



white paper

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Clinical Trials In Latin America

SYNOPSIS

In the past, few clinical trials were performed in Latin America because of a perception that the region's healthcare systems and potential investigator pools were not up to the standards used in North American and Western European trials. This view has changed substantially in recent years as Latin American governments have improved healthcare and related regulations. These investments and changes have paid off as more and more Latin American physicians are becoming involved in studies that comply with GCP and ICH standards.

Analysis of clinical study trends shows that the top Latin American markets of Brazil, Mexico and Argentina have seen a 1000 percent increase in clinical trials between 1995 and 2000. This paper expands the analysis to show that Latin American trials offer superior recruitment potential and support higher local sales.

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Latin America

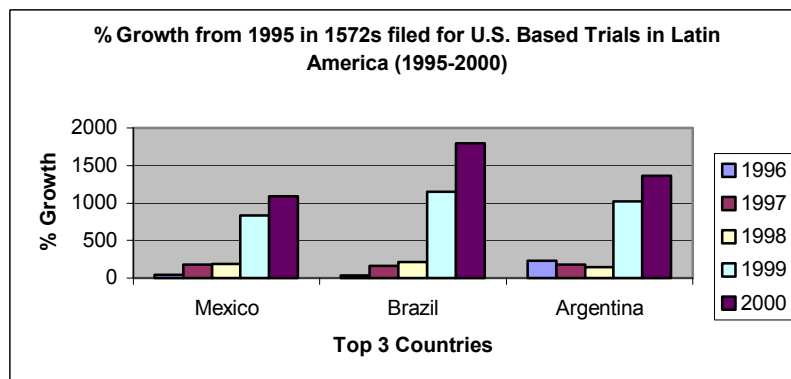
Latin America consists of the large South American subcontinent with its 13 countries as well as Central America and the countries of the Caribbean. Within this geography are 490 million people who can for the most part be categorized as treatment naïve (not on other medications that could interfere with experimental treatments). They can also be categorized as trial naïve—this massive source of potential trial subjects is largely untapped. Heart disease, arthritis, cancer, and infections are as prevalent as in the United States. Many of the seasonal disease states occur six months out of phase with North America, which permits year round recruiting in trials of seasonal ailments by combining Latin American with North American subjects. In addition, this potential trial-subject population is in large part located in several major cities, allowing recruitment via hundreds of multi-center sites in several countries at the same time.ⁱ According to CenterWatch, many Latin American investigators have access to thousands of patients, and a single metropolitan area in Latin America can have more than six to nine million patients within a 20-mile radius of the central urban hub.ⁱⁱ Since many of these patients fall into lower income brackets, participation in a clinical trial could often times provide them a better quality of treatment than they would get under normal circumstances. In a December 21st, 2000 *Miami Herald* article, Argentine oncologist Daniel Campos states, “These are mostly people who are born, live, and die in the same place,” adding that clinical trials offer them “free diagnosis and treatment”.ⁱⁱⁱ All of these factors combined make Latin America an attractive source of patient recruitment to help fill the need for patients in the upcoming years.

