MYER™

Near-shore Clinical Research

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Contents

1. Introduction

Clinical research is an essential component of modern healthcare, providing a pathway for the development and testing of new drugs and treatments. In recent years, there has been a significant increase in the outsourcing of clinical research to regions beyond traditional research hubs such as North America, Europe, and Japan. This trend has given rise to the field of near shore clinical research, which involves the conduct of clinical trials in regions geographically close to these traditional research hubs.

Near shore clinical research can offer several advantages, including access to larger and more diverse patient populations, lower costs, and faster trial recruitment timelines. However, the field also presents unique challenges, such as regulatory differences across regions, cultural and language barriers, and infrastructure limitations.

This book explores the complexities and nuances of near shore clinical research, providing an in-depth analysis of the field from various perspectives. In North America, the outsourcing of clinical research to near-shore locations has become increasingly popular in recent years, with countries such as Mexico, Costa Rica, and Canada emerging as attractive options for sponsors seeking to conduct clinical trials outside the United States. However, the region also faces unique challenges which are addressed in this book, such as navigating complex regulatory frameworks, overcoming language and cultural barriers, and ensuring patient safety and ethical conduct.

Mexico is rapidly emerging as a key player in the global clinical research industry, offering a range of advantages for sponsors seeking to conduct trials in the region. With a large and diverse patient population, a growing pool of trained healthcare professionals, and a favorable regulatory environment, Mexico has become an attractive location for near shore clinical research.

This specialized book explores the current status of clinical research and the pharmaceutical industry in Mexico, with a focus on the opportunities and challenges of conducting near shore clinical research in the country. The book covers topics such as regulatory considerations, cultural and language barriers, ethical considerations, and the role of technology in supporting near shore clinical research in Mexico.

Mexico's close proximity to the United States, combined with the recent passage of the United States-Mexico-Canada Agreement (USMCA), has opened up new business opportunities for the clinical research industry. The USMCA includes provisions that aim to streamline regulatory processes and enhance cooperation between the United States and Mexico, making it easier for sponsors to conduct clinical trials in Mexico and export pharmaceutical products to the United States.

2. Mexico’s clinical environment in a nutshell

Mexico is a strategic clinical research option for US based pharmaceutical and medical device companies to execute their near-shore clinical trial research and build upon their existing infrastructure and support network. The country is one of the established industry leaders in the

manufacture of pharmaceutical and medical devices within the Latin American region and is a growing exporter to the US market. Over 200 companies operate successfully in Mexico, including many blue-chip multinationals. These companies have sponsored thousands of successful clinical trials in Mexico.

Mexico's clinical research ecosystem offers a successful clinical research track record, a large, centralized patient population, and an attractive ethnology and etiology representative of genetically diverse populations. The rising demand for chronic disease treatments and motivated patient populations with limited access to healthcare services are a major factor contributing to high recruitment and retention rates in clinical trials. Further, its well-developed and rigorous ICH-GCP compliant regulatory landscape has attracted different levels of US FDA collaborative relationships, established an internationally renowned clinical-research infrastructure with growing capabilities, and fostered strong collaborations with academic and health care institutions. Lastly, its highly educated and skilled labor force, combined with a favorable and permissive trading environment, shared US time zones, the large gap observed due to fair market value differences, and proximity travel to US cities. Translating to significant cost savings over US based studies.

When you include Mexico as part of your clinical research strategy your organization achieves multiple advantages:

- Diverse and centralized patient base
- Cost Savings
- Improved Recruitment/Retention
- ICH/GCP quality

MYER's strategy is to leverage these advantages of near-shore drug development to accelerate therapeutic development to first-in-man clinical studies and successful completion of phase II – IV trials. Our primary objective is to catalyze and maximize a company's development program's value in order to support further capital raising rounds generating results and supporting clients in successfully reaching clearly demarcated milestones. MYER will ensure that near-shore studies are conducted following the highest ICH/GCP clinical research standards under COFEPRIS approval (Mexico's FDA equivalent). In parallel, the FDA's pre-submission guidance will be sought in order to facilitate and support subsequent US FDA submissions and ensure the continuity of US based clinical research. MYER's second key objective is to assist with entry into the Latin American market via partnering opportunities so as to create commercial opportunities and expand to untapped revenue driven markets.

To achieve these goals, MYER has assembled an experienced group of partners, advisors and consultants with proven track records conducting clinical research under ICH-GCP compliance and who successfully developed companies and SOPs that regularly passed rigorous audits and inspections from sponsors and regulatory bodies. MYER proposes to provide your organization with access to these near-shore clinical research opportunities and to the Latin American market, under a contract consulting and services agreement.

WHY MEXICO & LATAM?

3. Mexico is one of the regional industry leaders in pharmaceutical and medical devices

The Mexican pharma market is competitive and well-developed, with a presence of around 200 companies; including a certain number of blue-chip multinationals. As an important producer of

medicines, Mexico is projected to top $13 billion USD in pharmaceutical sales by 2028 (WEDC, 2022). The government's continued efforts to improve competitiveness in Mexico's pharmaceutical sector, combined with the country's economic out-performance of other LATAM countries being the largest exporter and the second economy in the LATAM region (EMBAMEX, 2021,) will improve Mexico's attractiveness to drug makers and medical device companies as well as those interested in conducting clinical research. Regulatory changes have incentivized multinational drug makers to prioritize the country's market. An indication that these efforts are working is Kearney's US Reshoring index from April 2021, which showed that most US manufacturers think that nearshoring to Mexico is more advantageous than reshoring to the US (Pharmaceutical Technology, 2022).

Mexico is among the best investment destinations in the world

According to PwC, Mexico is the 8th most attractive investment destination in the world (ProMexico, 2017). The country is the 2nd largest destination for foreign direct investment in Latin America; Mexico's network of free trade agreements grants preferential access to markets in forty-six countries with strong trade links to the US, Canada and the EU (ProMexico, 2017). At the same time, Mexico is the largest exporter of medium- and high-tech goods (as a percentage of GDP) in Latin America and the 3rd largest among the G20 countries, as medium- and high-tech products account for 61% of Mexican exports (ProMexico, 2017), and additionally, the country has signed thirty-two agreements for the promotion and reciprocal protection of investments (ProMexico, 2017).

Pharmaceutical investment

In recent years, there has been a boost in foreign pharmaceutical investment in Mexico which has been favored by improvements in regulation, production practices and certifications (Pharmexcil, 2020). It is estimated that, during the period 2005-2014, foreign companies invested a total of $3.2 billion USD. The largest investments came from the US (36.4% of the total), Luxembourg and Ireland (11.7% each), Germany (11.5%) and Spain (7.8%) (Pharmexcil, 2020). Low production costs are one of the reasons for the recent boost in Mexico: it is estimated manufacturing costs are 17.1% lower than those in the US, and the lowest amongst OECD nations (Pharmexcil, 2020).

More than 20 pharma and medical device blue-chip companies are aware of Mexico's capabilities

Foreign companies continue to invest in Mexico's emerging pharma and medical device markets, taking advantage of the country's high consumption rate of branded medicines, the governmental support of new medical devices, and subsidies of new life saving medical products of all kinds by national health insurance programs (Pharmexcil, 2020). Many multinational blue-chip pharmaceutical companies have a presence in Mexico; among them are Johnson & Johnson, Bayer, Sanofi, Roche, Pfizer, Boehringer Ingelheim, Novartis, AstraZeneca, Merck, and GSK, some

of which have operated in the country for decades. Recently in 2020, Pfizer invested $ 20 million USD in Mexico for clinical research, renovation of production lines and medical education (Valle, 2020). In 2022, Bayer announced an investment of $375 million USD for the next three years in its pharma, consumer, and agriculture sectors in Mexico (El Economista, 2022).

Exports from Mexico

Pharmaceutical exports from Mexico reached a total value of around $1.77 billion in 2021. The United States was the main destination for Mexico's pharmaceutical exports, with an export value of about $751.27 million USD. Second was France with nearly $139 million worth of pharmaceuticals exported (Statista, 2022).

Mexico has a variety of attractive economic and regulatory partnerships with the other LATAM countries, turning it into a natural bridge to the rest of the Latin American market; this will be discussed in more detail later in this report. In fact, Mexico is the leading exporter of pharmaceutical products in LATAM and the second largest market for the pharmaceutical industry in Latin America (ProMexico, 2017).

Mexico is recognized as an important player in the med-device industries. It was the number one exporter of medical devices within Latin America and the 3rd globally (2020), with $10.6 billion USD exported in medical instruments (OEC, n.d.). Leading med-device manufacturers in Mexico include Medtronic, Johnson & Johnson, Welch Allyn and GE Medical Systems (TACNA, 2021).

US-Mexico-Canada Agreement (USMCA)

In 2020, the US-Mexico-Canada agreement (USMCA) replaced NAFTA. The USMCA provides regulatory and trading ease in the pharmaceutical and med-device market. The main benefit of this is that applicants for commercial authorization of a drug in another country participating in the USMCA will have a quicker response. The approval in one country may be used as evidence that a drug complies with requirements for a foreign regulatory agency. USMCA also offers an improved intellectual property framework, facilitating the innovation environment (Uhthoff & Uhthoff, 2020).

