



EMERGING MARKETS: CLIMATE CHANGE IN LATIN AMERICA MAKES FOR SUCCESSFUL CLINICAL TRIALS

The change in local regulatory guidelines ensuring faster project start-up, the ability to run trials six months out of phase for seasonal disease states, and the availability of highly motivated patients for clinical trials has the clinical development climate in Latin America heating up.

The skill to integrate trials across the continent by managing multiple countries and cultures, tapping the potential of this emerging pharmaceutical market is a job that must be handled with the correct integrated project teams and good local relationships.

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Population diversity across the continent is a positive factor for patient recruitment.

Latin America, an area inclusive of South and Central America and the Caribbean region, with a footprint of 22 countries and 13.1 million square miles, represents many distinct cultures and heritages. The perceived commonality of Latino populations is a long held notion in many parts of the world. However, the Latin American culture is actually more different than alike. Latin Americans are diverse, comprised of a heterogeneous population in terms of ethnic composition and epidemiological profiles.

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Language is a common consideration when planning global trials. While the Spanish language is spoken across most countries, with the exception of Brazil where Portuguese is the official language, there are many local variations of the dialect that come into play. This is a real issue in the areas of site and patient communications and informed consent. It is a misnomer to assume that there is a common ethnicity making Latin America an easily accessed market for clinical development. There are many country specific differences in terms of culture, government, and regulatory requirements that require global expertise from an outsourcing partner with a strong local presence within these markets, as well as the scale to manage and integrate trials across the continent.

Population concentration in Latin American mega cities provides good dynamics for patient recruitment and retention.

More than 560 million people live in Latin America. The top three countries in Latin America for conducting clinical trials are Brazil, Argentina, and Mexico with 70% of the population centered in large metropolitan cities. Fifty percent of the continent's clinical trial activity is centered across these countries. Three mega cities – Sao Paolo, Buenos Aires, and Mexico City – with a combined population of 53 million citizens, make patient recruitment and clinical trial management more easily achieved from a logistics perspective.

Factors affecting the growth of clinical trials specific to Latin America include: a large and rapidly rising population of largely trial naïve people in Latin America, improved regulatory standards instituted in an effort to shorten clinical trial approval timeframes, a strong knowledge and practice of ICH GCP guidelines and existing western medicine standards, strong local physician-patient relationships contributing to good patient retention, and an emerging market for pharmaceuticals based upon improving economic status and similar diseases as North America.

Latin America provides excellent trial integrity as audited by the FDA.

One of the misconceptions concerning most emerging markets is the data and trial integrity accepted by the FDA with regard to out-of-country projects. The FDA recently reported global audit results of clinical investigators, Sponsors, and IRBs to check compliance with ICH GCP guidelines and to provide assurance that the data submitted to the FDA is substantiated by appropriate records. These audits were performed from 1997-2008 with the intent of measuring global site performance after the adoption of ICH GCP guidelines in 1996. Latin America, as part of a group segment, scored on par or better with regard to the following attributes: following the

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investigational plan, record keeping, drug accountability, and IRB compliance.¹ This finding supports the case for the ability of Latin America to deliver sound ICH/GCP guideline performance results as compared to other emerging markets.

Seasonal southern hemisphere dynamics allow recruitment advantages 12 months out of the year for more efficient studies.

Because of the seasonal variations between the southern and northern hemispheres, Latin America is a good choice when choosing sites for seasonally affected diseases within infectious disease, allergies, and seasonal viruses. In general, this ability is a highly attractive attribute in terms of speeding patient recruitment in an effort to improve speed to market.

A highly motivated government and improvement in regulatory submissions make the Latin America climate favorable for conducting multi-national trials.

An ultimate goal of any clinical trial is to produce the desired results more quickly at a lower cost per patient. Latin America can afford those results to Sponsors based upon a large, recruiter friendly and highly patient retentive environment. In addition, the population is centered within large metropolitan areas, making the cost to monitor trials lower than in geographically dispersed areas. Most countries in Latin America have worked diligently to improve the regulatory and approval environments to shorten study start-up timelines. Because Latin Americans are each bound by their individual governments, regulatory standards and regulatory bodies can be best navigated with local parties who understand the approval guidelines and standards.

Well qualified investigators are increasing in Latin America.

The rise of the scientific investigator for clinical trials in Latin America is well documented in recent years. In terms of published opinions of investigators according to *The Science Citation Index* and *Social Science Citation Index*, the rise in the number of journal articles accredited to Latin American investigators has soared 110% in the last ten years as compared to 15-50% in the US and Europe.²

1. *Clinical Trial Magnifier*
Volume 2:4 April 2009

2. *Journal of Investigative Medicine* – Volume 55,
Number 5 – July 2007

Strong local physician – patient relationships provide a high patient retention factor.

Not only are patients geographically concentrated in cities, the low rate of country specific mobility in Latin America countries encourages close relationships with patients and investigators. This being the case, there are many advantages to recruit patients in specific therapeutic areas and to improve patient retention. In addition, the low incidence of patient health insurance is a benefit for potential clinical trial participants who typically can expect to receive a standard of care higher than most of their peers by entering a clinical trial.

Recent regulatory submission improvements are contributing to faster development timelines and the ability to integrate patient recruiting across countries.

Increasingly, less regulated Latin America countries are joining the ranks of Brazil, Argentina, and Mexico in terms of complying with ICH and GCP standards. An increased focus on ethical guidelines supporting patient protection has also been established. Argentina has announced a new central clinical trial registry to track and coordinate all trials conducted in that country.³ New ANVISA changes with regard to submissions in Brazil should shorten general timelines after a short transition period.

