

# ASSESSING GENERIC AND BIOSIMILAR DRUG MANUFACTURING IN NORTH AMERICA & THE POTENTIAL OPPORTUNITY FOR THE CALIBAJA REGION

A STRATEGY PAPER DEVELOPED BY:



INSTITUTE OF  
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# I. Executive Summary

In recent years, the United States has experienced shortages of many essential medicines, putting at risk the stability of its healthcare systems and ability to meet the priority health care needs of its population. Over 90% of medicines consumed by Americans are generic drugs and biosimilars. The U.S. has become over-reliant on lower cost overseas sources, principally from China and India, for much of the active pharmaceutical ingredients (APIs) and key starting materials (KSMs) required to make many generic and essential drugs. While the United States is a world leader in developing and marketing patented branded prescription drugs, a significant portion of America's generic drugs are sourced from overseas, with a large percentage also coming from China and India. This dependence poses supply chain risks and national security concerns.

As the United States looks to strengthen and make its pharmaceutical supply chain more resilient, the CaliBaja region could play a valuable role. A 2021 [White House report](#) on building resilient supply chains highlighted the importance of “fostering greater international cooperation” and emphasized the need to “partner with allies.” The U.S. government has since taken steps to onshore essential medicine production and increase domestic production. The White House announced in late 2023 a plan to use the Defense Production Act (DPA) to produce more essential medicines in America. The drug shortage crisis and dependence on China for API and other essential medicines have also prompted Congress to consider legislation that would, if enacted, catalyze investment in the pharmaceutical sector to promote greater drug resiliency.

Although the White House report does not specifically name Mexico as a country to produce essential medicines, its proximity to the United States and membership in the USMCA trade agreement make it a logical partner. Mexico's pharmaceutical sector represents a significant component of that country's economy and includes multinational and domestic companies. A substantial portion of Mexico's pharmaceutical needs, particularly generics, is met by local production, but there is also a significant reliance on imported medicines and raw materials, again from China and India. Canada faces similar vulnerabilities.

The growing U.S. demand for essential medicines provides Mexican companies with an opportunity to invest in expanding their capacity to serve the U.S. market. The sector has also seen investment from foreign pharmaceutical companies, including from countries like India, which view Mexico as a gateway to Latin America and potentially the U.S. market. In October 2023, the Mexican government [issued a nationwide incentive program](#) to catalyze expanded investment in ten strategic sectors, including pharmaceuticals. However, Mexico's willingness and ability to seize this nearshoring opportunity have so far been limited by significant regulatory hurdles, among other factors.

Many of Mexico's pharmaceutical companies are concentrated in the greater Mexico City metropolitan area with other important centers in Guadalajara, Puebla, and Monterrey. In Baja California, there are currently only four companies producing generic drugs. Still, the binational CaliBaja region is positioned to play a potentially unique role in fortifying North America's pharmaceutical supply chain.



By leveraging its cross-border strengths, the CaliBaja region offers a unique opportunity to become a production hub for generics drugs and, in particular, biosimilar drugs serving the U.S. market that are deemed essential medicines. The region's strengths include world-class life sciences and bio-pharmaceutical clusters in Southern California; Baja California's strong manufacturing base, including in medical devices; best-in-class universities, technical colleges, and research institutions on both sides of the border; and access to skilled labor in Baja California at lower costs relative to California and the United States.

As of this writing, the U.S. Food & Drug Administration (FDA) has approved 46 biosimilar drugs<sup>1</sup> but this number is expected to grow over time as there are currently 118 biosimilar drugs under development in the United States<sup>2</sup>. Here, a key question is where these biosimilar drugs will be ultimately manufactured?

For the CaliBaja region to capitalize on the opportunity for generic and/or biosimilar manufacturing, collaborative initiatives across institutions and regulatory alignment between the United States and Mexico are critical. Stakeholders should focus on strengthening the workforce, improving border infrastructure, and enhancing cross-border transportation. To support the region's manufacturing capacity for generic and biosimilar drugs, consideration should be given to establishing dedicated industrial parks in Baja California with required infrastructure, including reliable access to water, clean energy, and security.

Success will depend on targeted investment, regulatory reforms, and cross-border collaboration. As one White House report noted, supply chain issues cannot be fixed solely through government action; they require industry, nonprofits, public-private partnerships, and governments working together to ensure stable supply chains and patient access to critical medicines.

San Diego and Tijuana's joint selection as the first binational [2024 World Design Capital](#) presents an unprecedented chance for the region's key stakeholders to think boldly about how to seize this historic moment. Through innovative private sector, non-profit and approaches, lower-cost production in Mexico, targeted government incentives, and more regulatory certainty, a stronger and more resilient North American pharmaceutical supply chain is in sight.



Bio-pharmaceutical lab, CICESI, Ensenada.  
Credit: Ensenada EDC





## II. Definitions



### Small molecule drugs:

The majority of pharmaceuticals available today are what are known as small molecule drugs, (otherwise known as conventional pharmaceutical drugs) and are the most common medications on the market. Small molecule drugs are organic compounds with a low molecular weight<sup>iii</sup> and manufactured through chemical synthesis. Small molecule drugs are meant to replicate natural compounds produced by plants, fungi and bacteria, using biochemical processes to prevent or treat a disease. The key advantage of small molecule pharma drugs is their low molecular weight and simple chemical structures. This means that they are stable, can be easily taken orally, and do not need to be stored in special conditions. Typical small molecule, conventional drugs include aspirin and statins.

**According to Research and Markets, small molecule drugs make up to 90% of the pharmaceutical drug market by volume. In 2020, 75% of all approved drugs were small molecule medications<sup>iv</sup>.**



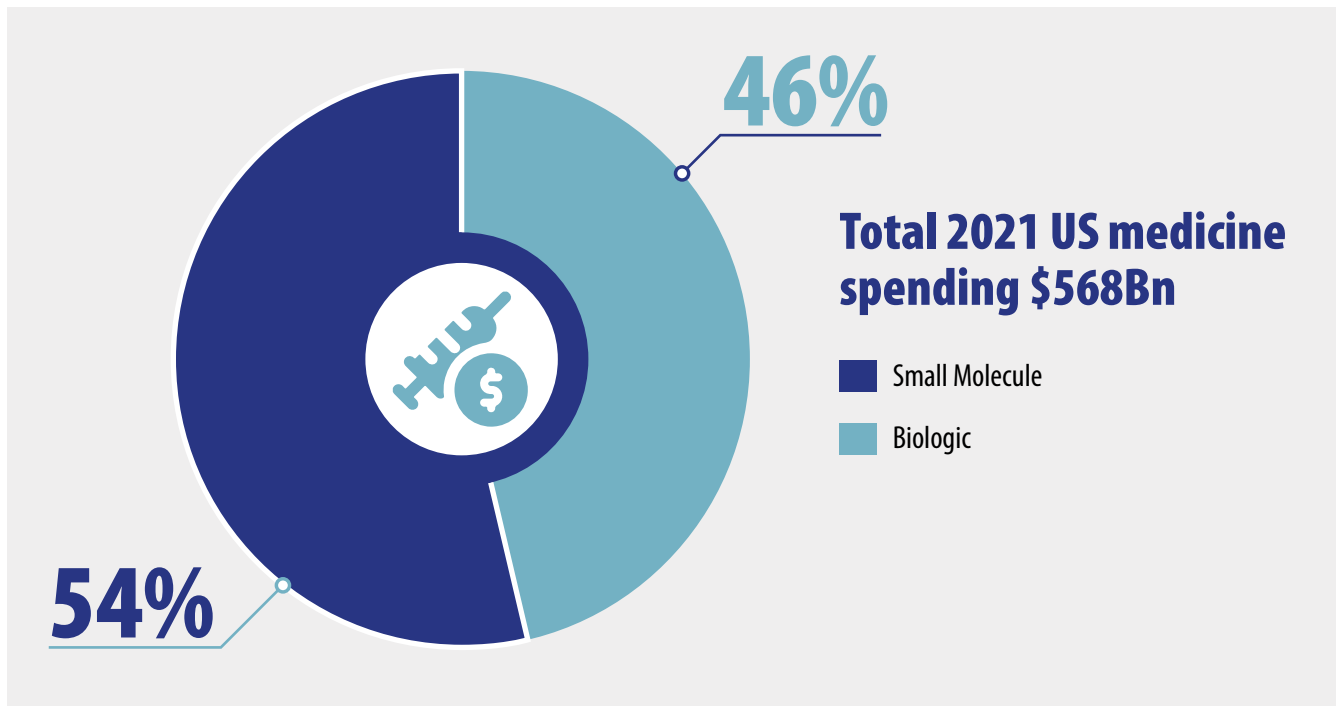
### Generic Drugs:

Small molecule drugs with expired patents can be reformulated into more affordable generic medications. Generic drugs are created to be the same as an already marketed brand name, patented drug in dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use. This means that generic drugs work in the same way and provide the same clinical benefits as brand-name, patented drugs, but are often available at a much lower cost.



