CRA Charles River Associates

Value of IP for health and growth

The economic benefits of strengthening the environment for innovation in Mexico

OCTOBER 2020

CONTENTS

1. Project objectives and methodology

BACKGROUND AND OBJECTIVES

INTERPAT and AMIIF asked Charles River Associates (CRA) to identify and quantify the economic benefits from strengthening the environment for innovation in Mexico.

The objective of the study is to:

1. Set out the **policy framework** for supporting innovation in Mexico and the current state of innovative activity.
2. Undertake a **case study analysis** on countries, outside the LATAM region, with potential lessons from other countries which may represent an opportunity for Mexico.
3. Develop **scenarios** as to how innovative activity could change in Mexico, if policies adopted in other countries were pursued.

The approach builds on a similar analysis applied to Argentina in 2018, Brazil in 2019.

THE PROJECT HAD FOUR STEPS

	1	2	3	4
	MEXICAN INNOVATION POLICY FRAMEWORK	**STAKEHOLDER VIEW OF THE CURRENT IP ENVIRONMENT**	**COMPARISON TO OTHER MARKETS AND BEST PRACTISE**	**DEVELOPMENT OF PEER REVIEWED PAPER**
ACTIVITIES	• Review the current IP framework in Mexico, - The current rules and regulations. - Recent changes in the regime and changes to enforcement. - Academic, grey literature on how it works in practice. - The existing policy debate. • Discussion with local academics.	• Interviews with INTERPAT members on investment decisions in Latin America and current perception of Mexico. • Collection of statistics in terms: - R&D Investment - FDI - Clinical trials - Patent applications - Patents granted - Backlog and delays • Interviews with policymakers, academics, SMEs, CROs.	• Develop comparable country case studies. - Development of metrics and recent changes. • Development of scenarios. - Application to Mexico.	• Draft INTERPAT white paper. - Incorporate comments. • Develop peer-reviewed paper for publication. • Participate meeting to disseminate findings.
DELIVERABLES	• A description of the current regime including challenges and opportunities	• Deeper understanding of current challenges • Pressure test potential for change	• Setting out ranking in terms of Lat Am • Case studies on the potential speed of improvement • Scenarios	• White paper Report with policy implications • Published paper on metrics and potential benefits

WE REVIEWED BOTH THE LOCAL AND INTERNATIONAL LITERATURE ON MEXICO'S INNOVATION ENVIRONMENT

- We have reviewed more than 50 international and local publications on the current challenges in the IP regime and innovation policy environment in Mexico as well as its innovative performance, with a focus on the pharmaceutical industry:

ACADEMIC PUBLICATIONS

International and local academic literature including Rios-Flores & Ocegueda Hernández (2018), Guzmán et al. (2018), García Galván (2017).

INSTITUTIONAL REPORTS

A review of institutional websites, including reports by PhRMA, AMIIF, IMPI, INEGI, CONACYT, OECD, Wilson Centre and WIPO.

GREY LITERATURE

Sourced through targeted Google searches, including online media articles, reviews and op-eds, from local and international sources.

WE HAVE CLOSELY FOLLOWED THE DEVELOPMENTS AND DEBATES ON THE NEW INDUSTRIAL PROPERTY LAW

- We have reviewed more than 30 international and local publications on the new Industrial Property Law:

INSTITUTIONAL REPORTS[1,2,3]

A review of institutional websites, including publications by the Mexican Senate and AMIIF.

GREY LITERATURE

Sourced through targeted Google searches, including online media articles, reviews and op-eds, from local and international sources.

TO UNDERSTAND MEXICO'S INNOVATION ENVIRONMENT, WE HAVE UNDERTAKEN A COMPREHENSIVE INTERVIEW PROGRAMME

- **INTERVIEWS WITH 9 INTERNAL EXPERTS** were used to provide industry view of Mexico IP policy and innovation environment and remaining key gaps and challenges.
  - AMIIF
  - PhRMA
  - Novartis
  - Pfizer
  - UCB
  - Roche
  - AbbVie
  - J&J
  - Grünenthal
- Local/ regional teams provided context and validation of findings identified through literature.

- **13 EXTERNAL INTERVIEWS** with former policymakers, academics, regulatory experts, local bio-techs and influencers of the current innovation environment were used to develop understanding of the broader innovation policy in Mexico.
- Policy experts revealed plans for imminent reforms to innovation policy, while academics and local industry provided suggestions for additional improvements.
- Interviews with experts from other relevant stakeholders groups were also requested.

2.
The innovative environment in Mexico and comparison to other markets

INNOVATION POLICIES IN MEXICO

THE SPECIAL PROGRAM FOR SCIENCE, TECHNOLOGY AND INNOVATION 2012-2037

- The Special Program for Science, Technology and innovation 2012-2037 (PECiTI) is a program aimed at strengthening and coordinating the STI capacities, orientate capacities towards strategic sectors, reinforce financing from the business sector and ensure that majority of financing for R&D comes from private sector.[6]

TECHNOLOGY TRANSFER OFFICES, 2012

- The Ministry of Economy and National Council for Science and Technology (CONACyT) created and operated Technology Transfer Offices to help licence new technologies and promote commercial innovation. They acted as intermediaries between research centres and universities and the private sector.[5]

EQUIVALENCE AGREEMENTS, MARCH 2011 – AUGUST 2014

- COFEPRIS has signed agreements with regulatory agencies in Australia, US, Canada, EU and Switzerland to accelerate the approval of new molecules. The approval is processed in 60 working days instead of the usual 360 days.[4]

PUBLIC-PRIVATE PARTNERSHIPS LAW, DECEMBER 2015

- The legal barriers preventing researchers receiving public funding to partner with the private sector to develop commercial patents were removed.[5]

INCOME TAX REDUCTION, 2016

- In September 2016, a corporate income tax reduction of 30% was proposed for R&D expenses, including investments in R&D. These expenses and investments need to be aimed for projects which represent a scientific or technological improvement.

RULES FOR PROTECTION AND OTHER INCENTIVES

ENACTMENT OF INDUSTRY PROPERTY LAW, JUNE 28 1991

- The new legislation abrogated the previous Technology Transfer Law and enabled broader protection of intellectual property.[9]

ENACTMENT OF THE NORTH AMERICAN FREE TRADE AGREEMENT (NAFTA), JANUARY 1994

- The NAFTA treaty set out the provisions on intellectual property rights: it required the parties to give patent owners the opportunity to obtain patent protection.

INTELLECTUAL PROPERTY RIGHTS LEGISLATION MODIFIED FOLLOWING WTO ENTRY, 1999

- WTO entry in 1995 and by 1999, IPR legislation was reformed to meet the conditions of the TRIPS agreement.[11]

SCIENCE AND TECHNOLOGY COMMISSION (CCYT) ARTICLE 77, MARCH 2003

- The CCyt increased the capacity of the Secretariat of Health (SH) to issue compulsory licenses in the case of health emergencies, simplifying the process by which 'serious illness' was declared and rapid issuance of CLs.[8]

FOX GOVERNMENT INTRODUCED A LINKAGE SYSTEM, 2003

- Health authorities are required to consult with IP office and deny market entry to drugs where patents are in effect to prevent generic entry.[8]

CHAMBER OF DEPUTIES AND SENATE BY PRESIDENT FOX, UPDATE TO THE CL REFORM, 2004

- Due to strong opposition by transnational pharmaceutical industry, the March 2003 provision was revised to make granting of CLs less likely by complicating the process by which serious illness is declared.[8]

DATA PROTECTION EXCLUSIVITY, 2012

- COFEPRIS publish an internal decree providing 5 year term of data protection to new chemical entities only and not biologics or new indications.[10]

UNITED STATES-MEXICO-CANADA AGREEMENT (USMCA) OCTOBER, 2018

- Agreement reached between Mexico, Canada and the US on November 30, 2018. When finalised, it will improve the IP environment in Mexico by enforcing the protection of pharmaceutical-related IP[7] including patent term extension for unreasonable delay to patent grants or curtailment to regulatory or marketing approval process and data exclusivity on new chemical entity for 5 years, new indications for 3 years and biologics for a term of 10 years.[10]

Key

○ Areas for improvement in innovation policy.

○ Pro-innovation policies/agreements.

The USMCA has been ratified by Canada in March 2020, the third and final country. From the date of ratification, Mexico will have 4.5 years to implement the obligations for patent term adjustment and 5 years for implementation for data protection.

THE LITERATURE REVIEW IDENTIFIED SIX MAIN WEAKNESSES IN MEXICO'S IP REGIME. SOME HAVE SINCE BEEN ADDRESSED THROUGH THE IP LAW*

* **DELAYS IN IP INFRINGEMENT RESOLUTIONS**	• **It could take between 5 to 8 years for a company to access reparation due to IP infringement. This is due to the bifurcated system which relies on IMPI to provide a review recourse report** verifying that there has been patent rights infringement before the company can take legal actions to get an award of damages.[17,18] Also, the alleged infringer can pay a counter-bond to lift the injunction. Due to extended infringement resolutions process, rights holders often choose not to claim compensation for damages.
* **LACK OF ROBUST REGULATORY DATA PROTECTION FRAMEWORK**	• In June 2012, COFEPRIS issued guidelines to implement RDP for new chemical entities for a maximum period of five years. • However, it is unclear **whether the guidelines apply to biological products and whether other key approvals (such as new formulations and indications) are protected. There remains a lack of implementation of RDP reform through federal legislation and uncertainty on the measures that could be used to enforce and observe RDP rights.**[13,14]
EXCLUSION OF BIOLOGICS IN THE USMCA	• **The assurance of 10 years' data exclusivity for biologics in the USMCA was removed from the tri-lateral trade agreement** in late 2019. This would have encouraged Mexico and Canada to provide improved data protection for.[15,16]
* **WEAK PATENT LINKAGE**	• **The Federal Committee for Protection from Sanitary Risks (COFEPRIS) appears to apply patent linkage inconsistently.** In some cases, **marketing authorizations (MA) have been issued despite patents listed in the Official Gazette, and this is attributed to the poor communication between IMPI and COFEPRIS.**[12] • There have been instances (at least three in April 2017) where **COFEPRIS granted MA for entry of products with a valid patent.**
* **NO PROVISIONS FOR PATENT TERM EXTENSION**	• There are **supplementary protection certificates in Mexican law. However, under the USMCA, after 2025 Mexico must adopt measures to adjust the patent term as compensation for delays from the Health Authority in the issuance of marketing authorisations.** Furthermore, the life term of a patent can be adjusted to compensate for delays from the Patent Authority (IMPI) under certain international treaties (e.g. USMCA) and the recently approved IP Law., The current Mexican law limits the normal life term of a patent to 20 years as from the filing date. • **No pharmaceutical company has successfully extended the life term of a patent in Mexico.**[19,20]
POTENTIAL ABUSE OF THE BOLAR EXEMPTION	• **Mexico fails to impose any limits on the amount of raw materials that can be imported in a patented pharmaceutical for "experimental use" (the Bolar Exemption).** • This **suggests some importers may be abusing the Bolar exemption** by stockpiling and/or selling patent-infringing and potentially substandard medicines.[14] However, the companies interviewed highlighted that this is not a key issue in Mexico's IPR.

PROVISIONS TO ADDRESS SOME OF MEXICO'S IP LIMITATIONS HAVE BEEN INTRODUCED THROUGH THE NEW INDUSTRIAL PROPERTY LAW

PREVIOUS GAPS IN MX IPR

IP INFRINGEMENT RESOLUTIONS	• Through the new IP Law, **the rules to claim damages have been modified in order to make it easier and to expedite the corresponding proceedings.** Furthermore, the enforcement measures have been reinforced to be effectively dissuasive of infringements. • A company can now seek damages through the civil courts or through IMPI – however there remain concerns around the expertise IMPI has to fulfil this role.
EXTENSION OF REGULATORY DATA PROTECTION	• Under the USMCA, **Mexico has agreed to extend the term for data protection of new agricultural chemical products, new pharmaceutical products and new indications. Thus, this does not include biologics.** • The USMCA prohibits generic manufacturers from referencing undisclosed test or other data concerning safety and efficacy of new pharmaceutical products for at least five years from the date marketing approval was first granted.[21]
IMPROVING THE LINKAGE SYSTEM	• From August 2018, IMPI started issuing a different special edition of the *Official Gazette* which **publishes petitions to list a patent in the Special Gazette for Medicaments (SGM) which were rejected.**[25] Through the new IP Law **the scope of linkage will be broadened** to include patents of inventions susceptible to be used in a pharmaceutical product. No marketing authorisation will be granted by COFEPRIS until IMPI agrees – thus it is expected to remove the need of litigation. This amendment addresses Mexico's **CPTPP obligation** of establishing a communication channel between the IMPI and COFEPRIS to prevent patent infringement.[27]
PATENT TERM ADJUSTMENT PROVISIONS	• **The new IP Law has introduced a "supplementary certificate"** to adjust the patent term due to: (i) unreasonable delays owing to the patent granting authority, and (ii) unreasonable curtailment of the patent term as a result of the regulatory or marketing approval process for pharmaceutical products. This will grant a day adjustment for every two days of delay. • However implementing regulations still required to enforce the Law.[26]
ACCELERATION OF PATENT GRANTS FROM IMPI COLLABORATIONS WITH USPTO AND EPO	• **IMPI has partnered with USPTO and EPO to accelerate patent applications previously examined by USPTO and EPO** in order to issue more patents, faster, as well as reducing the backlog.[22,33] • Furthermore, the collaboration between IMPI and EPO is aimed to **help promote the exchange of information and support IMPI's work with training, tools, and technical support from the EPO.**[24]

The new Industrial Property Law was approved by the Mexican Congress on June 30th, and it will be entering into force within the following 90 working days. The secondary regulations, which are subject of public consultations, will be discussed in the coming months. The controls to ensure that the Bolar exemption is not abused will be covered through secondary regulations.

THE OVERALL ENVIRONMENT IS STILL SUFFERING FROM A DE-PRIORITISATION OF INNOVATION AND LACK OF LEGAL IMPLEMENTATION

LACK OF GOVERNMENT INCENTIVES	• The government's **funding to support education in science and technology and academic research has been reduced**, and so has the **funding and tax incentives to support the private industry to invest in R&D and innovation**.
LACK OF PRIVATE-PUBLIC PARTNERSHIPS	• The government is not committed in investing in private-public partnerships and there is **no legal framework in place which provides the necessary legal certainty for the private industry to invest in such collaborations.** • Additionally, there are **no frameworks to incentivise academics to commercialise their patents**, and **there is a lack of Technology Transfer Offices in private and public universities.**
LACK OF RECOGNITION OF INNOVATIVE PRODUCTS	• The government **does not provide good access to innovative products**, and this is reflected by the fact that in 2020 COFEPRIS has not granted marketing authorisation to any new pharmaceutical product. • Additionally, **procurement regulations have not been respected and foreign low-cost medicines are imported into Mexico**, harming the local industry.
LACK OF STRONG LEGAL FRAMEWORK TO CONDUCT CLINICAL TRIALS	• **The lack of regulation on clinical trials and lack of RDP discourages pharmaceutical companies from conducting clinical trials in Mexico.** COFEPRIS takes a long time to get the clinical trials approved and at times COFEPRIS asks for further amendments to the protocol. Additionally, pharmaceutical companies are required to cover all the investment costs of clinical trials.
POOR COMMUNICATION BETWEEN THE PRIVATE AND GOVERNMENT INSTITUTIONS	• The **private industry it does not have a good communication with certain government institutions**, such as: COFEPRIS, the Ministry of Health and the Ministry of Finance (who is responsible of public policy and procurement). • Additionally, there is **poor communication between government bodies such as IMPI and COFEPRIS which hinders collaboration.**

CHALLENGES IN THE IMPLEMENTATION OF USMCA EXTEND BEYOND IP AND INCLUDE CHALLENGES IN GOVERNMENT PROCUREMENT PROCESS

DIVERSION OF PROVISIONS IN GOVERNMENT PROCUREMENT AWAY FROM USMCA COMMITMENTS

- In April 2020, a bill was introduced to Congress to amend the **Government Procurement Law.**[28] This new bill **fails to meet the standards and, in some cases, is in contradiction to what is agreed in the USMCA.**
- Provisions in the new Bill which contradict the USMCA include:
  1. The introduction of **'market research'** which enables different suppliers to make auctions, reducing the original price offered by suppliers and enables greater scope for negotiation.
     - This would essentially act as a summary proceeding for the open tendering which does not need to comply with the deadlines, timeframes and procedural stages agreed in USMCA.
  2. Broader definition of **'limited tendering'** where entities can directly contact a supplier of their choice.
     - The new Bill exceeds USMCA grounds by enabling limited tendering of a greater number of goods and hence, prevents fair competition.
  3. **National treatment and preference** in the instance where there are two finalists for a tendering procedure, the national supplier will be awarded the tender even if the price offered is 15% higher. This goes against the national treatment principle of USMCA.
  4. **Lack of domestic review** whereby the new Bill fails to designate one impartial administrative authority to implement the USMCA as agreed in the treaty.

IMPLICATIONS

- The Bill represents an example of Mexico's **inaccurate interpretation of the USMCA's provisions**.
- The Bill is contributing to **uncertainty around the procurement process.**
- Industry efforts to address the inefficient procurement process is a **trade-off of investment into innovation.**
- Nationalistic policies may **discourage foreign investment** in Mexico and could ultimately **harm patient access to medicines.**
- The Mexican government should take an informed, **"do no harm" approach** when considering implementation of legislation of the USMCA. Policies which fail to achieve the true goals of the USCMA could have **significant negative unintended consequences.**

THE FOLLOWING INDICATORS WERE ASSESSED TO UNDERSTAND THE OVERALL INNOVATIVE ENVIRONMENT

POLICY ENVIRONMENT → RESOURCES FOR INNOVATION

OVERALL INNOVATION SUPPORT

- National innovation plans.
- Targeted initiatives.

RULES FOR INNOVATION PROTECTION

- IP rules and patentability criteria.
- Patent filing and granting process.
- Regulatory data protection.
- Preliminary injunction process.
- Free Trade Agreements e.g. the USMCA.

INCENTIVES FOR INNOVATION

- R&D tax credits.

