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Navigating Latin America's Diverse Clinical and Regulatory Landscapes

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According to a recent article in the New York Times, 78 percent of the people who participated in clinical trials in 2008 were enrolled outside of the U.S.¹

That figure may come as no surprise to sponsors familiar with the cost savings of conducting trials in China, the diverse patient populations accessible in India, or the regulatory cohesiveness of the European Union. Yet the NYT report found that Central and South America boasted the highest number of patients enrolled per site, accounting for 26 percent of all patients enrolled in sites outside the U.S.

As these numbers prove, many sponsors are well-aware of the benefits associated with conducting clinical trials in Latin America. There are 550 million people in the region, many of whom are treatment-naïve, and their rates of heart disease, arthritis, cancer and infections are similar to rates in the United States. Obesity, diabetes and respiratory diseases also are common, making this an ideal patient population for trial recruitment.

Additionally, most Latin American countries use clinical trial standards similar to the International Conference on Harmonisation – Good Clinical Practice (ICH-GCP) standards, resulting in reliable data that can be combined with datasets from across the globe. There are many Latin American investigators who are eager to participate in trials, and they have the resources and infrastructure to do so.

Latin America offers convenience benefits as well: with only two official languages, Spanish and Portuguese, translating contracts and labels is much easier than in Europe or Asia. Additionally, Latin American time zones match those in the United States, making frequent communication and fast turn-arounds more feasible. Yet at the same time, a global trial that includes sites in Latin America's southern hemisphere can allow year-round recruiting for seasonal diseases like flu and allergy.

And of course, there are the cost benefits. While shipping, tax and translation costs may be higher than at U.S. trial sites, the professional fees for investigators and site monitors tend to run about 30 percent lower. And as the middle class in many Latin American countries expands, sponsors have an opportunity to tap into a large potential market for their drugs.

Despite Latin America's many benefits for clinical trial sponsors, establishing a foothold in the region isn't easy. Brazil, Argentina and Mexico are the most established in conducting clinical trials, which is to say they have the clearest regulatory pathways. But unlike in the European Union, every country in Latin America has its own specific rules and regulations, and each has its own idiosyncrasies. That's why it is essential for sponsors considering Latin American trial sites to work closely with a CRO that has representatives on the ground in the region.

Other recommendations for sponsors seeking to establish trial sites in Latin America include:

Consider Latin America's regulations early in the trial design process

Some countries in Latin America will allow a placebo-controlled trial only if there is no established standard of care. In other countries, a placebo arm is acceptable as long as it does not put the patient at risk, but sponsors must provide a detailed explanation of why the placebo

arm is needed and how the patient will be protected. If a sponsor is even considering Latin American trial sites as part of a global clinical trial plan, it is critical to understand the position of the ethics committees and regulatory authorities in each country on such matters.

Additionally, sponsors should consider that in Latin America, as in many countries outside the U.S., the sponsor is required to cover the cost of the investigational drug and any other concomitant or comparator medications used in the study. If the sponsor is seeking to combine its investigative product with an expensive targeted cancer drug, trial costs will be significantly increased at sites outside the U.S.

Establish a Latin American presence

If a sponsor does not have an affiliate or subsidiary located in Latin America, then the company will need to grant its CRO power of attorney to represent it with the regulatory authorities in each country. Local legal representation and local insurance may also be needed.

Once the presence in Latin America is established, it must be nurtured. Constant communication with regulatory authorities throughout a trial is critical to ensure that the dossier is not misplaced, or that a strike or other administrative issue does not delay the trial. Additionally, a strong relationship with regulators might result in more satisfying responses to questions, which can speed the review process.

Allow plenty of time to prepare your paperwork

While European regulators allow import license preparations to be conducted in parallel, this process must be managed sequentially in Latin America. First, the sponsor must obtain approvals from the ethics committee and the hospital. Second, the sponsor must apply for regulatory approvals from the Ministry of Health. Only then can the sponsor apply for an import license.

This entire process, from start to finish, might take four to eight months, depending on the country. For example, in Brazil, the requirements are relatively straightforward, but in Argentina, sponsors are required to obtain additional approvals from the hospital director, the governing authority in the jurisdiction where the hospital is located, and the Ministry of Justice for the informed consent form. In Peru, investigators and ethics committee must be registered and have approval to participate in a trial, details that must be sorted out ahead of time in order to avoid delaying the start of the trial.

