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Latin America's Trials Climate

By Karen Politis Virk

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Several countries in Central and Eastern Europe, Asia, and Latin America are among the most prominent new locations for outsourcing clinical trials. In the past, few clinical trials were conducted in Latin America due to a number of factors including poverty, political instability, and lack of infrastructure. Most importantly, however, regulatory requirements did not meet with international standards. Recently, governments in this region have made considerable efforts to improve their health care regulations, including the gradual implementation of ICH-GCP guidelines in clinical research.

Argentina currently has the most advanced regulatory legislation in Latin America.¹ Another problem that is gradually being overcome is the lack of adequate patent protection in Latin America. Between 1991 and 1995, new patent protection laws were established in several Latin American countries, including Peru, Argentina, Mexico, Chile, and Brazil.² This has further facilitated the growth of clinical research and development in this region.

Despite the advantages of outsourcing clinical trials, language remains a major issue, even in Latin America, where one language dominates. Spanish is officially the main language, with the exception of Portuguese in Brazil. This reduces the complications that arise in regions where translation of regulatory documents must be done in multiple languages. The use of a common language also reduces language barriers in conducting multinational clinical trials, particularly compared to other newly expanding regions such as Eastern Europe and Asia.

However, the issue of language in Latin America should not be underestimated. For one thing, there are several regional differences in the Spanish spoken. Furthermore, these differences among Latin American countries can introduce barriers to research if they are not addressed.

In addition, differences in cultural attitudes and medical practices must also be taken into account. While there are many advantages to conducting studies in this region, successful clinical trial management requires that language and cultural differences be taken into consideration.

Emerging reasons

Therapeutic Opportunities

In addition to the cost effectiveness for conducting research in Latin America, there are several advantages specific to the region. For one thing, due to the increasing prevalence of heart disease, arthritis, cancer, and infections in the region (diseases that are typically prevalent in the United States) research in these areas has recently evolved.

In particular, Latin America is dominant in breast cancer, lung cancer, and cardiovascular studies due to a recent emphasis on clinical research in these therapeutic areas. Furthermore, seasonal diseases in Latin America occur at different times than in North America. This allows for year-round recruitment of these subjects and an increased number of clinical studies in this area.

Therapeutic Opportunities

Among emerging research markets, Latin America is becoming a desirable location for conducting clinical trials for a range of reasons, mostly related to subject recruitment.

According to DataEdge,³ Latin America is the world's fourth largest clinical trials market. The concentration of the region's population of 500 million people in urban areas (where 70% of the total population lives) facilitates rapid subject enrollment. The four largest cities in Latin America—Mexico City, Rio de Janeiro, Sao Paulo, and Buenos Aires—are among the largest cities in the world, accounting for over 40 million people.

Due to such large numbers of drug-naïve subjects, their proximity to urban centers, the high success of subject enrollment and retention, and reduced costs for clinical research, Latin America is understandably playing a growing role in global clinical trials.

Mexico, Brazil, and Argentina are the three most established Latin American countries in clinical research due to improvements in their regulatory legislation. Other countries in Latin America are evolving their health care-related legislation, and thus regulatory environments are continually improving.

Currently, Argentina, Brazil, Mexico, Chile, Colombia, and Peru are the primary Latin American countries conducting clinical trials. This is in large part due to the fact that their combined populations account for approximately 80% of the region's total population,⁴ greatly facilitating their ability to meet subject enrollment requirements. The importance of these large populations in recruiting subjects for multinational, multicenter trials, which are increasingly common particularly in Phase III, reflects the expansion of clinical trials in the area over the last decade.

The primary reason that recruited subjects in Latin America are more eager to enroll in clinical trials is that for much of the population no other treatment options are available. Due to the fact that many trial subjects come from lower economic backgrounds, they do not have the resources or access to current and effective medical therapies available in more developed parts of the world. Thus, the ability to participate in a clinical study may be the only opportunity to receive treatment for their particular ailment, and following regulatory approval, such therapies may become more readily available.

