WHY YOU SHOULD RUN CLINICAL TRIALS IN LATIN AMERICA

Challenges & Opportunities
Why running Clinical Trials in Latin America?

Latin America has become a great ally for clinicians when developing Clinical Trials. This region provides many advantages and facilities other regions just can't match.

Over 20 countries, starting from Mexico in North America to Chile and Argentina in the South. Approximately 600 millions of people inhabit Latin America. Most of them are potential subjects for trials and patients for marketed drugs.

Sponsors should be aware of the great advantages this region have to offer. Advantages that helps medicine reach FDA approval faster than any other region. The reason for that is called: Diversity.

FDA Action Plan

In 2012 the Food and Drug Administration Safety and Innovation Act was published. Most of this FDA Action plan is based to encourage researchers to include safety and effectiveness data by demographic subgroups, including sex, age, race, and ethnicity. ¹

Section 907 of the FDA Safety and Innovation Act of 2012 also includes recommendations for improving the completeness and quality of analyses of data on demographic subgroups.

In other words, most scientist, physicians and researchers are aware on how some treatments and medicines usually work differently on the demographic spectrum, some of them even harming a group while benefiting another. New research should include data from all the spectrum to ensure that particular medicine or treatment would work properly.

More about FDA Action Plan - Why is it important?

FDA shares a common goal with patients, health professionals, researchers and the biomedical industry: safe and effective medical products must be available to the broad range of patients who need them. When participants in a clinical trial for a medical product reflect a diverse, real-world population (males and females, young and old, various racial and ethnic backgrounds, and patients with differing comorbid diseases and conditions) and when the subgroup data from the trial are appropriately analyzed, much more information can be known about the product and more meaningful clinical data can be communicated to the public.

The plan is divided into three overarching priorities—quality, participation and transparency.

- **Priority One:** Improve the completeness and quality of demographic subgroup data collection, reporting and analysis (Quality).
- **Priority Two:** Identify barriers to subgroup enrollment in clinical trials and employ strategies to encourage greater participation (Participation).
- **Priority Three:** Make demographic subgroup data more available and transparent (Transparency).

Pharmaceutical executives should recognize that collecting and analyzing demographic data on sex, race, and age may be critical to identifying population-specific signals and a required part of their marketing applications.

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Why focus on Hispanics?

Quick facts about Hispanic Population in the U.S.

- The current population of Hispanics in the U.S. is over 57 MM, which mean they are over 17% of the population in the United States.
- Hispanic population growth is 2.2%, this mean the population would grow to over 119 MM by 2060.
- California, Texas and Florida are the states with the most Hispanic density in the U.S.

Number of Hispanic clinical trials in United States

According to the web page clinicaltrials.gov there are only 60 open trials focused only on Hispanics. From those 42 are in the United States. That represents only 0.21% of the clinical trials that are open in the United States.

According to a 2011 report from the conference “Dialogues on Diversifying Clinical Trials,” sponsored by FDA’s Office of Women’s Health and the Society for Women’s Health Research and supported by the Office of Minority Health:

“Hispanics make up 16% of the population but only 1% of clinical trial participants.”

Other sources confirm that Hispanics are underrepresented in clinical trials. The following data comes from a report presented by the NIH in 2013. This report shows the percentage of people enrolled in domestic NIH clinical research and compares it to the information from the US Census Data.

Figure 1. Minority Groups Underrepresentation in NIH Clinical Research

<table>
<thead>
<tr>
<th>Minority Group</th>
<th>US Census Data (%)</th>
<th>% enrollment in domestic NIH clinical Research (FY2012)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanics</td>
<td>17.6</td>
<td>8.4</td>
</tr>
<tr>
<td>African Americans</td>
<td>13.3</td>
<td>11.1</td>
</tr>
<tr>
<td>Asians</td>
<td>5.6</td>
<td>6.9</td>
</tr>
<tr>
<td>American Indians</td>
<td>1.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Pacific Islanders</td>
<td>0.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Quick facts about Latin America²

- The current population of Latin America and the Caribbean is 646,107,010 as of Wednesday, April 12, 2017, based on the latest United Nations estimates. It is consider to be an equivalent of 8.62% of the total world population.
- It is formed by 22 countries segregated in North America, Central and South America.
- The population density in Latin America and the Caribbean is 32 people per Km2 (83 people per mi2).
- The median age in Latin America and the Caribbean is 29.6 years and the life expectancy at birth was 74.94 by 2014³.

