, the use of Spanish is universal. This allows for multinational trials to be conducted primarily in one language, thus simplifying the translation process to some extent. However, differences in local dialects and cultural differences among Latin American countries must be taken into account. The ability to distinguish between subtle differences in Spanish among these different countries can only be accomplished by well-qualified, local translators and localization experts.

Conclusion

Clinical trials are being pushed into emerging markets including parts of CEE, Asia, and Latin America, because of faster subject recruitment as well as cost effectiveness in these regions. According to CenterWatch, 86% of U.S. clinical studies fail to recruit the required number of subjects on time. It is therefore logical that pharmaceutical and biotech companies would turn to outsourcing. Clinical research abroad is greatly facilitated by recent efforts to standardize regulatory procedures, as well as the improved regulatory legislation and ethical practices throughout these regions. New technologies have helped standardize multinational data collection. However, the role of native language communication in international clinical research should not be underestimated. Furthermore, language challenges associated with conversion to electronic data methods involving languages with alphabets other than Latin must also be taken into account.

Although the benefits of global clinical trials are clear, the challenges of conducting clinical research in countries with non-native English speakers may offset these benefits to a great extent if language and culture issues are not addressed. In multinational trials, documentation must be consistently and accurately translated to avoid miscommunications. Informed consent must take language and cultural differences into account. Finally, cultural factors which affect medical attitudes and patient compliance must be well understood. These processes for understanding and addressing language and cultural differences must be incorporated into the planning stages in order to ensure the success and quality of clinical trials abroad.

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