### Biologic Drugs:

Biologic drugs, on the other hand, are generally large, complex molecules and heat sensitive, so require refrigeration. Biologic drug products may be produced through biotechnology in a living system, such as a microorganism, plant cell or animal cell.<sup>v</sup> Biologic drugs include a wide range of vaccines, blood and blood components, antidiabetics, HIV antivirals, allergenics, somatic cells, gene therapies, tissues and recombinant therapeutic proteins,<sup>vi</sup> including the RNA COVID-19 vaccines. According to the Association of Accessible Medicine (AAM), **only 2% of US patients use biologics.<sup>vii</sup> That said, in 2021 46% of prescription drug spending in the United States was on biologics.** See Figure 1. **These classes of biologic drugs —for immunology, antidiabetics, and oncology— account for 70% of all biologic spending.<sup>viii</sup>**



Source: IQVIA Institute, November 2022



### Biosimilar Drugs:

**A biosimilar drug is similar to another biologic drug that is already FDA-approved (known as the original biologic).** Insulin is a well-known biosimilar drug. It is normal and expected for both biosimilars and original biologics to have minor differences between batches of the same medication<sup>x</sup>. Biosimilars must have no clinically meaningful differences from their original biologic and must be given the same way, have the same strength and dosage form, and have the same potential side effects. Like biologic drugs, biosimilars are rigorously and thoroughly evaluated by the FDA before approval.<sup>x</sup> To date, the FDA has approved 46 biosimilar drugs for the U.S. market.



## III. Background

**While currently over 90% of medicines consumed by Americans are generic drugs and biosimilars<sup>vi</sup>**, over the past few years the United States has experienced a growing prevalence of generic drug shortages for many essential drugs, some of which were attributed to COVID-19 supply chain disruptions. In fact, according to a report by the U.S. Senate's Committee on Homeland Security, between 2021 and 2022, the United States experienced drug shortages for more than 15 essential drugs<sup>xii</sup>. The essential patented and generic medicines that have experienced shortages have included [heart medications](#), cancer treatments, and [ADHD medications like Adderall](#).

The United States faces another key challenge. The country has become over-reliant on lower cost overseas sources, principally from China and India, for not just most of its generic drugs but also a growing number of the active pharmaceutical ingredients (APIs) and key starting materials (KSMs) required for many essential drugs. Over time, America's over dependency on China and India has positioned both countries to have a comparative advantage of cost competitiveness for generics, APIs and KSMs through value chain integration clusters, lower cost utilities, high-capacity utilization and economies of scale that is today more difficult for U.S. manufacturers to compete.

**As the Senate report observed, between 90-95% of generic sterile injectable drugs for critical acute care in the U.S. rely on APIs from China and India.** This over-reliance on China for not just generic drugs but also mission-critical APIs and KSMs raises obvious national security concerns given growing bilateral tensions and the potential to affect patient's lives. Another key concern relates to drug quality and safety, as highlighted by the worldwide recall in 2007 of heparin —**a widely used blood thinner**— that had been adulterated at a manufacturing facility in China and caused dozens of American patients to suffer adverse reactions, including death<sup>xiii</sup>.

America's drug shortages, supply shocks, and the country's over-reliance on just two foreign sources for generic drugs are attributed to various factors. These include the low profit margins for generic drugs in comparison to their patented alternatives, the high costs associated with overcoming [regulatory hurdles](#) for FDA approval for any new product, challenges related to building any new manufacturing operation (environmental and speed to market) as well as hiring and retaining a skilled workforce, and the need to ensure standards of quality are maintained for the generic drugs ultimately produced.

In response to recent drug shortages and generic and biosimilar drug market dynamics in the United States, the U.S. Department of Health and Human Services (HHS) established a public-private consortium with the goal of advancing manufacturing and onshoring domestic essential medicine production. This led to the convening of 183 leading subject matter experts (SMEs) in the National Forum to Secure America's Supply Chain for Essential Medicines (Forum). The Forum generated a [list](#) of [86 essential medicines](#) critically needed for acute patient care.



Forum SMEs also contributed to a White House [report](#) published in June 2021 that issued four key recommendations to promote greater national resiliency for our country's supply of essential medicines. **These included: 1) increasing supply chain coordination, security and transparency; 2) increasing domestic manufacturing capabilities and innovation in research and development; 3) expanding purchasing, stockpiling and distribution approaches; and 4) expanding both domestic onshore as well as nearshore production capacity.** To expand the potential for essential drug nearshoring, the report highlighted the critical importance of "fostering greater international cooperation" and emphasized the need to "partner with allies." It observed that promoting cooperation on the friend-sourcing front could be improved by collectively developing solutions that reduce identified risks by, among other things, developing a centralized shared API (Active Pharmaceutical Ingredient) supplier database as well as "**coordinating production in geographically accessible locations**" among allies<sup>xiv</sup>. Accelerating API domestically requires overcoming substantial environmental concerns that may slow domestic development but also includes the opportunity to develop new methods of manufacturing that could be accomplished more rapidly by nearshoring with North American allies.

It will take a broad North American response to address the supply chain imbalance and potential national security threat. While the focus today is on small molecule generic drugs, the potential for biosimilar alternatives to branded biologic drugs has the potential to follow a similar path. This is where the CaliBaja border region offers potential solutions, most notably in becoming a future hub for biosimilar innovation and manufacturing. This strategy paper examines both the North American response to the issues of today and the potential role that the CaliBaja region can play in responding to the need for expanded essential medicine access for the United States and Mexico.



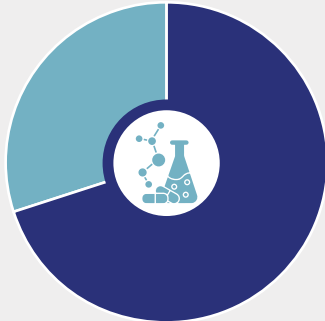




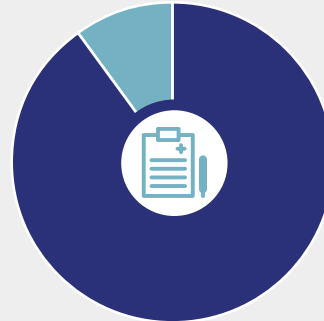
## IV. Current Landscape



### a) United States



The United States is the world's largest pharmaceutical drug market with nearly **70%** of Americans taking at least one prescription drug and more than half of the population taking two<sup>xv</sup>.



Of drugs prescribed, over **90 %** are generics or biosimilars, which account for less than 18% of spending.<sup>xvi</sup>



While the United States is a world leader in developing and marketing patented branded prescription drugs, due to intense price competition and other competitive factors, the manufacturing of generic drugs intended for U.S. consumption increasingly occurs internationally, primarily in China and India<sup>xvii</sup>.

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Manufacturing drugs (patented or generic/off-patent) either in the United States or internationally require several actions that are regulated by the U.S. Food & Drug Administration (FDA) before drugs can be produced and/or marketed for final consumption in country. The initial set of steps involves making essential biochemical ingredients (raw, bulk or starting materials, KSMs) and creating intermediates. During the second step in the process (undertaken at the same or different location) these bulk or intermediate materials are then combined in a form that is biologically active but not readily consumable by patients, otherwise known as active pharmaceutical ingredients or APIs. The last step, again at the same or another location, the API is converted into consumable formulations in the form of tablets, capsules, or ointments, otherwise known as final dosage forms (FDFs). Only FDFs and their APIs that are manufactured in accordance with the FDA's basic quality standards can be legally marketed in the United States by drug makers, operating either domestically or internationally.