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² http://www.worldometers.info/world-population/latin-america-and-the-caribbean-population/
Number of clinical trials per country

According to the webpage clinicaltrials.gov in Latin America there are over 16 thousands studies in Latin America. Most of them conducted in Brazil, Mexico, Colombia and Argentina.

Figure 2. Number of Clinical Studies per Country

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>2,187</td>
</tr>
<tr>
<td>Brazil</td>
<td>5,580</td>
</tr>
<tr>
<td>Chile</td>
<td>1,241</td>
</tr>
<tr>
<td>Colombia</td>
<td>1,010</td>
</tr>
<tr>
<td>Ecuador</td>
<td>108</td>
</tr>
<tr>
<td>Peru</td>
<td>866</td>
</tr>
<tr>
<td>Mexico</td>
<td>2760</td>
</tr>
<tr>
<td>Central America</td>
<td>2805</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>16,844</strong></td>
</tr>
</tbody>
</table>

Source: clinicaltrials.gov
Elaborated by: FOMAT Marketing Department

Latin America is one of the unexplored regions for Clinical Trials. The region only has about 6% of the total Active Studies in the world and about 11% of total studies according to the website clinicaltrials.gov.

Figure 3: Active Studies per Region

Source: https://clinicaltrials.gov/ct2/results/map?recr=Active%2C+not+recruiting&map=PA
Causes of mortality and morbidity

**Figure 4. Leading Causes of Mortality**

<table>
<thead>
<tr>
<th>Leading Causes of Mortality</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Heart Disease</td>
<td>9.21</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>7.7</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>6.54</td>
</tr>
<tr>
<td>Influenza and Pneumonia</td>
<td>4.54</td>
</tr>
<tr>
<td>Cardiac Insufficiency</td>
<td>3.56</td>
</tr>
<tr>
<td>Assaults Resulting in Homicide</td>
<td>3.45</td>
</tr>
<tr>
<td>Hypertensive Disease</td>
<td>3.45</td>
</tr>
<tr>
<td>Chronic Diseases of the Lower Respiratory Tracts</td>
<td>3.3</td>
</tr>
<tr>
<td>Cirrhosis and Other Diseases of the Liver</td>
<td>3.06</td>
</tr>
<tr>
<td>Motor Vehicle Accidents</td>
<td>3.02</td>
</tr>
</tbody>
</table>

Source: Mortality and Morbidity in Latin America and the Caribbean
Elaborated by: FOMAT Marketing Department

**Figure 5. Leading Causes of Morbidity**

<table>
<thead>
<tr>
<th>Leading Cause of Morbidity</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Communicable Diseases</td>
<td>74%</td>
</tr>
<tr>
<td>Communicable, Nutritional, Maternal and Perinatal</td>
<td>14%</td>
</tr>
<tr>
<td>Injuries</td>
<td>10%</td>
</tr>
<tr>
<td>Ill-defined Causes</td>
<td>2%</td>
</tr>
</tbody>
</table>

Source: Mortality and Morbidity in Latin America and the Caribbean
Elaborated by: FOMAT Marketing Department
Opportunities

A year round Research

In the Latin American Region, specifically South America, seasons are inverted from the Northern Hemisphere, which means that some studies often stop during several months. Pharmaceuticals and/or CROs can extend their research in the region to full-fill a year-round research in conditions such as pneumonia, flu, or allergies just for quoting examples. Not only that, but for studies with too many patients to recruit get over saturated sites Latin America is a great option to continue the research and accomplish the recruitment goals.