Biotech clusters and hubs

The Mexican government is promoting the development of biotech clusters, which are meant to operate through public-private partnerships with domestic drug makers and universities. Several biotechnology institutes were founded in recent years by several universities: UNAM in Morelos, UANL near Monterey, and Monterey Technology Institute in Queretaro. These clusters and hubs are intended to accelerate local biotech discovery and production in the country, and increase

drug exports. This can also facilitate networking with local key opinion leaders in preclinical and clinical R&D, Manufacturing, Distribution, and Commercialization channels.

In 2010, the "Derecho de planta" law was abolished, which requires pharma companies selling their products in Mexico to have at least one manufacturing facility in the country (Pharmexcil, 2020). The most densely populated areas are Mexico City and its close states (State of Mexico and Morelos), where most of the pharma research and manufacturing facilities are (ProMexico, 2014).

Skilled & Educated Industry Labor

Mexico has a well-trained, skilled, and cost-effective workforce; the country also has a solid base of human capital with around 130 universities offering more than 614 programs related to biotech and pharma (ProMexico, 2014). The number of medical school students have increased in recent years as well, representing an incremental value of 47% from 2010 to 2018 (Secretaría de Salud, 2018).

4. Mexico has a successful clinical research track record

Mexico's clinical research experience

In alliance with national institutions, the industry has completed over 2,448 interventional clinical studies in Mexico (NIH, n.d.).

With its trained workforce, Mexico has more than four decades of experience in clinical research, operating in the most stringent regulatory standards; this workforce combined has backgrounds in all therapeutic indications and population sectors (children, adults, and senior citizens). Principal investigators, research nurses, clinical research coordinators and medical doctors at clinical research sites have experience implementing complex protocols with diverse epidemiological profiles, including transmissible, non-transmissible, chronic-degenerative, and rare diseases (Pharmexcil, 2020).

Mexico also offers a high level of specialization for clinical research in all phases. Mexico counts with more than 120 ethics and research committees for the approval of research protocols, inspected clinical research sites, extensive hospital infrastructure with comprehensive protocols to handle adverse events and systems for the monitoring of patients' medical care throughout and after a clinical trial (ProMexico, 2017).

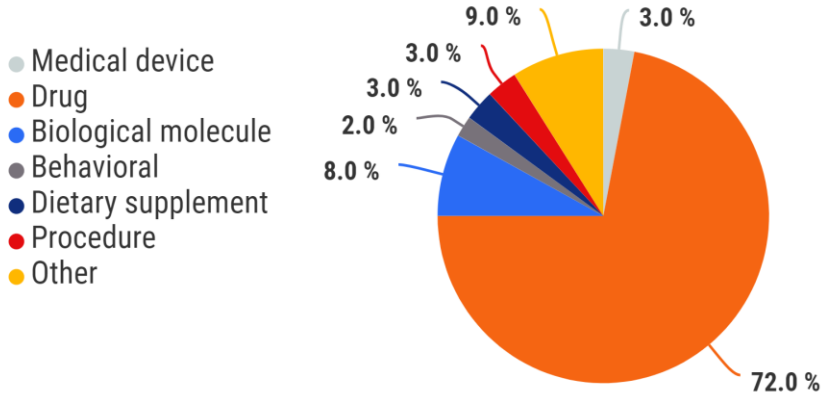
Number of clinical studies in Mexico

As of August of 2022, more than 2,400 interventional studies have been completed in Mexico. Furthermore, eight-hundred-and-sixty clinical trials are active, either in process or in recruitment stages (NIH, n.d.).

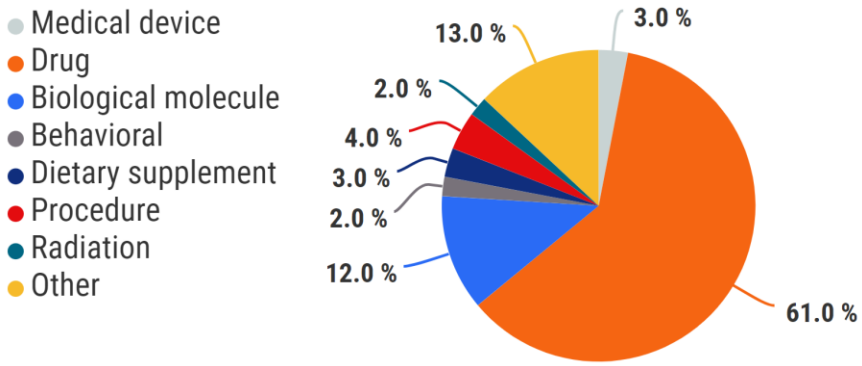
Mexico is experienced in research with more than seven therapeutic intervention types

Mexico's trials have involved mostly pharmaceutical and biological molecules. However, the country has experience with a variety of intervention types:

Therapeutic interventions in Mexico (completed studies, clinicaltrials.gov)



Therapeutic interventions in Mexico (active studies, clinicaltrials.gov)



See the *Supplementary content* section for further detail on data processing from clinicaltrials.gov site.

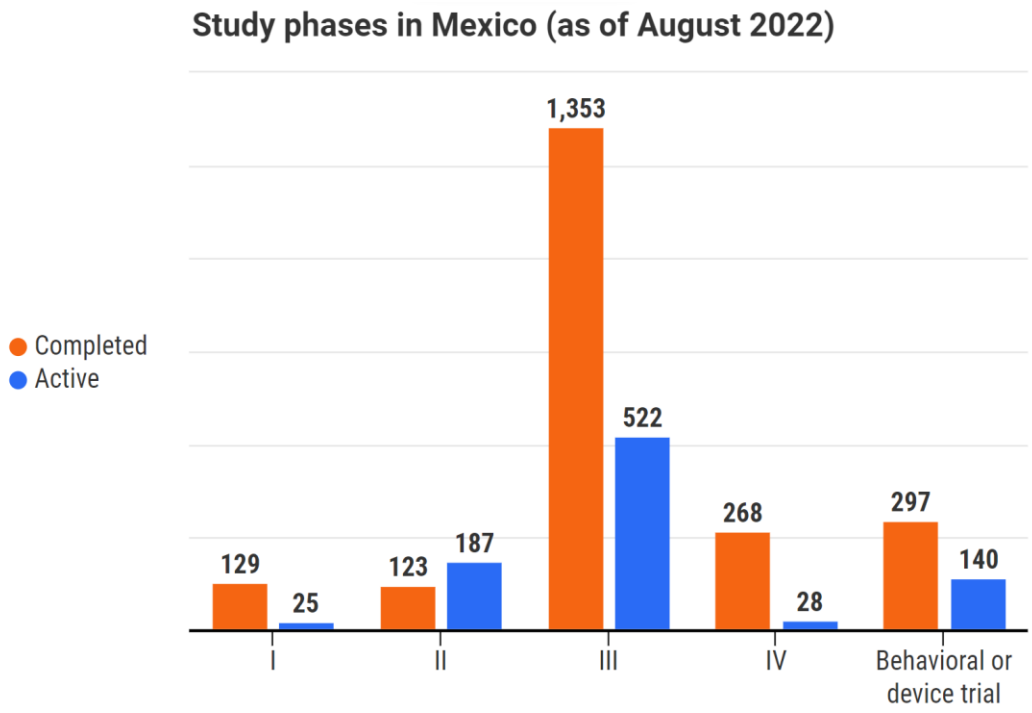
Breakdown by Disease Indications

The following table is a breakdown of clinical research indications undertaken; these include oncology, immunology, metabolic, cardiovascular, infectious, psychiatric, and chronic-degenerative diseases (NIH, n.d.).

Number of clinical trials per indications and type of intervention (active and completed studies, not all indications are included) (clinicaltrials.gov)					
Drugs		**Biological molecules**		**Medical devices**	
Breast cancer	130	Breast cancer	130	Respiratory	2
Diabetes	433	Diabetes	11	Lens (optical)	14
Multiple sclerosis	40	COVID-19	32	Articular	2
Crohn's disease	23	HPV	11	Transcranial device	4
Stroke	16	Lupus	16	Obesity related	3
Bladder cancer	5	Psoriasis	3	Diabetes related	14
Prostate cancer	33	Rheumatoid arthritis	26	Bone allograft	1
Lupus	85	Prostate Cancer	5	Menorrhagia related	4
Overweight/obesity	38				
COPD	13				
Colorectal cancer	14				
Alzheimer	28				
Parkinson	10				
Epilepsy	39				
Depression	17				
Lung cancer	79				
COVID-19	93				
Psoriasis	18				
Schizophrenia	40				
Rheumatoid arthritis	96				
Leukemia	43				

Breakdown by Study Phase

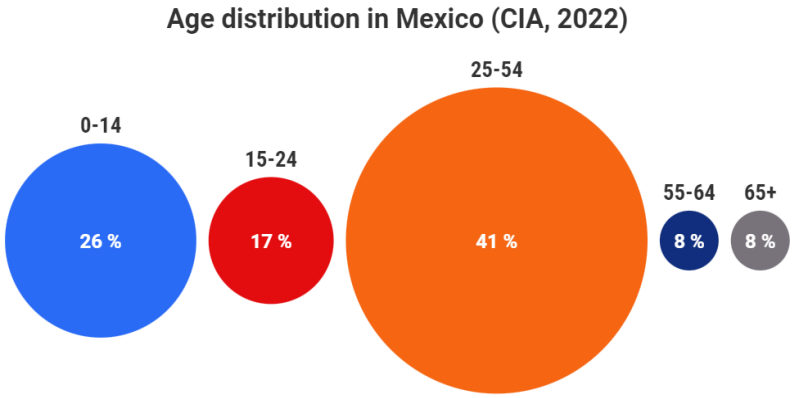
Mexico has performed clinical studies for all research phases.