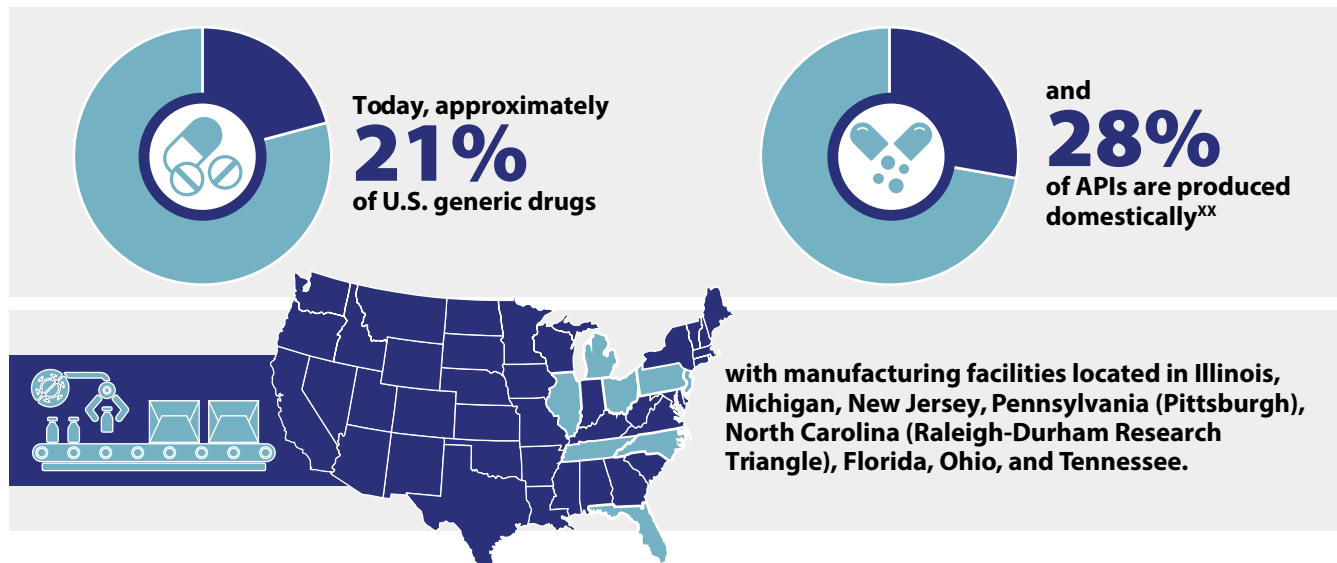
In the case of new, patented drugs, an applicant must file a New Drug Application ("NDA") that includes details of extensive clinical trial evidence of safety and efficacy as well as documentation of compliance with Current Good Manufacturing Practice (cGMP) regulations as a condition of NDA approval.



### Generics:

For generic drugs, the approval process for an Abbreviated New Drug Application (ANDA) is less onerous, as an NDA with clinical trials is not required. Generic drug applications must include evidence of the drug's pharmaceutical and bioequivalence to the reference drug as well as manufacturing to cGMP standards. This requires that generic drug makers submit as part of their ANDA details regarding the chemistry, manufacturing, and controls for their APIs and/or FDFs.

In accordance with the General Drug User Fee Act (GDUFA), the FDA collects applications and annual fees from ANDA applicants and ANDA holders to offset the cost of domestic and international facility inspections. In theory, both domestic and international generic drug manufacturers should be inspected equally.



Source: Safeguarding Pharmaceutical Supply Chains in a Global Economy, US FDA Testimony before House Committee on Energy and Commerce, Subcommittee on Health, October 19, 2019.

Leading U.S. manufacturers include Viatris (formed in 2020 through a merger of Mylan, N.V and Upjohn) , Teva Pharmaceuticals (Israel), Hospira, Inc. (acquired by Pfizer in 2015) and Sun Pharma-USA States (India). Other U.S. generic manufacturers include Endo Pharmaceuticals, JHP Pharmaceuticals, and UPM Pharmaceuticals. Due to competitive pressures and other legal issues, three U.S. generic manufacturers —**Akron<sup>xxii</sup>, Lannett<sup>xxiii</sup>, and Mallinckrodt<sup>xxiv</sup>**— have recently filed for bankruptcy protection.<sup>xxv</sup>

For most of the late twentieth century, Puerto Rico was one of the major sources of brand name and generic pharmaceutical products for the United States, but its role has diminished due to the elimination of Section 936 tax provisions that incentivized pharmaceutical manufacturing on this U.S territory<sup>xxvi</sup> as well as the increased risk of natural disaster.<sup>xxvii</sup>



### Biosimilars:

As a result of stiff competition and low margins in the generic drug market, U.S. drug makers have increasingly focused on more complex generics and biosimilars. Biosimilars are non-original biological medicine produced through recombinant technology and approved through an abbreviated pathway. In the United States, the market for biosimilars emerged through the passage of the Biologics Price Competition and Innovation Act (BPCIA) enacted in 2010. As of this writing, the FDA has approved 46 biosimilars across 14 molecules since 2006. Of these biosimilars, 15 are currently manufactured in the United States and just three are made in China.

**Today, the United States has a dominate position in the global biosimilar market with over 39% of the total market share in 2022<sup>xxviii</sup>.** Key biosimilar manufacturing regions include Boston/Cambridge, MA; the San Francisco Bay Area; Southern California; Research Triangle Park, North Carolina; Montgomery County/Baltimore, MD; New Jersey, Pennsylvania; and the Midwest (Indiana and Illinois). U.S.-headquartered market leaders in biosimilar manufacturing include Pfizer, Catalent, Amgen (Thousand Oaks, CA), BioGen, Viatrix, Johnson & Johnson, and IQVIA.

Though there are currently no generic or biosimilar manufacturing operations in San Diego, Genentech (a leading biotech company owned by Roche) operates a 575,000 SF biologics drug substance manufacturing facility in Oceanside, California<sup>xxix</sup>. Also in Oceanside, Gilead Science supports clinical drug manufacturing<sup>xxx</sup>.

Increased awareness of U.S. vulnerability to the supply of generic drugs resulting from shortages, drug quality and safety concerns, supply chain shocks, and other geopolitical factors, have led to increasing calls for re-shoring or friend-shoring production of more of the essential medicines that the United States requires. The White House has responded with a plan announced in November 2023 to use the Defense Production Act (DPA) to make more of these essential medicines in America. President Biden will issue a Presidential Determination to broaden the Department of Health and Human Services' (HHS) authorities under Title III of the DPA to enable investment in domestic manufacturing of essential medicines, medical countermeasures, and critical inputs that have been deemed by the President as essential to the national defense. Further, the Department of Defense (DOD) will also [soon](#) release a new report on pharmaceutical supply chain resilience aimed at reducing reliance on high-risk foreign suppliers.



### b) Mexico

Though the previously cited White House report does not specifically name Mexico as an option to produce essential medicines, its proximity to the United States and membership in the USMCA trade agreement make it a logical choice. In 2021, Mexico accounted for **18.5% of total pharmaceutical imports to the United States by quantity and volume, behind only China totaling 149,587,712 kgs.<sup>xxxi</sup>** In dollar value, Mexican pharmaceutical sales to the United States were just over \$1 billion in 2022<sup>xxxii</sup>.

**By weight, 57% of pharmaceutical imports to the United States come from China, Mexico and India<sup>xxxiii</sup>. The majority of these combined imports are generic drugs.**

Like the United States, Mexico shares its own challenges in obtaining critical supplies of essential medicines. The volume of generic drugs consumed in Mexico is like the United States, with over 90% of Mexican consumers relying on generic drugs for their medical needs<sup>xxxiv</sup>. **That said, among the total volume of drugs produced by the Mexican pharmaceutical industry, only 12.1% of drugs are generic, with 74.7% being patented drugs.**



As of 2020, there were 678 pharmaceutical companies manufacturing drugs in Mexico<sup>xxxv</sup>. The largest of these firms are multinational companies. As in the United States, the focus of these multinationals is the **production of patented drugs, which total over 85% of the volume produced in-country annually**. By contrast, **Mexican national pharmaceutical companies are mostly privately held, concentrate 95% of their total production on generic drugs**, and are focused on supplying the domestic Mexican market. The growing U.S. demand for essential medicines provides these companies with an opportunity to invest in expanding their capacity to serve this larger market north of the border.

Nationally, most of Mexico's pharmaceutical companies are concentrated in the greater Mexico City metropolitan area with other important centers in Guadalajara, Puebla, and Monterrey. In Baja California, there are currently only four companies producing generic drugs, according to COFEPRIS, Mexico's drug regulatory agency.

Mexican companies producing generic drugs face challenges like their U.S. counterparts given the globally competitive nature of generic drug manufacturing. While the costs of producing generic drugs in Mexico are lower than in the United States, the country's generic drug companies face another set of challenges related to delays in getting approval for bringing new drugs to market –a result of significant budget cuts to COFEPRIS. Also, many Mexican generic drug manufacturers have limited access to the capital required to bring new off-patent drugs to market. As a result, there is a significant lag in the number of newly off-patented drugs that are available to Mexican consumers.

Though challenges remain in both the United States and Mexico to developing a more resilient supply of generic drugs for their respective markets, geopolitical tensions and the risk of future pandemics or other national emergencies have increased the urgency for essential medicines be to be produced closer to home.



### c) Canada

Like the United States and Mexico, Canada has become overly reliant on China and India as a primary source for generic drugs and many active pharmaceutical ingredients (API)<sup>xxxvi</sup>. **In fact, 91% of Canada's drug shortages are attributed to generic drugs, most coming from these two countries.**<sup>xxxvii</sup> Canada's over-reliance on China for not just generic drugs but also mission critical APIs raises obvious security concerns for our northern neighbor.<sup>xxxviii</sup> In response to Canada's own drug shortages, Health Canada has established Canada's Drug Shortages Task Force. As mentioned, a similar task force was established by the United States in 2021 leading to a list of 86 essential medicines.