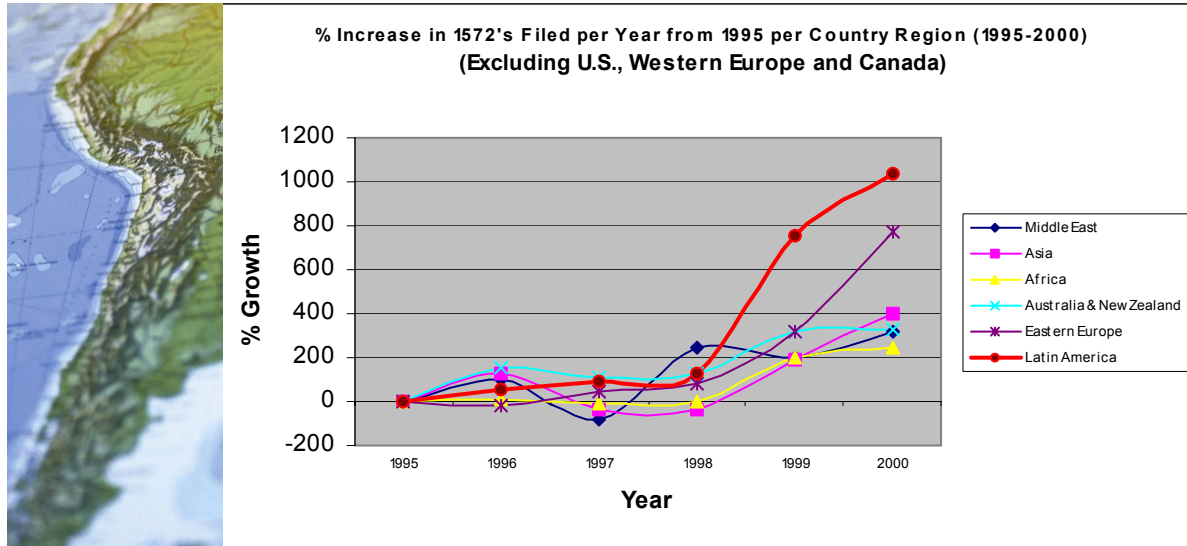
Conducting Trials in Latin America

Latin American investigators are enthusiastic about participating in research and have excellent patient retention. According to Dr. Jorge Guerra, Executive Director of Clinical Research Operations at Merck, “Drop-out rates in the region are about half of what you see elsewhere.”^{iv} Based on a 10-site study conducted by CenterWatch, investigative sites in Latin America have on average seven years of experience in clinical research and conduct approximately two trials per year.^v As investigators increase in proficiency and improve standards of operation, so too are some individual Latin American governments becoming more formalized in their handling of clinical research. They recognize the potential benefit to their countries by participating in clinical trials, and are preparing to realize that benefit in coming years. The three largest markets--Brazil, Argentina and Mexico-- are the most established in conducting clinical trials and have enacted clear controlling processes and relevant legislation.^{vi} All three of these countries require authorization of clinical trials by ethics committees and regulatory authorities, and the approval process spans two to four months on average.

Growth in Latin America

According to an analysis done by researchers at **DataEdge** (a Fast Track Systems, Inc. business unit located in Fort Washington, Pennsylvania), the number of 1572s submitted for U.S. based trials executed in Latin America increased over tenfold from 1995 to 2000, with the yearly totals for the three largest markets increasing dramatically (in some cases well over 1000 percent) from 1995.





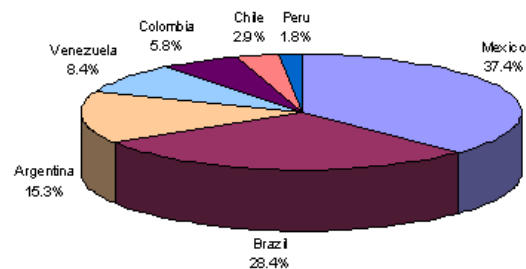
Additionally, DataEdge did a similar analysis of growth in the annual number of 1572s by geographic region (excluding the United States, Western Europe and Canada). The preceding diagram illustrates that the number of clinical trials in Latin America is increasing at a faster rate than other geographies. Latin America has become the fourth largest clinical trials market and has gained on Canada (3rd largest market) dramatically over the past 5 years (1572s submitted for Latin America were 10% of that of Canada in 1995, by 2000 the same ratio grew to 63%).

Last year, more than 200 clinical trials were begun in Argentina and the number of ongoing trials in Brazil is estimated at over 1000. During the first eight months of 2000, Costa Rica received 42 new trial applications from the U.S. and Europe.^{vii} According to industry observers, providing market conditions are favorable, an increase of as much as tenfold can be expected over the next five years.^{viii} This growth is reflected by the appearance of several of the large CROs in the region. In the past few years, ClinTrials, Covance, Quintiles, ICON, and others have opened offices in Latin America to help support their efforts in this area. With the expected expansion of the number of trials clearly indicating a corresponding need for expanded infrastructure, other CROs can be expected to respond by starting operations or opening offices in Latin America.