(NIH, n.d.)

Demographics

- Estimated population of 128 million, 10th global as of 2022 and a 0.51 % growth rate
- Around 50-50 % distribution of males and females.
- 30 % of the population lives in the 6 most densely populated cities (Mexico City, Guadalajara, Monterrey, Puebla, Toluca, and Tijuana)
- Around 18 % of the population lives in Mexico City alone.



(CIA, 2022)

A diverse population for robust research

According to World Atlas (2019), Mexico's population is around 62 % of mixed-ancestry (*mestizo*), mostly Amerindian-European but also Asian, African, and Arab to a lesser extent. Approximately 21 % are Amerindian predominantly and 7 % purely. The remaining 10 % is composed of almost only white/European population (World Atlas, 2019) corresponding to around 12 million white people. It must be noted the vast diversity of the Mexican population which aids to meet FDA diversity guidelines to guarantee robustness of clinical trials in different populations. Nonetheless, a population-wide ancestry genetic profiling study has never been conducted in Mexico. This opens an opportunity to perform such research in order to confirm the statistics and generate a more detailed genetic profile of the Mexican population which would support the information about the population's diversity.

Mexico has a large patient population with a wide variety of epidemiological profiles

It is expected that the rate of chronic disease will increase in upcoming years despite national campaigns to improve general healthcare. This is anticipated to generate an increased demand for medications, creating investment opportunities for drug makers and clinical research. Approximately 75 % of all deaths in Mexico are caused by non-communicable diseases characterized by a high burden of metabolic diseases (mainly diabetes), cardiovascular disease, cancer and neurological disorders (mental and behavioral) (Pharmexcil, 2020).

Metabolic disease (diabetes)

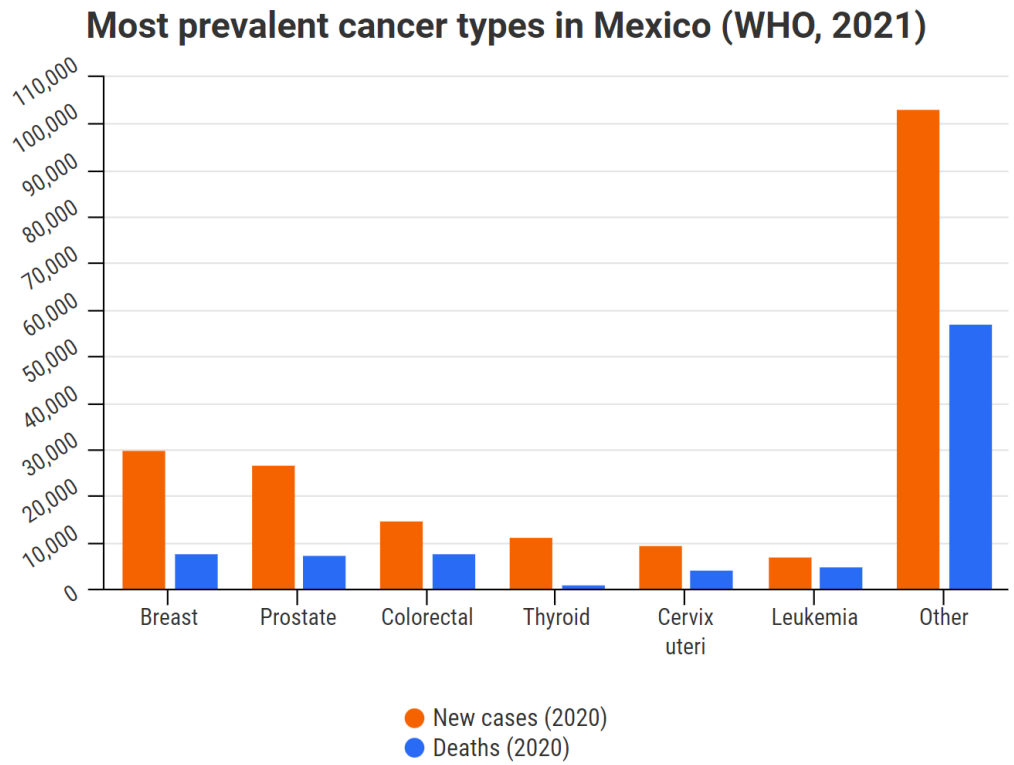
It was estimated in 2021 that 16.9 % of the Mexican adult population had diabetes (14 million adults), an increase of 10 % in comparison with 2011. Furthermore, 11 million adults have impaired glucose tolerance, making them prone to developing diabetes type 2. On the other hand, 1 % of diabetes diagnoses correspond to type 1. In general, diabetes is the leading mortality cause in the country (International Diabetes Federation, 2021).

Cardiovascular diseases

In 2020, heart disease accounted for 20.8 % of deaths related to health issues in Mexico (COVID-19 was 15.9 %) (INEGI, 2021). Around 70 % of the adult population has at least one cardiovascular risk factor: hypertension (17 million adults), diabetes, overweight or obesity (35 million), dyslipidemia (14 million) and smokers (15 million) (Lizárraga, 2017).

Oncology

In 2020, there were almost 200,000 new cancer cases in Mexico and the number of prevalent patients (over 5 years) was 530,000 (WHO, 2021).



Neurologic and psychiatric diseases

Several neurological diseases affect the Mexican population. Between 2014 and 2017, 28,457 new cases of Parkinson disease were diagnosed (Rodríguez-Violante, 2019). Since 1990, the number of new stroke cases has increased 70.7 %, leading to 107,719 cases in 2019. These

included ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage (Cruz-Góngora, 2022). On epilepsy, in 2015 it was estimated that nearly 2 million Mexicans suffered from it (Fundación Carlos Slim, 2015).

In 2018, seventeen-percent of the Mexican population had a psychiatric disorder and 1 in 4 were expected to have at least one during their lifetime. Around 13 % of the population suffered depression, 1.9 % bipolarity, 1 % schizophrenia, 15 % some kind of phobia (most common is agoraphobia) and 14 % anxiety disorders (INCyTU, 2018). All of these before the onset of the COVID-19 pandemic, which leads to infer that these percentages are higher now.

From common to rare diseases: some conditions MYER has worked with

Rare Diseases - Hemophilic Arthropathy

As an example of rare diseases in Mexico, according to the 2018 "Annual Global Survey", Mexico had 4,761 patients with hemophilia A and 724 with hemophilia B, and around 1,060 carrier mothers (López-Arroyo, 2021). In 2011, seventy-five-percent of hemophilia-related bleeding cases attended in IMSS were reported to be caused by arthropathy (Carlos-Rivera, 2016). The IMSS, or the Mexican Institute of Social Security, is a governmental organization that assists public health, pensions and social security in Mexico operating under the Secretariat of Health. It also forms an integral part of the Mexican healthcare system.

Diabetic Neuropathy

Diabetes mellitus (DM) is a disease with a very high prevalence in Mexico and of the chronic disease with the most frequent complications, the earliest of which, in its natural history, manifests as diabetic neuropathy (DN). DN can present itself in a variety of ways, and nearly 50% of patients are asymptomatic. When not treated properly, it contributes significantly to an increased risk of amputations, falls, and a negative effect on quality of life.

The prevalence of this complication in Mexican patients is unknown; however, some publications indicate that its prevalence in Mexico is higher than in other countries. For example, in the United States, a prevalence of peripheral neuropathy among adults is reported to be 28 % and the SEARCH for Diabetes in Youth study reports DN in 26 % of youth with type 2 diabetes (Sánchez, 2020).

In the ACCORD study, 42 % of adults with type 2 diabetes at baseline had DN. In another large study, known as the Veteran Affairs Diabetes Trial, it was identified in 39 % of adults; whereas in BARI 2D, fifty-one-percent of adults with type 2 diabetes already had a history of peripheral neuropathy at the beginning of the study. In Mexico, Ibarra et al. were able to use a validated instrument in test of this: The Michigan Neuropathy Screening Instrument (MNSI) using a sample of 240 subjects diagnosed with diabetes from 5 to 15 years of diagnosis, , and identified DN in 69 %. In addition, demonstrating a direct relationship with the time of diagnosis of DM, at 5, 10 and 15 years of evolution, the prevalence was 59, 69 and 77 %, respectively. In this cohort, 50 %

of DN patients had dry skin, 2 % had ulcers, 43 % had abnormal vibration perception, and 29 % had abnormal monofilament testing (Sánchez, 2020).

The estimated prevalence of Diabetic Peripheral Neuropathy (DPN) in Latin American Countries was 46.5 % (95 % CI: 38.0–55.0) with a significant heterogeneity (I2 = 98.2 %; p<0.01), and Mexico had a prevalence of 68.7 %, according to the authors from Prevalence and incidence of diabetic peripheral neuropathy in Latin America and the Caribbean: A systematic review and meta-analysis (Aldana et al., 2021).

5. Mexico has a well-established healthcare and research infrastructure

The Mexican health system offers a range of clinical research alternatives in both the private and public sectors, where health care services are extremely diversified. This leads into enormous potential within the country for the recruitment of patients; this can take place on a large scale with third parties or support units authorized to issue preliminary opinions on the approval of clinical research protocols.

