Changing Regulatory Environment Improving Clinical Research Outlook for Brazil

Eduardo Pizolato
Lead Regulatory Affairs Officer

Livia C Patricio
Associate Manager, Clinical Monitoring
Introduction
Brazil has successfully transformed from a regional to a global force over the past decade and a half. This trend towards internationalism is most evident when Brazil’s marked economic growth is examined. In 2004, its gross domestic product (GDP) was not one of the top ten in the world; at that moment, there were no entries from the Southern Hemisphere and Mexico held the number 10 position. In 2006, Brazil’s GDP exceeded $1 trillion (the U.S. was first with a GDP of nearly $14 trillion); as a result, it made its first appearance on the list. During the last 10 years, Brazil has been a fixture on the list, peaking at number 6 in 2011 [1]. And according to projections by Bloomberg Business, Brazil’s economic presence will remain substantial for years to come. By 2030, Brazil will boast the sixth largest economy in the world, with a predicted GDP of $4 trillion (the U.S. will continue to lead, with a predicted GDP near $25 trillion) [2].

Brazil’s financial statistics are mirrored by its population figures, both in terms of current snapshot and future projections. As of 2015, the country has a total population of nearly 204 million; that number is expected to jump to 223 million by 2030 and 231 million by 2050 [3]. Brazil is currently the fifth largest country in the world (by population) and is expected to remain in the top 10 for decades to come [4]. The vast majority of Brazilians reside in cities, as Brazil’s rate of urbanization stands at 85.4% (the U.S., by comparison, has a rate of 81.4%) [5].

Brazilians are not only growing in number, but in voice as well. A Forbes.com article from 2013 presents a strong case that Brazil is the second most active country in the world in terms of social media use, referencing data to show that Brazilians only trail Americans in usage of Facebook, YouTube, and Twitter [6]. The implications are twofold: first, Brazilians are eager to communicate both nationally and internationally; second, Brazil is a prime target for foreign advertising and commerce.

Brazil’s economic strides and population increases have coincided with greater world influence. As a member of BRICS (along with Russia, India, China, and South Africa), Brazil is recognized as a rapidly emerging industrial nation. Brazil has achieved this status partly because it has strived to maximize its agricultural potential, and because it has adeptly exported its valuable commodities. All of this financial growth and collaboration has fueled success in other areas. Brazil has assumed a larger voice in the geo-political dialogue, including having served a record-tying 10th term as an elected member of the United Nations Security Council in 2010-11. Finally, Brazil has enjoyed a greater role on the world stage, having been selected to host the two largest sporting events in the world: the 2014 World Cup and the 2016 Olympics.

An Attractive Destination for Clinical Research Trials
To an international contract research organization (CRO), Brazil should be viewed as an attractive place to conduct business. It has a well respected medical community that is very experienced in clinical research. As the economy flourished, the government was able to dedicate more resources to the study of sciences in universities, resulting in an increase in awarded advanced degrees. This, in turn, led to a dramatic rise in the publication of peer-reviewed scientific papers originating in Brazil; in a ten-year period ending in 2007, the number more than doubled to 19,000 [7]. Clearly, this demonstrates dialogue and collaboration between Brazilian scientists and their colleagues abroad.

“Brazilians are not only growing in number, but in voice as well.”
– Eduardo Pizolato
Brazil has proved its desire to create partnerships around the world, and sustain a vibrant long-term economy. The decision-makers of CROs can clearly observe that Brazil seeks to continue to find ways to observe accepted universal standards, and to more actively participate in world markets. In fact, on March 3, 2015, Brazil made significant steps in streamlining its process for granting approvals to run clinical research trials by enacting new regulatory legislation. The changes came after a public consultation in 2014 that included 641 contributions from their biomedical sector [8].

Because of the expanding economy, large population base, experienced research community, and faster approval procedure, clinical research trials in Brazil have become more viable and therefore more appealing.

The Former Process
In the past, it could be argued that Brazil had missed out on international pharmaceutical research because of the lengthy—and cost-prohibitive—timelines in clinical trial approvals. The process as a whole could have lasted up to a year, which was understandably not enticing to CROs and their biotechnology company trial partners. The failure to attract clinical research trials meant the loss of business, but it also meant the loss of opportunity for thousands of Brazilian patients who could have volunteered for participation.

