ADVOCACY ASSISTANCE

Patient advocacy organizations are critical partners in the recruitment of patients for clinical trials in any country, says Leone Atkinson, M.D., senior director of clinical development at PTC Therapeutics.

"As the operations of advocacy networks outside the United States may vary, it is essential to share clinical-trial information in ways that account for a group's capabilities and cultural sensitivities, including its method of communication with patients and native language," she says. "To facilitate patient recruitment for our pivotal Phase IIb clinical trial of ataluren in patients with nonsense mutation Duchenne and Becker muscular dystrophy, PTC tailored clinical trial and disease education materials for advocates in 11 countries, including translation into eight languages."

Dr. Atkinson says a challenge is to ensure that both the clinician and patient communities are well-informed about the study and its enrollment requirements, as soon as possible.

"Participation in a clinical trial is always associated with some burden for patients and their families, so efforts to minimize these burdens may assist in improving enrollment," she says "Such efforts include, assisting with travel requirements, arranging for some procedures to be performed at the patients' home or more local to them, and providing them with tools to help organize and complete study requirements." ✦

An Approach to Language in GLOBAL Trials

Most international sponsors who conduct multinational clinical trials are aware of the importance of native language communication in clinical research.

Informed consent procedure requires that written consent be translated into the patient's native language, and any unique cultural aspects be taken into account. In addition, many countries have multiple language translation requirements, depending on the population demographics.

When linguistic differences and key cultural factors are not considered, they can ethically compromise the process of informed consent, decrease patient compliance, and negatively affect patient enrollment. These factors, therefore, must be well-understood before initiating clinical trials in a specific region.

CENTRAL AND EASTERN EUROPE AND RUSSIA

The most dominant Central and Eastern Europe countries in clinical research include many countries that have recently joined the European Union, such as the Czech Republic, Poland, Hungary, Romania, and Bulgaria. Approval for clinical trials in Central and Eastern Europe is divergent and still in flux. No two countries have the same review structure or evaluation procedures for IRBs. In Bulgaria, for example, the local Ethics Committee of the respective clinical site must approve clinical trials, and approval times by the Ministry of Health may average up to nine weeks. In Russia, the Ministry of Health must first issue approval, which usually takes up to two months.

In addition, clinical-trial applications must be reviewed by the National Ethics Committee, which may take an additional month (Cordab 2006). Currently, the European Union member states are striving to harmonize their regulatory approval procedures.

Following the addition of several Central and Eastern Europe countries to the EU, many physicians proficient in English left in pursuit of better work opportunities in Western Europe. Thus, the rate of English proficiency among investigators has decreased. In addition, English proficiency among subjects in CEE is lower than in Western Europe (European Commission Survey; February 2006).

Each country requires that all documents be translated into its native language(s). Some countries may have multiple language translation requirements, such as Ukraine where both Ukrainian and Russian translations are necessary. Each of these countries has a unique culture that should be considered separately. However, CEE and Russia have some common cultural factors that affect clinical research, especially the patient/physician relationship. In contrast to the United States where patients are more likely to question their physician's recommendations, the majority of patients in this region are more amenable to following their physician's suggestions, including the recommendation to participate in clinical trials.

LATIN AMERICA

Argentina, Mexico, and Brazil currently have the most established

regulatory environments and conduct the largest number of clinical trials. In most Latin American countries, the approval times for the Ministries of Health can range from 30 to 90 days. Several Latin American countries have specialized Ethics Committees for the approval of clinical trials involving indigenous populations. Approval times for the majority of Ethics Committees or IRBs are typically 30 to 60 days. Most Latin American regulatory bodies are working to increase their clinical-trial resources and shorten approval times (Glanczspigel 2003).

Clinical-trial documents must be translated into Spanish in most of Latin America, with the exception of Portuguese in Brazil. But there are many regional differences in spoken Spanish as a result of influences from dominant indigenous and immigrant groups. These differences must be taken into account, especially during patient recruitment. In addition, every country in Latin America has a unique culture, and there are regional differences within each country. For example, Argentine and Mexican Spanish differ significantly, and Mexico City is different from Mexico's Yucatan Peninsula in terms of local dialects and culture.