Mexico has a large, motivated, and centralized patient base within its six most densely populated cities, which provide a large pool of potential volunteers (healthy and diseased) for research in all population groups (ProMexico, 2017).

Most healthcare costs in Mexico are paid out-of-pocket, therefore for a significant portion of these patients it is difficult to cover the costs associated with disease, thus increasing motivation to participate in clinical trials. Additionally, Mexico is known to have strong doctor-patient relationships, facilitating the recruitment of treatment-naive and eager patients, which augments enrollment rates. All these factors support increased patient recruitment into trials. Moreover, low dropout rates facilitate a quicker completion of clinical trials in Mexico (Arman et al., 2013).

Public sector

The IMSS (Mexican Social Security Institute) covers 58 million people, it is a tripartite system funded equally by the employee, employers, and the federal government. IMSS, along with other national health institutions, potentially have access to over 70 % of the country's patient population (ProMexico, 2017) and offer a wide range of therapeutic areas for the implementation of clinical research protocols.

Private hospital systems

As of 2011, private health systems have been allowed to have their own ethics and research committees; thus, it allows for a significant increment in the number of clinical research protocols executed within the private sector. In 2015 and 2016, private institutions registered 97 % of clinical trials in Mexico (Antunes, 2017). Public institutes have to come to realize this and have significantly improved their regulatory access to be able to stay *competitive* with the private sector. In 2017, sixty-eight-percent of clinical research was conducted in the private sector, 23 % in public hospitals and 6 % in universities (COFEPRIS, 2017). However, collaboration between private and public hospitals is possible in order to improve patient access while leveraging access to higher resources available to private entities.

Clinical Research centers

There are established clinical research centers across Mexico with many years of operating experience. The Mexico Centre for Clinical Research (MCCR) in Mexico City was founded in 2011 and has important clients, including Novartis, Pfizer, Roche, and more; CIMOVA in León, Guanajuato has 19 years of experience and has worked with Sanofi; the Mexican Association for Clinical Research (AMIC) was founded in 1988 and is located in Pachuca, Hidalgo; among their clients are Bayer, Pfizer, Janssen, Eli Lilly, AZ and several others. These are only a few clinical research centers, as there is a range of companies which offer high quality services for varied therapeutic areas and in different regions of the country.

In 2015, it was reported that Mexico had 2,511 medical and research centers. In addition, the Clinical Research Organizations Alliance of Mexico (ACROM) represents companies that conduct clinical research (14 multinationals and two Mexican companies). Together, these companies account for: 2,000 researchers, 1,400 employees and 400 monitors (ProMexico, 2017).

Universities

Universities are also a site for clinical trials: college hospitals such as “Dr. José Eleuterio González” hospital from UANL (public) and Tec Salud’s Clinical Research Center from Monterrey Technology Institute (private), both in Nuevo Leon state; in Guadalajara, there is the Experimental and Clinical Therapeutics Institute from Guadalajara’s University (UdG, public), and in Mexico City, UNAM’s Medicine School has carried out clinical trials, as well.

6. Mexico has an ICH-compliant regulatory framework

On top of being a leading pharmaceutical market in the region, Mexico is known to set regulatory trends.

COFEPRIS

The regulatory body in Mexico (responsible for pharmaceuticals and other health-related technologies) is known as the Federal Commission for Protection against Health Risks (COFEPRIS in Spanish), which is the counterpart of the US FDA. In 2012, COFEPRIS obtained level IV certification as a national regulatory authority, with the capacity to perform duties recommended by the PHO/WHO. This guarantees drug efficacy, safety, and quality standards. Additionally, in 2014, COFEPRIS was acknowledged as a benchmark health agency authorized to issue equivalence registration certificates valid in other countries, thanks primarily to COFEPRIS bilateral agreements with the US FDA (more of this in the following sections).

ICH-GCP

COFEPRIS joined the ICH in 2021. It was the first Spanish-speaking regulatory agency to be a member and the fourth in America (COFEPRIS, 2021). Since then, the regulatory process has been evolving to comply with international requirements.

European cooperation

Under the Mexico-European Union Competitiveness and Innovation Program (PROCEI), thirty-one Clinical Research Units (UIC) were integrated and obtained certification in the ISO 9000-2008 standard by virtue of their quality management model (ProMexico, 2017).

7. Advantages of Near-shore trials

Use near-shore clinical trial data for FDA acceptance

The submission process to COFEPRIS is analogous to the US FDA process, since both follow similar requirements (more on this in a later section).

Leverage resources with 30-60 % cost savings in Mexico and extend financial runway

The cost savings of clinical research in Mexico are around 30-60 % compared to typical US costs (Pharmaceutical Technology, 2022). Mexico's cost basis is the lowest among countries in the OECD because of the tax and incentive treatment given to R&D expenditures. Additionally, Mexico has significantly lower labor costs and overheads. The cost differential is significant enough to allow earlier entry to first in man trials than would be possible with a US based clinical research program. The Near Shore strategy may allow an organization to meet milestones objectives sooner and a successful trial may potentially help with additional funding raising efforts. In the case of startups and emerging companies, Mexico's lower costs may help to

decrease burn rates, thereby improving operational efficiency and saving budgets. Alternatively, Mexico's more accessible cost basis might be leveraged to explore additional indications or research opportunities.

Mexico is the ideal gateway to the rest of the LATAM market

Mexico's closeness, geographically and economically, with the US, makes it a perfect bridge and the ideal first step for entering the LATAM market. Moreover, thanks to the recognition of COFEPRIS as a benchmark regulatory health agency and its bilateral agreements with other OECD nations, drugs or med-devices previously tested and approved in Mexico can be registered in other ICH regulated countries around the world. Latin American countries with bilateral agreements with Mexico include Panama, Colombia, Chile, Paraguay, and Argentina (COFEPRIS, 2014; COFEPRIS, 2018; DESISA, 2022). Additionally, Mexico's major cities are just a few hours away from the US by airplane and it shares the same time zones as in US cities, which makes scheduling and logistics more manageable.

8. MYER has assembled an experienced group of clinical research partners

MYER has built a network consisting of partners, advisors and consultants, with expertise in clinical research, development, regulatory and submission strategies focused on the Mexico and Latin America region. MYER's goal is to assist your organization in achieving its human health and commercialization goals by offering high impact, high-quality clinical research, with unmatched speed and affordability under a consulting and services agreement.

MYER has partnered with a network of clinical research units in Mexico which will be responsible for conducting the clinical research studies for our Sponsors' programs. As mentioned above, this clinical network was founded in 2013 and has experience supporting clinical trials from phase I to phase IV. Their sites are located in Guadalajara, Aguascalientes, and Mexico City, offering a range of coverage to access a larger number of patients and principal investigators. The clinical network has experience with studies involving biomedical research, pharmaceuticals, medical devices, health products, emerging biotechnologies, nutraceutical products, among others.

Their clinical network research centers have obtained approvals and certifications from COFEPRIS and the Society for Clinical Research Sites (SCRS), and have recently successfully passed an FDA inspection. Among their sponsors are national and multinational CROs and pharma companies such as ICON, AMGEN, Bayer, Eli Lilly, Roche, Pfizer, Janssen, Merck, and others.

Another MYER strategic partner is a Mexican CRO currently performing the oversight of clinical research in neuroscience, diabetes, oncology, pain, orthopedics, and software as a medical device. The CRO will be tasked with providing a clinical research oversight function for the Sponsors' programs. This CRO was founded by the same CEO of the clinical research network, recruited directors from these clinical research sites, and attracted business executives from

executive leadership positions in Mexico and the US, to hold important R&D, regulatory, monitoring, business, finance, legal, and operational country study manager roles.

MYER and partners have been involved in hundreds of clinical trials

The clinical network team has participated in more than 70 studies of all phases for treatment of a variety of diseases and conditions. Moreover, for the past 12 years, the clinical research sites executed over 400 clinical trials for big international firms, in multiple therapeutic indications. The research sites are strategically located across three of the largest and most populated cities in Mexico. Most of the trials the sites have executed are considered rescue trials for big pharmaceutical, biotechnology, and medical device companies. Rescue trials are those trials for which other clinical sites were unable to recruit and retain sufficient patients to meet study objectives. The clinical network has a strong record of high patient recruitment and retainment.