FUNDING FOR INNOVATION

- Public and private funding for research.
- Foreign Direct Investment.

EXPERTISE AND INFRASTRUCTURE

- University quality and education attainment.
- Care: Hospital infrastructure and physician availability.
- Collaboration and clusters.

HEALTH SYSTEM STRENGTH

- Care provision indicators.

INNOVATIVE ACTIVITIES → ECONOMIC ACTIVITIES

EARLY AND BASIC RESEARCH

- Publications.
- Public private collaborations.

PRODUCT DEVELOPMENT

- Clinical trials by phase, type and funder.

OUTPUTS OF INNOVATION

- Number of patents filed, granted both domestic and international.

EMPLOYMENT

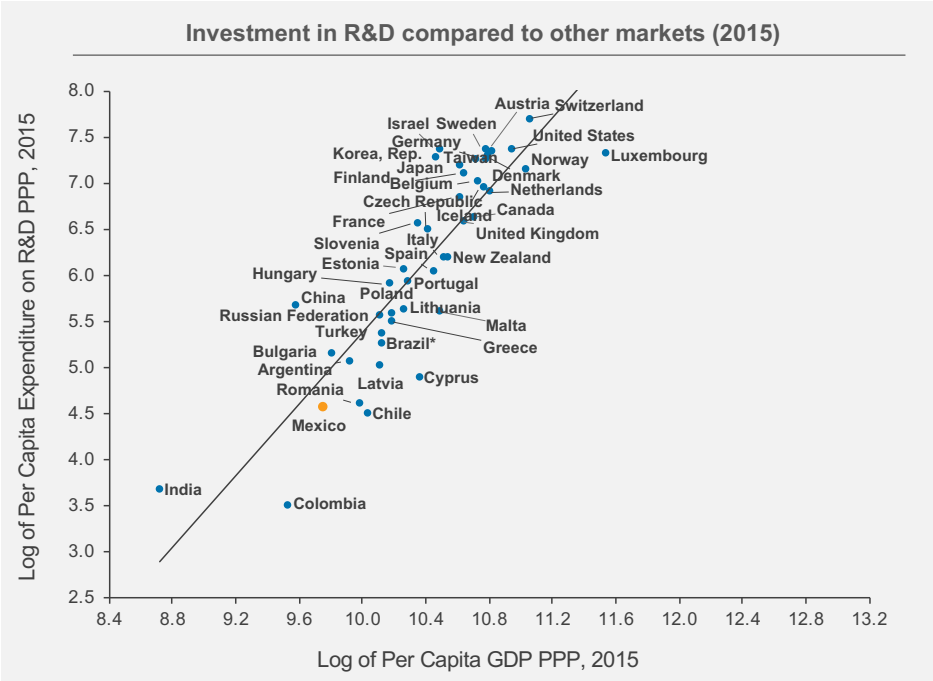
- Researchers employed in pharma.
- Types (roles) of employees in pharma in the country.
- Compensation levels.

TRADE

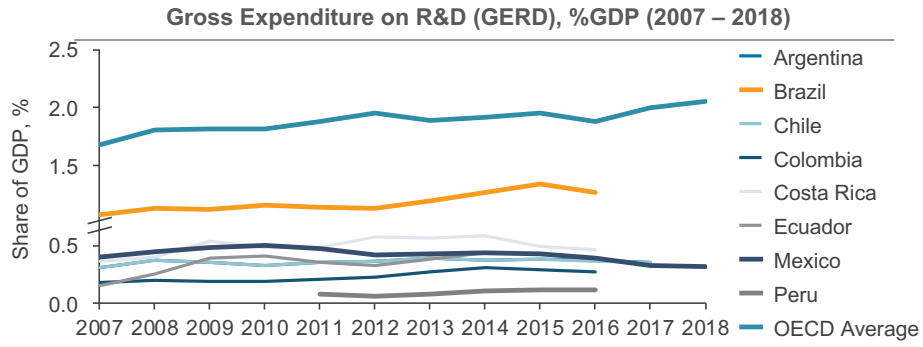
- Imports vs exports in pharma and biotech.

RESOURCES FOR INNOVATION:
INVESTMENT IN INNOVATION & R&D

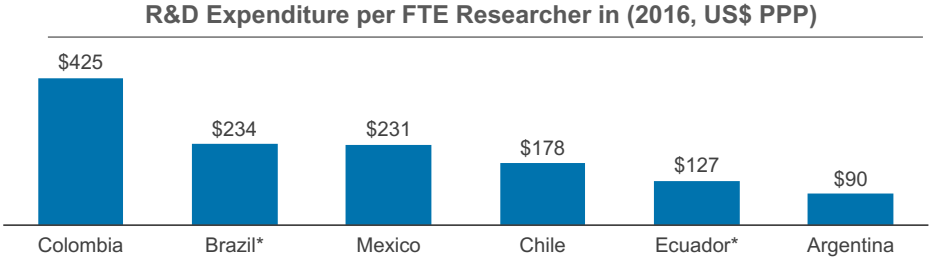
- Mexico falls short of the OECD average in R&D investment relative to its GDP per capita by 1.7 percentage points (2018) but performs better than Chile and Colombia with comparable GDP per capita.
- However, between 2014 and 2018 Mexico has experienced a reduction in R&D as a share of GDP, in contrast to the increasing trend observed in the OECD average.



Sources: World Bank Innovation Policy Platform; OECD Data for GDP per capita, PPP; OECD Data 2018; Argentina Central Bank 2016.
Note: *Brazil data on R&D investment is from 2014.



Source: Ibero-American Network, Science and Technology Indicators (2020); OECD Main Science and Technology Indicators (2020).

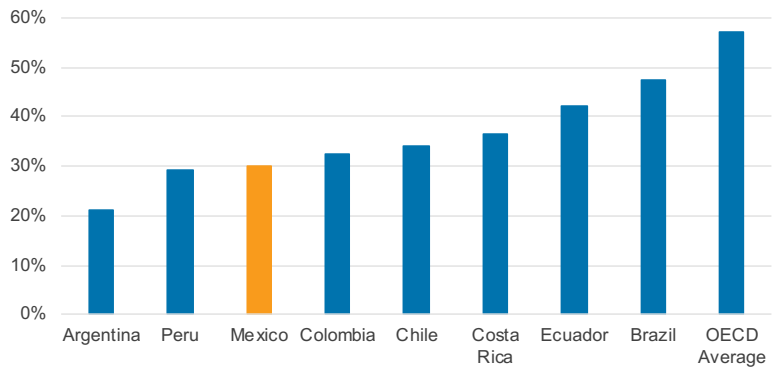


Ibero-American Network, Science and Technology Indicators 2018; OECD Main Science and Technology Indicators (2019). Note: * Latest data from 2014.

RESOURCES FOR INNOVATION:
INVESTMENT IN R&D COMPARED TO LATAM AND OECD

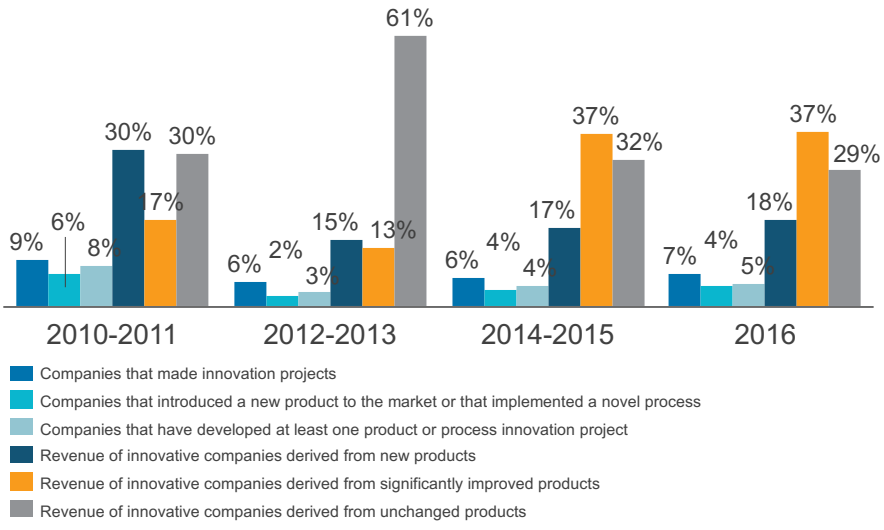
- In Mexico the majority of R&D investment is funded by the government and it estimated that only 10-15% of private companies conduct R&D.[29]
- Private investment in R&D as a percentage of GERD in Mexico is lower than that of other LatAm markets and falls short of the OECD average – such private R&D investment predominantly focused in the motor vehicle, electrical equipment and pharmaceutical manufacturing industries.[30] The private sector is demanding that the government offers more incentives to invest in R&D.[31]
- In 2016, 16% of companies have invested in an innovative project or process, or have developed at least one innovative product – this contrasts to 23% of companies' in 2010-2011.
- In 2016, 55% of the revenue of innovative companies derived from products with an innovative components (versus 47% in 2010-2011).
- Although there were more companies investing in R&D and in innovative processes and projects in 2016 than there were in 2010-2011, more incentives are need to be introduced by the government for Mexico to be a leading LatAm market in R&D.[44]

Business Expenditure on R&D (Latest available year, % GERD)



Source: World Bank Innovation Policy Platform 2018; Brazil Ministry of Science, Technology, Innovations and Communications Indicators (2019). Note: BR – 2016; AR, MX, CO, CL – 2015; CR, EC - 2014.

Research, technological development and innovation metrics (2010-2011, 2012-2013, 2014-2015; 2016)

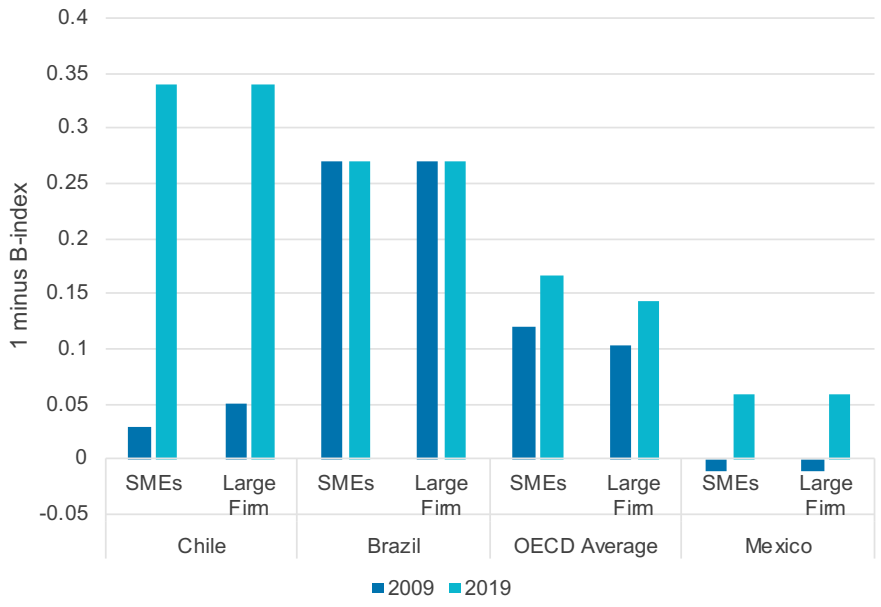


Source: INEGI 2020.

RESOURCES FOR INNOVATION:
R&D TAX INCENTIVES

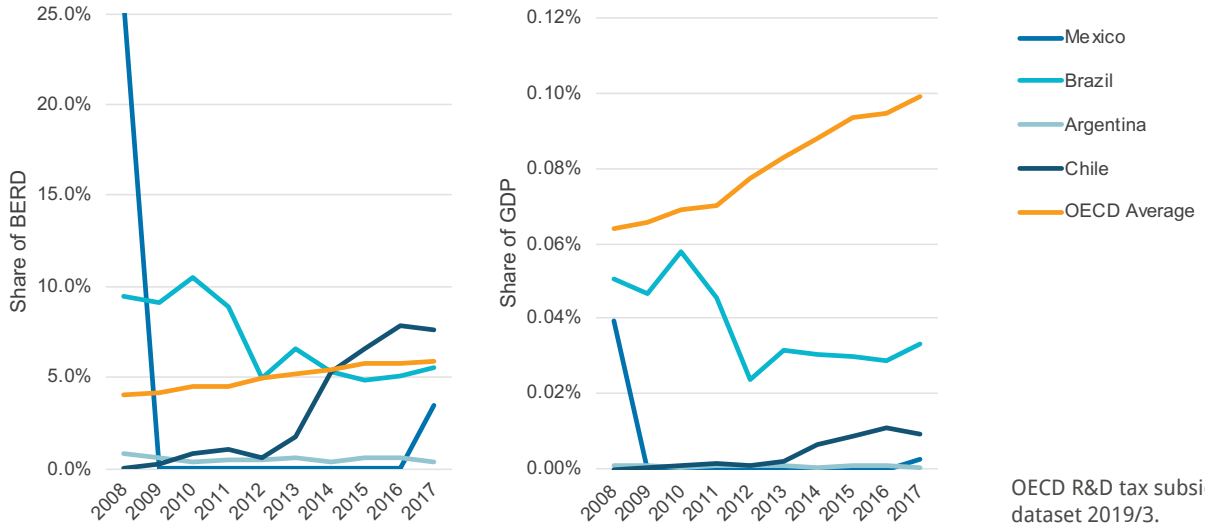
- Mexico reintroduced R&D tax incentives in the form of an incremental R&D tax credit in 2017, following a previous experience up to 2008; during 2000-2001, Mexico offered an incremental tax credit which was replaced by a more generous volume-based tax credit in 2001 – however, this tax incentive was abolished in 2008.[32]
  - A tax credit rate of 30% applies to eligible R&D expenditure in excess of the average R&D expenses incurred in the previous three years;
  - In case of insufficient tax liability, unused credits can be carried-forward over 10 years;
  - A ceiling of MXN 50 million applies to the value of the R&D tax relief provided.
- The R&D tax credit introduced in 2017 is significantly less than the volume-based tax credit available from 2002-2008, however it is still an incentive for companies to invest in R&D. The current government has made the process of tax incentives more cumbersome to distinctive companies from applying for it.[33]

Implied tax subsidy rates on R&D expenditures (2009 and 2019)



OECD R&D tax subsidy (RDTAXSUB) dataset 2019/3.

Indirect government funding through R&D tax incentives (2008 – 2017)

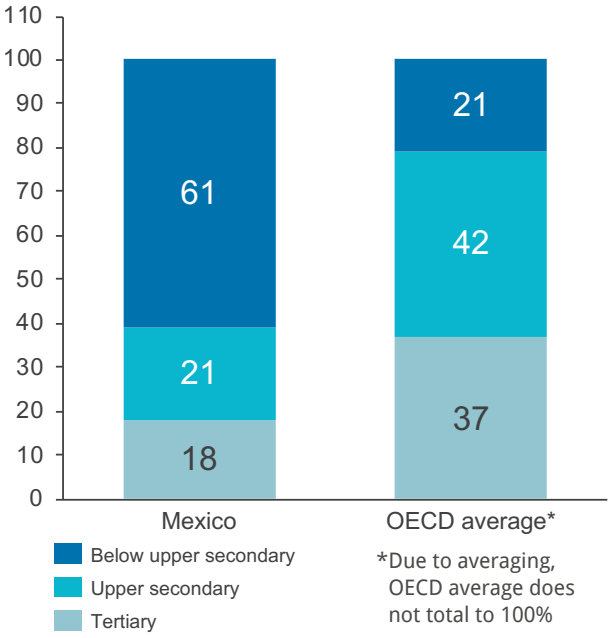


OECD R&D tax subsidy (RDTAXSUB) dataset 2019/3.

RESOURCES FOR INNOVATION: AVAILABILITY AND STRENGTH OF RESOURCES AND EDUCATION

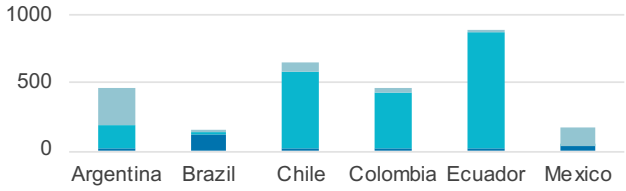
- The proportion of 25-64 year olds in Mexico with tertiary education falls short of the OECD average and amongst graduates with tertiary level education, however, Mexico has the second largest PhD medical science graduates and the largest proportion of STEM graduates when compared to other LatAm countries. Additional, the PISA Science scores in Mexico are the second largest in LatAm and the OECD average.[34]
- Thus although Mexico has room to improve its educational attainment, it has a strong workforce of PhD medical science and STEM graduates which could fuel innovation.
- Although locally there are capability and talents to conduct research, entrepreneurship spirit is still lacking and is a key barrier to convert research into innovation.[35]

Educational attainment of 25-64 year olds (2018, %)

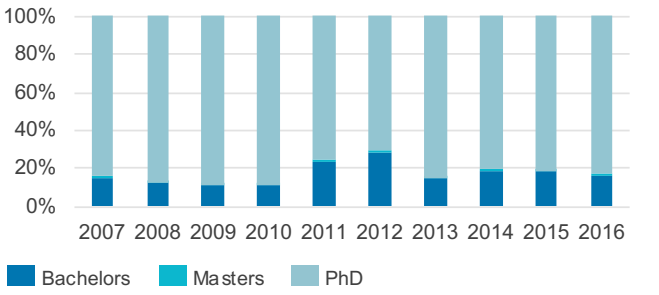


Source: OECD Data, 2018
STEM - Science, Technology, Engineering and Mathematics

Number of medical science graduates by grade (2014)

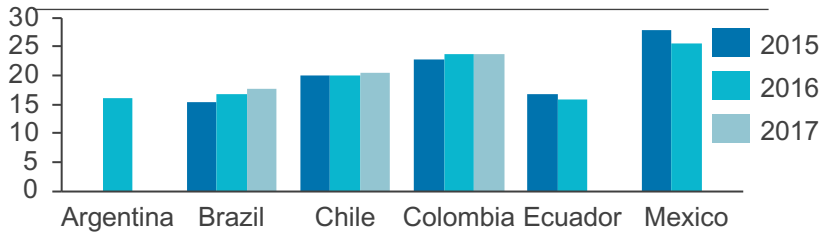


Medical science graduates by grade (2007-2016, %)



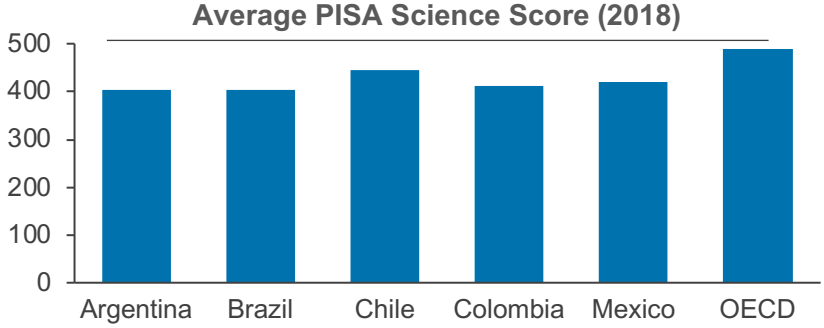
Source: RICYT, 2014.