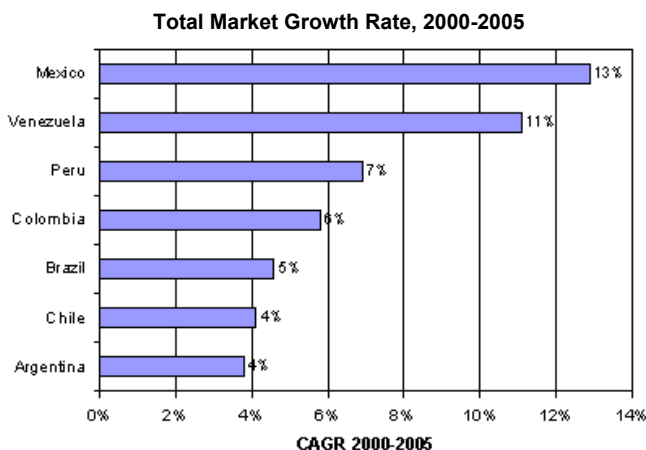
A Growing Latin American Pharmaceutical Market

The large Latin American population not only offers an untapped source of patients as a powerful draw to companies for starting trials in Latin America, but it also creates impressive market potential for pharmaceutical drugs--another justification for entry into this new market. Three of the top 15 largest pharmaceutical markets can be found in Latin America. Yet, despite a population almost twice the size of that of the U. S., the Latin American ethical pharmaceutical market is less than 20% of the size of the same market in the U. S.^{ix} Further analysis reveals that the Latin American market share for ethical pharmaceuticals from researched-based pharmaceutical companies (excluding the United States) is 11.52% of the total or approximately \$4.7 billion.^x

Forecast Breakdown of the Latin American Market by Country (2005)



Graph Source: IMS Health Pharma Prognosis Latin America, 2000-2005



Graph Source: IMS Health Pharma Prognosis Latin America, 2000-2005

Of this overall sales figure, the top three growing markets in Latin America are Mexico, Brazil, and Argentina, respectively, which also show the largest growth in trial activity over the past 5 years. According to IMS Health, by 2005 Mexico, Brazil, and Argentina will account for over 81% of the overall Latin American market for pharmaceutical sales, with Mexico overtaking Brazil as the largest single Latin American market (Mexico's growing economic strength in NAFTA and recent moves by the Mexican government to expand healthcare are cited as the reasons for this gain).^{xi} If the view is expanded to the seven largest Latin American pharmaceutical markets, the Compound Annual Growth Rate of the combined market is expected to be 7.3% per year on average, spurred in part by new product patent-protection regulation and enforcement, which makes the region more appealing to multinational companies.^{xii} Despite this swelling volume of sales, however, Research and Development spending in Latin America by PhRMA members is only 1.6% of total global R&D expenditures, or \$78.5 million.^{xiii} This is the fourth largest spend but almost an order of magnitude smaller than the top three geographical areas posted in this same PhRMA report.

Trials and Increased Sales

Recent studies conducted by DataEdge researchers have demonstrated that investigators who participate in clinical studies subsequently prescribe the drug studied more frequently on an ongoing basis. This study used a matched case/control analysis of 3431 Phase III and Phase IV investigator sites from the company's PICAS Database, involving 2596 unique investigators and 2596 control physicians from the IMS prescriber database. By examining trials at these sites from seven indication groups (asthma and allergic rhinitis, hypertension, osteo- and rheumatoid arthritis, depression, pneumonia, hypercholesterolemia and diabetes), DataEdge was able to statistically prove that trialists prescribe the study drug at significantly higher rates than do control physicians. Specifically, this study found that in Phase IIIa studies:

- Trialists display a Uniform System of Classification (USC) product market share ten points higher than controls at three, six and 18 months after product launch.
- Trialists' total prescriptions written are nearly 80% higher than control physicians for the 18 months following product launch.
- In contrast to the controls, trialists also show a statistically significant higher prescribing rate of sponsor drugs other than the drug being studied.





Additionally, for Phase IIIb/IV studies:

- Trialists prescribe a statistically significant ten points higher market share, at three, six and 18 months following the Phase IV study completion or new product launch.
- Trialists' total incremental prescriptions are 50% higher than for controls during the 18-month post-launch period.