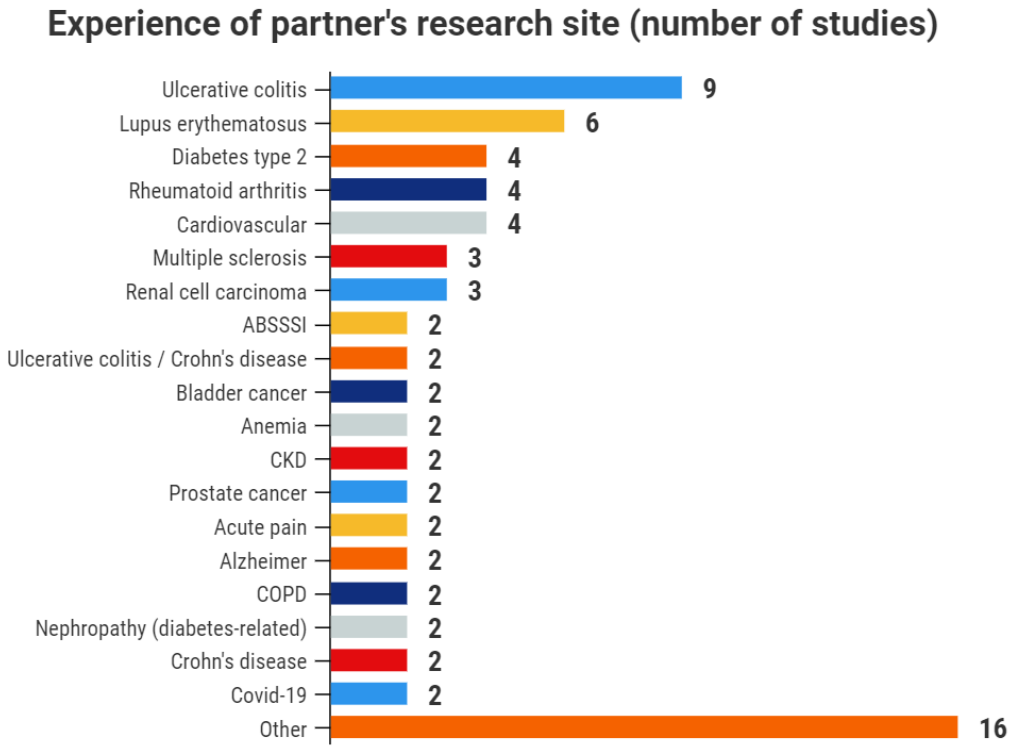
Following are a few representative studies conducted within the clinical network.

Clinical trial	Sponsor	Phase	Indication	Project
MNK14304067	Mallinckrodt	4	Lupus Erythematosus	A Multicenter, Randomized, Double Blind, Placebo Controlled Study to Assess the Efficacy and Safety of Acthar Gel in Subjects With Persistently Active Systemic Lupus Erythematosus Despite Moderate Dose Corticosteroids
64091742PCR 3001	Janssen	3	Prostate Cancer	A Phase 3 Randomized, Placebo-controlled, Double-blind Study of Niraparib in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone in Subjects With Metastatic Prostate Cancer
3151 201 008	AstraZeneca	2	Ulcerative Colitis	A 54-Week Treatment, Multicenter, Randomized, Double-Blind, Double-Dummy, Placebo and Active-Controlled, Parallel-Group Phase 2 Study to Assess the Efficacy and Safety of Brazikumab in Participants With Moderately to Severely Active Ulcerative Colitis
TX05-03E	Tanvex BioPharma USA	3	Early Breast Cancer	A Double-blinded Extension Study to Provide Adjuvant Treatment With Single Agent Herceptin® or TX05 and Assess Continued Safety and Immunogenicity in Subjects With HER2-positive Early Breast Cancer Following Neoadjuvant Treatment and Surgical Resection in Protocol TX05-03
204957	GlaxoSmithKline	2	Rheumatoid Arthritis	A Randomised, Multi-center, Double Blind (Sponsor Open), Placebo-controlled Study to Assess the Efficacy, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of GSK3117391 in Subjects With Severe, Active rheumatoid arthritis
I8B-MC-ITRN	Eli Lilly	3	Type 2 Diabetes Mellitus	A Prospective, Randomized, Double-Blind Comparison of LY900014 to Insulin Lispro, Both in Combination With Insulin Glargine or Insulin Degludec in Adults With Type 2 Diabetes PRONTO-T2D

Disease indication experience to date

The clinical network and its teams have performed a large percentage of trials for oncology indications. However, the sites have also conducted work on a wide range of other therapeutic indications. These include Type 2 Diabetes Mellitus, COPD, Pneumonia, Obesity, Lupus, Kidney Disease, Ulcerative Colitis, Acute Coronary Syndrome, renal disorders, neuropathic pain,

Migraine, Alzheimer's Disease, neurodegenerative diseases, neurology, Rheumatoid Arthritis, Lupus, Crohn's Disease and COVID-19. Amongst the oncology domain, these research sites have performed work in blood cancer, breast cancer, prostate cancer, bladder cancer, kidney cancer, brain cancer, and lung cancer.



Study phase experience to date

The clinical network has extensive experience with phase I through phase IV clinical research including pharmacovigilance studies for drugs and biologics, and techno-vigilance studies for medical devices. Most of these trials have had complex inclusion and exclusion criteria, making it challenging to screen for patients that qualify for the trials. However, the clinical network sites have consistently exceeded recruitment and randomization quotas. The CRO and clinical network have been inspected by the US FDA and completed the inspection successfully.

Exceed recruitment and retention rates with MYER and partners

The clinical network team has a proficient marketing group which focuses on recruitment using digital media plus a network of referring doctors that help surpass recruitment goals. The recruitment and retention of patients tend to be a bottleneck for clinical research. However, the clinical network has faced these issues successfully: Less than 3 % of their subjects have been lost to follow-up and there is 96 % rate of meeting subject recruitment goals with 80 % of studies exceeding stipulated goals.

MYER's partnered research center's ethics committee provides an answer in just one week

The clinical network has 4 research units in the country with staff and infrastructure for all research phases. Apart from their 3 owned units, the clinical network is allied with the Hispano Hospital in Guadalajara, with the infrastructure for Phase I studies and studies that require hospitalization of patients. The clinical network is staffed with a qualified and experienced clinical operations team of nurses, study coordinators, and administrative staff. This allows the more than 30 principal investigators with different areas of experience to focus on recruitment and patient care.

All the trials are conducted in strict adherence with ethical guidelines, under ICH and GCP standards. The clinical network sites have their own committees (Ethics, Research and Biosafety; these are certified by COFEPRIS for approval and vigilance and have sovereign decision-making ability and act independently from the clinical network sites and CRO. This results in a quicker and more efficient process to start clinical trials and provides for a more personalized regulatory process that is fully independent and governed by the National Committee of Bioethics. The response time for reviews is 5 business days at a maximum. They accept online submissions and offer the highest quality service, process excellence, and qualified personnel mindful of seeking benefit for patients.

9. COFEPRIS submission process

Registration and regulatory requirements

All the documentation should be submitted in Spanish and a local sponsor is required for the process. Legal documents which are originally in English should be submitted in original English and translated to Spanish by an authorized translator that certifies the translation quality and preserves the medical intent of the documents. The local sponsor is defined as "an individual or corporation willing to undertake responsibility to participate and finance a research project or

protocol, in full or in part". The local sponsor may hire a CRO and delegate responsibilities to it as well. Either the local sponsor or the CRO can be responsible for the feasibility and selection of the research site(s) that will be conducting the clinical research study. The applicant must obtain a research protocol authorization from COFEPRIS but, prior to that, a Research Ethics Committee (REC) and Research Committee (RC) must approve the protocol (equivalent to the Institutional Review Board in the US). Typically, each research site or health institution has its own REC and RC. Sometimes approval of a Biosafety Committee (BC) is required as well. The REC must approve the Informed Consent Document as well. In certain cases, the REC and RC might require an in-person interview with the applicant or a representative. The approval time depends on the committees involved; therefore, it is important to select the appropriate site or institution to conduct the trial to ensure timely processing.

COFEPRIS needs to ensure that the test pharmaceutical is produced under GMP before importing it. A GMP certificate from another regulatory agency namely the FDA can be validated by COFEPRIS as well.

Comparison of an FDA's IND and a COFEPRIS dossier submission

Quick comparison		
	Mexico COFEPRIS	**US FDA**
Trial application language	Spanish	English
Regulatory authority & ethics committee review may be conducted at the same time	No	Yes
Clinical trial registration required	Yes	Yes
In-country sponsor/representation required	Yes	No
Age of minors	Under 18	Determined by state
Specimen export allowed	Yes	Yes

The REC, RC, and BC (if necessary) in Mexico will require the following documentation:

IRB (US)	REC (Mexico)
• Clinical protocol • Informed consent forms (ICFs) and participant information • Participant recruitment procedures • Investigator's brochure • Safety information • Participant payments and compensation • Investigator(s) current Curriculum Vitae (CVs) • Each IRB may require additional documentation	• Research protocol • Protocol summary • Summary of previous studies • Summary of therapeutic product research • Documentation stating research participant, researcher, institution, and if applicable, sponsor commitments • Report describing maintenance measures and life support for research participants and insurance policy agreements • Report on procedures and people responsible for keeping participants informed of study developments • Investigators resume • Statement specifying external funding source information if applicable • Statement providing study costs and expenses if no external funding source • Sponsor data report • Report on supporting material to be used for participant recruitment • System/mechanism to protect participant privacy and maintain confidentiality during study • Methodology to obtain informed consent • System and procedure to communicate results to participants • Informed consent letter • Investigator's manual • Required documentation for participants • Amendments to previously approved documentation • For previously rejected protocols, information on modifications made to address earlier issues

Consultation should be sought from the committee for a given research site to obtain their specific information and format requirements.

The decision by committees in Mexico is not simultaneous to the review by COFEPRIS, in contrast to the US FDA's typical IND process. Once the ethics and research committees approve the protocol, COFEPRIS will review the application and will require the next documents:

FDA IND	COFEPRIS Dossier
• Cover sheet (Form FDA 1571 (USA-76)) • Table of contents • Introductory statement and general investigational plan • Investigator's brochure • Protocols • Chemistry, manufacturing, and control data • Pharmacology and toxicology data • Previous human experience with the investigational drug • Additional information • Relevant information	Application: • Authorizations, Certificates and Visits form • Proof of payment of rights • Application document About the research protocol: • Research protocol document • Informed consent model letter • Description of imported investigational products and quantity • Study's financial budget or insurance • Study schedule About the API or the research product: • Investigator's manual • GMP certificate or application for a COFEPRIS revision • If applicable, stability studies or proof of undergoing studies

Note that COFEPRIS requires documentation from other participating entities: the sponsor, the committees, research site and research team (principal investigator and others).