Graduates from STEM degrees in tertiary education (%)



Source: UNESCO UIS.Stat, 2015-2017.

Average PISA Science Score (2018)

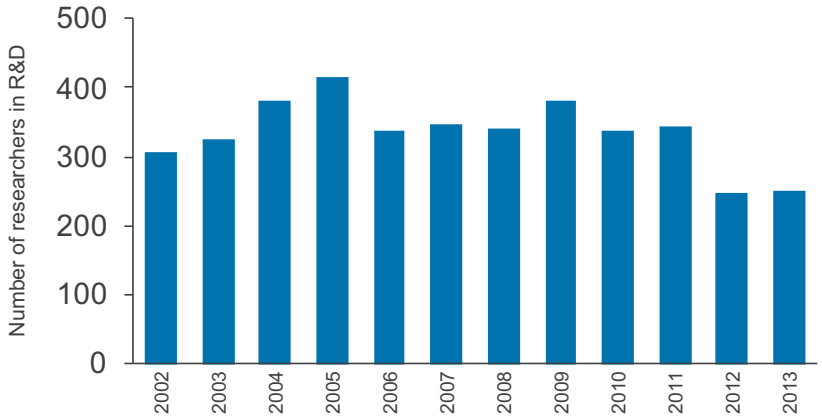


Source: OECD Data, 2018.

RESOURCES FOR INNOVATION:
AVAILABILITY AND STRENGTH OF RESEARCHERS

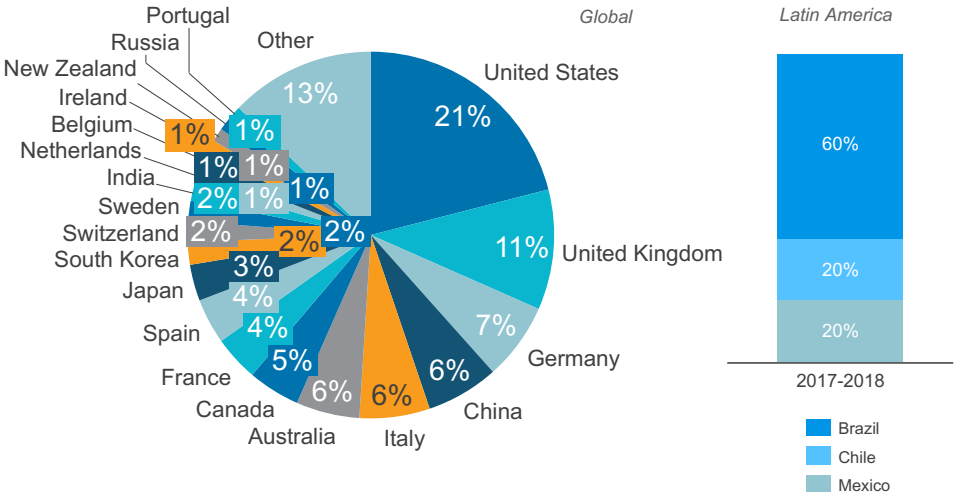
- In 2013, number of researchers in R&D for Mexico was 251.8 per million people. Though the number of researchers in R&D fluctuated substantially in recent years, it tended to increase through 1999 - 2013 period ending at 251.8 per million people in 2013.[36]
- The Mexican university of Monterrey Institute of Technology is ranked as one of the top 500 world universities in Life Sciences research.[37]
- However, the funding allocated to research by CONACYT has decreased recently and CONACYT's Innovation Stimulus Program and the Sectorial Innovation fund have been halted. Further cuts are expected.[38,39]

Number of researchers in R&D by institution (2002-2012, per million people)



Source: The World Bank (2002-2013).

Proportion of top 500 The World University Rankings in Life Sciences research (2020, %)

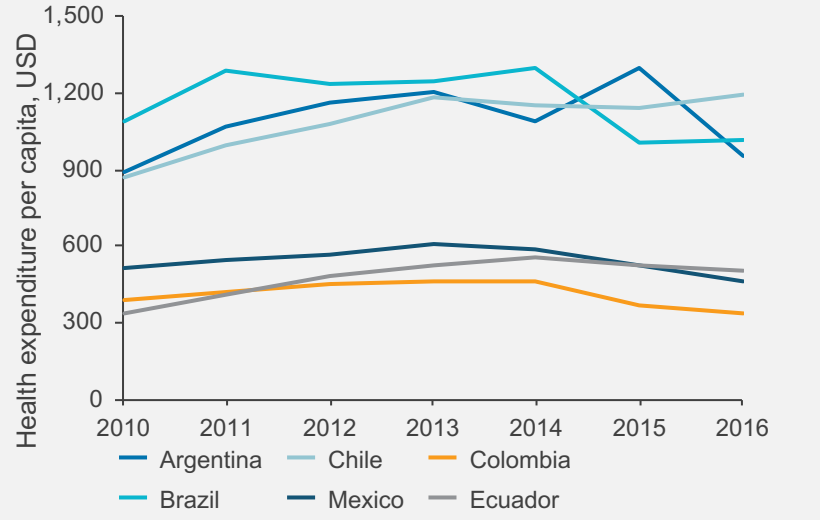


Source: Nature Publishing, 2018.

RESOURCES FOR INNOVATION:
HEALTH BUDGET AND INFRASTRUCTURE

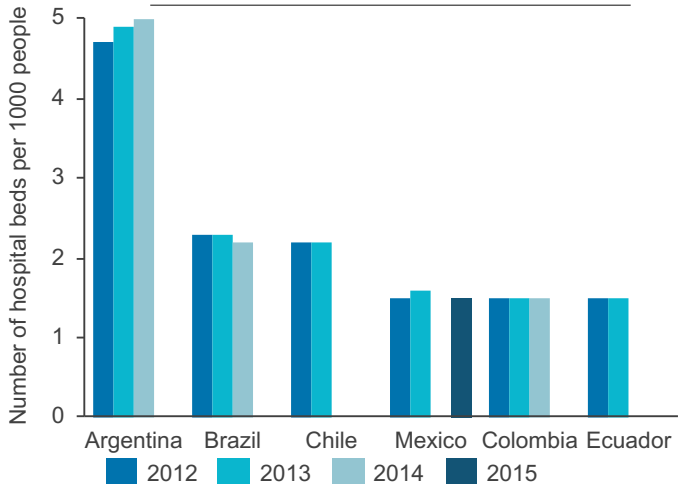
- Between 2010 and 2016 , Mexico spent less on health expenditure per capita than Argentina, Brazil and Chile. Furthermore, between 2014 and 2016 the expenditure per capita has been declining.
- In terms of infrastructure, Mexico has a lower number of hospital beds per capita than Argentina, Brazil and Chile – and a comparable number of hospital beds per capita to Colombia and Ecuador. On the other hand it has the second largest number of physicians per capita in the LatAm region.

Health expenditure per capita (2010-2016, USD)



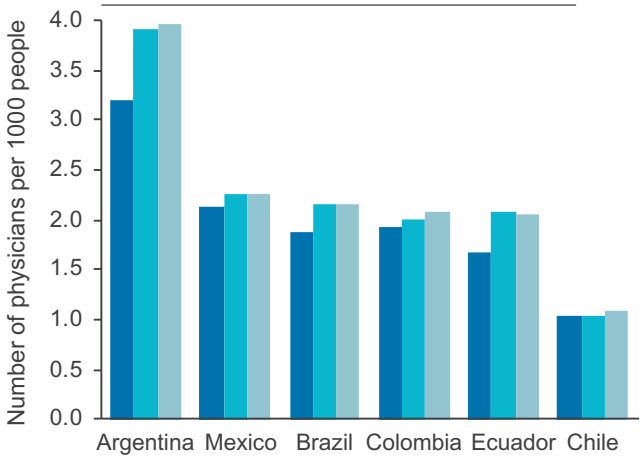
Source: World Bank, 2018.

Hospital beds per 1,000 people (2012-2015)



Sources: World Bank Data 2018.

Physicians per 1,000 people (most recent available data)

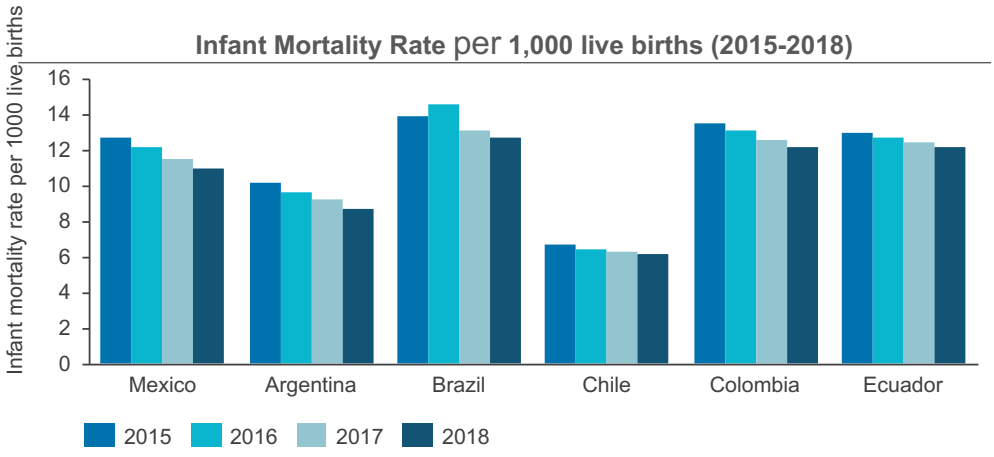


Sources: World Bank Data 2018;
*Most recent available data, clarification in notes.

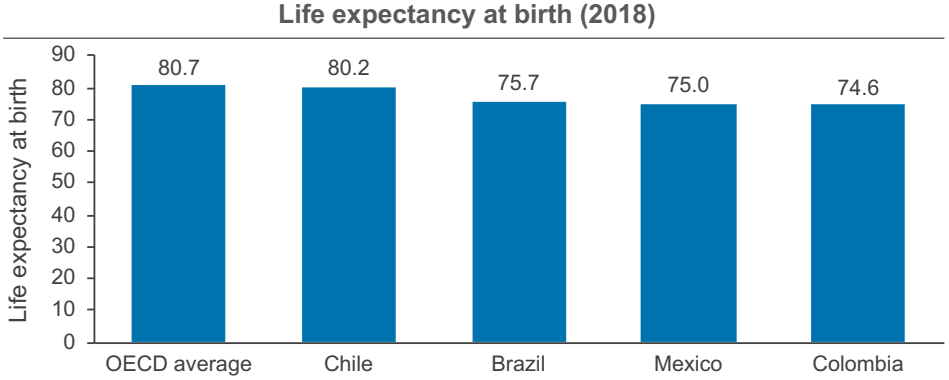
Note the years for Physicians (per 1,000 people): Argentina: 2010, 2013, 2017; Brazil: 2013, 2017, 2018; Chile: 2008, 2009, 2016; Mexico: 2014-2016; Colombia: 2015-2017; Ecuador: 2011, 2015, 2016.

RESOURCES FOR INNOVATION:
HEALTHCARE SYSTEM AND CARE

- The public healthcare is funded by government contributions, employer contributions and employee contributions – and the public healthcare is provided by a number of payer stakeholders, including IMSS, SPS, ISSSTE, PEMEX, SEDENA and MARINA. In 2003, it was estimated that approximately 3% of the population had a private health insurance.[40,41,42]
  - In 2018, Mexico spent 5.5% of GDP on health, less than the OECD average of 8.8%, which is equivalent to $ 1,138 PPP per capita per year (the OECD average is $ 3,994 PPP in 2018).
  - In 2018, out-of-pocket spending in Mexico constitutes 41.8% of the income of the health system and approximately 4.0% of household spending.
- In terms of provision of care, Mexico lags behind Argentina and Chile in terms of infant mortality rates per 1,000 live births.
- Moreover, Mexico performs moderately in the LatAm region when comparing life expectancy at birth and falls short of the OECD average.
- Patients gain access to new medical products with a delay, and this is partially attributed to the fact that COFEPRIS has significant delays in granting marketing authorisation of new products.[43] The Mexican Federal government aspires to amending the national healthcare system to one similar to the Nordic-style healthcare system.[43]



Source: World Bank, 2015-2018.

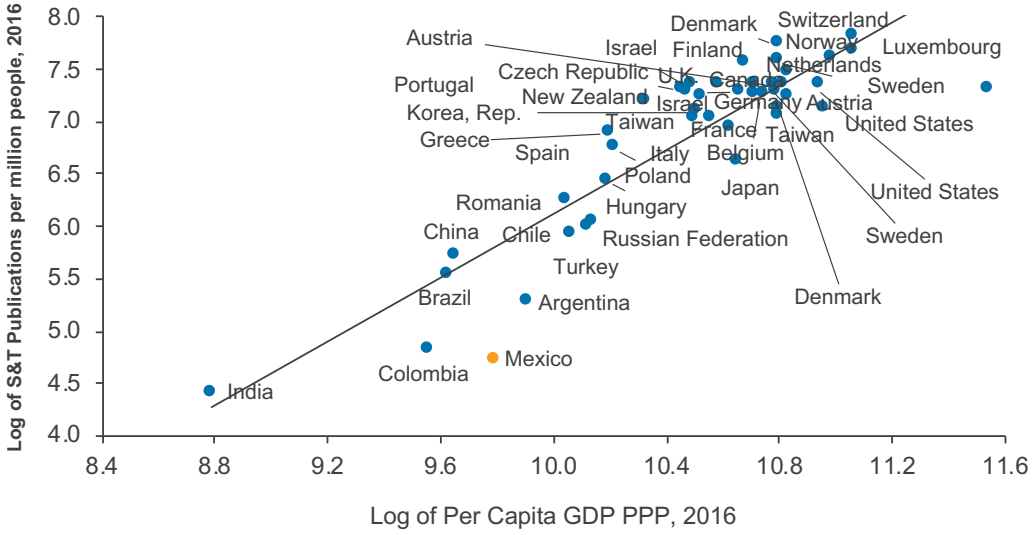


Source: OECD data, 2018.

RESOURCES FOR INNOVATION:
BASIC RESEARCH OUTPUT

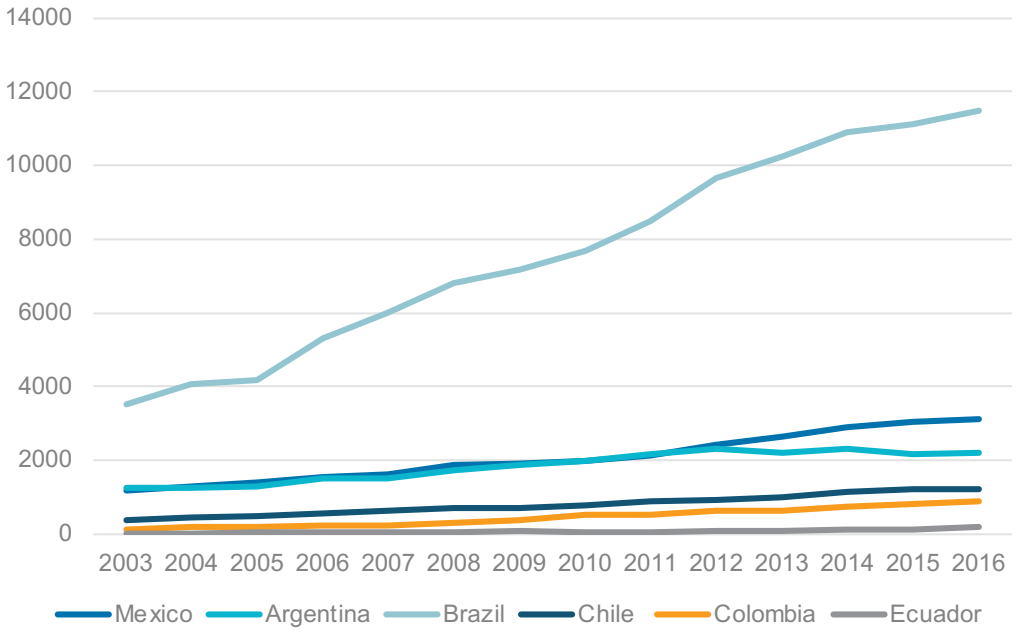
- In 2016, basic research output in Mexico (as measured by the number of scientific publications) remained low relative to its economic size.
- However, in terms of the absolute number of publication in Biological Sciences, Mexico is leading the majority of the Latin American countries as researchers are highly driven by journal publications as an indicator of prestige.[44]
- Though, Mexico is still significantly lagging behind Brazil who have an output several folds larger.

Scientific output compared to other countries (2016)



National Foundation Survey for the number of publications in 2016. World Bank Data for population. World Bank Data for GDP per capita, PPP, except Taiwan sourced from the International Monetary Fund, World Economic Outlook Database, 2015.