Other factors that affect patient recruitment in the region are poverty and illiteracy. The importance of family in Latin American culture, and family decision making regarding medical treatment, must also be taken into account. Similar to Central and Eastern Europe, patients in Latin America do not often question their physician's recommendations. As a consequence, their physician's recommendation greatly influences the decision to enroll in clinical trials.

In addition, economic factors play a significant role among many patient populations in Latin America, as many patients have no other treatment options available to them.

8 FACTORS LIKELY TO AFFECT THE FLOW OF OUTSOURCING TO EMERGING COUNTRIES

1. Competing demand for sites and patients in the West may in fact diminish as the pull-back in biotech and small pharma funding is likely to lead to fewer studies, even with big pharma acquisitions. The biotech and small pharma companies often focused their clinical activities close to home in the West, hence any pull-back in trials will be disproportionate in the West.
2. The supply of investigators in the West may stabilize. There are physician/clinical surveys indicating that as the result of stock and equity decline many of the most productive investigators in the West who were nearing early retirement cannot afford to do so for several more years.
3. The supply of nurses available as study coordinators may actually increase. A large number of nurses who left nursing practices in affluent countries (especially the United States) may return to the fold for economic reasons.
4. The relative supply of CRAs and other trial management staff in the West may actually increase with the current rate of big pharma and biotech layoffs.
5. Adverse economic conditions may make clinical-trial participation a more intriguing option for a broader socio-economic range of patients in the West.
6. There is growing coverage in mainstream press (even the Wall Street Journal) about the "abuses" by the industry in international trial conduct. Also in India, a key emerging market, there are growing voices of concern expressed about abusive practices of the clinical research industry.
7. In many of the most important emerging countries, the escalating influx of studies has saturated the limited number of ICH GCP qualified investigators.
8. There could be an escalation in U.S. FDA regulatory inspection and enforcement actions that focus on international clinical-trial locations. The FDA is opening new offices in key emerging countries, and the GAO has very recently put focus on the need for inspections of foreign manufacturing sites.

Source: Larry Meinert, M.D., senior VP, medical and scientific affairs, clinical development services, Covance. For more information, visit covance.com

INDIA, CHINA, AND SOUTHEAST ASIA

South Korea and Singapore are currently the most efficient and predictable for regulatory approval in Asia. For example, the process in South Korea has been so streamlined, that approval by the Korea Food and Drug Administration (KFDA) can be completed within one month. The IRB approval process occurs in parallel, further facilitating the process.

China and India have become primary offshoring locations. China currently has the longest approval time in the region, up to nine months, because of the fact that clinical-trial applications must pass through six regulatory approval bodies. In India the average time for regulatory approval is 10 to 16 weeks. Approval from local Ethics Committees at the site level occurs in parallel, facilitating the initiation of clinical trials (Varawalla 2006).

Although English is considered a second language in the majority of Asian countries involved in clinical research, many of the less educated subject populations have limited, if any, proficiency in the language. Despite the prevalence of English in India, for example, English proficiency is low among many clinical-trial subjects, and several other languages are dominant among much of the population.

In China, low English proficiency among the majority of Chinese subjects is an even greater issue. In addition to Mandarin Chinese, there are several other secondary languages, which present further communication barriers.

In addition to language barriers, there are several cultural differences that must be taken into account. For example, it is less culturally acceptable for physicians to disclose a patient's complete diagnosis, especially in the case of terminally ill patients. As a result, physicians will often only partially disclose potential risks to study participants.

Family hierarchy plays a major role in Asia. The more senior family members, predominantly males, are generally responsible for making decisions about medical issues.

Patient/physician relationships are traditionally different in the East than the in West. Recommended participation in clinical trials is widely accepted without question. In India and China, as well as several other countries in Asia, economic factors and access to medical care also play a pivotal role in patient recruitment. ✦

Source: Language Connections. For more information, visit languageconnections.com.