Start your clinical trial in 6 months or less

COFEPRIS is actively working on accelerating review processes; however it can take up to 6 months to receive an approval and start the clinical trial. MYER can assist you in reducing this time to 4 months with proven strategies that have been followed in the past by our collaborators.

Furthermore, the applicant may request a pre-assessment through an Enabled Pre-Assessment Support Unit (UHAP in Spanish), analogous to a pre-IND meeting by the FDA. If approved, the pre-assessment facilitates a positive decision from COFEPRIS. If the pre-evaluation is rejected, the UHAP institution emits its observations and allows the applicant to address the issues within the next 30 business days. If the issues are not addressed, the reassessment will be rejected and

another UHAP should be filed (note that this step is not mandatory). For COFEPRIS, the response time might remain the same, even with an approved UHAP pre-assessment.

When an applicant receives the COFEPRIS approval, the applicant has a maximum of 5 working days to register the trial in the National Registry of Clinical Trials (RNEC).

FDA data registration from foreign clinical trials

The Food and Drug Administration accepts foreign clinical trial's data as long as the research complies with the FDA requirements, and it was conducted under an IND registration. If the trial was not done under an IND, the FDA might conduct an onsite validation of the study's data. MYER can assist you in obtaining an IND as well for simultaneous trials in the US and Mexico.

Mexican industry and government organizations

MYER maintains an active and ongoing communication and networking effort with various Mexican Industry Organizations and Government Organizations that promote business between the US, Mexico and Latin America in the pharmaceutical, biopharmaceuticals, medical device and medical research segments.

Mexico based pharmaceutical companies

MYER has recently initiated a communication and networking effort with various Mexican based companies, including manufacturers, distributors, and pharmacies in the Pharmaceutical, Biopharmaceutical and medical device industries in order to explore potential collaborations or partnerships on behalf of its contracted clients.

10. Project management team

Rey Magaña, MYER Research Inc, Founder and CEO, USA

Rey Magaña is a serial entrepreneur with over 30 years of experience in preclinical and clinical R&D operations and business development. He has worked in the pharmaceutical, biotechnology, medical device, and nutritional industries. He has managed projects and R&D programs in cancer, diabetes, cardiovascular, and other therapeutic areas. He is a co-inventor and was part of the team that pioneered Extracellular vesicle and Exosome nucleic acid technologies for applications in molecular diagnostics, drug delivery, and therapeutics. He co-founded Proxy Life Science Holdings, a biotechnology company organized to develop those technologies and held the positions of Vice President and Director of Business Development. He also co-founded Perry Scientific, a contract research organization specializing in pre-clinical research services supporting early-stage pharmaceutical, biopharmaceutical, and medical device companies. The company catered to both emerging and established blue-chip companies. Mr. Magaña was responsible for strategy, business development, and operations. He held the title of VP and Chief Operations Officer. His key duty was the development and delivery of custom research services including efficacy, pharmacokinetics, and safety studies in areas as diverse as

oncology, metabolic diseases, cardiology, dermatology, immunology, drug delivery, cosmetics, nutraceuticals, and medical devices. He also co-founded NutraClinical Inc. a near-shore clinical research organization delivering clinical trial services for the nutritional industry. Mr. Magaña attended the University of California of San Diego, where he studied Biology.

11. Clinical research team

Marco A. Cid, MBA, Senior Clinical Research Operations, MX

Graduated from La Salle University (CDMX), as a Pharmaceutical Chemist Biologist.] Postgraduate in Clinical Research at York College in Toronto, Canada. MBA from ITESO (GDL), Senior Management from IPADE, InnovAD from IPADE. General Director of THE CLINICAL NETWORK holding, for more than 12 years, and pioneer in the development of business models focused on research and development in Mexico. Immersed in philanthropy, developing Universal Health AC, being part of the advisory council of Children and Adolescents in Armonía A.C. It has developed 5 successful companies, which stand out, two of research and development, a private capital fund, a chain of clinics focused on medical services: and one more company of human talent. DROX Health Science recently opened its doors in Florida, USA, attracting research and development projects to Mexico and Latin America. Founder of the most important kidney research center in Latin America, in Guadalajara, Jalisco, and an oncology mixture center in Aguascalientes, Aguascalientes, are also being completed. A lover of evolutionary biology, and a tireless dreamer, Marco firmly believes in Mexico as a world player in the development and research of new therapeutic options.

Valeria Alvarez, MS, Senior COFEPRIS Regulatory Advisor

Born in the city of Guadalajara, Valeria graduated from the University of Guadalajara, as a Nutritionist in 2015, passionate about clinical and sports nutrition, she began her career in clinical research in 2018 as coordinator of the Ethics and Research Committees of the Hispano Hospital in Guadalajara, where she developed her passion for regulation and compliance with the Standards. In 2020, She began as a Regulatory Affairs Specialist at CidViD Biomedical Research, monitoring the status with COFEPRIS of its research centers, offices, pharmacies, and laboratories, as well as providing advice to clients for the registration and marketing of different products such as medicines, supplements, and cosmetics. She is currently a vocal member of the Research Ethics Committee of the Hispano Hospital and works as a Regulatory Affairs Specialist at the DROX HEALTH SCIENCE company, providing regulatory support from preclinical phase research to health registration and marketing of health supplies such as medical devices and drugs.

Carolina Gomez, Senior Clinical Management Advisor, MX

As a Master in Pharmaceutical Sciences, for more than five years Carolina collaborated at Sophia Laboratories, working mainly as Sr. Clinical Research Associate, performing monitoring tasks and visits for designated projects according to relevant SOP's, study specific procedures and Latin American regulation, for Phase III and Phase IV clinical trials. Extensive experience implementing research site activities: research site contracts, ethical and regulatory submission, and review and

finalization of essential documents. She has many years of experience coordinating and preparing resources for clinical trials for another major global CRO and pharmaceutical company. At DROX, Carolina is a Country Study Manager, leading all the project management and monitoring efforts for the end-to-end services from our preclinical to phase IV.

Carmen de la Rocha, Ph.D., Sr. Clinical Research Advisor and R&D Director, MX

Born in 1985 in Celaya, Guanajuato, Mexico. At the age of 18, Carmen went to León to study Nutrition and Food Science at the University. She spent a year in a third-level hospital designing specialized oral, enteral, and parenteral diets at all stages of life. She then spent two years in private practice as a nutritionist. Later, she started the Master of Science in Biochemical Engineering and later the Doctor of Science in Biotechnology, where I focused on the investigation of factors in epigenetics in murine and human models. Later, she joined Investigacion Biomedica para el Desarrollo de Farmacos (CidVID Investigacion Biomedica), to focus on clinical research, which she has been in for almost four years, initially as coordinator of clinical studies (around 15) and later in the area of Research and Development focused on health products and services. Simultaneously, she works at the University of Guadalajara as a part-time professor in the Nutrition degree and as a visiting professor in Doctorate in Sciences in Translational Nutrition, where she also collaborates in various lines of research. Since the beginning of the pandemic, she leads a team of PhD level scientists focused on proposing solutions and understanding the causes from various perspectives, such as the application of low-cost drugs as a possible treatment (NCT04407507) and observational studies (unpublished), and designing intelligent clinical trials and drafting all the necessary documentations for submissions of clinical trial protocols.

Blanca Ivette Venegas López, Deputy Director, MX

Graduated as a Nutritionist from the “Universidad del Valle de Atemajac” with a masters in Health Administration from the “Universidad del Valle de Mexico”, Blanca also has a Diploma in Business Administration from the IPADE, Business School. She started her professional career with private consultations as a nutritionist. She also worked in the pharmaceutical industry in different areas such as business administration, regulatory business and research and development of new drugs in prestigious enterprises like Nestlé and Terumo Medical. For over 3 years she was president of the Ethical Committee from the Hispano Hospital. For the past 10 years, she has served as the Deputy Director of iBiomed.

Gabriela Sierra, Clinical Operations Manager, MX

Obstetric Surgeon from the Universidad de Guadalajara, specialized in Rheumatology, Gabriela has a Master in Rheumatology Research from the University of Texas and a Master in Social Marketing in Public Health from the University of South Florida. With over 25 years of experience, she has participated in more than 150 clinical studies as a Researcher. She has collaborated with prestigious Pharmaceutical Companies like Roche Syntex Group where she served as Clinical Monitor. She has published over 20 articles and books. She has also participated as a Public Speaker in both national and international Medical Congresses. She currently serves as Clinical Operations Manager in iBiomed.

Jorge Ramirez, BS, Senior Technology and Data Science Advisor, MX

Born on July 8, 1996, in Oaxaca, Mexico, Jorge has a degree in computer Science from University of Guadalajara. Passionate about web development and technology, he became a seasoned web developer with years of experience in developing and creating the best digital solutions for businesses of diverse industries. In 2021 he discovered clinical research developing websites and creating various digital solutions at CidVid Biomedical Research. At DROX Health Science he holds the position of System Analyst developing digital solutions for the clinical industry and as administrator of current systems. He leads the development of an In-House Electronic Data Capture (eDC) system and Case Report Forms (CRFs).