## d) Siting Considerations

Whether in the United States or Mexico, siting a pharmaceutical and biopharmaceutical manufacturing facility involves several critical considerations to ensure compliance with regulations, operational efficiency, and safety. Key considerations include:



• **Regulatory Compliance:** In addition to drug safety regulatory considerations (U.S. FDA and COFEPRIS-Mexico), new facilities are required to meet a variety of local and state zoning requirements, environmental regulations, and building codes.



• **Accessibility & other Supply Chain Considerations:** A site with good access to transportation networks (road, airports, ports) is key to allowing ease of movement of raw materials (including API), finished products, and workforce.



• **Infrastructure:** Access to clean energy, water, and waste disposal is essential. Water is of particular importance. A medium-sized pharmaceutical facility may use between 50,000 to 200,000 gallons (about 75,7082 liters) of water per day with larger facilities consuming significantly more.



• **Human Capital:** Access to a skilled workforce is key. For most pharmaceutical manufacturing facilities, a combination of life science professionals and semi-skilled technicians with a high school diploma, associate degree, or equivalent is essential. Chemistry-based talent is of specific importance in manufacturing API. For biopharmaceutical and biosimilars manufacturing, having ready access to a strong professional life sciences talent pool is critical.



• **Security:** Robust security measures are critical for facilities, employees, and the products manufactured. These include both physical and cyber security measures to protect sensitive data and information.



• **Cost Analysis:** Generic drug manufacturing is highly cost sensitive, so labor, real estate, utilities (electricity and water), and transportation costs are key considerations.



• **Incentives:** Given the highly competitive nature of generic drug manufacturing and high cost associated with any new pharmaceutical manufacturing plant, government incentives are another key consideration for companies considering investing in this sector.





## V. Mobilizing a North American Response

Given the emerging nearshoring opportunities and growing interest from business and policymakers, a number of solutions are emerging across North America.



### a) Re-Purposing Underutilized U.S. Capacity

Research from the [Center for Analytics and Business Insights](#), at Olin Business School at Washington University (WASHU), finds the United States has the capacity to make the nation's most essential and critical drugs, yet most of that capacity is sitting idle. The WASHU research team surveyed 37 U.S. generic pharmaceutical manufacturing sites and found they are producing at just half of their production capacity annually, **with an aggregate excess capacity of nearly 50%**<sup>xxxix</sup>. In fact, only two of the 37 manufacturing sites are producing at full capacity. If these sites became fully operational, 30 billion additional doses of essential and critical medicines could be produced without incurring the expense of building new manufacturing plants. This would also shorten the time to make generic medicines available from domestic sources, according to the report<sup>xl</sup>.



### b) Tax and other Fiscal Incentives

The growing drug shortage crisis and dependence on China for API and other essential medicines have prompted Congress to actively consider legislation that would, if enacted, catalyze expanded investment to promote greater drug resiliency for the United States by offering a variety of fiscal incentives including tax breaks, grants and long-term contracts. Various legislative bills are currently under consideration in the U.S. Congress.

In October 2023, the Mexican government issued its own nationwide incentive program to catalyze expanded investment in ten strategic sectors, including pharmaceuticals, through a recently enacted presidential decree.<sup>xlvi</sup> **The decree permits investors to claim an up-front deduction of between 56% to 89% of the total investment value** in fixed assets and income tax payments during the fiscal year in which companies make an eligible investment. **The decree also includes a 25% deduction for investments in workforce training**<sup>xlvi</sup>.



### c) Non-U.S. Foreign Direct Investment in Mexico

Mexico has recently benefited from inward foreign investment in its generic drug market. In October 2020, six generic drug makers, mostly Indian —**Dr Reddy's Laboratories (Hyderabad, India), Cadila Pharmaceuticals (Gujarat, India), Glenmark Pharmaceuticals (Mumbai, India), Torrent Pharmaceuticals (Ahmedabad, India), Hetero Drugs (Telangana, India), and Ackerman Pharma (State of Mexico, Mexico)**— signed a deal with the Mexican state of Hidalgo to set up a large pharmaceutical cluster for production and logistics. The move was facilitated by the Indian Ministry of Commerce and Industry and is expected to help these companies also penetrate neighboring Latin American markets.<sup>XLVIII</sup> Also, in April, 2022 a Strategic Partnership and Technology Transfer Agreement was signed between Birmex, a majority state-owned company, and Cipla, a pharmaceutical company in India, to ensure a short-term supply of oncological and retroviral drugs to Mexico and a technology transfer arrangement to ensure that Birmex has the capacity to manufacture these products to supply the country.



### d) Increased Supply from Domestic Mexican Pharmaceutical Companies

Mexico City, the country's densely populated capital city, has the largest number of pharmaceutical manufacturing facilities, **accounting for 50% of all FDA and/or European Medicines Agency (EMA) approved sites (56% of sites with any regulatory approval)**. Most of these sites offer commercial dose manufacturing (56%), **with 27% offering active pharmaceutical ingredient (API) chemical production**, as well as one site operated by Sanofi (Paris, France) offering API biologics (protein and peptide), commercial dose injectables and commercial packaging. The state of Morelos, located on the south border of Mexico City, has the second largest number of facilities and predominantly contains facilities with API chemical capabilities<sup>XLIX</sup>.

On October 17, 2023, the Wilson Center Mexico Institute in collaboration with United States Pharmacopeia (USP) and the U.S. Embassy-Mexico convened a binational seminar to promote expanded cross-border engagement with the goal of strengthening the U.S.-Mexico binational pharmaceutical supply chain.

The seminar aimed to **1) describe the current framework that could allow interactions between U.S. and Mexican players to partner on pharmaceutical nearshoring efforts to build up a strong binational quality supply chain for APIs and medicines; 2) show commitment, policies, and initiatives of both governments to strengthen the bilateral pharmaceutical quality supply chain through nearshoring initiatives; and 3) show the capabilities of the innovative and generic pharmaceutical industries to provide quality APIs and medicines to strengthen the U.S.-Mexico supply chain.**

Historically, domestic, family-owned pharmaceutical companies have been content with supplying the domestic market and exporting to Latin America and Europe. Several Mexican pharmaceutical manufacturers, including PiSA Pharmaceutical, SBL Pharmaceuticals, and Laboratorios Zeyko, indicated an interest in expanding capacity, and in some cases are doing so with the intention of not only supplying domestic and Latin American demand, but also producing volumes capable of supplying the U.S. market. In one example, PiSA Pharmaceutical is bringing an oncology drug product factory online that can fully support domestic **demand with 10-15% of its capacity**, allowing the company to export several drugs on the U.S. Essential Medicines list. While each company expressed an interest in international regulatory harmonization, they all communicated plans intent on meeting the high standards expected of an FDA-compliant drug product.



## e) Emerging Non-Profits

The St. Louis-based API Innovation Center (APIIC)<sup>LII</sup> is a registered 501c3 non-profit organization established in 2022 and focused on strengthening the domestic pharmaceutical drug supply chain by reshoring active pharmaceutical ingredients and de-risking the process through partnerships, collaboration, innovation, and research. APIIC has facilitated stakeholder partnerships with key players and innovators in the bioscience, pharma, tech, and advanced manufacturing industries to create a sustainable network for the U.S. production of lomustine and other essential drugs. Their public-private model to build a resilient pharmaceutical manufacturing base could be a successful model for the nation.



Pathway to Build Supply Chain Resilience for Critical Drugs



### API Innovation Center, St, Louis, Missouri

<https://apicenter.org/>

- **Non-profit enabling delivery of market-competitive, U.S.-made active pharmaceutical ingredients (APIs) to address national health security**
- Leverages the St. Louis region's **strengths in bioscience, healthcare, and advanced manufacturing**
- **Collaborate with private companies, academic and research institutions, and startups spanning the API advanced manufacturing supply chain**
- Create a diverse talent pipeline by partnering with local educational and apprenticeship **programs that focus on technical education.**

On September 12, 2023, the White House summarized progress in “Strengthening the supply chain for cancer drugs.” According to the report, leaders from across the generic oncology drug supply chain, patient advocates, caregivers, and health care providers all agreed that supply chain issues cannot be fixed solely through government action. They identified key areas where industry, nonprofits, public-private partnerships, and government can work together to change the status quo and implement nonprofit initiatives to ensure patient access to needed medicines<sup>LIII</sup>.