Approximate approvals and timelines for regulatory submissions for Latin America:

| Country | Approvals Required | Regulatory Timelines (months) | Regulatory Agency |
|------------------|--|-------------------------------|-------------------|
| Argentina | IEC, LEC, T&R Committee, Ministry of Justice, RA, IL | 4.5–5.0 | ANMAT |
| Brazil | Local EC, Central EC, RA, IL | 6–7.5 | CONEP-ANVISA |
| Chile | REC + RA + Uso y Destino | 3.5–4.5 | ISP |
| Colombia | LEC + RA + IL | 4–5 | INVIMA |
| Mexico | LEC + RA + IL | 3–4 | COFEPRIS/SSA |

There are potential challenges for clinical trials in Latin America.

While the major countries – Brazil, Argentina, and Mexico – have embraced clinical development, there are many local areas within all Latin America countries where the regulatory submissions criteria are still in transition. Countries such as Brazil have seen the need to shorten approval cycles and have worked diligently to process approvals to better serve the needs of pharmaceutical companies shorten regulatory timelines.

3. *Scrip*, “Argentina creates the region’s first clinical trial registry”, April 2, 2009

Well integrated teams can overcome multi-national challenges for clinical trials.

Running successful trials in Latin America requires a local presence on the ground. The selection of local sites and investigators can be challenging; however, given the presence of therapeutic and clinical operations professionals and past site experience, local trials can be extremely successful. In terms of regulatory challenges, one must pay attention to lengthier review time vs. North America, unexpected protocol concerns and occasional difficulties in resolving queries.

Medpace understands the best practices for success in Latin America.

Latin America, though not without its challenges as an emerging market, cannot be ignored in putting together key pieces of global trials. However, choosing the right partner with local representation is a critical first step in the process. Other best practices throughout the trial process are to understand the cultural differences, emphasize good and frequent communication with the team especially during the trial start-up. As patients are recruited rapidly it is recommended to schedule the first monitoring visit immediately after the first patient is randomized. Frequent monitoring visits are also recommended with sites experiencing rapid recruitment.

The Medpace advantage in Latin America is integration across countries.

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alignment with all Medpace countries and offices. If patient recruitment will be slower in other countries, Medpace has the ability to recruit for the same trial in countries with the ability to move more quickly like Mexico. The recruitment effort can take the burden off another country like Brazil where the timeline may be longer. This balance between countries and sites keep the recruiting numbers moving and keeps the trial on pace.

The Medpace advantage is project teams at the local level with deep expertise in driving clinical trials to successful completion.

As an emerging market in clinical trial development, Latin America offers Sponsors a world that is increasingly attractive in terms of patient availability and retention. In terms of project management, integrating clinical trials across Latin America countries remains a challenge for most CROs with multiple offices. Medpace is expert in not only managing, but beating recruitment deadlines as a result of balancing patient recruiting across multi-country sites to take advantage of multi-country flexibility in study start-up timelines and regulatory requirements.

A combination of knowledgeable and integrated project teams, deep therapeutic and regulatory expertise, and the proliferation of strong local investigator relationships can truly change the climate of your current development project.

The Medpace Latin America team has experience in the following therapeutic areas:

| Oncology | Metabolic Disease | Cardiovascular | CNS | Infectious Disease | AIID | Other |
|---|-------------------|------------------------|---------------------|------------------------------|----------------------|---|
| Refractory Solid Tumors–CNS, Osteosarcoma, NB | Type II Diabetes | Hypertension | Epilepsy | HIV / AIDS | Rheumatoid Arthritis | Neonatal Respiratory – Hyaline Membrane |
| Breast Cancer | | Pulmonary Hypertension | Diabetic Neuropathy | Hepatitis | Psoriasis | |
| Lung Cancer | | Homozygous FH | Dementia | Pediatric Infectious Disease | Asthma | Erectile dysfunction |
| Neuroblastoma | | Stroke | Schizophrenia | Chronic HBV Infection | | Urinary incontinence |
| Adrenal Cancer | | Venous Thromboembolism | | Rotavirus | | Osteoporosis |
| Retinoblastoma | | | | | | Endometriosis |
| Gastric Cancer | | | | | | Acute Otitis Media |
| Colorectal Carcinoma | | | | | | |
| GIST | | | | | | |
| Ovarian Cancer | | | | | | |
| Pancreatic Cancer | | | | | | |
| Prostate Cancer | | | | | | |

Medpace Latin American Office

The Medpace office, located in Sao Paulo, Brazil, is home to Medpace employees with many years of experience in clinical development within Latin America and a wide range of therapeutic expertise. Team leaders at Medpace include industry expert Lais Koelle.



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Lais C. Koelle, MPharm, MBA; Director, Clinical Operations



Lais Koelle earned a Pharmacist degree in 1998 and a post graduation in Business and Administration in 2004 from Faculdade Getulio Vargas – EAESP. She started her career in 1998 at Johnson & Johnson in research and development of over the counter products; she also worked at Pfizer for almost 5 years in clinical research and training.

Lais has worked on phase II, III, and IV trials in various areas, including diabetes, erectile dysfunction, cardiovascular, pediatric hypertension, pediatric epilepsy, pulmonary hypertension, urinary incontinence, GERD, and diabetic neuropathy.