Aquiles Sanchez, Clinical Research Coordinator, MX

Aquiles graduated from the Bachelor of Psychology from the Universidad de Guadalajara. Diplomate in Clinical Ethics from the IMSS specialty hospital. Workshop for clinical research coordinators by the Mexican CRO´s alliance. Diplomate in Clinical Research by the National Institute in Medical Science and Nutrition "Salvador Zubiran". With more than 15 years of experience, Aquiles has collaborated with distinguished institutions as Clinical Research Coordinator, such as the Mexican Institute of Social Security (IMSS), Security Institute and Social Services of the State Workers (ISSSTE) and in the Dermatological Institute of Jalisco "Dr. Jose Barba Rubio'' for over 11 years. He has participated in clinical trials from very important pharmaceuticals, such as GlaxoSmithKline, Bayer, Pfizer, Novartis, Bristol-Myers Squibb, Eli Lilly, Janssen Cilag, among others; this studies were conducted in different therapeutic areas like Cardiology, Dermatology, Traumatology, Orthopedics, gastroenterology, among others.

Nathalie Geraldo, Clinical Research Coordinators, MX

Graduated as Medical Surgeon and midwife by the Universidad de Guadalajara. Nathalie's first steps in the medical field were offering first level attention to the Mexican Institute of Social Security (IMSS) patients. She also worked in the bioequivalence field, as medical sub-investigator in different phase 1 studies. During the last 5 years, she has collaborated in more than 100 clinical trials. She also worked as Principal Investigator in UNEBI (third approved by COFEPRIS). She is currently part of the Clinical Research Coordinators in iBiomed.

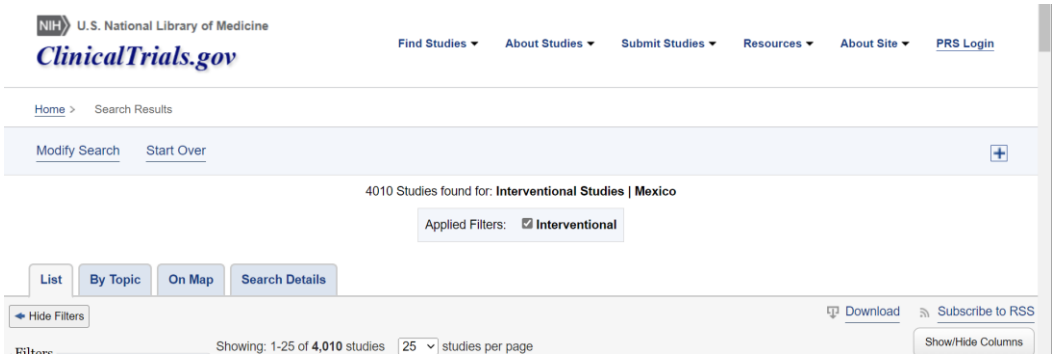
Mildred González, Quality Supervisor, MX

Mildred graduated with excellence in BPC (Biotechnological Pharmaceutical Chemist) from Technological University of Guadalajara (UTEG). With a great trajectory within different corporations such as MexLab S.A de C.V. where she was in charge of the quality department in medical devices with support to the development of reagents for febrile reactions tests, as well as in Farmiral S.A. de C.V. where she served as leader of quality assurance in food supplements. She currently serves as Quality Supervisor at iBiomed.

12. Supplementary content

Generation of graphs and tables from “clinicaltrials.gov” data

The search in clinicaltrials.gov was delimited to only Mexico interventional type studies.

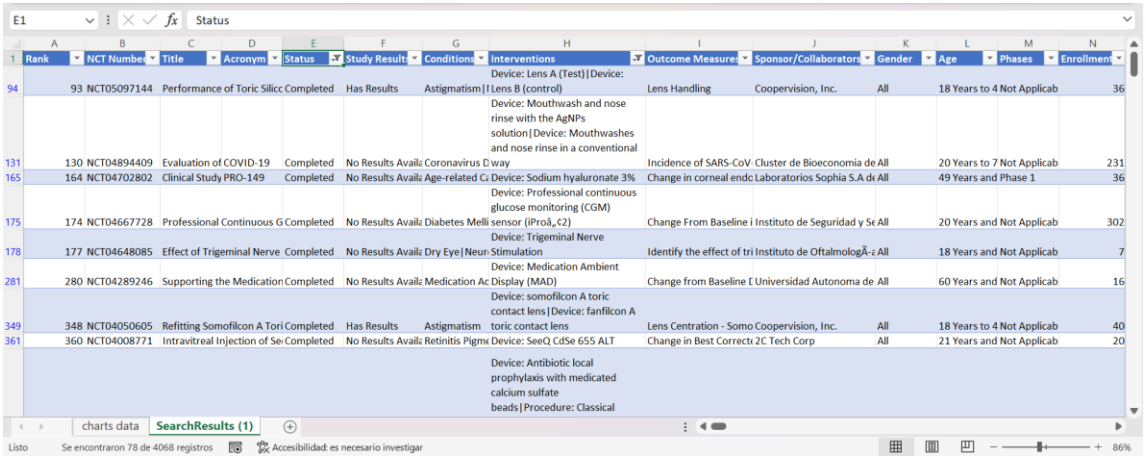


The entire data from all of the Mexico interventional studies was downloaded as a “comma separated values” file and processed in Excel.

The “Filter” function in the “Data” section was used to start analyzing the number of different intervention types, indications and phases of the studies, completed or active.

The “Phases” column was filtered for each of the four stages of clinical trials to know the amount of trials from each phase.

For completed studies, the “Status” column was filtered to show only studies with the value “Completed” resulting in 2449 studies. Filters for the “Interventions” column were applied to distinguish the amount of studies involving medical devices, drugs, biological compounds or others. Here is an example of the displayed table when applied filters for only completed medical devices’ studies and the legend “78 out of 4068 coincidences”.



The same was done then for active studies (filter containing “active”, “recruiting”, “not yet recruiting”) to know the number of each intervention type. Graphs were done from this data:

Completed								Intervention type
Medical Devi	Drugs	Biological mc	Behavioral	Dietary suppl	Procedure	Radiation	Other	
78	1973	205	66	90	82	7	241	
Active								
Medical Devi	Drugs	Biological mc	Behavioral	Dietary suppl	Procedure	Radiation	Other	
31	648	131	24	31	41	20	140	

Note that the sum of trials is more than the total displayed by "clinicaltrials.gov" (active or completed. Suspended or terminated studies were not considered) as some studies involved more than one intervention type and so were counted for each category.

13. References

Antunes, N.T. (2017, April 5). *¿Puede México convertirse en una potencia regional para los ensayos clínicos?* International Society of Drug Bulletins. Retrieved August 28, 2022, from https://www.saludyfarmacos.org/lang/es/boletin-farmacos/boletines/ago201704/26_puede/

Arman, C., Lopez, A., & Sanchez, S. A. (2013, May 23). *Clinical trial regulation in Mexico*. PMLiVE. Retrieved September 18, 2022, from https://www.pmlive.com/pharma_intelligence/clinical_trial_regulation_in_mexico_477081

Carlos-Rivera, F., Gasca-Pineda, R., Majluf-Cruz, A., & García-Chávez, J. (2016). Impacto económico de la hemofilia tipo A y B en México Economic impact of hemophilia type A and B in Mexico. *Gaceta medica de Mexico*, *152*(1), 19–29.

CIA. (2022, September). *Mexico - The World Factbook*. CIA. Retrieved September 18, 2022, from https://www.cia.gov/the-world-factbook/countries/mexico/

COFEPRIS. (2014, April 3). *México y Panamá firman acuerdo de cooperación regulatoria en materia de medicamentos*. Gobierno de México. Retrieved September 18, 2022, from https://www.gob.mx/cofepris/prensa/mexico-y-panama-firman-acuerdo-de-cooperacion-regulatoria-en-materia-de-medicamentos-58828

COFEPRIS. (2017, November 22). *El 68% de la #InvestigaciónClínica[Tweet]*. COFEPRIS. Retrieved September 18, 2022, from https://twitter.com/COFEPRIS/status/933399136426131456

COFEPRIS. (2018, September 14). *ANMAT y COFEPRIS firman Lineamientos de Buenas Prácticas de Fabricación (BPF) de Medicamentos*. Gobierno de México. Retrieved September 18, 2022, from https://www.gob.mx/cofepris/prensa/anmat-y-cofepris-firman-lineamientos-de-buenas-practicas-de-fabricacion-bpf-de-medicamentos?idiom=es

COFEPRIS. (2021, November 17). *México, primer país hispanohablante miembro de ICH, máximo foro regulatorio de productos farmacéuticos*. Gobierno de México. Retrieved September 18, 2022, from https://www.gob.mx/cofepris/es/articulos/mexico-primer-pais-hispanohablante-miembro-de-ich-maximo-foro-regulatorio-de-productos-farmaceuticos?idiom=es

Cruz-Góngora, V. D. la, Chiquete, E., Gómez–Dantés, H., Cahuana-Hurtado, L., & Cantú-Brito, C. (2022). Trends in the burden of stroke in Mexico: A national and subnational analysis of the global burden of disease 1990–2019. *The Lancet Regional Health - Americas*, *10*, 100204. https://doi.org/10.1016/j.lana.2022.100204