Proven Quality for Research

The Food and Drug Administration (FDA) conducts careful inspections of regulated facilities to determine a firm’s compliance with regulations and the Food, Drug and Cosmetic Act. Inspections are one of many ways FDA protects the public health. FDA audits and classifies the facilities they inspection according to their results according to the observations they have found. These classifications are NAI (No action indicated) VAI (Voluntary Action Indicated) OAI (Official Action Indicated). According to the results from the Inspections Classifications from 10-1-2008 through 9-30-2016. Facilities in Latin America Region have a 63.8% of NAI results. This number is not significantly different from facilities in United States (66%), Asia Pacific Region (64.8%) or China. (63.9%)

![Figure 6: FDA Inspections 2008-September 2016](image)

<table>
<thead>
<tr>
<th>REGION</th>
<th>Inspections</th>
<th>NAI</th>
<th>VAI</th>
<th>OAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>144064</td>
<td>66.1%</td>
<td>30.3%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Asia Pacific</td>
<td>153195</td>
<td>64.8%</td>
<td>31.4%</td>
<td>3.8%</td>
</tr>
<tr>
<td>China</td>
<td>160866</td>
<td>63.9%</td>
<td>32.2%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Latin America</td>
<td>162451</td>
<td>63.8%</td>
<td>32.3%</td>
<td>3.9%</td>
</tr>
<tr>
<td>CEE</td>
<td>17115</td>
<td>46.1%</td>
<td>47.6%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Western Europe</td>
<td>17573</td>
<td>46.1%</td>
<td>47.7%</td>
<td>6.2%</td>
</tr>
<tr>
<td>CIS</td>
<td>9107</td>
<td>44.4%</td>
<td>49.3%</td>
<td>6.3%</td>
</tr>
</tbody>
</table>

Source: Inspections Classifications from 10-1-2008 through 9-30-2016
Elaborated by: FOMAT Marketing Department

Why does it happen?

Physicians in Latin America are highly trained, most of them have completed their postgraduate studies and specialty qualifications in the U.S. or EU. Professionals in the research industry are respected in their community, which is continually exchanging clinical and scientific expertise. Not to mention a high percentage of sites are well-equipped. The combination of both perks has let us experience that research conducted in Latin American Investigator sites provide reliable and high-quality data in the required timeframe.

Most physicians are often willing to participate in clinical trials. Not only for the professional challenge and prestige they represent but to the opportunity to bring medical advantages to their patients.

All Latin American countries have adopted the International Conference for Harmonization (ICH) Good Clinical Practice (GCP) guidelines, and the area boasts several laboratories that have been certified by the College of American Pathologists. The local Ethics Committees and Ministries of Health conduct routine audits of facilities.
Strong patient/physician bond

Latin America enjoys excellent patient retention. Physicians and patients in these areas have strong bonds that result in high rates of patient compliance and study retention. Among the Hispanic culture there’s a core belief where their personal doctor is the highest authority in health. For example, in a study published by the Journal of Health Communication: International Perspectives⁴, researchers discovered that Hispanics trust doctors so much, that a sense of confusion was created when doctors asked patients about a treatment decision, such as participating in a clinical trial. These patients expected the doctor to tell them what to do.

Diverse population

In August 2014, Margaret A. Hamburg, M.D., Commissioner of Food and Drugs wrote an introduction for the FDA report: FDA Action Plan to Enhance the Collection and Availability of Demographic Subgroup Data. Which states:

“One of the core tenets of rigorous biomedical research, as well as a guiding principle of the FDA’s goal to meet the health needs of patients across the demographic spectrum, is the importance of encouraging diversity in clinical trials. When a more diverse population participates in clinical trials, we increase the potential to know more about the extent to which different subgroups—males and females, young and old, people of various racial and ethnic backgrounds, and patients with differing comorbid diseases and conditions—might respond to a medical product. And when subgroup data are analyzed, we have available more information about the product that can be communicated to the public. The result is greater assurance in the safety and effectiveness of the medical products used by a diverse population.”