Phlow Corp, a public benefit drug manufacturing company<sup>LV</sup> launched with the help of \$354 million in initial funding from the U.S. federal government through the Biomedical Advanced Research & Development Authority (BARDA)<sup>LVI</sup>, is working to re-imagine essential medicines from start to finish using flow chemistry and other advanced processes in development and manufacturing a resilient end-to-end solution that is U.S.-based, comprehensive, and fully integrated. Through the use of continuous-flow processes and other green chemistry approaches, Phlow is working to reduce costs and waste, improve quality and yield, and offer a more environmentally friendly alternative to batch manufacturing. They are also a key partner in the Alliance for Building Better Medicine<sup>LVII</sup>, a Virginia-based cluster of advanced pharmaceutical manufacturers and researchers in the Richmond-Petersburg region with the objective of fixing the broken and disconnected supply chain for the most vital medicines. As of this writing, Phlow has six essential medicines available with additional ones under development<sup>LVIII</sup>.



**ALLIANCE  
FOR BUILDING  
BETTER MEDICINE**

### **Alliance for Building Better Medicine (Richmond-Petersburg, Virginia)**



- **An alliance driven by an immediate and urgent need** to create a reliable supply of safe, high-quality, and affordable medicines for all;



- **Multi-jurisdictional public and private sector stakeholders** in the Richmond-Petersburg region;  
<https://buildingbettermedicine.com/>



- The Alliance is working together to define a new era in R&D, **advanced pharmaceutical manufacturing, workforce and supply chain development.**





## f) Key Starting Materials (KSMs)

According to a White House report issued in June 2021, **87% of generic API facilities are located overseas**, which has helped reduce costs by trillions of dollars in the past decade but also left the U.S. health care system vulnerable to shortages of essential medicines.<sup>LX</sup> There are several efforts underway to address this imbalance in API; however, an equally concerning trend exists with KSMs.

Given the current comparative advantage of both China and India in the production of APIs and KSMs, the likelihood of scale production of both in North America is unlikely without an industrial policy similar to recent efforts to rebuild semi-conductor supply chain resiliency through the U.S. Chips & Science Act.

To prioritize opportunities, the region can make use of the work performed by United States Pharmacopeia (USP) in creating a Medicine Supply Map (MSM) that identifies, characterizes, and quantifies risk in the upstream pharmaceutical supply chain. To date, USP has mapped the manufacturing locations of **91% of U.S. drug products and 44% of those producing API**. The previously referenced, API Innovation Center has taken an analytical approach in identifying opportunities for their work by reviewing approved FDA molecules. These organizations have identified specific opportunities with respect to cardiovascular and oncology drugs. While the work in identifying API manufacturing locations and opportunities is clear, the critical raw materials used in their production, KSMs, requires more analysis and is expected to have a similar global profile. While the analysis is warranted, several FDA-approved drugs have been traced back to a single manufacturing location; in one example it was found that **88% of oncology drugs are manufactured from one KSM in China**.

As noted previously, President Biden **issued** a Presidential Determination to broaden the Department of Health and Human Services' (HHS) authorities under Title III of the Defense Production Act (DPA) to enable investment in domestic manufacturing of essential medicines, medical countermeasures, and critical inputs that have been deemed by the President as essential to the national defense. HHS has **identified** \$35 million for investments in domestic production of KSMs for sterile injectable medicines.

The majority of KSMs are chemically synthesized and North America has strong subnational regions with a long history of chemical manufacturing success by both domestic and multinational companies. To advance this initiative more quickly, Mexico would be advantaged in creating new facilities at a lower cost than in the United States.



Bio-pharmaceutical lab, CICESI, Ensenada.  
Credit: Ensenada EDC





## VI. CaliBaja's Regional Opportunities

As the largest integrated economic zone along the U.S.-Mexico border that is home to 7 million inhabitants, with a regional GDP of \$250 billion and \$70 billion in cross-border trade flows<sup>LXI</sup>, CaliBaja sets itself apart from other regions of North America. Due to the binational nature of its economy, CaliBaja is more than just a sum of its parts. When the combined productive capacities of San Diego and Baja California are considered, the CaliBaja region is strategically positioned to offer solutions, under the right conditions and leadership, as a potential destination for future generic and biosimilar drug manufacturing.

View of Torrey Pines Mesa, home to San Diego's life sciences cluster, anchored by UC San Diego and a number of private research institutions, including Scripps Research, the Salk Institute, and the Sanford Burnham Prebys Medical Discovery Institute. Many leading biopharmaceutical companies are also located in the region including Bristol Myers Squibb, Eli Lilly, Illumina, Pfizer, and Takeda. Photo Credit: Alamy



The region has unique cross-border comparative advantages including:



• **Established life sciences and bio-pharmaceutical clusters** in Southern California (San Diego and Los Angeles) with expanding cross-border potential.



• **Strong manufacturing** base in Baja California, particularly in the area of medical devices.



• **The existing eco-system** of Southern California-based life science companies that are establishing information technology-focused subsidiaries in Tijuana to respond to their growing data management needs.



• **Skilled cross-border STEM workforce.**



• **Best-in-class universities, technical colleges, and research institutions** on both sides of the border including UC San Diego, San Diego State University, University of San Diego, Universidad Autónoma de Baja California (UABC), CICESE, and UNAM's Center for Nano Science & Nano Technology (Ensenada campus).



• **Access to skilled labor** in Baja California at lower labor costs relative to California and the United States.



• **Affordable professional development programs in the life sciences and biotechnology**<sup>LXII</sup> through California Assembly Bill 91, making community colleges in the San Diego and Imperial Counties accessible to Mexican students at in-state tuition costs for those interested in pursuing careers as biopharmaceutical technicians.<sup>LXIII</sup>

While these strengths serve the region well, there are challenges that need to be addressed to capitalize on the opportunities as noted in the following Strengths-Weaknesses-Opportunities and Threats (SWOT) analysis.



# CaliBaja SWOT Analysis



## Strengths:

- Comparative advantages listed above (established Southern California life science and bio-pharmaceutical clusters, Baja California medical device presence, skilled cross-border life sciences focused, STEM workforce with access to lower cost in Baja California)
- Well-developed infrastructure on both sides of the border, including transportation and logistics networks
- Experienced facility development & construction, including the ability to move faster and at a lower cost in Baja California



## Weaknesses:

- Regulatory uncertainty and delays in Mexico; lack of regulatory alignment between the U.S. & Mexico
- Perceived protectionism favoring Mexican generic pharmaceuticals over other manufacturers, particularly from Indian pharmaceutical companies seeking to invest in country
- Profitability concerns of drug companies limiting investment in building/expanding manufacturing
- Lack of existing KSM and API manufacturing in the CaliBaja region and limited current biotech presence in Baja California.
- Regional water/energy/security concerns
- High cost of living and housing affordability in San Diego.



## Opportunities:

- The U.S. Government is focused at highest levels on making pharmaceutical supply chains more secure and resilient, especially for essential medicines
- Potential for U.S. Congress to establish a CHIPS-like bill to secure nation's drug supply
- New Government of Mexico leadership could embrace nearshoring initiatives, including pharma
- CaliBaja could become a regional hub for biosimilars, leveraging biotech and life sciences clusters
- Possibility for US Department of Defense (DOD) / DLA financial engagement
- Potential Indian FDI to develop/manufacture for generics and biosimilars to access U.S. market. Collaboration options with Mexican domestic manufacturers
- Expanded cross-border research collaborations between San Diego and Ensenada based life science research institutions and companies.
- Proposed San Diego-Ensenada high speed ferry service could improve connectivity for San Diego-Ensenada's life sciences community and expand cross-border options for affordable housing making the region more competitive with other potential pharma/biopharma regional clusters.



## Threats:

- New GOM leadership fails to seize nearshoring opportunity.
- Fentanyl / counterfeits / corruption pose insurmountable risks to U.S.
- U.S.-Mexico relations sour under new U.S. administration, dampening prospects for collaboration.
- U.S. efforts to secure our pharmaceutical supply chain and prevent shortages of essential medicines stall or bypass Mexico for more reliable partners.



The geography of the U.S. generic pharmaceutical sector has over the years skewed towards key metro areas of the Northeast and Midwest for a variety of reasons, including lower cost of labor, land, and proximity to FDA regulators. Over time, generic pharmaceutical clusters evolved, in parallel with patented drug manufacturers, achieving certain economies of scale and agglomeration.<sup>LXIV</sup> Likewise, most of Mexico's pharmaceutical companies are concentrated in the greater Mexico City metropolitan area with other important centers in Guadalajara, Puebla, and Monterrey.

With San Diego's strong biotech presence and considerable talent, biosimilar manufacturing is an opportunity for the region, beginning with production in the county itself. Ensenada's strong life sciences research cluster—**located at Punta Morro and hosting the campuses of CICESI, UNAM, and UABC**—further expands the region's cross-border potential as a future destination for biosimilar manufacturing.

While the generic pharmaceutical market remains highly competitive, under the right conditions and with the proper leadership, opportunities do exist for the CaliBaja region in the areas of generic and biosimilar pharmaceutical manufacturing.