Number of Science and Engineering articles in Biological Sciences (2003-2016)



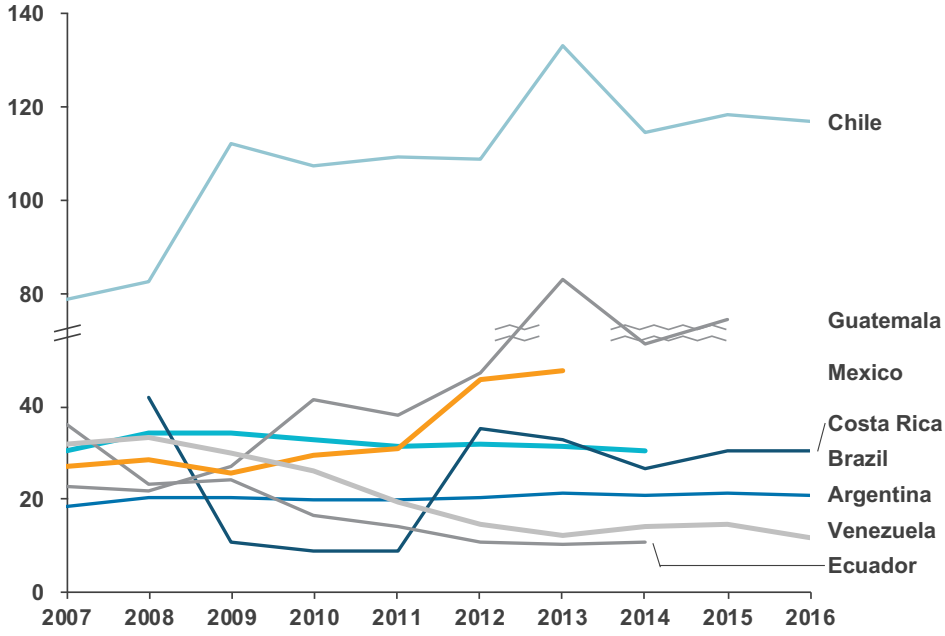
National Science Board, Science & Engineering Indicators 2018.

Note: Life Sciences includes the following areas listed by the Ministry of Science, Technology, Innovations and Communications – Biochemistry, genetics and molecular biology; Immunology and Microbiology; Medicine; Neuroscience and Pharmacology, toxicity and pharmaceuticals.

INNOVATIVE ACTIVITY:
RESEARCH PRODUCTIVITY COMPARED TO LATAM

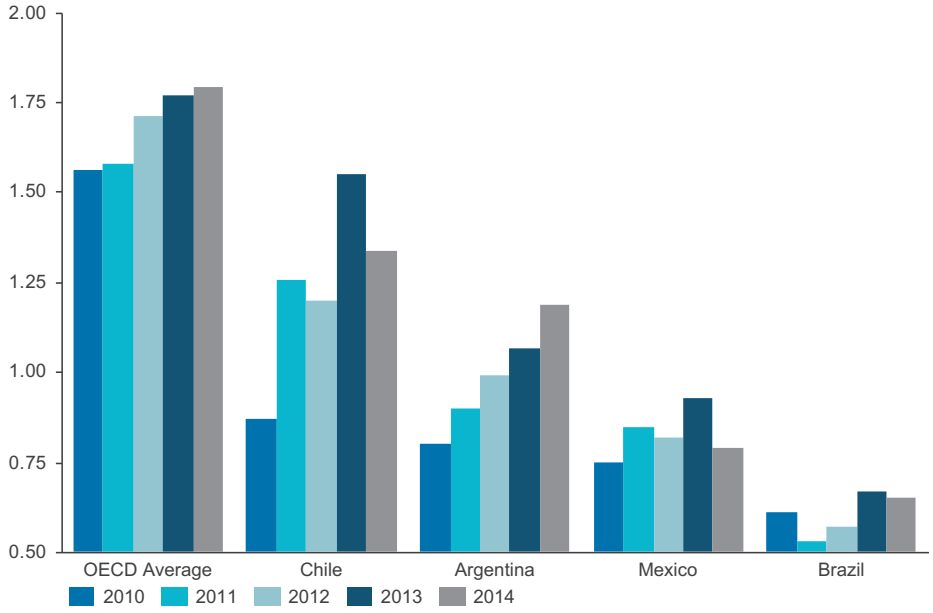
- The research productivity across 2007 – 2013,in terms of the number of Science and Technology (S&T) publications per 100 FTE researchers, Mexico falls behind Chile but is still one of the leading countries in Latin America region.
- The impact of its scientific research, as measured by share of top 1% most cited articles in Scopus, lags behind other LatAm and OECD countries and has not shown a clear trajectory of improvement therefore, research productivity and the quality of academic publications is thus an area requiring continued improvement.

Number of S&T Publications per 100 FTE Researchers (2007 – 2016)



Ibero-American Network for Science and Technology.

Share of top 1% Most Cited Publications in Scopus* (2010 – 2014)



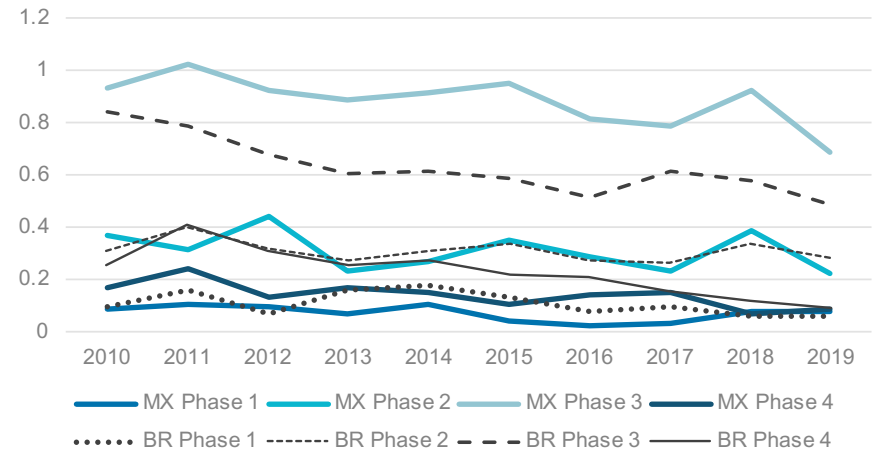
National Science Foundation Survey 2018.

Notes: *Scopus is Elsevier's abstract and citation database launched in 2004. Scopus covers nearly 36,377 titles from approximately 11,678 publishers, of which 34,346 are peer-reviewed journals in top-level subject fields: life sciences, social sciences, physical sciences and health sciences.

INNOVATIVE ACTIVITY:
CLINICAL TRIALS

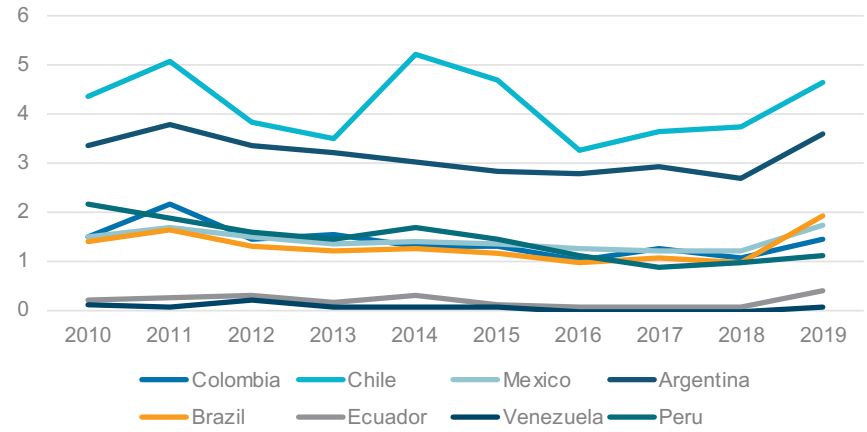
- In terms of the total number of clinical trials, Mexico is comparable with Brazil with around 2 trials per 1M people, but lags behind Argentina and Chile with nearly double the number of clinical trials per million people. Furthermore, the majority of research in Mexico are in late stage research (Phase 3 trials).
- Despite Mexico and Brazil having comparable levels of clinical trial activity, Mexico has a higher number of phase 3 trials per 1 million people suggesting more developed infrastructure to support late stage research
- Interview findings suggest that if COFEPRIS were to improve the efficiency for clinical trial approvals, there would be an increase in the number of clinical trials conducted in Mexico. The number of clinical trials can increase 3-5 fold of the current level if the local procedure through COFEPRIS improves. There is significant potential for clinical trials given the size of the population in Mexico and the fact that the population is largely naïve to clinical trials.[44,45]

Number of Clinical Trials per 1M People by Phase in Mexico and Brazil (2010 – 2019)



CRA Analysis of Clinicaltrials.gov.

Number of Clinical Trials per 1M People in LatAm Region (2010 – 2019)

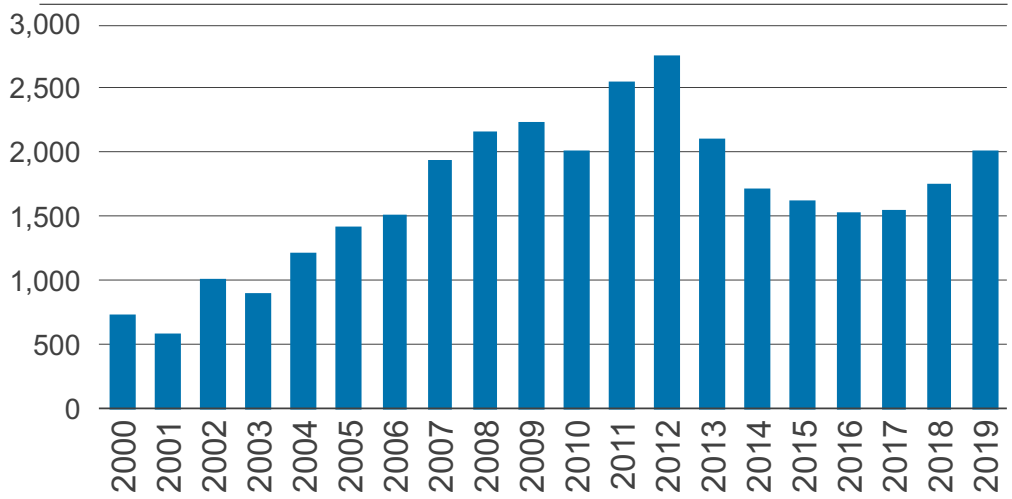


CRA Analysis of Clinicaltrials.gov.

INNOVATIVE ACTIVITY:
PATENTS (IMPI)

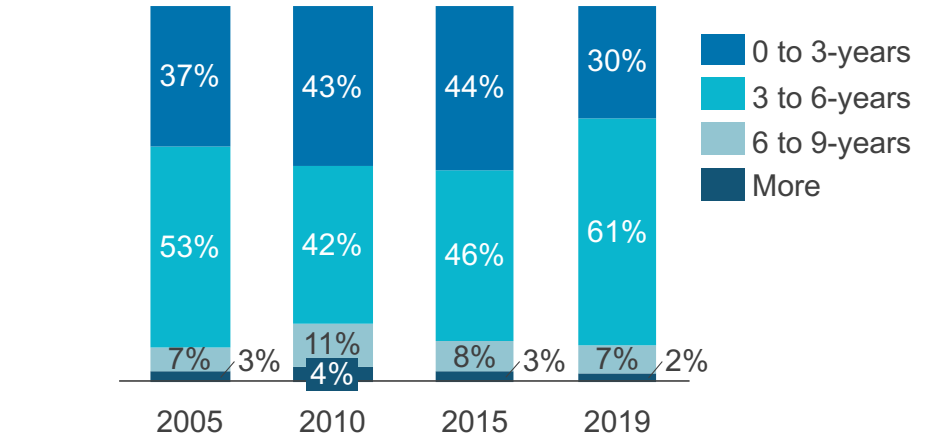
- The Mexican Institute of Industrial Property (IMPI) is ranked 10th in terms of the number of patents granted.[44] However, it has a long-standing backlog problem; for example, in 2019, more than 60% of the granted patents had submitted the patent application between 3 and 6 years ago – in order to address this backlog IMPI has partnered with EPO and USPTO.[46]
- In 2019, a partnership between the European Patent Office (EPO) and IMPI was established to enhance the use of Mexican resources dedicated to the examination of national patents, as well as to accelerate applications previously examined by EPO in order to issue more patents, faster, as well as reducing the backlog.[47]
- Similarly in 2020, the United States Patent and Trademark Office (USPTO) and IMPI agreed to launch a new work-sharing arrangement that will accelerate the process of obtaining a patent in Mexico for businesses and individuals already in possession of a corresponding U.S. patent.[48]
- Additionally, IMPI is implementing measures to shift its services electronically as a way to reduce the process timeframes.[50]

Number of Granted Pharmaceutical Patents (2000 - 2019) [51]



Source:IMPI, clase A61K.

Percentage of Granted Pharmaceutical Patents per Year of Patent Application (2005, 2010, 2015, 2019) [52]

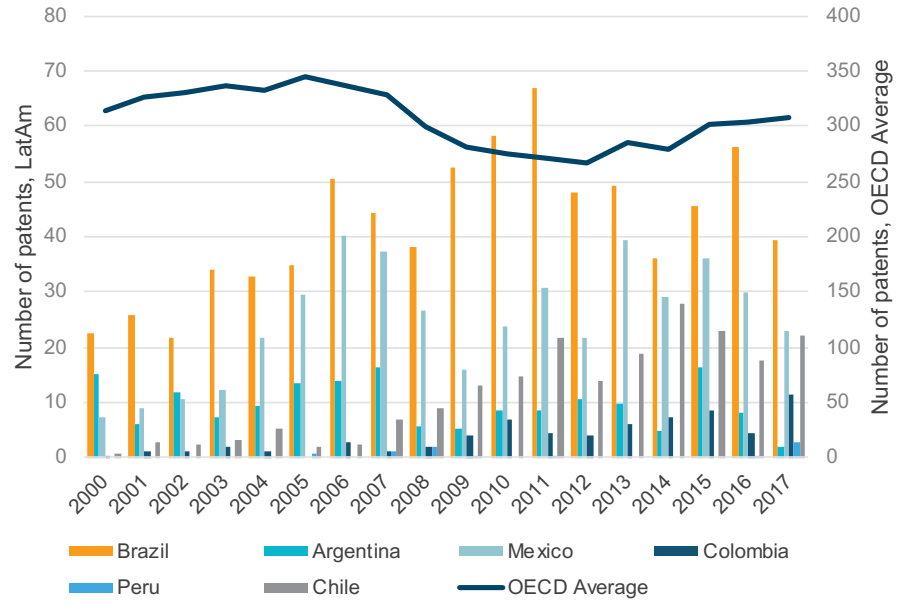


Source: IMPI, clase A61K

INNOVATIVE ACTIVITY:
PATENTS (PCT & USPTO) (1/2)

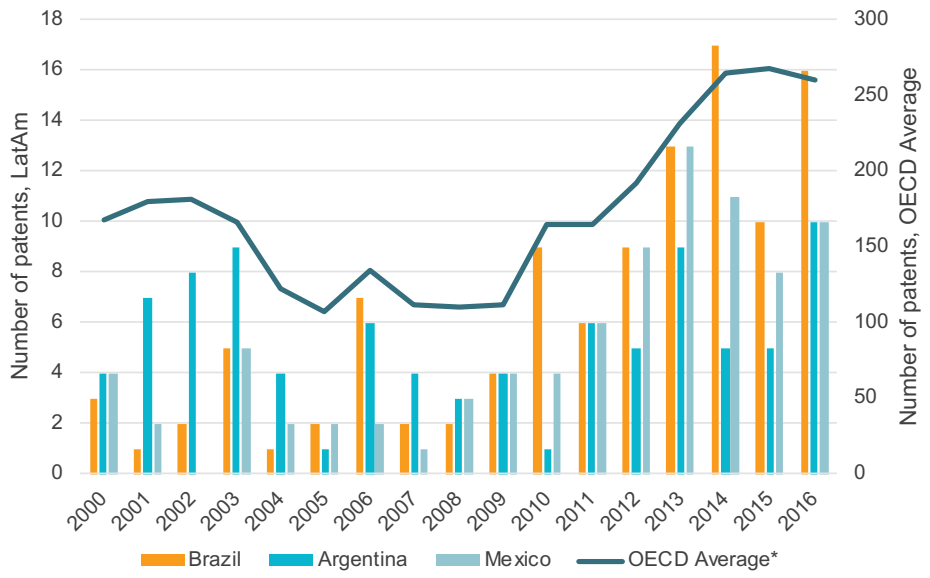
- In terms of the absolute number of pharmaceutical patent applications under the Patent Cooperation Treaty (PCT) and patents granted to Mexico nationals by the U.S. Patent and Trademark Office (USPTO), Mexico is lagging behind Brazil and the OECD Average.
- Local researchers are incentivised to file patents with IMPI to improve their university ranking, however there are no incentives for local researchers to file patents with PCT and USPTO. This limits the potential commercial potential of a patent as if a commercial product were to be developed it could only be marketed in Mexico and thus it is less attractive for foreign investors to invest in.[45]

Pharmaceutical Patents Filed Under PCT (2000 – 2017)



OECD Patents by Technology, 2020.

Pharmaceutical Patents Granted to Nationals by USPTO (2000 – 2016)

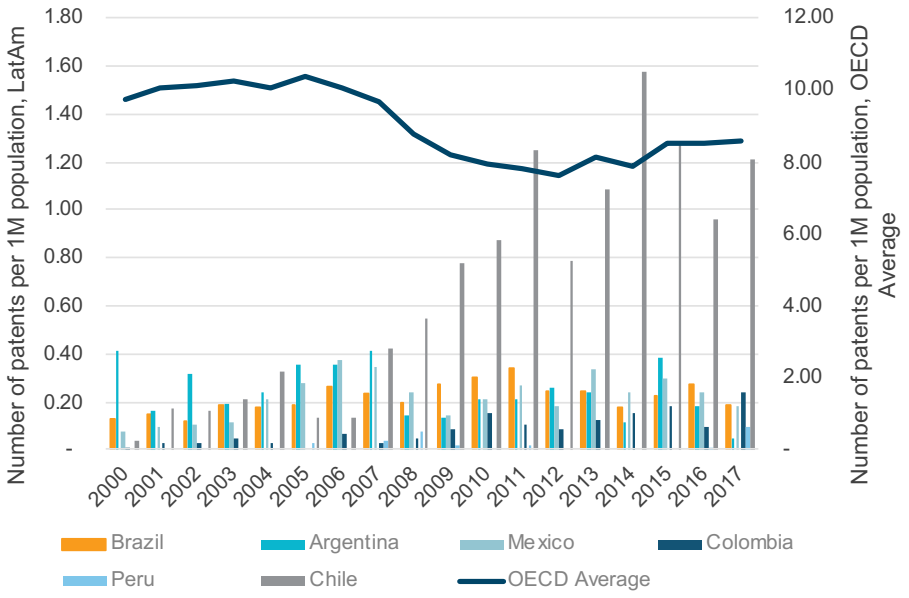


National Science Foundation Survey, Science and Engineering Indicators 2018.*Selected countries with available information.