One of the FDA’s goals is to create consciousness and make professional researchers aware about certain populations which may be more at risk for certain diseases—such as diabetes and heart disease—than others. It is important for researchers to include patients who are more likely to be treated for a condition that is common in those populations and recruit them in a trial.

Beside, data gathered over the years have shown that there can be important differences in how people from diverse groups respond to different medical treatments. Researchers should test these products in all groups and ensure they are safe and effective in everyone who will use them.

Information on those differences can then be included in the product labeling to help doctors and patients make treatment decisions.

Meeting these standards could be difficult in most regions. Nevertheless, Latin America offers vast diversity for a rapid recruitment, most countries are multicultural and had become a great location to develop a broad-spectrum research.

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⁴ How to boost Hispanics’ participation in clinical trials? Relate to them, study shows.

Source: https://www.sciencedaily.com/releases/2013/06/130627102619.htm
As you can see, these key countries in Latin America are highly diverse. Making it easier to complete a recruitment process to study diverse data in less time than in any other region.

**A dense population - Easy access to patients**

Latin America has dense urban areas, according to the Colombia Reports, LatAm has been referred as the most urbanized region in the world. Large cities continue to grow, many end up absorbing the territories of other municipalities, generating urban areas of greater dimension. These cities have been the principal economic motors of Latin America. 79.7% (516,362,168 people) of the population is living in cities, a percentage which is estimated to grow to 89% by the year 2050.5

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**Figure 7: Population Makeup in Key Latin American Countries (%)**

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Argentina</th>
<th>Brazil</th>
<th>Chile</th>
<th>Colombia</th>
<th>Ecuador</th>
<th>Guatemala</th>
<th>Mexico</th>
<th>Peru</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>97</td>
<td>47.7</td>
<td>52</td>
<td>20</td>
<td>6.1</td>
<td>9</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Mestizo</td>
<td></td>
<td>44</td>
<td>58</td>
<td>71.9</td>
<td>60</td>
<td>60</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>2.5</td>
<td>43.1</td>
<td>14</td>
<td>7.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>7.6</td>
<td></td>
<td>4</td>
<td>7.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amerindian</td>
<td>0.5</td>
<td>2.5</td>
<td>4</td>
<td>7</td>
<td>40</td>
<td>30</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0.5</td>
<td>1.1</td>
<td>0.8</td>
<td>0.4</td>
<td>1</td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Interethnic ad mixture and evolution of Latin America populations, 2014
Elaborated by: FOMAT Marketing Department

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5 Latin America most urbanized region in the world: UN

Dense urban areas mean that access to potential patients in the population is easier and more effective. Also the number of hospitals or potential Clinical Investigation Sites is greater in these areas.

Not to mention that a survey conducted by the Hispanic Federation in the US revealed that seven out of ten Hispanic patients are willing to participate in clinical trials if the physician advises them to do so.\(^6\)

**Figure 9: Number of Hospital Beds per 1000 Population, by Country**

![Number of Hospital Beds per 1000 Population, by Country](image)

Substantial market for sales

Since 2008, the region is by far the fastest growing pharmaceutical market in the world. By 2017, Brazil will become the fourth largest Pharma market, behind the U.S., China and Japan. Latin America's $100 billion pharmaceutical industry is today dominated by Latin American firms. Brazilian, Argentine and Cuban generics producers already export their goods to other emerging markets in Asia, Africa and the mid-East. It may not be long before Latin American pharmacy giants do the same.\(^7\)

According to the World Bank website, Latin America & Caribbean Gross Domestic Product (GDP) was around $5.294 Trillion in 2015. In this region Pharma sales are around $82Bn on the first trimester of 2017. Making a per capita Pharma sales range from $96 to $222. And not only that but most governments are increasing their healthcare spend, for example Brazil’s Compound Annual Growth Rate (CAGR) in Current Public Healthcare Provision has grown since 2012 up to 12.7\(^8\).