### **a) Generic Drugs: Domestic Mexican Companies, FDI & Partnerships**

Mexico and the rest of Latin America will benefit from the initiatives already in motion through both foreign direct investment and increased domestic company investments in the pharmaceutical sector. While new U.S. pharmaceutical company investment in Mexico currently remains flat, the opportunity for Baja California could come from expanded regulatory collaboration between the United States and Mexico as well as increased access to U.S. markets by Mexican manufacturers.

With increased market access, established Baja California manufacturers and larger domestic producers in other Mexican states would have the opportunity to leverage the Government of Mexico's export-focused incentives to increase drug production capacity.

Much of Mexico's generic pharmaceutical production begins with imported KSMs and APIs. In fact, the port of Ensenada is an entry point for much of these materials entering the country from China. As noted previously, domestic Mexican manufacturers are expressing interest in the U.S. market and a few are specifically interested in Baja California as a location for both API and final drug packaging.

The region, and in particular the State of Baja California, also has an opportunity to attract foreign investment, particularly large Indian pharmaceutical manufacturers that are already beginning to invest in Mexico. Here, an opportunity exists for some of these companies to establish binational operations to leverage the well-established biotech community in San Diego and the emerging life science IT cluster in the CaliBaja region.

The opportunity for partnerships between domestic Mexican manufacturers and established multinational companies exporting to the United States can reduce financial risk and increase regulatory access.





## **b) Biosimilars**

Given the region's leadership in the life sciences as well as the need for lower cost biologic medicines and greater supply chain resiliency, CaliBaja has the potential to emerge as a future super cluster for biosimilar production. The key driver in siting both biopharmaceutical and biosimilar manufacturing companies is a skilled life sciences workforce which CaliBaja is well positioned to provide today and can be further strengthened through binational collaboration in building a biotech workforce in Ensenada.

As in the case of API Innovation Center, a non-profit private/public partnership leveraging the strengths of San Diego and Baja California is an option worth further consideration, especially given the State of California's recent commitment to invest in building in-state generic drug manufacturing capacity through the legislative mandate under SB- 852 and the establishment of CALRx.

San Diego's well-known biotech community includes over 500 companies and top research institutions (e.g. Burnham Institute for Medical Research, Salk Institute for Biological Studies, Sanford Burnham Prebys Medical Discovery Institute, Scripps Research and the J. Craig Venter Institute) and UC San Diego. For its part, Ensenada based CICESI already has an established track record in R&D of marine biopharmaceutical drugs.

Local companies in both San Diego and Baja California can provide important building blocks required in final manufacturing. Contract manufacturers with global operations and innovative process knowledge are headquartered in the region.

While current conditions are compelling companies to evaluate their business cases for biosimilar solutions, new investments in capacity are more likely to be made after industry has time to digest early commercial examples and evolving government policies. The state of the biosimilar sector allows the CaliBaja region to formulate a clear strategy and mobilization plan.

Leveraging San Diego's innovative process knowledge necessary to produce complex biosimilars in combination with Baja California's regulatory-trained, highly skilled and economically competitive workforce, the region has the opportunity to add biosimilars to the successful life sciences sector in the mega region.

Biopharma scientist, CICESI, Ensenada.  
Credit: Ensenada EDC





## VII. What would it take in CaliBaja?



### a) Collaborative Initiatives

The CaliBaja region has a unique set of institutions that could be mobilized to pursue these opportunities.

Anthony Sardella, Chair of the API Innovation Center, recently testified before the House Energy and Commerce Oversight and Investigations Subcommittee that examined the root causes of drug shortages and potential solutions. Mr. Sardella observed that the optimal public-private model to address current API shortages was the creation of regional nodes across the country. These nodes would bring together a super-cluster of innovators, researchers, investors, and commercial manufacturers into project consortiums to commercialize new technologies that drive U.S.-based biomanufacturing<sup>LXV</sup>. According to Mr. Sardella, a coordinated approach between federal and state public entities and regional private enterprise has the greatest likelihood of de-risking the challenges of building stronger and sustainable supply chains<sup>LXVI</sup>. The question is whether the CaliBaja region could leverage its comparative advantages to become a regional node for biosimilars?



### b) Regulatory Alignment & Trade Facilitation

Drug shortages and associated national security risks remain a priority for the U.S. Government. As observed by FDA commissioner, Robert Califf, "I did not come back to FDA to spend all my time on supply chain, but that is what's happened. And I feel like I know a lot about it, and I am pretty fired up to do something about it."<sup>LXVII</sup> Califf also confirmed that U.S. drug shortages now constitute a "national security threat."<sup>LXVIII</sup>

Regulatory alignment was on the agenda in meetings of the U.S.-Mexico High-Level Economic Dialogue (HLED) in 2023. During the September 2023 HLED, the United States and Mexico explored deepening collaboration in ongoing lines of effort, including medical device and pharmaceutical regulatory collaboration<sup>LXIX</sup>. While there has been progress with respect to medical devices, minimal effort is being directed toward pharmaceuticals. Regulatory harmonization is key to any significant contribution by Mexico to better balance the global supply chain to serve North American markets.

Beyond North America, there is an opportunity for the United States to review its policies towards India in order to incentivize Indian generic pharmaceutical companies to expand their foreign direct investment into Mexico and/or encourage joint venture partnerships with domestic Mexican pharmaceutical companies. Indian FDI could increase the supply of generic drugs, APIs, and KSMs for export on the United States.



### c) Infrastructure & Investment Incentives

During the COVID-19 pandemic, the U.S. Department of Health & Human Services (HHS) recognized the need for new and innovative countermeasures to address public health emergencies. HHS invested, via the Administration for Strategic Preparedness and Response (ASPR) and the Biomedical Advanced Research and Development Authority (BARDA), in the previously referenced four-year, \$354-million project with private industry to produce **—from raw materials to finished drug product—** generic sterile injectable medicines for public health emergencies and the national stockpile. In press statements, HHS cited the need to reduce U.S. dependence on foreign suppliers and manufacturers of pharmaceutical raw ingredients, APIs, and finished dosage forms and noted that the project would provide immediate, U.S.-based capacity to produce APIs and the chemical compounds for those ingredients to help alleviate or prevent drug shortages.

To address the scale of the supply chain imbalance and potential threat to national security, a U.S. Government incentive program will need to continue at a much greater level of funding. In addition to executive branch action, attention by the U.S. Congress is critically needed given the national security implications for the United States of potential future drug shortages.

Nicole Longo, the senior director of public affairs at PhRMA, expressed the pharmaceutical industry's desire for policies to offset the costs of manufacturing drugs in the United States. Ms. Longo explained that **“other countries continue to make significant public investments, coupled with other incentives, that offset the costs related to infrastructure, including buildings, and operating new facilities. Without similar programs in the United States, this leaves the biopharmaceutical industry in our nation at a significant disadvantage to other nations when it comes to costs for labor, energy, raw materials, and other critical cost components. To continue to recognize the full economic benefits of biopharmaceutical manufacturing in the United States, policymakers should look for ways to expand collaborations between the public and private sectors tied to innovative biomanufacturing technologies.”**<sup>LXXV</sup>

To encourage expanded investment in generic and biosimilar manufacturing, the Government of Mexico should establish a “one-stop shop” for would-be investors that would streamline regulatory approvals and required permits. Such a one-stop shop would be similar to Pro Mexico that was active in prior administrations. Additionally, Mexico would benefit from increasing the staffing capacity of its food and drug regulatory agency, COFEPRIS, as well as establishing regional offices, including one in the State of Baja California, to facilitate approvals for new facility and drug production.



### d) Baja Infrastructure – Pharmaceutical “Free Trade Zone”

To catalyze CaliBaja's manufacturing capacity for generic and biosimilar drugs, consideration should be given to incentivizing the establishment of dedicated industrial parks in Baja California with the required basic infrastructure, including access to water, clean energy and security.

To streamline the cross-border shipment of pharmaceutical products to the United States, a special effort should be made for drug companies investing to Baja California to enroll in the U.S. Customs & Border Protection (CBP)'s Trusted Trader Program (TTP), a voluntary public-private partnership established under authority of the Customs-Trade Partnership Against Terrorism or CTPAT<sup>LXXVI</sup>, rewarding qualified participants with expedited clearance, minimized changes of random inspections and other benefits. Already, many Mexican manufacturers and Mexican long-haul carriers are enrolled.