INNOVATIVE ACTIVITY:
PATENTS (PCT & USPTO) (2/2)

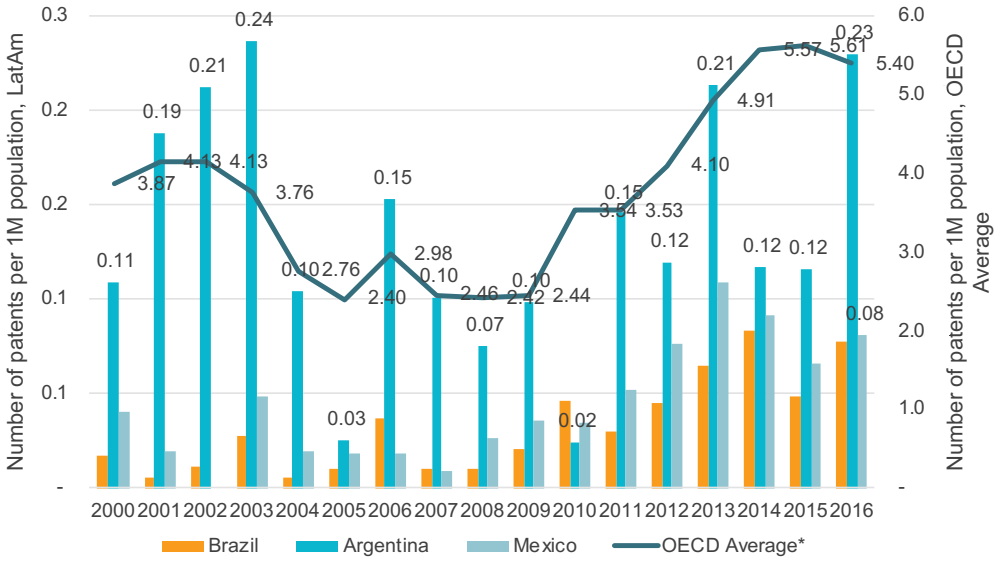
- In 2017, 0.18 pharmaceutical patents were filed under PCT per one million Mexican nationals, this is comparable to Brazil (0.19) and lower than Colombia (0.24), Chile (1.21) and the OECD average (8.56). Similarly, in 2016 0.08 pharmaceutical patents were filed under USPTO per million Mexican nationals, lagging behind Argentina (0.23) and OECD average (5.61).
- In light of this, in the period 2011-2015 79,019 patent applications were filed, according to data released by the IMPI, the Mexican Intellectual Property Institute. Only around 8% of all the patent applications came from Mexican applicants – reflecting the limited amount of local innovation - a number that is lower than Brazil, where 18% of the applications in the country are filed by residents.[53]

Pharmaceutical Patents Filed Under PCT per 1M People (2000 – 2017)



OECD Patents by Technology, 2019.

Pharmaceutical Patents Granted to Nationals by USPTO per 1M People (2000 – 2016)



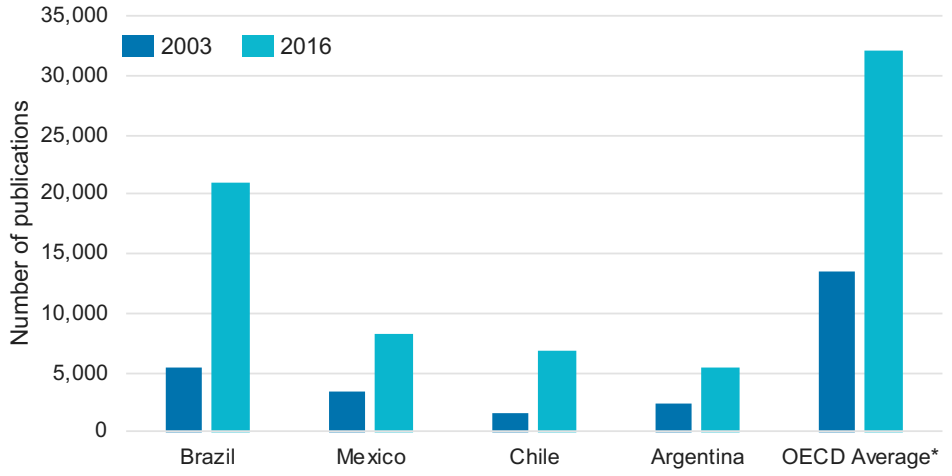
National Science Foundation Survey, Science and Engineering Indicators 2018.

*Selected countries with available information.

INNOVATIVE ACTIVITY:
CLUSTERS & COLLABORATIONS

- International collaboration as measured by co-authorship of publications in Mexico lags behind the OECD average as well as Brazil, one of the leaders in the Latin America region.
- Mexico is leading in the Latin America region in terms of collaboration between innovative SMEs and academic and government institutions. The levels are comparable with the OECD countries. However, collaboration with large companies are lacking – this is partially due to cultural barriers amongst local academics in engaging with private industry but also due to lack of funding being allocated to strengthen the private-public partnerships.[44]
- Partnership between public and private bodies are particularly important for the commercialisation of early stage molecules and such collaboration is hindered by the limited number of Technology Transfer Offices in Mexican universities and by University Regulations which do not permit private-public partnerships.[44]

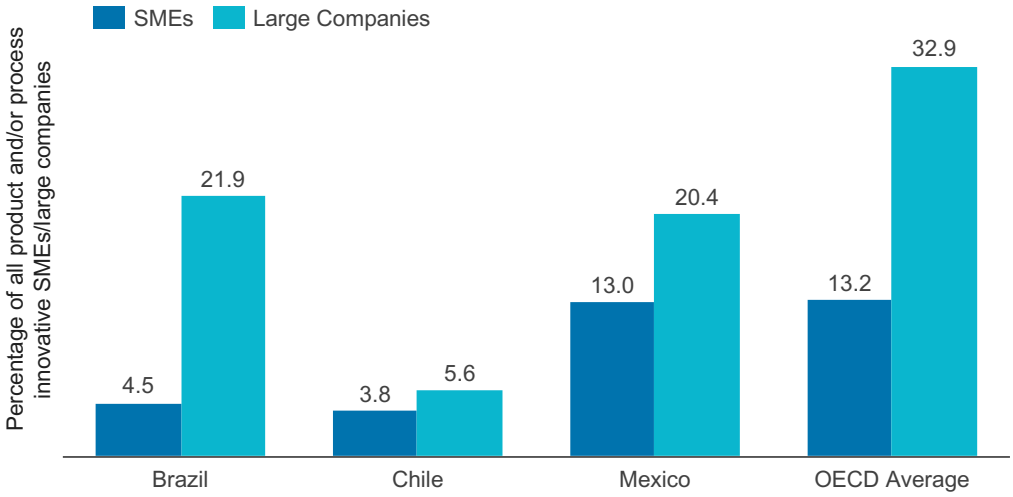
Internationally co-authored science & engineering publications (2003, 2016)



National Science Foundation Survey 2018.

Note: Selected OECD Countries (n=27).

Firms collaborating with higher education or government institutions (2017)



OECD Innovation Indicators 2017.

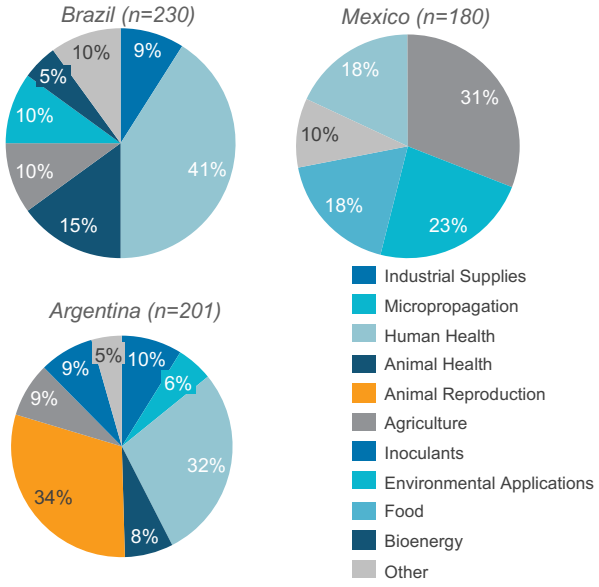
INNOVATIVE ACTIVITY:
CLUSTERS & COLLABORATIONS

- In 2011, the federal and state governments introduced incentives for the development of biotechnology clusters. In response, the government of the central state of Morelos invested US$25 million in a new science and technology park specifically targeting biopharmaceuticals producers.[54]
- The cluster in Nuevo León is focused on Biotechnology.[55] ITESM (el Instituto Tecnológico de Estudios Superiores de Monterrey) in Nuevo León and UNAM (Universidad Nacional Autónoma de México) in Morelos are the respective life sciences biotech leader in the biotech clusters of their State.[44,56]
- Many of the clusters in Mexico - some of which are advertised by their state governments - implemented a triple helix model in which there is collaboration between public institutions, academic and the business sectors.[55]

Main Biotechnology Clusters in Mexico (2015)

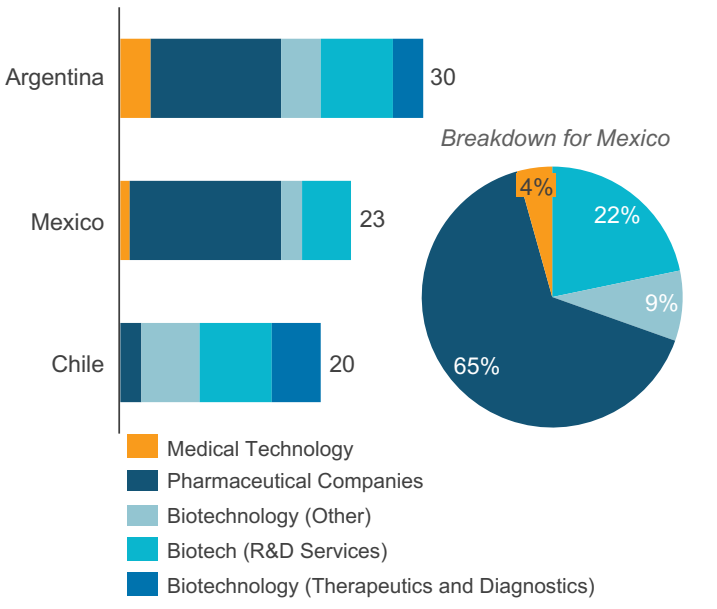
Source: ProMexico.

Biotechs by Sector (2011)



Sources: Ministry of Science, Technology and Innovation; Haar, J., Wilson Center Latin American Program.

Life Sciences Companies (to date)

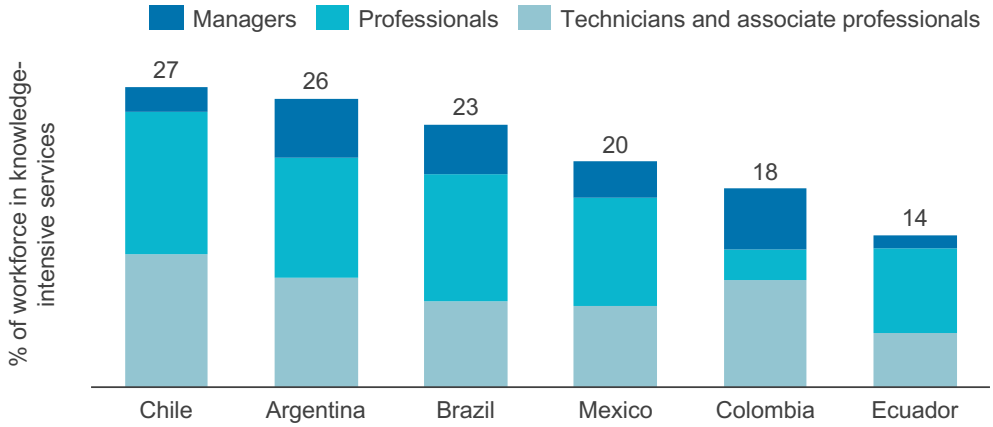


Biotech Gate.

ECONOMIC ACTIVITY: EMPLOYMENT

- In Mexico, in 2019, 20% of the workforce were employed in knowledge intensive services – lagging behind Chile (27%), Argentina (26%) and Brazil (23%), however, superior to Colombia (18%) and Ecuador (14%).
- Again, Mexico hold a middle ground position in terms of employment in the biopharmaceutical industry (652 per million) in terms of number of biopharmaceutical jobs per million inhabitants, when compared to Argentina (902 per million) and Brazil (464 per million).[57]
- However, the nominal salary in the pharmaceutical industry has increased by 29% between the years 2003-2013, whereas the real salary has decreased by 15% during the same period.

Employment in knowledge-intensive services (2019, % of workforce)



Source: International Labour Organisation, 2019.

Average annual salary in the pharmaceutical manufacturing industry remuneration (2003, 2008, 2013, thousand pesos)

Source: INEGI, 2003, 2008, 2013.

Employment in the Biopharmaceutical Industry per million inhabitants (LatAm)

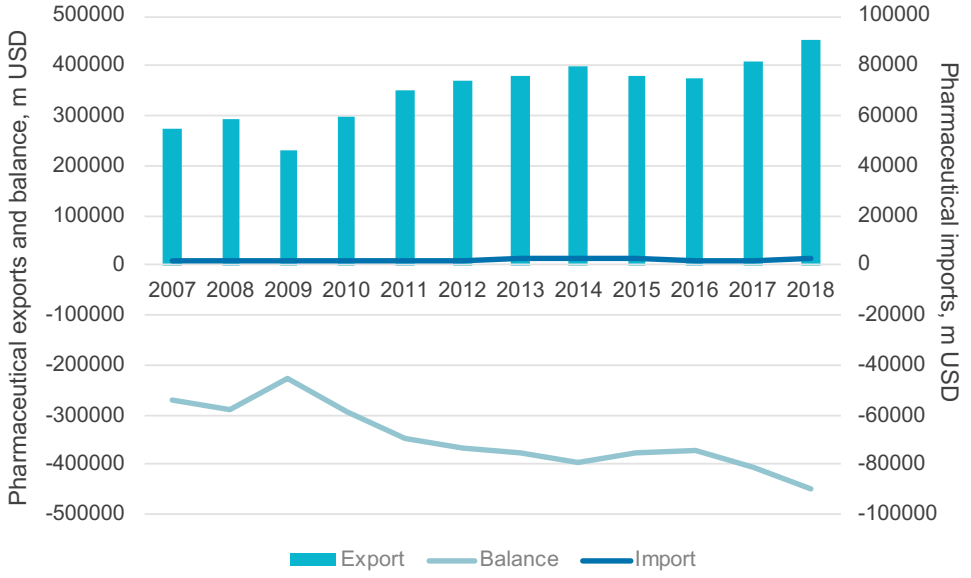
Sources: OEDE-MTEySS; INADEM Mexico; SINDUSFARMA, latest data available, clarification in notes*

*2014 data for Argentina and Mexico, 2016 data for Brazil.

OTHER ECONOMIC ACTIVITY
LINKED TO THE PHARMA SECTOR

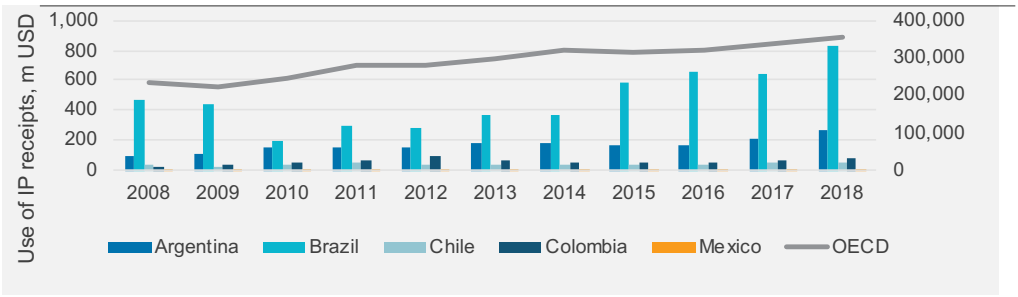
- Between 2009 and 2018, Mexico has had an increasing trade surplus in pharmaceutical goods, indicating that the pharmaceutical industry is a key industry in Mexico.
- Between 2008 to 2018, the FDI inflow into Mexico was on average USD 30,740.9 million – which is lower than the level of FDI outflow (which was on average USD 9,752.5 million over the same period).
- However, Mexico is lagging behind Brazil and average OECD in the levels of payments from licensing intellectual property.

Evolution of pharmaceutical imports and exports (2007-2018, m USD)



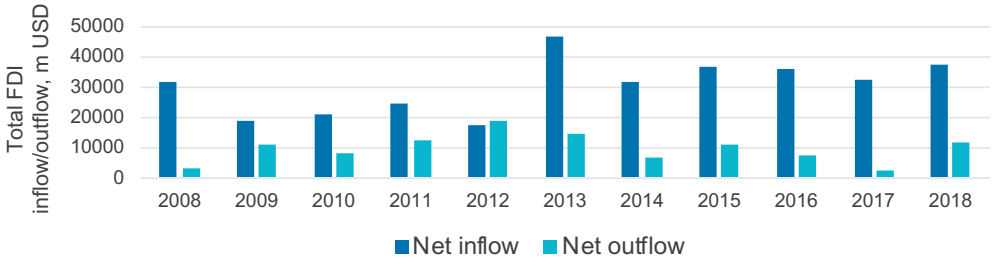
Source: UNCTADstat, 2007-2018.

Receipts for the use of intellectual property (licensing payments) (2008-2018, m USD)



Source: World Bank, 2008-2018.

Total FDI inflow/outflow in Mexico (2008-2018, m USD)



Source: World Bank, 2008-2018.