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\(^7\) [LATIN AMERICA’S BOOMING PHARMA INDUSTRY IS A LOCAL AFFAIR](https://www.imshealth.com/files/web/Global/Services/Services%20TL/IMS_Pharmerging_WP.pdf)

\(^8\) [Pharmerging markets](https://www.imshealth.com/files/web/Global/Services/Services%20TL/IMS_Pharmerging_WP.pdf)
As you can see in Figure 9, the expected incremental sales in Latin America are the highest with $2.5Bn. Making it a great market for developing pharmaceutical products. IMS Health has estimated that the region will generate 10% of global pharmaceutical sales by the end of 2017.

Also keep in mind that regulatory agencies in Latin America do not reject commercialization authorizations when the product has already been approved in countries with high vigilance. In other words, if the product was already approved by the FDA or EMA, it is most certain it could be commercialized in Latin American countries.
Challenges

Time

Latin America although is a region with many similarities, it also is a region with significant differences. Latin America different countries represent different governments and different regulations.

![Figure 11. Average Regulatory Turnaround Times by Country](image)

As you can see in figure 10 different countries have different regulatory times. It mostly depends on their individual politics and patient protection laws. They’re very strict, people in charge need to know every procedure will not intend to harm any patient or that studies are ethical. The approval process can be lengthy and somewhat hard to predict, despite published target approval timelines. These can range from an average of 9 weeks in Ecuador to an average of 40 weeks in Brazil.

Culture

Trying to comprehend the Latin-American culture is not an easy task. Different countries have different ways of using the language, idiosyncrasies and habits. Sometimes confusion is not easy to avoid. This issue is solved by companies who work with local partners in each country. They usually have better understanding of the local procedures and a strong relationship with the country’s MoH.

Cost

Some researchers often get confuse with the ways some companies communicate clinical trials in Latin America. Most promotions content is based on announcing cheaper cost for studies within the region. Nevertheless, it doesn’t mean that is operational cost in the region are really low. It’s true that marginal cost are significantly lower but it doesn’t mean Clinical Trials in Latin America are a quarter of the cost than a Clinical Trial in any other region.

Even though there are some companies whose expertise can lead you to save important amount of resources, including money, in Clinical Trials within the region.
Conclusions

Hispanic community is one of the groups that have been forgotten by the clinical researchers. For many different reasons including the inexperience from both sides; researchers and patients. Efforts should be re-directed to encourage the inclusion of this community in order to provide better healthcare, medicine and treatments for them.

In the U.S. many institutes and colleges are aware of this situation and are already creating plans and educating patients and doctors to manage this issue.

By the other hand, an unexplored region for most pharmaceutical companies, Latin America offers diversity of data, shorter recruitment times and important savings in money if you know how to manage these studies around the region. It’s highly recommended to contact experienced partners to help you move through the region effectively.

And also it is important to keep in mind that pharmaceutical markets in the Latin American region are far from being saturated.

To summarize, Latin America is also an important region to develop clinical trials. Its many advantages provides opportunities to small, mid-size or even big pharmaceuticals and CROs to provide the world with new and better treatments.

About FOMAT Medical Research

FOMAT Medical Research is an international company focused on innovating Healthcare for Hispanics throughout the Americas. In the US, we are a Hispanic focused Site Management Organization (SMO) and in Latin America, we are a SMO with local Contract Research Organization (CRO) capabilities pioneering Clinical Trials throughout the region.

FOMAT Medical Research has over 10 years of experience participating in Clinical Research, including most therapeutic areas. In the US, we manage high producing sites and diversify your clinical trials data by researching through the Hispanic community. We help you accomplished the FDA requirements to research abroad the whole demographic spectrum in order to get more reliable data, which help you develop better treatments and medicine.

For more information about FOMAT Medical Research please visit: www.fomatmedical.com

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