The startup (the collection and organization of documents, translations, insurance forms, and labels) took about six weeks. Next, a local ethics committee (LEC) would commence its review, followed by a central ethics committee (CONEP); this part of the process, in a best-case scenario, could have lasted up to seven and a half months. (The ethics committees are made up of numerous professionals, including doctors, lawyers, and clergy, and their task is to investigate and discuss the ethical implications of the research). Beginning a month after the ethics review and then running concurrently, the Brazilian Health Surveillance Agency (ANVISA) would conduct its own review of the clinical trial application, or CTA (known there as the Drug Development Clinical Briefings, or DDCM). It is important to note that ANVISA’s reviews would take up to six months on average. If the submissions and reviews went as planned and no questions were posed by the Competent Authority (CA), then—10 months after the original date and sometimes 12 months—DDCM approval was given, import licenses and customs clearances were granted, trial materials could be imported, and testing could begin.

The lengthy process was unique to Brazil, as it had not yet unified its approval practices with the international community. But as it has continued to demonstrate in recent times, Brazil was eager to invite input and enact the necessary modifications to its regulations in order to become a global partner.

An Evolving Regulatory Environment
One dramatic improvement occurred three years ago, long before the adoption of any of the new legislation. Since early 2012, all clinical trial application materials were submitted through Brazil’s national and unified electronic database called Plataforma Brasil. Because of the implementation of the Plataforma Brasil system, the ethics component of the clinical trial approval process was reduced by approximately three months, now averaging four and a half.
As for the newly enacted law, Resolution RDC No. 9 imposed definitive review periods for clinical trial approvals that are consistent with international standards. The expedited process will significantly shorten the time period between DDCM submission and trial commencement. There is now a 90-day (maximum) period for reviewing international Phase III clinical trials for synthetic drugs. If there is no response within those 90 calendar days, the clinical trial can be initiated after obtaining LEC and CONEP approvals [9].

The process timeline as a whole is dramatically improved. The startup period is now down to approximately one month (from six weeks). As previously stated, the ethics committee reviews now take four to five months due to Plataforma Brasil. But the most significant impact is observed in the CA review, which has been reduced from nearly six and a half months to a maximum of 90 days. Finally, even the import licenses and customs clearance portion of the process has been greatly shortened, from a month down to a week. The current total timeline from the first day of application to ultimate approval is roughly half what it had been before all of the positive modifications.

Additionally, the DDCM must be submitted by the Brazilian affiliate of the Sponsor, but if the Sponsor does not have a Brazilian affiliate, a CRO may assume this responsibility and submit the DDCM to ANVISA.

In all cases, the DDCM is the investigational product development plan that covers all clinical trials with this study drug. If the DDCM submission includes three clinical trial studies, it is permissible for three separate CROs to conduct each of the studies. Finally, the approval letter generated by the CA will be issued per study drug; thus, all clinical trials to be conducted in Brazil with the same investigational product will be approved at the same time by a single document.

By simplifying the process, Brazil is now a much more attractive destination for CROs and their biotechnology company partners conducting new trials. And because Brazil has standardized its procedures with the rest of the world regarding Phase III clinical trials, tests that are underway in other countries can be more easily consolidated there.

**Remaining Challenges**

Even though the environment in Brazil has become much more hospitable to conducting clinical research studies, there are legitimate remaining challenges. The review periods have not been reduced for Phase I and II trials. The process can take up to 180 days, and a response by ANVISA is mandatory before a trial can be commenced. The same time period is also in effect for all clinical trials utilizing biological drugs (including vaccines).

Trials using placebos are allowed in Brazil only if no “standard of care” treatment is available. This limits the types of trials that can be conducted in Brazil because if there is a standard of care option available, the trial must compare the investigational product versus the approved standard of care.

In the end, Brazil needs to overcome the misguided preconception that its country is a difficult place to conduct clinical research. Clearly, it is country with an emerging economy driven by a large and active population. Brazil also has a respected medical professional community and established clinical study sites. By enacting laws that allow for better integration and cooperation with the rest of the world with regard to

---

“Brazil is now a much more attractive destination for biotech and pharma companies conducting new trials.”

– Livia C Patricio
clinical trials, Brazil is rapidly reshaping its reputation and becoming a target country for CROs conducting clinical research.

References