These statistically significant differences hold whether the drug is novel or not, or reaches a high market share or not; and whether the physician is board certified or not, or is a high prescriber of the sponsor company's drugs before the study commences. Since the market potential is high and growing in Latin America, it can be inferred that those companies that begin to conduct more trials in Latin America will also be positioned to benefit from increased investigator brand awareness with an increased likelihood of investigators prescribing products produced by sponsors of trials in which the investigator has participated.

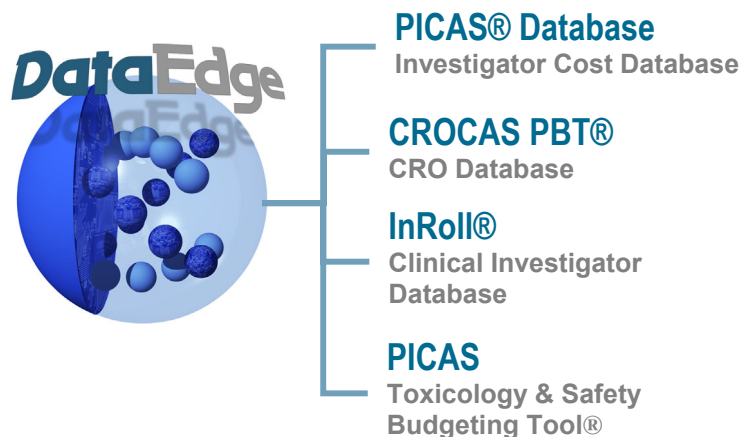
New Latin American Module From DataEdge

For the past ten years, DataEdge has offered a suite of clinical trials cost benchmarking products that have become an industry standard for estimating and planning budgets for clinical trials. The PICAS Database product improves the investigator planning process by providing a near census of information on the costs of clinical trials in the US and Europe. By utilizing anonymous, high quality industry data to support the budgeting process, the time needed to plan, negotiate, and budget clinical studies is reduced.



This data allows pharmaceutical organizations to compare equivalent sets of data that are organized by country, study phase and disease indication. Additionally, the data allows users to:

- Stratify institutions by overhead charged in order to focus recruiting on the most cost-effective clinical research providers (institutional and hospital overheads are a significant expense for most drug companies).
- Manage internal costs of clinical procedures (e.g., chest X-rays) by using industry data to negotiate appropriate fees. Procedure costs can be analyzed by country, disease indication, or the institution where the study will take place.
- Speed preparation of study budgets by using a flexible budget template that can help save time and improve adherence to company budgeting policies.





The new PICAS Database **Latin America** option will enable users to examine data from past trials and trials currently underway in the same way that the existing DataEdge tools allow users to analyze similar data from the United States and Europe. Researchers at DataEdge have been collecting and encoding contract and protocol data from Latin American countries with the largest amount of clinical trial activity such as Argentina, Brazil, Chile, and Mexico. This data will be encoded, sanitized, and available in the first quarter of 2002 as an additional module in the existing PICAS Database product.

The PICAS Database Advantage

For companies currently working in or planning to enter the Latin American market, the PICAS Database for Latin America will provide a valuable reference tool for estimating and planning trial costs. In their initial dealings with Latin American investigators, pharmaceutical companies may find themselves struggling to come to an agreed understanding of the type of work to be performed and the cost to do this work. For example: Overhead costs in Argentina range from 10-20%, while in Chile they range from 10-30% but are not applicable in public institutions. For public institutions an equivalent donation is usually requested. By providing this type of information to help sponsors understand the pricing dynamics of the new market, the Latin American module of PICAS Database can help to minimize the learning curve for effectively negotiating investigator grants, thereby facilitating the planning and execution of projects in a faster, more seamless and cost-effective fashion.

“Some of the main advantages in conducting clinical trials in Latin America are the abundance of patients for all possible disease areas, the large number of children, excellent investigation centers and the increasing rise of opinion leaders in the area.

The dramatic increase in clinical trials in Latin America can be attributed to the improvement of medical science as a whole in the region. Most opinion leaders are following American schools and are using the same methodological guidelines as those used in the United States.”