MEXICO:
ASSESSMENT OF PERFORMANCE

- Compared to the LatAm region, Mexico comparatively has strong human resources and a strong healthcare system. The general de-prioritisation of innovation from the government is a significant barrier which limits the level of collaboration between public and private entities. There is limited investment in early stage research in clinical trials and poor implementation of IP laws dis-incentivises FDI. If more investment were to be allocated to innovation, Mexico would experience higher innovative and economic activity.
- With the new Industrial Property Law and the USMCA provisions, Mexico could attract more FDI and pharma confidence to conduct local clinical trials.
  - However, these reforms should be complemented with new innovative policies that foster private-public partnerships.

	INDICATORS	COMPARED TO LATAM	COMPARED TO OECD*
HUMAN RESOURCES	Universities		
	Education attainment		
	Collaboration		
	Researchers		
HEALTHCARE SYSTEM STRENGTH	Infrastructure		
	Effective and safe care		
INVESTMENT IN INNOVATION	R&D investment		
	FDI		
INNOVATIVE ACTIVITY	Early research (publications)		
	Clinical trials		
	Patents		
ECONOMIC ACTIVITY	Employment		
	Trade		

Improving performance →

* Where OECD average not available, comparison was made against World: higher income countries average.

ENABLERS OF INNOVATIVE ACTIVITY AND CHALLENGES IN MEXICO

- Drawing from the analysis on policies, innovation base and resulting activities and discussions with global and local experts in IP, research, academia, clinical research and industry, Mexico exhibits:
  - Strong IP legislation, good human capital and expertise particularly in basic research and local innovation hubs, large population, but
  - Lags behind on private investment in R&D, communication between government entities, enforcement of legislation, and technology transfer and collaborations and leveraging its diverse population for clinical trials
- The rest of the analysis focuses on potential gains from improving the enablers and particularly the strength of having a strong enforcement of the legislation and in fostering private-public collaborations

	AREAS	DESCRIPTION IN MEXICO
ENABLERS	**Strong IP legislation**	Through the new IP law, Mexico will have a strong IP legislation which incorporates the USMCA provisions.
	Human capital and expertise	Good availability of top universities and education attainment to higher degrees and good standards.
	Size of population	Being highly populated, Mexico represents an attractive market for foreign manufacturers and could be an attractive location for clinical trials if the regulations were to be simplified.
	Private investment in R&D	The government can introduce incentives to attract private R&D investments.
	Communication between entities	Poor communication between IMPI and COFEPRIS hindering the performance of both institutions.
	Enforcement of legislation	Poor enforcement of legislation hindering pharma industry trust and investment in Mexico.
	Technology transfer and collaborations	University regulations and lack of Technology Transfer Offices hindering private-public partnerships and commercialisation.

High	Enablers in Mexico	Low

3.
The benefits of an improved environment for innovation

LESSONS FROM COMPARABLE MARKETS

The second step of the project aims to investigate the performance of "similar" markets to Mexico (drawing from regions outside of Latin America).

Choice of case studies: We chose to focus on markets where:

1. **The government has prioritised innovation through policies which strengthen the IP regime, support funding of research and foster collaboration.**
   - Introduced policies to support education in science and technology and academic research.
   - Incentives for collaboration between private and public sector.
   - Prioritized innovation from government level down to academic researchers.

2. **There has been robust implementation of IP policies in response to international commitments such as Foreign Trade Agreements.**
   - Strengthened IP regime in response to international agreements to develop the country as a local innovation hub.
   - Prioritized pharma innovation policies e.g. implementation of RDP.

3. **Show an observable impact on innovative activity**
   - Timing of policy change means that observations on impact can be made.

WE USE CASE STUDIES TO DRAW LESSONS FROM COMPARABLE MARKETS

Using case studies, our aim is to investigate

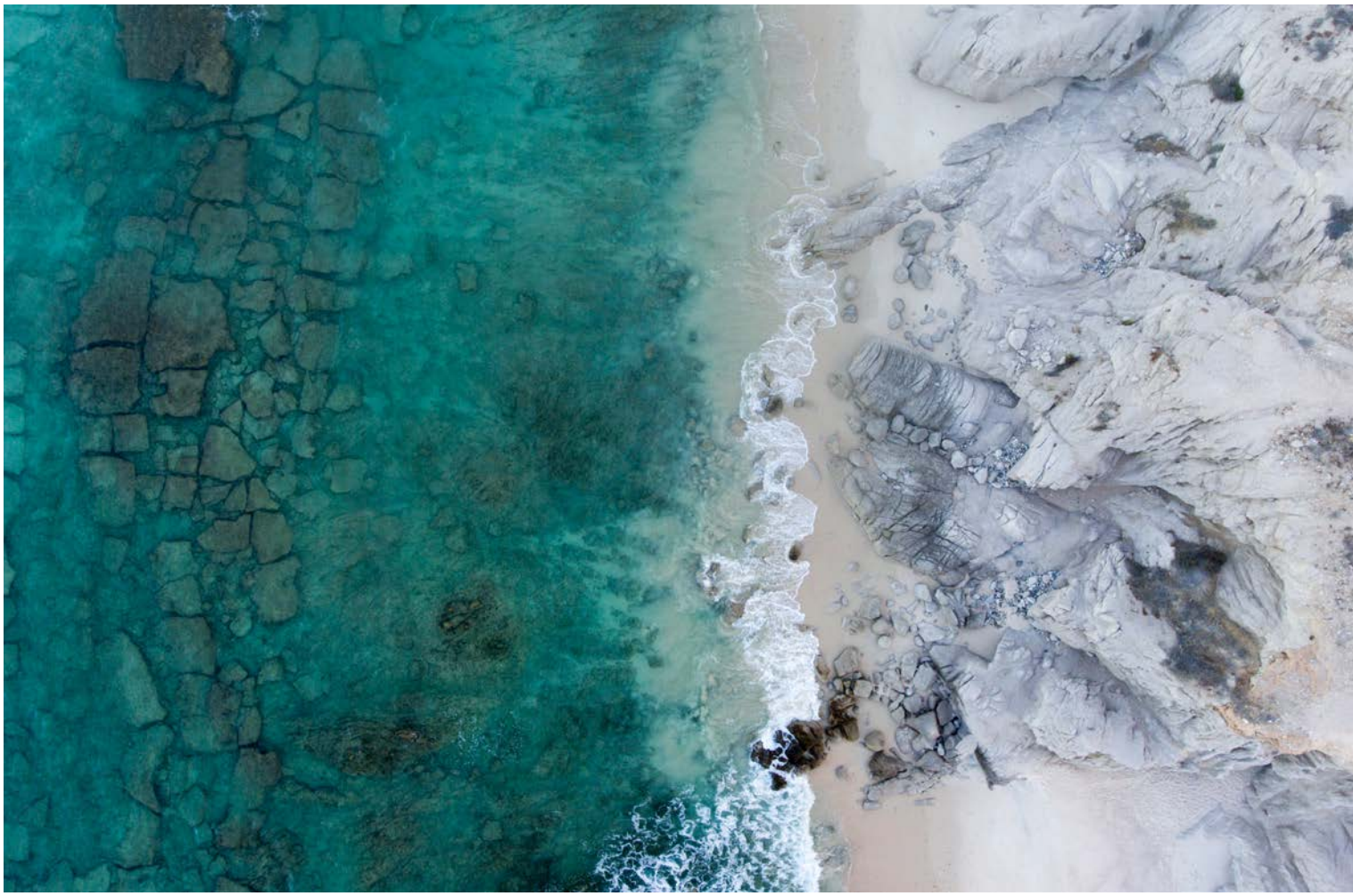
1. The changes in the policy regime supporting innovation.
2. The innovative environment and economic activities related to innovation across a range of areas.
3. Whether there is any relationship from changes in the policy regime to innovation activity by analysing the growth changes in indicators before and after key policy changes.

It is important to note that this is a challenging approach, due to:

- Many factors affect innovative activity.
- Factors work together and need to be considered as package rather than in isolation.
- Changes in innovative activity can only be observed over time and may occur in anticipation of a change – making causation difficult to interpret.
- Certain indicators take a longer time to experience the impact from policy changes – making the determination of impact more difficult.
- We need to test results are robust to differences between markets (role of off-patent sector).

We use key dates of significant policy changes and examine whether there is a reflected change in the innovative environment through a:

- Change in growth rates.
- Change in average level (where an apparent step change).
- A statistical analysis to try to identify a causal link.



Aerial views from the beach and reef of Cabo Pulmo, Mexico, shutterstock.com/it/g/photonatura.

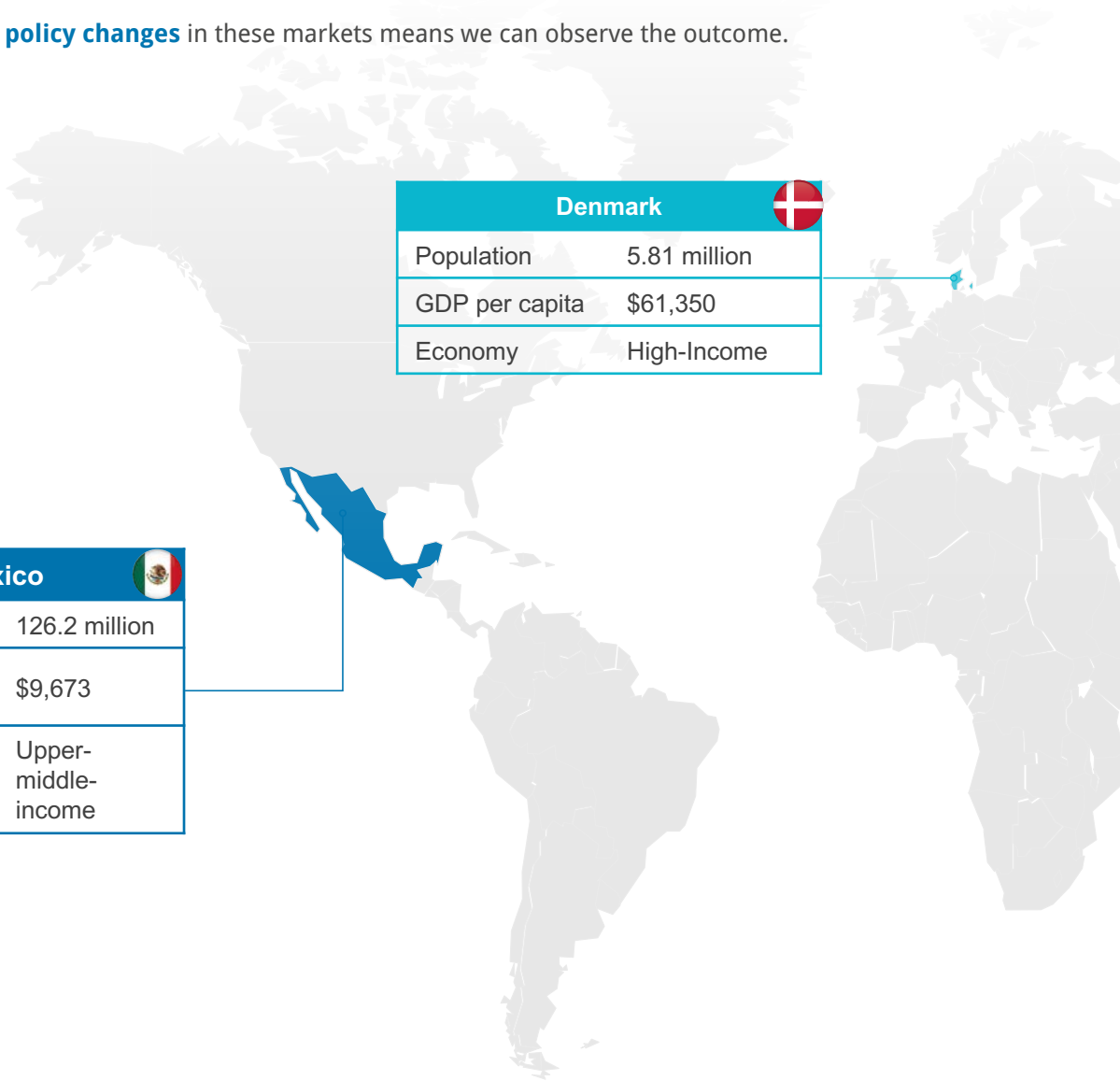
APPROACH TO CASE STUDY ANALYSIS AND SCENARIOS

Our research and interview insights reveal that Mexico's key innovation policy gaps are:

1. Government de-prioritisation of innovation together with a lack of incentives and legal certainty for companies to invest in innovation and collaborations.
2. Lack of enforcement of legislation and delays in infringement resolutions.
3. Patent Linkage is being applied inconsistently and this is attributed to the poor communication between government bodies.
4. Inconsistencies in the granting of RDP and no legal instrument available to ensure RDP protection.

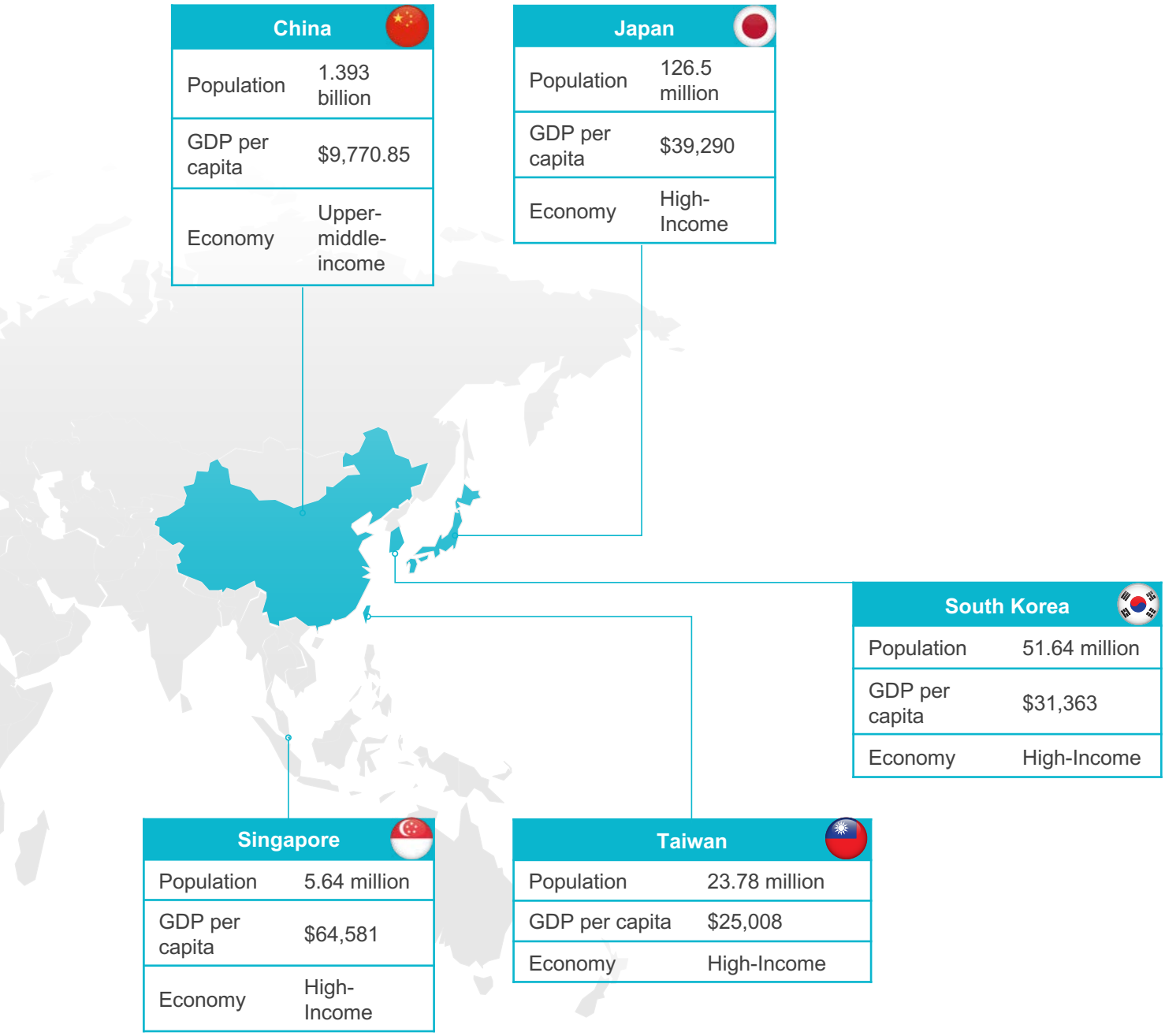
Our selection criteria for our case study markets include:

- Have shown a **focus on strengthening innovative environment**, particularly the IP protection.
- Placed **broadly in the same income, size and development category as Mexico** when started focusing on innovation.
- Show an observable impact on **innovative activity**.
- The **timing of policy changes** in these markets means we can observe the outcome.



Our research and interview insights reveal that Mexico's key innovation policy gaps are:

1. **Denmark and China's** government prioritisation of innovation and implementation of incentives to secure innovation environment:
2. **Singapore's** implementation of legislation to enforce international agreements and provisions for infringement resolutions.
3. **Taiwan and South Korea's** implementation of a robust patent linkage system:
4. **South Korea, Japan, Taiwan, Singapore's** implementation of RDP through legislation.