DESISA. (2022, April 11). *Alianza de autoridades sanitarias INVIMA, ISP y COFEPRIS - Blog Desisa*. Grupo DESISA. Retrieved September 18, 2022, from https://grupodesisa.mx/blog/alianza-de-autoridades-sanitarias-invima-isp-y-cofepris/

El Economista. (2022, March 10). *Bayer prevé inversión de 7,500 mdp en México en los próximos tres años*. El Economista. Retrieved September 18, 2022, from

https://www.eleconomista.com.mx/empresas/Bayer-preve-inversion-de-7500-mdp-en-Mexico-en-los-proximos-tres-anos-20220311-0008.html

EMBAMEX. (2021). *Overview of the Mexican Economy*. EMBAMEX Secretaría de Relaciones Exteriores. Retrieved September 18, 2022, from https://embamex.sre.gob.mx/filipinas/index.php/negocios-y-comercio/overviewmexicaneconomy

Fundación Carlos Slim. (2015, February 2). *Nearly 2 million people have epilepsy in Mexico*. Fundación Carlos Slim. Retrieved September 18, 2022, from https://www.salud.carlosslim.org/english2/nearly-2-million-people-have-epilepsy-in-mexico/

INCyTU. (2018). *Salud Mental en México*. Retrieved September 1, 2022 from https://www.foroconsultivo.org.mx/INCyTU/documentos/Completa/INCYTU_18-007.pdf

INEGI. (2021, July 29). *CARACTERÍSTICAS DE LAS DEFUNCIONES REGISTRADAS EN MÉXICO DURANTE 2020, PRELIMINAR*. INEGI. Retrieved September 18, 2022, from https://www.inegi.org.mx/contenidos/saladeprensa/boletines/2021/EstSociodemo/DefuncionesRegistradas2020_Pre_07.pdf

International Diabetes Federation. (2021, November 12). *1 in 6 adults are now living with diabetes in Mexico*. IDF. Retrieved August 28, 2022, from https://www.idf.org/index.php?option=com_attachments&task=download&id=2645:WDD2021_MEXICO_PR_Final#:~:text=These%20findings%20from%20the%2010th,in%20the%20past%20two%20years.

Lizárraga, J. (2017). *Enfermedades Cardiovasculares, principal causa de muerte entre los mexicanos*. Asociación Ale. Retrieved September 18, 2022, from https://asociacionale.org.mx/enfermedades-cardiovasculares-principal-causa-de-muerte-entre-los-mexicanos/

López-Arroyo, José L., Pérez-Zúñiga, Juan M., Merino-Pasaye, Laura E., Saavedra-González, Azucena, Alcivar-Cedeño, Luisa María, Álvarez-Vera, José Luis, Anaya-Cuellar, Irene, Arana-Luna, Luara L., Ávila-Castro, David, Bates-Martín, Ramón A., Cesarman-Maus, Gabriela, Chávez-Aguilar, Lénica A., Peña-Celaya, José A. de la, Espitia-Ríos, María E., Estrada-Domínguez, Patricia, Fermín-Caminero, Denisse, Flores-Patricio, Willy, García Chávez, Jaime, García-Lee, María T., González-Pérez, María del Carmen, González-Rubio, María del Carmen, González-Villareal, María Guadalupe, Ramírez-Moreno, Fabiola, Hernández-Colin, Ana K., Hernández-Ruiz, Eleazar, Herrera-Olivares, Wilfrido, Leyto-Cruz, Faustino, Loera-Fragoso, Sergio, Martínez-Ríos, Annel, Miranda-Madrazo, María R., Morales-Hernández, Alba, Nava-Villegas, Lorena, Orellana-Garibay, Juan J., Palma-Moreno, Orlando G., Paredes-Lozano, Eugenia P., Peña-Alcántara, Paula, Pérez-Lozano, Uendy, Pichardo-Cepín, Yayra M., Reynoso-Pérez, Ana Carolina, Rodríguez-Serna, Mishel, Rojas-Castillejos, Flavio, Romero-Rodelo, Hilda, Ruíz-Contreras, Josué I., Segura-García, Adela, Silva-Vera, Karina, Soto-Cisneros, Paulina M., Tapia-Enríquez, Ana L., Tavera-Rodríguez, Martha G., Teomitzi-Sánchez, Óscar, Tepepa-Flores, Fredy, Valencia-Rivas, María D., Valle-Cárdenas, Teresa, Varela-Constantino, Ana, Javier-Morales, Adrián, Martínez-Ramírez, Mario A., Tena-Cano, Sergio, Terrazas-Marín, Ricardo, Vilchis-González, Shendel P., Villela-Peña, Atenas, Mena-Zepeda, Verónica, & Alvarado Ibarra, Martha. (2021). Consenso de hemofilia en México. *Gaceta médica de México*. https://doi.org/10.24875/gmm.m20000451

NIH. (n.d.). *Search of Interventional Studies in Mexico*. ClinicalTrials. Retrieved August 28, 2022, from https://clinicaltrials.gov/ct2/results?cntry=MX&age_v=&gndr=&type=Intr&rslt=&Search=Apply

OEC. (n.d.). *Medical Instruments in Mexico | OEC*. The Observatory of Economic Complexity. Retrieved September 18, 2022, from https://oec.world/en/profile/bilateral-product/medical-instruments/reporter/mex?redirect=true

Pharmaceutical Technology. (2022, February 21). *Mexican manufacturing: so far from EU, so close to US*. Pharmaceutical Technology. Retrieved September 18, 2022, from https://www.pharmaceutical-technology.com/comment/mexican-manufacturing-eu-us/

Pharmexcil. (2020, August). *Mexico pharma market & REGULATORY report*. Mexico Pharma Market & Regulatory Report. Retrieved September 18, 2022, from https://pharmexcil.com/uploads/countryreports/Mexico_Market_Regulatory_report2020.pdf

ProMexico. (2014). *México: Biotecnología*. ProMexico, Gobierno de México. Retrieved September 18, 2022, from https://www.gob.mx/cms/uploads/attachment/file/75579/05052014_DS_Biotecnologia_ES.pdf

ProMexico. (2017). *Clinical Research? Take a look at Mexico*. ProMexico.

Rodríguez-Violante, Mayela, Velásquez-Pérez, Leora, & Cervantes-Arriaga, Amin. (2019). Incidence rates of Parkinson's disease in Mexico: Analysis of 2014-2017 statistics. *Revista mexicana de neurociencia*, *20*(3), 136-140. Epub August 28. 2022.https://doi.org/10.24875/rmn.m19000043

Sánchez, H. (2020, April 1). *NEUROPATÍA DIABÉTICA Epidemiología, clasificación fisiopatología y tratamiento*. Galena MED. Retrieved September 1, 2022, from https://med-cmc.com/neuropatia-diabetica/

Secretaría de Salud. (2018, June 13). *Se incrementa en 43 mil el número de estudiantes de medicina en los últimos 8 años*. Gobierno de México. Retrieved September 18, 2022, from https://www.gob.mx/salud/prensa/239-se-incrementa-en-43-mil-el-numero-de-estudiantes-de-medicina-en-los-ultimos-8-anos

Statista. (2022, July 6). *Mexico pharmaceutical exports by country 2021*. Statista. Retrieved September 18, 2022, from https://www.statista.com/statistics/478682/mexican-pharmaceutical-exports-by-country/

TACNA. (2021, August 26). *An Overview of Mexico's Growing Medical Device Industry - TACNA*. Tacna. Retrieved September 18, 2022, from https://tacna.net/mexicos-growing-medical-device-industry/

Uhthoff, S., & Uhthoff, G. (2020, March 18). *Effects of the USMCA (US-Mexico-Canada agreement) in the Mexican pharmaceutical industry*. Lexology. Retrieved September 18, 2022, from https://www.lexology.com/library/detail.aspx?g=d850f261-22c8-43be-b92f-6e763341a22d

Valle, A. (2020, January 27). *Pfizer invertirá 20 mdd en México en 2020*. Expansión. Retrieved September 18, 2022, from https://expansion.mx/empresas/2020/01/27/pfizer-invertira-20-mdd-en-mexico-en-2020

WEDC. (2022, March 28). *Mexico's pharmaceutical industry grows | WEDC*. Wisconsin Economic Development Corporation. Retrieved September 18, 2022, from https://wedc.org/export/market-intelligence/posts/mexican-pharmaceutical-industry-grows/

WHO. (2021, March). *Mexico*. Global Cancer Observatory. Retrieved September 18, 2022, from https://gco.iarc.fr/today/data/factsheets/populations/484-mexico-fact-sheets.pdf

World Atlas. (2019, July 18). *Largest Ethnic Groups In Mexico - WorldAtlas*. World Atlas. Retrieved September 18, 2022, from https://www.worldatlas.com/articles/largest-ethnic-groups-in-mexico.html

Yovera-Aldana, M., Velásquez-Rimachi, V., Huerta-Rosario, A., More-Yupanqui, M. D., Osores-Flores, M., Espinoza, R., Gil-Olivares, F., Quispe-Nolazco, C., Quea-Vélez, F., Morán-Mariños, C., Pinedo-Torres, I., Alva-Diaz, C., & Pacheco-Barrios, K. (2021). Prevalence and incidence of diabetic peripheral neuropathy in Latin America and the Caribbean: A systematic review and meta-analysis. *PloS one*, *16*(5), e0251642. https://doi.org/10.1371/journal.pone.0251642

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