Some countries, like Argentina, also require that a signed copy of the site contract be submitted to the regulatory authorities before the contract is submitted to the ethics committee. And in one Buenos Aires province, an actual signed contract must be submitted – a process that can be time-consuming.

And there are additional requirements to be prepared in advance. For example, contracting for locally applicable insurance and securing information related to study drugs, study drug supplies and labeling. Copies of insurance certificates are commonly required by ECs as well as by most regulatory agencies. In addition, copies of study drug labels must be included for approval as part of the regulatory agency submissions in countries like Peru and Chile.

Leverage the strength of the investigator network

Investigative sites in Latin America have, on average, seven years of clinical research experience and conduct two trials per year. Sponsors will find Latin American investigators eager to participate in trials, and many investigators speak English thanks to training received in the U.S. or Europe.

Much of Latin America also has the resources and infrastructure to run clinical trials. The internet is widely available, and an estimated 80 percent of investigators have experience with electronic data collection. Electronic patient diaries also are being introduced in the region and experience with them is increasing rapidly.

However, some individual Latin American countries have specific regulatory requirements for investigators, such as documentation of clinical trial experience, certified GCP training, or registry with a central authority. Such requirements should be assessed before selecting a site.

Patients come first, in Latin America as in the rest of the world

The number of ethics committees in Latin America is on the rise, and in 2005 a group of pharmaceutical industry and regulatory representatives released “Good Clinical Practice: Document of the Americas,” a guideline based on the ICH-GCP standards. This document is widely relied on by regulatory agencies across Latin America, although as noted, each country has made its own adjustments.

Regulatory agencies in Argentina, Peru and Chile have implemented GCP inspection programs to ensure compliance with local regulations. Patient rights are further protected by informed consent forms, which in Argentina require the signature of a witness and in Mexico require two witnesses.

In summary, if sponsors can navigate the ever-evolving clinical and regulatory landscape of Latin America, the rewards are significant in terms of access to a large patient population and cost-savings. At INC Research, we understand the importance of having teams based across Latin America that can provide in-depth knowledge of the regulations and the regulatory authorities in each country. Some of our team leaders have been at the forefront of developing clinical trial standards for the region, participating in the working group that produced the “Good Clinical Practice: Document of the Americas” guidelines and working closely with Latin American regulators to develop certification courses for investigators and site monitors.

To understand how the Latin American team at INC Research can support your clinical trial needs, please contact Silvia Zieher at szieher@incresearch.com or visit www.incresearch.com.

About the Author

Silvia Zieher, M.D., Executive Director, Clinical Development, Latin America has 15 years experience in clinical research as clinical team leader, clinical development manager of a top ten pharmaceutical company in Argentina and as a CRO clinical research director and head of clinical operations for Latin America. She joined the CRO industry in 2004.

Her responsibilities have included operations and project leadership activities related to the conduct of global clinical trials and the implementation of studies in Latin America. She has had direct line management responsibility of project teams. She has contributed to the development of training, quality control activities and development of processes and SOPs at the regional and global level. She has served as the local safety officer with pharmacovigilance responsibilities for a pharma country affiliate. Dr. Zieher contributed to the preparation of the PAHO (Pan American Health Organization) guidelines: titled: “GCP: Document of the Americas” that was published in 2005, being the FIFARMA (Latin America Global Pharma industry) representative of the GCP expert working group at PANDRH (Pan American Network for Drug Regulatory Harmonization). This guideline is the foundation of all new regulations in Latin America. She has conducted academic activities in clinical research and is a frequent presenter at international conferences as DIA.

Prior to entering the pharmaceutical industry, she worked for 8 years as a pediatric physician public and private institutions in Buenos Aires, Argentina, and taught at the Faculty of Medicine of the University of Buenos Aires, where she also completed postgraduate studies in clinical pharmacology. Dr. Zieher was awarded the Clinical Research Professional of the Year in 2009 by the GCPj/Scrip.

¹ <http://www.nytimes.com/2010/06/22/health/research/22trial.html?scp=1>