To further facilitate essential medicine production in Baja California and promote greater drug safety and efficacy, consideration could also be given by the FDA to establish a pilot satellite field office at the U.S. Consulate-Tijuana as part of its Latin American Office (LAO) that currently has a presence at the US Embassy-Mexico. Though such a commitment would take time and require a demonstrated investment into the region, there is some precedent to such an approach. For example in India, the FDA operates a main office in New Delhi, six zonal offices, four sub-zonal offices, 13 port offices and seven laboratories across the country.<sup>LXXVII</sup>



## e) Workforce Development & Training

Interviews with regional industry leaders from the bio-pharmaceutical sectors have highlighted the importance of ready access to a trained workforce. Recent shortages of qualified personnel in some medical device and electronics manufacturers in Tijuana highlight the need for increased investment in Baja California in the area of workforce development and training.

While it is worth noting the CaliBaja region has several highly regarded academic institutions focused on STEM and the life sciences —including **UC San Diego, San Diego State University, the University of San Diego, UABC, CICESE, UNAM Center for Nano Science & Nano Technology (Ensenada campus), as well as additional technical and community colleges**— greater attention is needed on expanding cross-border academic partnerships. Such collaboration would help to catalyze the region's potential to become a hub for future generic and biosimilar pharmaceutical investment. Relatedly, would-be life science technicians in Baja California would be able to take advantage of reduced in-state tuition for San Diego and Imperial County community colleges offering such programs.



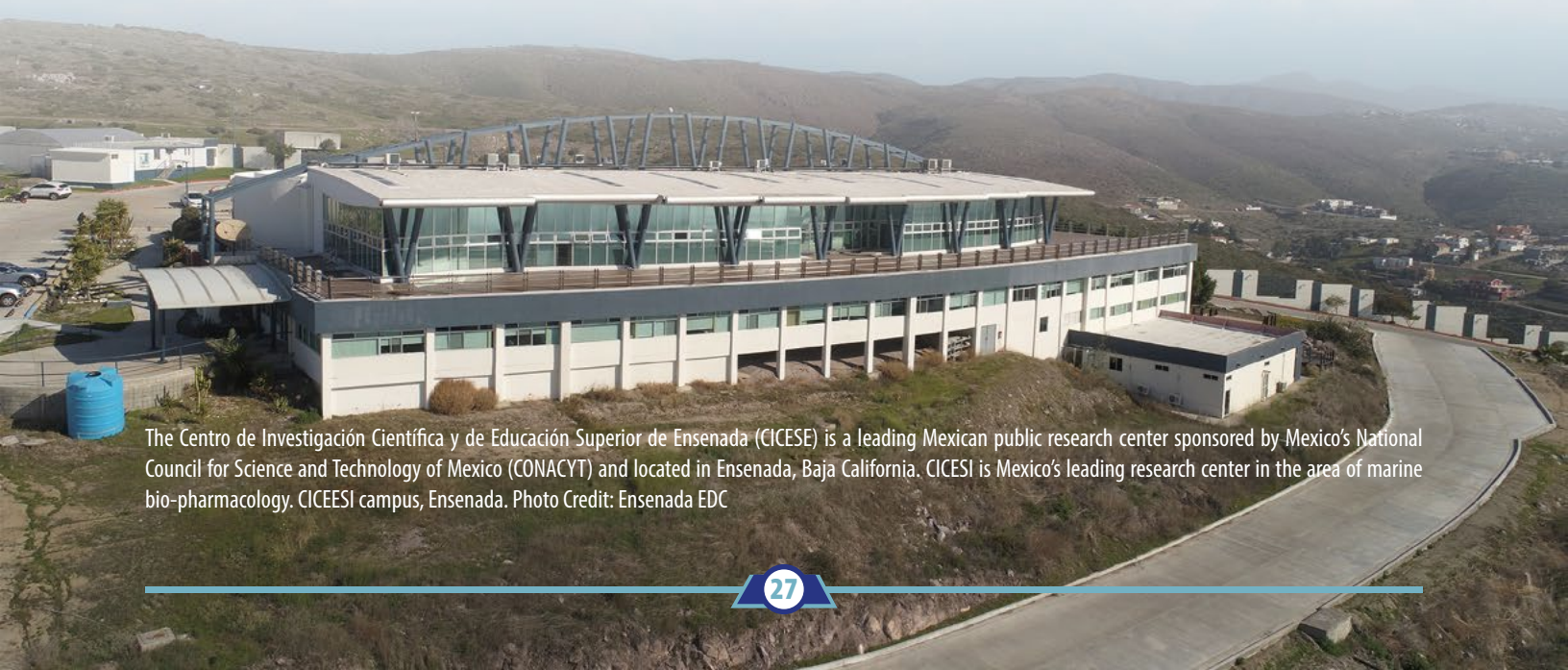
UC San Diego ranks as one of the top public universities in the United States and is a center for research and innovation in the areas of biological sciences and bio-engineering. In fiscal year 2023, UC San Diego received over \$1.76 billion in sponsored research funding. Photo Credit: Alamy





Expanded cross-border knowledge sharing and professional development could also be promoted by expanding UC San Diego's Extended Studies' Spanish language Mi Universidad program<sup>LXXXIII</sup> beyond pre-college to ongoing professional development programs in the life sciences, which could be sponsored and supported by industry.

Most importantly, the region will need to partner with industry in developing more biology and chemistry-based talent in Baja California in the same way it mobilized to meet the electrical, mechanical and software engineering to support existing sectors dependent key talent.



The Centro de Investigación Científica y de Educación Superior de Ensenada (CICESE) is a leading Mexican public research center sponsored by Mexico's National Council for Science and Technology of Mexico (CONACYT) and located in Ensenada, Baja California. CICESI is Mexico's leading research center in the area of marine bio-pharmacology. CICEESI campus, Ensenada. Photo Credit: Ensenada EDC



## f) Affordable Housing & Improved Cross-Border Transportation Corridors

As noted above, given the existing life sciences eco-system in San Diego and the difficulty of producing complex molecule biologic drugs, San Diego County is a more likely candidate for future investment in biosimilars manufacturing than Baja California, at least initially. Biosimilar manufacturing facilities will require trained life sciences technicians and scientists. However, compared to other generic and biosimilar manufacturing locales across the United States, San Diego faces challenges in attracting the required workforce, including lab technicians, given the region's high cost of housing.

While high housing costs remain a barrier, one of San Diego's comparative advantages is its close proximity to Baja California. Already, there are an estimated 80,000 daily cross border commuters traveling back and forth from Tijuana to San Diego.<sup>LXXIV</sup>

Improvements to border infrastructure and expanded options for transportation (including the proposed Azteca Ferry<sup>LXXV</sup> service between Ensenada-San Diego ferry) would go a long way towards helping to create a unique binational life sciences community, providing expanded cross-border inter-connections between scientists and innovators in San Diego and Ensenada while also providing current San Diego area life science professionals with options to remain in the region with the prospect of one day owning a home, albeit south of the border. Such an opportunity is reinforced by recent investments in two life science focused R&D centers in downtown San Diego, IQHQ R&D Development District (RaDD)<sup>LXXVI</sup> and Genesis San Diego<sup>LXXVII</sup>, both in close proximity to the Broadway Pier where the Azteca Ferry service would operate.

View of Ensenada. Photo Credit: Ensenada EDC





## VIII. Conclusion: A North American Call for Action & CaliBaja's Potential Role

Nearshoring offers a potential for the United States to reduce its reliance on any one or small group of countries for critical drugs, leading to a stronger and more resilient supply chain. Through innovative nonprofit approaches, lower cost production in Mexico, targeted government incentives and regulatory reform, a more-balanced and resilient pharmaceutical supply chain can be achieved.

No doubt, North America would greatly benefit from expanded collaboration by a newly formed regional coalition of like-minded countries that could together work to expand essential medicine resiliency across the continent.

Given CaliBaja's established life sciences eco-system and unique comparative advantages, this binational region is distinctively positioned to play a role in meeting North America's growing demand for essential medicines, particularly in the area of biosimilars.

As of this writing there are 46 FDA approved biosimilar drugs. According to the IQVIA Institute, there are now 118 biosimilar drugs now under development in the United States. Here, a key question is where these biosimilar drugs will be manufactured?

The success of public-private partnerships like the API Innovation Center, and the Alliance for Building Better Medicine highlight the potential to establish a similar public benefit company in the CaliBaja region dedicated to generic and biosimilar drug production. Such an entity could successfully leverage the talent and expertise of the San Diego biotech cluster and Baja California's regulatory-trained, highly skilled and economically competitive workforce to position CaliBaja as a future binational biosimilar development and manufacturing hub.

Given the realities of the highly competitive genetic pharmaceutical sector and nascent biosimilar market, these opportunities will take time to fully materialize. Also, questions remain about whether the CaliBaja region will be able to seize potential opportunities for future generic and biosimilar production. Much will depend on whether Mexico and the state of Baja California proactively address several critical issues to maintain the region's competitiveness, including strengthening its regulatory framework; improving security; ensuring adequate water supplies; providing clean, reliable & affordable energy; strengthening infrastructure (ports of entry, seaports, rail); and providing a skilled workforce.