Dr. Alfredo Souza
Medical Manager
Aventis - Brazil

Summary

In 2000, prescription drug sales reached \$132 billion annually with over \$35 billion being funneled back into research and development. Of that \$35 billion, almost \$5 billion was spent on investigator and CRO contracts for the testing of chemical entities on human subjects. According to CenterWatch, approximately 33,000 principal investigators, along with another 13,000 sub investigators, conducted approximately 60,000 clinical trials in the United States in 2000.^{xiv} This number equates to over 7100 projects worldwide in discovery through clinical today and it is predicted by IMS International that this number will increase to approximately 10,000 projects over the next three years.^{xv} It is estimated that as many as 4000 evaluable patients are included in each NDA that is submitted and that this number increases by as much as 15% each year.^{xvi} With the current large markets having reached the saturation point for patient recruitment, there exists a potential problem of not having enough viable patients to fill the needs of the increasing study load. The population of the United States consists of approximately 274 million people but according to CenterWatch, only four to six million Americans participate in clinical trials.^{xvii} Included in that number are a large number of people who move from trial to trial, which decreases even more the percentage of the total available population utilized. The fact that this apparent saturation point has been reached is leading some pharmaceuticals to look to other geographic areas for the necessary subjects.

With a total population that is almost twice the size of the United States and one-third as large as Western Europe, Latin America has the potential to become a significant player in research activities and add significant dollars to pharmaceutical sales in the coming years. As greater investment is placed in government regulations, research infrastructure and healthcare reform, Latin America will grow exponentially as a premier market for pharmaceutical and biotech activities.

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ABOUT FAST TRACK

Fast Track Systems, Inc. improves the clinical development process by applying advanced medical informatics technologies to the labor-intensive, paper-based processes used in today's clinical trials. The company is providing substantial benefits and return-on-investment to pharmaceutical and biotechnology companies who need to reduce the time and cost of developing new drugs and medical devices.

TrialSpace™, the company's Internet-based product suite, connects all trials constituents through a standard operating platform that enables a complete systems approach to clinical trials. At the core of TrialSpace is an industry-exclusive technology called **iCP™** (Intelligent Clinical Protocol). Researchers use the TrialSpace planning tools to design and optimize trials through real-time simulation and modeling feedback. The result is an optimized model of a trial (an iCP) that generates and manages all data required for efficient trial execution.

DataEdge, a Fast Track business unit, offers a suite of applications and databases that contain the world's largest library of clinical trials grants and protocols. Working independently or in conjunction with the TrialSpace platform, DataEdge helps sponsor organizations to set-up and launch clinical trails more effectively. For more details about DataEdge, visit www.dataedge.com.

More information about Fast Track and its family of products and services can be found at: www.fast-track.com.

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ⁱ Source: Miami Herald, December 21st, 2000 "Latin America is Ripe for Trials and Fraud"

ⁱⁱ Source: CenterWatch Volume 5, Issue 5 May 2000 "Latin American Fever"

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^{iv} Source: CenterWatch Volume 5, Issue 5 May 2000 "Latin American Fever"

^v Source: CenterWatch Volume 5, Issue 5 May 2000 "Latin American Fever"

^{vi} Source: Applied Clinical Trials, November 1999, "A Clinical and Regulatory Perspective on Conducting Clinical Trials in Latin America"

^{vii} Source: Miami Herald, December 21st, 2000 "Latin America is Ripe for Trials and Fraud"

^{viii} Source: CenterWatch Volume 5, Issue 5 May 2000 "Latin American Fever"

^{ix} Source: CenterWatch Volume 5, Issue 5 May 2000 "Latin American Fever"

^x Source: Pharmaceutical Research and Manufacturers of America, PhRMA Annual Survey, 2001

^{xi} Source: i-Squared by IMS Health, "Vigorous Growth Returns to Latin America", March 20th, 2001

^{xii} Source: i-Squared by IMS Health, "Vigorous Growth Returns to Latin America", March 20th, 2001

^{xiii} Source: Pharmaceutical Research and Manufacturers of America, PhRMA Annual Survey, 2001

^{xiv} Source: CenterWatch Volume 8, Issue 4 April 2001 "Anticipating a Clinical Investigator Shortfall"

^{xv} Source: CenterWatch Volume 5, Issue 5 May 2000 "Latin American Fever"

^{xvi} Source: CenterWatch Volume 5, Issue 5 May 2000 "Latin American Fever"

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