In addition, the number of qualified clinical investigators is increasing to meet the growing demand in clinical research in the region. The advantages of conducting clinical research in Latin America are clear, however, there are important barriers that must be overcome.

Language hurdles

With the previously noted exception of Brazil, all key regulatory documents involved in Latin American clinical trials must be translated into just one language, facilitating the use of EDC methods as well as translation procedures. However, one must keep in mind that there are regional differences in locally spoken Spanish as well as important cultural differences among Latin American countries.

Although they may share a common language, Latin American countries have subtle linguistic differences that can result in miscommunications if they are not properly addressed. These regional differences, or dialects, are influenced by the indigenous languages of Latin America, as well as by the native languages introduced by immigrants from other countries such as Germany, Italy, and France.

For example, many words from the original indigenous languages in each region have permanently replaced certain Spanish words. Although the educated populations including clinical investigators may speak Castilian Spanish, and even English, many patient populations more commonly speak their own regional Spanish.

In spite of the fact that many languages of the native Latin American people are no longer used, some still maintain their influence. The most widely spoken

indigenous language, Quechua, is the native language of at least 10 million people across several Latin American countries including Brazil, Colombia, Argentina, Bolivia, Ecuador, and Peru, where it is one of the official languages.

The issue of language in Latin America is more complex than one might expect. Therefore, accurate translation of study documents by native Latin American speakers from each country plays an important role in the success of trials in the region. Most importantly, to ensure informed and voluntary consent, patient informed consent forms must be translated into the regional Spanish of the participant. In addition, all patient-related study documents such as diaries must also be translated into local regional Spanish.

Since certain populations in Latin America are especially vulnerable, due to poverty and illiteracy, efforts to protect their rights have been evolving. Particularly in the case of indigenous subjects, it is common procedure in several Latin American countries to submit study protocols to local ethics committees following subject enrollment.⁵

Translation of such patient documents by native localization experts is the best way to ensure the patient's clear understanding of the study in which they will participate. In addition to patient-related documents, all regulatory documentation for clinical trials in Latin America must be translated into Castilian Spanish for local regulatory authorities. In Brazil, the same holds true for Portuguese translations.

Additional considerations

In addition to language barriers, there are cultural and socioeconomic factors that have been shown to directly impact clinical research in bilingual studies in the United States, as well as research conducted in emerging markets. One such study conducted in 1995 and in 1999 involving less educated, U.S. Spanish-speaking subjects reported problems with compliance because of the patients' inability to follow written instructions effectively.⁶

Similar problems have been reported in Latin America, where there are several indigenous populations and literacy rates are reportedly low among some of them. The indigenous populations of Latin America account for approximately 40 million people, percentages varying among different Latin American countries.⁷ Moreover, because of geographic diversity and influences from different ethnic groups throughout Latin America, there are some important cultural differences. These differences must be well understood as they can negatively affect clinical research. For example, a patient who is participating in a study while practicing herbal medicine may fail to report such use at the time of a study due to cultural attitudes. Several indigenous populations have traditionally used herbal therapies throughout Latin America, however, they may not report herbal practices because of the marginalization of indigenous herbal medicine in Latin America.⁸

Despite specific population differences among Latin American countries, there are some common traits that affect clinical research in this region. Cultural attitudes, for example, which influence medical practices and the manner in which information is communicated can greatly affect how clinical research is conducted.