CASE STUDY: DENMARK
USING IP TO FOSTER A CULTURE OF INNOVATION OPENNESS AND COLLABORATION BETWEEN ACADEMIA AND INDUSTRY IN DENMARK

MEDICON VALLEY ACADEMY (NOW ALLIANCE), 1997

Medicon Valley Alliance (MVA) is a non-profit membership organization in Medicon Valley (a life sciences cluster in Copenhagen), which aims to strengthen the collaboration, networking and knowledge-sharing in the life science community through research grants and tax schemes to support R&D.[58]

ACT ON INVENTIONS AT PUBLIC RESEARCH INSTITUTIONS, 2000

Th Act gave universities ownership of all inventions developed by employees during their work, even when that work is carried out in collaboration with third parties (e.g. industry). Due to this, between 2000-2004 Danish scientists were participating in fewer industry patents than before the new law but by 2008, large companies in particular have established agreements and pursuing work with the Danish academic institutions.[58]

TECHNOLOGY TRANSFER OFFICES, 2000

In response to the new Act on Inventions at Public Research Institutions, Technology Transfer Offices were set up at every university to facilitate cooperation between academics and industry.[58]

NORDIC PATENT INSTITUTE, 2006

In 2006, the Nordic Patent Institute - which is a partnership of the national patent offices of Norway, Denmark and Iceland – was established to provide Global Prior Art Searches (patent and non-patent) for businesses and IP law firms.[61]

INDUSTRIAL PROFESSORSHIPS, 2014

Universities establish research positions in collaboration with the industry: The researcher is thus employed by both the university and industry and spends time at both the university and industry.[63]

GLOBALIZATION STRATEGY, "DENMARK—BUILDING ON TRADITION" 2006

Council consisting of government, pharma industry and academics resulted in a national strategy to improve innovation. Among other commitments, included promise to increase funding for R&D to 3% of GDP, with 1% from public sources.[60] Expert panel recommended areas of focus e.g. infectious diseases and chronic disease.

THE DANISH COUNCIL FOR RESEARCH AND INNOVATION POLICY, 2014

The Council is responsible for providing the Minister of Higher Education and Science and others with independent and expert advice on research, technological development and innovation at system level.[61]

DEVELOPMENT CONTRACTS, 2016

In 2016, in order to increase regional national knowledge cooperation and collaboration to foster technology transfer a supplement development contracts were further expanded. Through these contracts, universities set goals to increase the number of research and innovation projects with private individual companies as well as increasing the number of student projects.[63]

OPEN ENTREPRENEURSHIP, 2017

Open Entrepreneurship is a project which aims to find new ways to commercialize research in areas where universities have strengths - including developing general models and concepts that can be disseminated to other universities and more research areas. Companies such as Novo Nordisk have benefited from this project.[60]

LEGAL COSTS OF PATENT LITIGATION, 2019

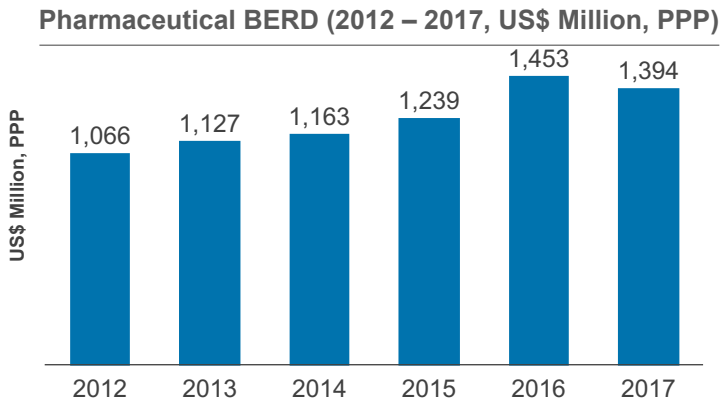
In August 2019, the Danish High Court (Eastern Division) decided that prevailing parties in patient litigation may now expect to receive costs that reflect the actual costs incurred as a result of the litigation, rather than the previously low costs that were awarded in Denmark.[59]

Key

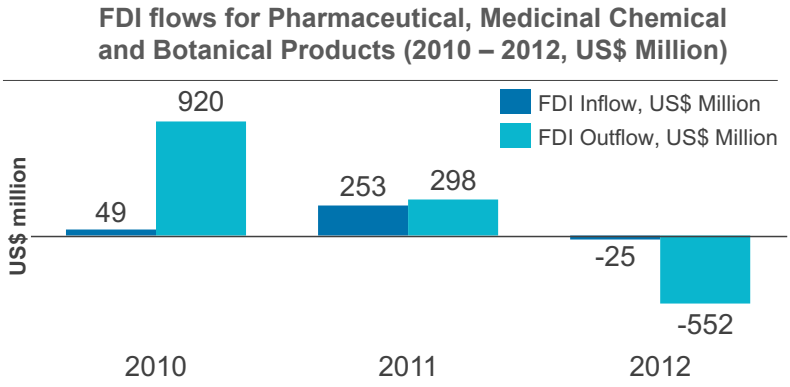
- Changes to the IP regime.
- Changes to the Innovation Policy Landscape.
- ★ NOTE – Regulation market with a star will be used as proxy for change in estimating growth differences.

INVESTMENT IN R&D AND FDI

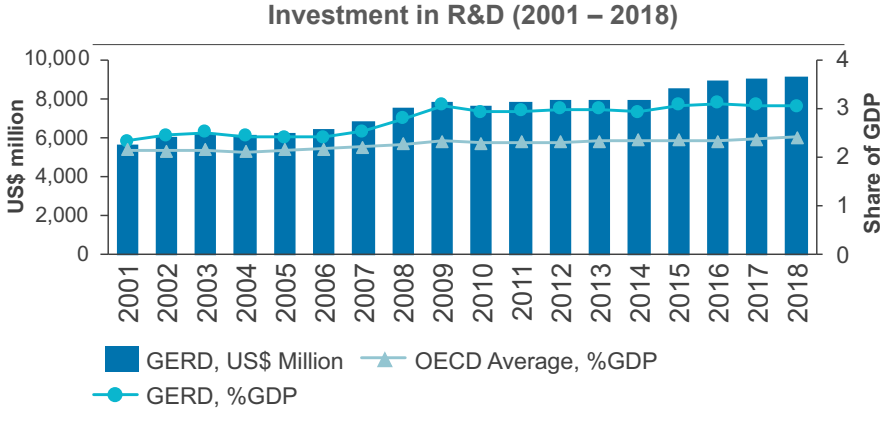
- In 2018, Denmark was ranked 2nd in the world for the researcher concentration and 6th in the world for the R&D intensity ranking number six in the world.[66] Additionally, in 2018 Denmark ranked higher than the OECD average for investment in R&D.[67]
- In 2012, public and private investment in R&D accounted for 1.6% and 2.03% of GDP, ranking Denmark fourth and seventh out of all OECD countries for public and private R&D investment, respectively.[64,68]
- FDI Outflow have consistently generated a higher rate of return than the return on FDI Inflow and this can be attributed to the Danish pharmaceutical patents registered abroad, which generate a high level of earnings relative to the investment.[65]



Source: OECD Data, 2019.



Source: OECD Data, 2020.

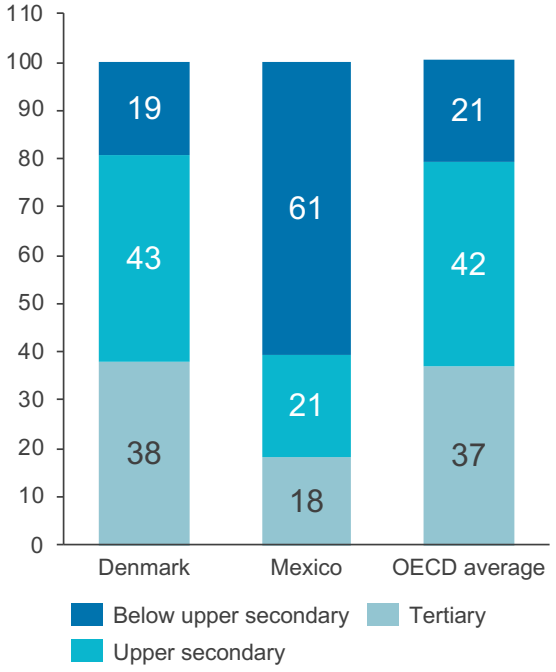


Source: OECD Data, 2020.

UNIVERSITIES AND QUALITY OF EDUCATION

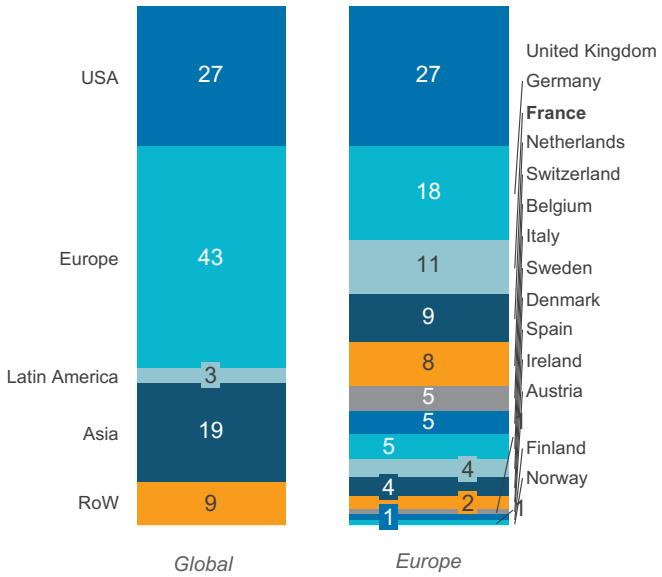
- The level of educational attainment (below upper secondary, upper secondary and tertiary education) in Denmark is similar to the OECD average. Moreover, the average PISA score in Science is also on par with the OECD average.
- Denmark represents ~4% of the European universities in the top 200 for biological sciences and falls in the bottom half of the European universities in terms of contribution.

Educational attainment of 25-64 year olds (2018, %)



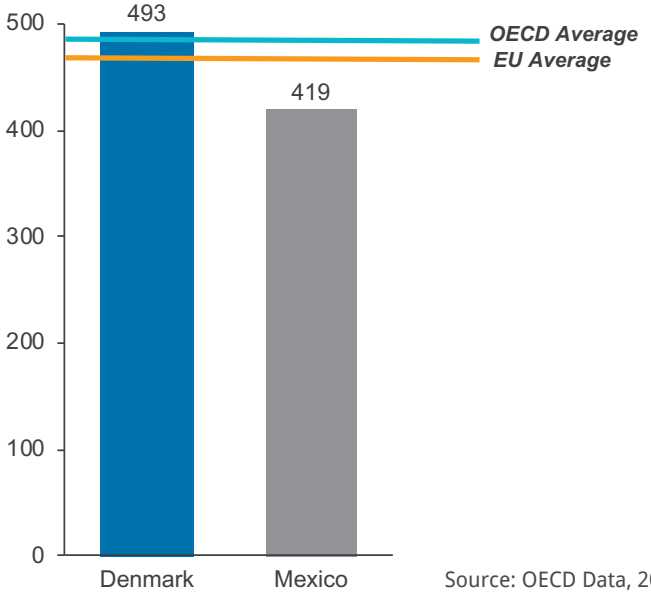
Source: OECD Data, 2018.

Universities in Top 200 Universities for Biological Sciences (2020, %)



Source: Top Universities, 2020.

Average PISA Score in Science (2018)

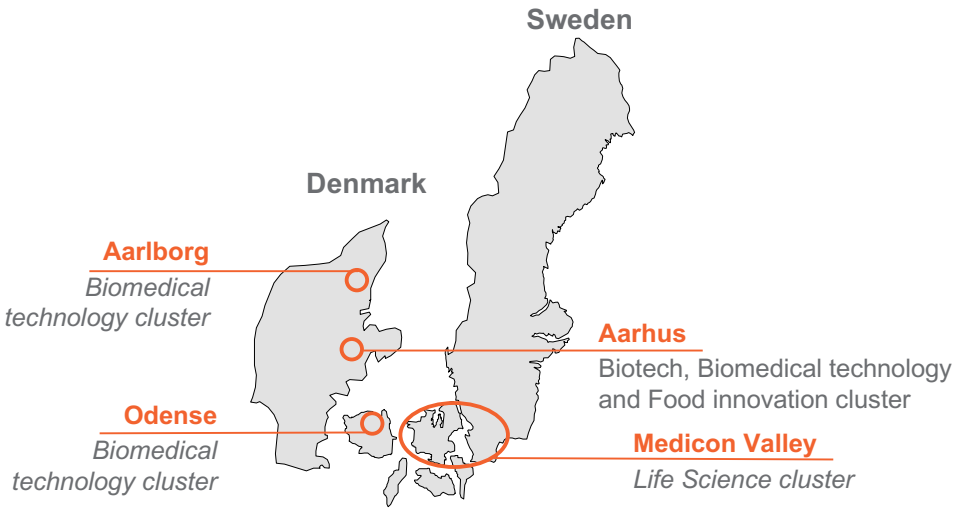


Source: OECD Data, 2018.

COLLABORATION AND INFRASTRUCTURE FOR RESEARCH

- There has been growing focus on economic clusters including medical research and biotechnology. The most notable of these clusters is the Medicon Valley in the Oresund region, the cross border region between Copenhagen and Southern Sweden. The Ministry of Foreign Affairs of Denmark notes Medicon Valley as one of the top 3 biotech clusters within Europe.[69]
  - Within the Medicon Valley, there are more than 7 science parks with a concentration of research intensive multinational companies, SMEs and educational and research institutions specialising in life sciences; the majority of pharmaceutical and biotech firm reside on the Danish side.

Map of biotech/biomedical clusters



Source: OECD Publishing,[70] Ministry of Foreign Affairs of Denmark.[71]

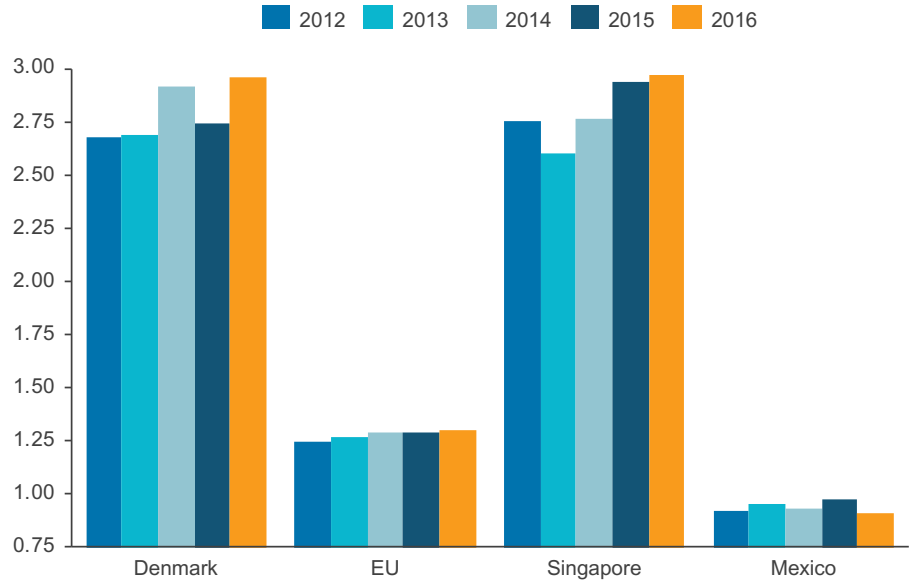
Pharmaceutical and biotech companies within Medicon Valley

International companies with major research centers within Medicon Valley

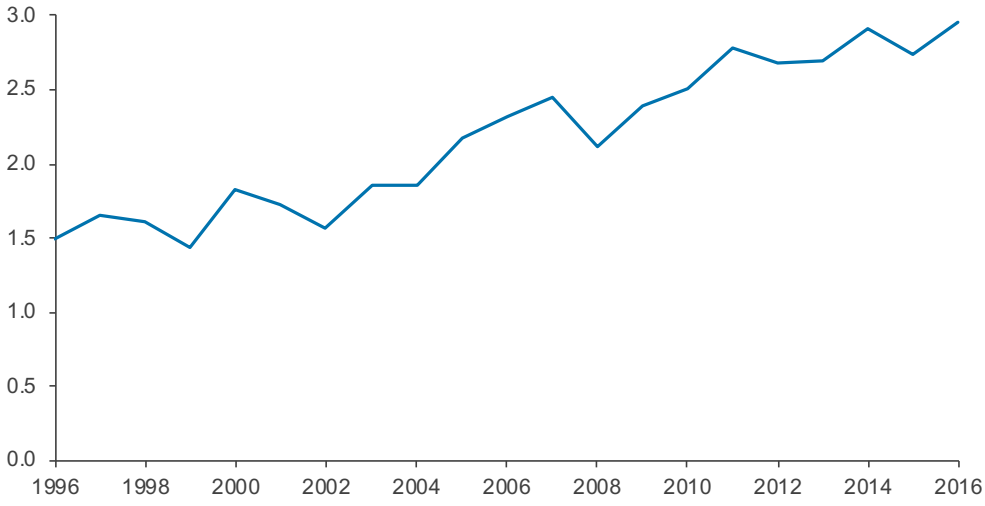
INNOVATIVE ACTIVITY: PUBLICATIONS

- The strength and influence of Danish publications have grown significantly and steadily, its share of Science & Engineering publications in the top 1% most-cited articles tin the Scopus database has doubled between 1996 and 2016.[72]
- To compare within the region, Denmark outperforms the European average by more than two times between years 2012-2016.

Share of top 1% Most Cited S&E Publications in Scopus* (2012 – 2016)



Share of Denmark S&E publications in the top 1% most-cited in the Scopus database (1996 – 2016)

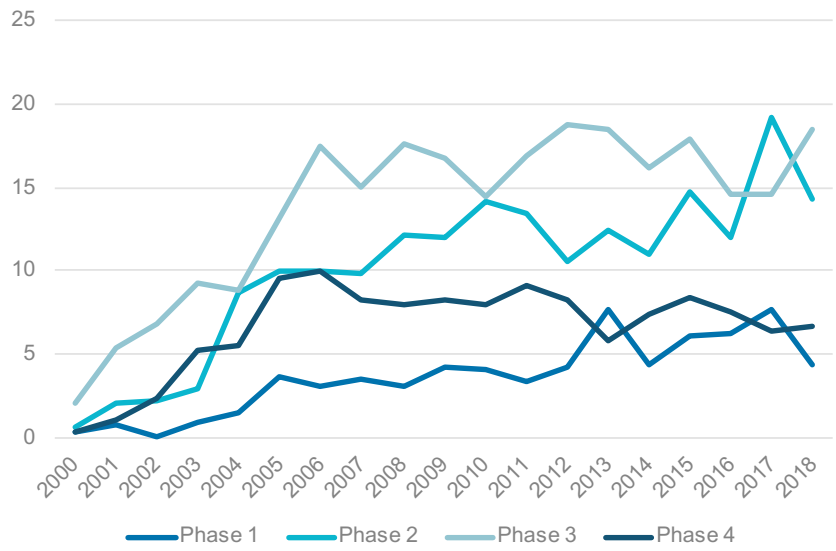


Sources: Scopus database; National Science Foundation Survey 2020.