Given the high cost of housing in San Diego relative to other pre-existing biosimilar manufacturing locations (New Jersey, North Carolina, Pennsylvania, Ohio and Illinois), Baja California offers the potential for more affordable housing options for the binational region's life science workforce, particularly, technicians. Yet, to fully realize this opportunity more must be done to reduce border wait times and expand cross-border public transportation options. Here, San Diego and Tijuana's joint selection as the first binational 2024 World Design Capital presents a unique opportunity for the CaliBaja region's key stakeholders to think boldly about how to seize this historic moment, which holds the promise not only to create tens of thousands of quality jobs (including in the life science sector) and expand Baja California's regional economy, but also to improve the quality of life for residents on both sides of the border.



## Glossary

**Active Pharmaceutical Ingredients (API):** Bulk or intermediate materials in a form that is biologically active but not readily consumable by patients

**Abbreviated New Drug Application (ANDA):** An Abbreviated New Drug Application (ANDA) is a written request to the U.S. Food and Drug Administration (FDA) to manufacture and market a generic drug in the United States. ANDAs are “abbreviated” since they do not require the applicant to conduct clinical trials and require less information than a New Drug Application (NDA).

**COFEPRIS:** COFEPRIS is the acronym the Comisión Federal para la Protección contra Riesgos Sanitarios, Mexico’s Federal Commission against Health Risks that provides regulatory authority over food safety, pharmaceutical drugs, medical devices, organ transplants and environmental health protection. It is the Mexican equivalent to the U. S Food & Drug Administration (FDA).

**Current Good Manufacturing Practice (CGMP):** CGMP refers to the Current Good Manufacturing Practice regulations enforced by the FDA. CGMP provides for systems that assure proper design, monitoring, and control of manufacturing processes and facilities.

**Final Drug Form (FDF):** A drug product in the form in which it will be administered to a patient, such as a tablet, capsule, solution or topical product.

**General Drug User Fee Act (FDUFA):** PDUFA was created in 1992 and authorizes the FDA to collect fees from companies that produce certain human drug and biological products. Since the passage of PDUFA, user fees have played an important role in expediting the drug and biological product approval process.<sup>LXXVIII</sup>

**Key Starting Materials (KSMs):** critical raw materials that undergo various reactions involving chemicals and solvents to form an API.

**New Drug Application (“NDA”):** The NDA application is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S. The data gathered during the animal studies and human clinical trials of an Investigational New Drug (IND) become part of the NDA<sup>LXXIX</sup>.



<https://www.fda.gov/drugs/biosimilars/biosimilar-product-information>

<sup>ii</sup>IQVIA Global Biosimilars Database, Sep 2022; IQVIA Institute, Nov 2022 .

<sup>iii</sup><https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9695118/>

<sup>iv</sup><https://www.businesswire.com/news/home/20221107005722/en/Global-Small-Molecule-Drug-Discovery-Market-Report-2022-Increase-in-RD-Spending-Boosts-Sector-Growth---ResearchAndMarkets.com>

<sup>v</sup><https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/what-are-biologics-questions-and-answers>

<sup>vi</sup>Ibid

<sup>vii</sup><https://biosimilarsresources.org/about-biosimilars/>

<sup>viii</sup>Biosimilars in the United States: 2023-2027, IQVIA Institute, 2023, page 5

<sup>ix</sup><https://www.fda.gov/consumers/consumer-updates/biosimilar-and-interchangeable-biologics-more-treatment-choices#:~:text=A%20biosimilar%20is%20a%20biologic,batches%20of%20the%20same%20medication>

<sup>x</sup>Ibid

<sup>xi</sup>The U.S. Generic & Biosimilar Medicines Savings Report, Association for Accessible Medicines, September 2023, page 2

<sup>xii</sup><https://www.hsgac.senate.gov/wp-content/uploads/2023-06-06-HSGAC-Majority-Draft-Drug-Shortages-Report.-FINAL-CORRECTED.pdf>

<sup>xiii</sup>U.S. Government Accountability Office (October 2010). Food and Drug Administration: Response to Heparin Contamination Helped Protect Public Health; Controls That Were Needed for Working With External Entities Were Recently Added. (Publication No. GAO-11-95).

<sup>xiv</sup>A report by the White House, Building Resilient Supply Chains, Revitalizing American Manufacturing, and Fostering Broad-Based Growth: 100-Day Reviews under Executive Order 14017, June 2021, page 249

<sup>xv</sup><https://www.consumerreports.org/prescription-drugs/too-many-meds-americas-love-affair-with-prescription-medication/>

<sup>xvi</sup>The U.S. Generic & Biosimilar Medicines Savings Report, Association of Accessible Medicines, September 2023, page 2.

<sup>xvii</sup>Shivdasani Y, Kaygisiz NB, Berndt ER, Conti RM. The geography of prescription pharmaceuticals supplied to the USA: levels, trends, and implications. J Law Biosci. 2021 Jan 29;8(1):Isaa085. doi: 10.1093/jlb/Isaa085. PMID: 33986950; PMCID: PMC8109232.

<sup>xviii</sup>Geography of prescription pharmaceuticals supplied to the USA, pg. 3-4

<sup>xix</sup>Gibson, Rosemary; Singh, Janardan Prasad. China Rx (pp. 142-143). Prometheus. Kindle Edition

<sup>xx</sup>Safeguarding Pharmaceutical Supply Chains in a Global Economy, U.S. FDA, Testimony before the House Committee on Energy and Commerce, Subcommittee on Health, October 30, 2019. <https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019>

<sup>xxi</sup><https://www.viatris.com/en>

<sup>xxii</sup><https://www.fiercepharma.com/manufacturing/akorn-pharma-bankrupt-calls-it-quits-closes-all-us-sites-and-cuts-entire-workforce>

<sup>xxiii</sup><https://www.financierworldwide.com/fw-news/2023/5/4/lannett-company-files-for-chapter-11-bankruptcy>

<sup>xxiv</sup><https://www.reuters.com/business/healthcare-pharmaceuticals/drugmaker-mallinckrodt-files-second-bankruptcy-us-2023-08-28/#:~:text=The%20Ireland%2Dbased%20company%20initiated,wipe%20out%20existing%20equity%20shares.>

<sup>xxv</sup>In the case of Akron, bankruptcy was attributed to a litany of FDA warning letters which compromised its planned sale to Fresenius. Mallinckrodt's bankruptcy was tied to a \$1.7 billion opioid settlement.

<sup>xxvi</sup>Yashna Shivdaskani, Neriman Beste Naygisiz, Ernest R. Berndt, and Rene, M. Conti, [The geography of prescription pharmaceuticals supplied to the United States: levels, trends, and implications](#), Journal of Law and the Biosciences, 1-28, doi:10.1093/jlb/Isaa085

<sup>xxvii</sup>Eric Palmer, Shortages of drugs and saline reported as Puerto Rico hurricane damage lingers, Fierce Pharma, October 12, 2017. Available at: <https://www.fiercepharma.com/pharma/shortages-drugs-and-saline-reported-as-puerto-rico-hurricane-damage-lingers>

<sup>xxviii</sup><https://www.grandviewresearch.com/industry-analysis/biosimilars-market#:~:text=The%20global%20biosimilars%20market%20size%20was%20estimated%20at%20USD%2021.8,USD%2076.20%20billion%20by%202030.>

<sup>xxix</sup><https://www.gene.com/contact-us/visit-us/oceanside>

<sup>xxx</sup><https://www.gilead.com/news-and-press/company-statements/gilead-to-expand-footprint-in-oceanside>

<sup>xxxi</sup><https://prosperousamerica.org/skyrocketing-pharmaceutical-imports-to-the-u-s-endanger-national-security/>

<sup>xxxii</sup><https://www.statista.com/statistics/478682/mexican-pharmaceutical-exports-by-country/#:~:text=The%20United%20States%20stood%20as,of%20pharmaceuticals%20exported%20from%20Mexico.>

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<sup>xxxiv</sup>La cuestión de las patentes en el Tratado México-Estados Unidos-Canadá: ¿un obstáculo para el desarrollo de medicamentos genéricos en México?, Senado de la Republica Mexicana, Temas estratégicos 86, Diciembre 2020., pg. 6.

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<sup>xxxvi</sup><https://www.canada.ca/content/dam/pmprb-cepmb/documents/npuis/analytical-studies/posters/capt-2022/CAPT2022-Poster-Drug-Shortage-Canada-en-fr.pdf>



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- <sup>XXVIII</sup> <https://www.drugshortagescanada.ca>
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- <sup>XL</sup> <https://olin.wustl.edu/about/news-and-media/news/2022/09/olin-research-shows-us-does-indeed-have-capacity-to-manufacture-essential-drugs.php>
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