In contrast to U.S. patients, Latin American patients tend to rely primarily on the recommendations of their physician when making decisions about their health. This can lead them to enroll in a study without questioning. Thus, in addition to issues of language and literacy, informed consent can be adversely affected by cultural issues.⁹

Furthermore, revealing a patient's complete diagnosis prior to conducting a study is not always common practice in many Latin American countries. This is especially the case in dealing with terminal illnesses such as cancer. Many times the involvement of the family is an important factor in the treatment of the patient, and full diagnosis may only be given to the patient's family members. Thus, the extent of information disclosed to a subject during a study may also be influenced by culture.¹⁰

Lingering past

According to a study commissioned by the U.S. National Bioethics Advisory Board, in many Latin American countries there is a general distrust of signing documents. This was not because of illiteracy, as people in countries with higher literacy rates such as Argentina also exhibited this behavior, but rather a developed mistrust of authority as a result of past experiences with oppressive regimes. These cultural attitudes were found to interfere with the signing of informed consent forms, and as a result new methods were adapted for ethically obtaining informed consent.¹⁰

Finding success

The outsourcing of clinical trials to Latin American countries has steadily increased over the last 10 years, primarily due to the demands for greater subject enrollment. As Latin American governments continue to improve their health care and regulatory environments, this region will continue to be an important location for clinical research.

In addition to regulatory issues, many factors play a role in the success of clinical research at international sites, including differences in medical practices, language, and culture. The differences between Latin American countries must be well understood and taken into careful consideration when conducting clinical research in this region. The process of informed consent, in particular, relies on a better understanding of cultural and linguistic differences.

The success of clinical research in Latin America is therefore necessarily dependent on language and cultural barriers being overcome. Proper clinical trial management requires that expert translation and localization strategies be implemented at all stages of clinical research.

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References

1. K. Barnes. "Paraxel Talks Clinical Research in Latin America," Outsourcing Pharma.com (July 12, 2007).
2. J. Fordis and L. Stevens, "Where in the World is the Best for Patent Filing?" *National Law Journal*, October 30, 2006, <http://www.law.com/jsp/article.jsp?id=900005551832> [http://www.law.com/jsp/article.jsp?id=900005551832/ [http://www.law.com/jsp/article.jsp?id=900005551832]~http://www.law.com/jsp/article.jsp?id=900005551832/%0a%09%09%09%09].
3. D. Kline, "Clinical Trials in Latin America," White Paper, DataEdge, Fast Track Systems Inc., <http://www.fast-track.com/pdfs/ClinicalTrialsLatinAmerica.pdf> [http://www.fast-track.com/pdfs/clinicaltrialslatinamerica.pdf]~http://www.fast-track.com/pdfs/clinicaltrialslatinamerica.pdf%0a%09%09%09%09] (November 2001).
4. S. Gambrill, "Fighting the Logjam in Latin American Drug Trials," *Clinical Trials Today*, September 2006, 5-6, http://www.clinicaltrialstoday.com/2006/09/fighting_the_lo.html [http://www.clinicaltrialstoday.com/2006/09/fighting_the_lo.html]~http://www.clinicaltrialstoday.com/2006/09/fighting_the_lo.html%0a%09%09%09%09].
5. H. Creed-Kanashiro et al., "Conducting Research in Developing Countries: Experiences of Informed Consent Process from Community Studies in Peru," *The Journal of Nutrition*, 135, 925-928 (April 2005).
6. D. Schillinger et al., "Association of Health Literacy with Diabetes Outcomes," *Journal of the American Medical Association*, 288, 475-482 (July 2002).

7. A. O'odham, "The Indigenous Languages of Latin America," *The Archives of the Indigenous Languages of Latin America*, 1-9.
8. T. Jagtenberg and S. Evans, "Global Herbal Medicine: A Critique," *The Journal of Alternative and Complementary Medicine*, 9 (2) 321-329 (2003).
9. P. Marshall "Informed Consent in International Health Research," *Journal of Empirical Research on Human-Research Ethics*, 1 (1) 25-42 (2006).
10. N. Kass and A. Hyder, "Attitudes and Experiences of U.S. and Developing Country Investigators Regarding Human Subject Regulations," *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries II: Commissioned Papers*, National Bioethics Advisory Commission, Bethesda, MD B1-189, <http://bioethics.georgetown.edu/nbac/clinical/Chap3.html> [http://bioethics.georgetown.edu/nbac/clinical/chap3.html]. (2001).

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Therapeutic Opportunities

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