INNOVATIVE ACTIVITY: CLINICAL TRIALS

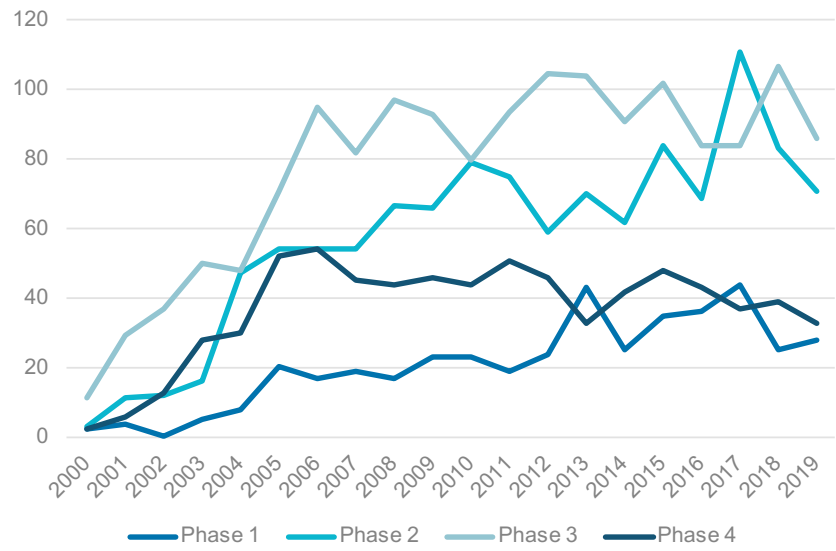
- The level of clinical trial activity has been fairly constant in Denmark since 2005 across all stages of clinical trials, with minimal year on year fluctuations.
- The largest growth was observed between the years 2003-2006 with largest growth in later stage development i.e. Phase 3 trials. Absolute numbers increased from 48 to 95 between 2004-2006.

Number of New Clinical Trials per 1M Population (2000 – 2018)



Source: Clinicaltrials.gov.

Absolute Number of New Clinical Trials (2000 – 2019)

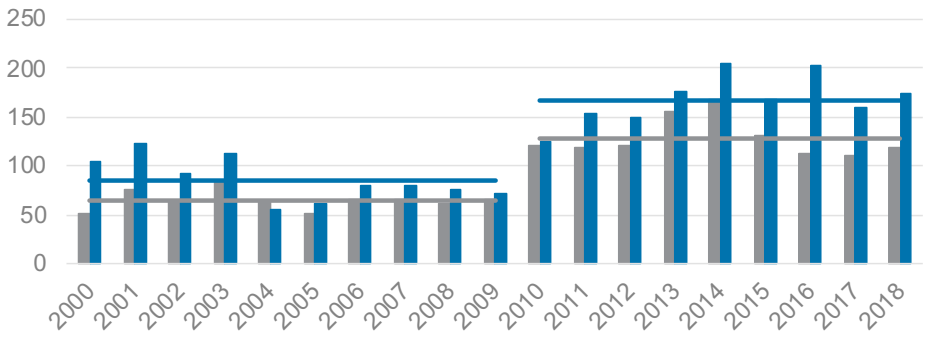


Source: Clinicaltrials.gov.

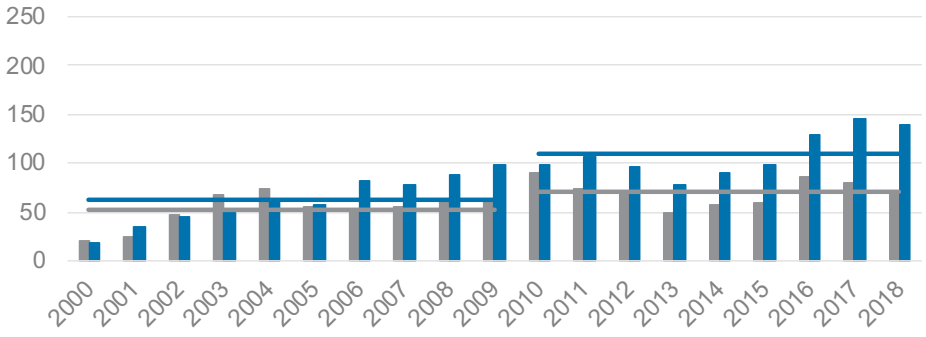
INNOVATIVE ACTIVITY: PATENTS

- Between 2006-2018, the percentage of annual filed patent applications with a Danish applicant with the Danish Patent and Trademark Office varied between 84-92% of the annual filed patent applications - however, the percentage of annual granted patents with a Danish applicant varied between 58-81% of the annual granted patents.[74,75]
- Between 2013 and 2017 the cumulative number of patents issued to Danish companies has grown by 11%. Between 2013 and 2017, the number has grown from 15,665 to 17,450.[76]

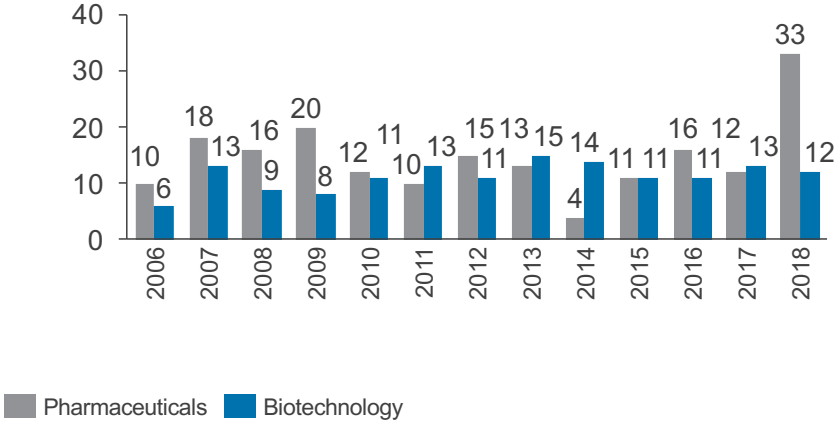
USPTO Pharmaceutical and Biotech patents granted to Danes[73]



EPO Pharmaceutical and Biotech patents granted to Danes[73]



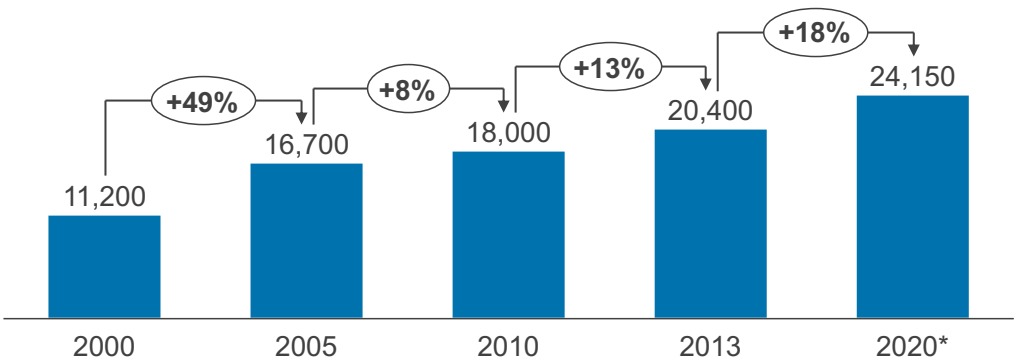
Filed patent applications at Danish Patent and Trademark Office[74,75]



EMPLOYMENT IN THE BIOTECH SECTOR

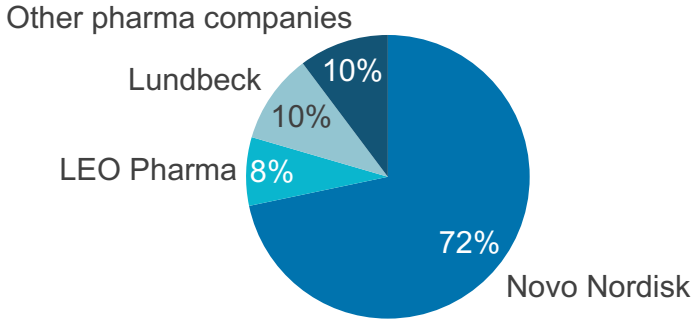
- In 2016, Denmark is ranked as the Best Country in Europe for development of biotechnology by Scientific American and this is attributed to the presence of world-class universities, university hospitals, research centres and private companies of various sizes, all working at the forefront of biotech research, targeting medicine as well as environmentally friendly products and solutions.[77]
- Additionally, the Danish educational system focuses on teaching students to work together in an interdisciplinary context, resulting in efficient teamwork and innovative research and products.[77]
- Denmark is home to more than 160 dedicated biotech companies. The Danish biotech industry employs 40,000 people, 5,000 of which are dedicated to R&D.[77]
- The European Spallation Source, which is one of the largest science and technology infrastructure projects being developed today, is a pan-European project with Sweden and Denmark as the host nations.[77]
- Through the TTIP agreement between the EU and the US resulted in non-tariff barriers to trade between the US and the EU in the pharmaceutical sector and this agreement is expected to provide benefits to Denmark, including DKK 3 billion worth of additional exports of pharmaceuticals, resulting in 650 new jobs in the pharmaceutical industry.[78]

Denmark Pharmaceutical Industry Headcount[78]



*Estimated – increase partially attributed to the Transatlantic Trade and Investment Partnership (TTIP).

Key companies employing pharma headcount (based on 2013)[78]



Copenhagen, Denmark, shutterstock.com/S-F.

CASE STUDY:
APPLYING LESSONS FROM DENMARK TO MEXICO

Changes in the policy regime to support innovation

Prioritisation of innovation.

- The purpose of the Act on Inventions at Public Research Institutions is to ensure that **research results generated by public funds are utilized for the Danish society through commercial exploitation**. The act on inventions at public research institutions **provides clarity on the ownership of intellectual property**.[79]
- In response to the new Act on Inventions at Public Research Institutions, Technology Transfer Offices (TTO) were set up at every university as from 2000. However, with time Danish universities started fostering the business-partner model rather than relying on the traditional linear TTOs.[80]
- The Act **allows universities to invest in patenting** and take equity in spinouts and offers an incentive structure, where commercial revenues are shared between institutions and the inventing researchers.[79]
- During the introduction phase (from 2000-2012) the new legislation **was backed by a national budget grant.**[79] For example, in the first four years, the law was accompanied by an appropriation of **DKK 58 million.**[80] These funds were used for a variety of related initiatives such as: university patenting cost; development of technology transfer concepts; training for tech-transfer professionals; proof of concept-projects (early stage gap-funding).[79]

The Danish government has a **strong vision on fostering innovation.** For example:

- VTU is an agency within the Ministry of Science, Technology and Innovation and its responsibilities include: **public research funding; prioritisation of research initiatives; commercialisation of research; and innovation policy.**[81]
- The Danish Council for Research and Innovation Policy (DFiR) provides research policy and innovation policy to the Minister of Higher Education and Science and others.[82]

Various polices have been introduced in Denmark to **facilitate innovation funding**:

- **Vaekstfonden**, the Danish government's investment fund, invests seed capital in companies at a stage deemed too immature and risky for ordinary venture capital. Life sciences companies that benefited from this fund include: Survac which was sold to Merck (Germany) in 2004 and Neurodan which was sold in 2005 to Otto Bock (Germany).[84]

Creation of innovation environment to provide legal certainty for technology transfer.

In Denmark, innovation is fostered through industry-science collaboration.[85] The Denmark innovation cluster is among the strongest in Europe and aims to openness to encourage private-public partnerships **and collaborations**.[87] For example:

- Medicon Valley Alliance (MVA) encourages networking and knowledge-sharing in the life science community to realise the full potential of Medicon Valley.[84]
- Matchmaking activities and private-public partnerships are encouraged through various initiatives, for example: AIM-day; Industrial professorships; Supplement contracts; and Open Entrepreneurship.[83]
- Four out of five companies in the Danish life science sector collaborated with a Danish university between 2014 and 2016.[86]

Impact of changes in policies on innovation activity

- In total, **654 inventions were reported** in the period 2000-2003, steadily increasing from 117 in 2000 to 206 in 2003. The increase in the number of reviews from 2000 to 2003 has been greatest for hospitals (86%) and universities (80%), while the increase for sector research institutions (44%) has been more modest (this is because employees of research institutions were already required to report inventions).[88]
  - The number of interventions for which were universities have acquired the rights increased by 68%.
- In the period 2000-2003, **the institutions submitted a total of 284 patent applications,** growing from 55 applications in 2000 to 87 applications in 2003.
- Overall, during the period 2000-2003, **133 inventions were transferred:** 61 from universities, 19 from hospitals; and 53 from research institutions. This includes 24 spin-outs.

Main expected effects of policy change

- The enactment of the Act on Invention at Public Research Institutions contributed towards an observed increase in the number of: inventions (and in the inventions in which the institution has acquired rights); patents; licensing agreements, patents sold and spin-outs.[89]
- The development of Medicon Valley bio-cluster as a regional leader has had significant impacts on local innovation.[90]
  - Danish patent applications to the European Patent Office increase 10% between 2017-2018.
  - Local employment increased (44,000 employees in 2017 a 3.4% increase from the year) before.
  - The quality of basic research has increased were the region's researchers are cited significantly more often than those outside of the region.[90]

CASE STUDY: SINGAPORE

CHANGES IN THE IP REGIME OF SINGAPORE

THE SINGAPORE PATENTS ACT (SPA), 1995

- Prior to the establishment of the SPA, the only way one could get patent protection in Singapore was by registering the corresponding United Kingdom or European patent.[91]

BIOMEDICAL SCIENCES INITIATIVE, 2000

- Launch of national Life Sciences strategy, with objective of becoming a leading drug discovery centre and the "biopolis of Asia". Singapore's Economic Development Board (EDB) and Singapore's Agency for Science, Technology and Research (A*Star) worked together to overcome challenges such as limited private investment and competition against larger regional rivals. Phase 1 (2000-05) was to develop foundation for basic biomedical research and Phase 2 (2006-2010) was to strengthen translational and clinical research. The Initiative is credited with Singapore's position as a hub for pharma innovation.[98]

ESTABLISHMENT OF IP COURTS, 2002

- Singapore created a specialized IP Court to handle increasingly complex IP cases.[96]

SINGAPORE-US FREE TRADE AGREEMENT, 2004

- Provided regulatory data exclusivity for 5 years, enforced linkage between patent status and marketing approval and provided ability of patent holders to limit parallel importation through licensing contracts.[94]

THE PATENTS (AMENDMENT) ACT, 2004

- Singapore permits an extension of term of up to 5 years for a patent which includes "any substance which is an active ingredient of any pharmaceutical product" if there was an "unreasonable curtailment", e.g. the delay between filing for marketing approval and the date marketing approval was obtained from the Health Services Authority must have been more than 2 years.[92,93]

INTELLECTUAL PROPERTY HUB MASTER PLAN TEN-YEAR PLAN, 2013 AND 2017

- Based on the recommendations of the Committee on Future Economy in 2017, the Intellectual Property Office of Singapore (IPSOS) updated the 2013 Plan to transform "ideas into assets" and provided billions in innovation funding. It also included the Intellectual Property Development Incentive ("IDI") to encourage the use of IP arising from R&D (an approved IDI company is eligible for a reduced corporate tax rate.[95,96]

RESEARCH, INNOVATION AND ENTERPRISE PLAN 5-YEAR PLAN, 2020

- The Singapore Government has committed to invest nearly US$2.4 billion over 5 years to advanced pharma development. The fourth and current phase (2016 - 2020) aims to focus on areas where Singapore has the potential to be internationally competitive, and to align R&D efforts with national healthcare strengths and needs to deliver on health and economic outcomes.[95,97]

Key

○ Changes to the IP regime

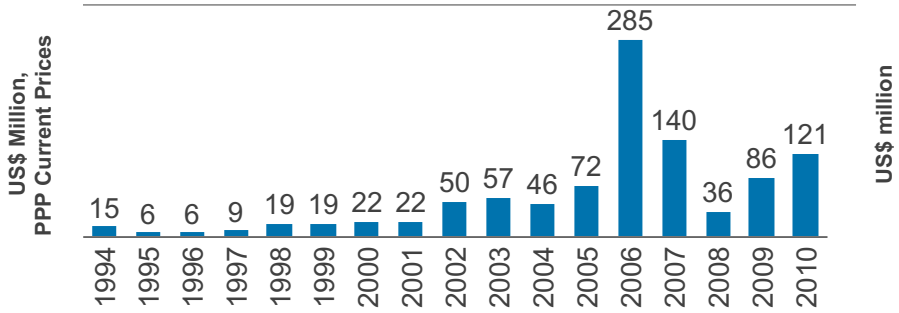
○ Changes to the Innovation Policy Landscape

★ NOTE – Regulation market with a star will be used as proxy for change in estimating growth differences

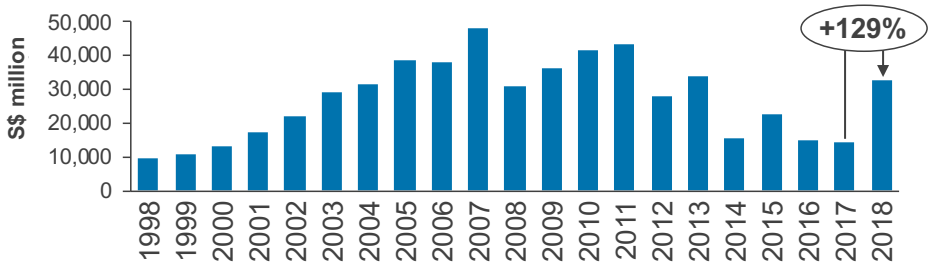
INVESTMENT IN R&D AND FDI

- The FDI in manufacturing sector grew by 22.0 per cent in 2018, and this is partially attributed to the strong growth in FDI in the manufacturing of pharmaceutical & biological products.[102]
- There are more than 65 different companies actively conducting biomedical R&D in Singapore and local Singaporean companies and research centres are investing in R&D.[103,104]
- S$4 billion in public sector research funding has been committed to the Health and Biomedical Sciences Domain.[104,105]

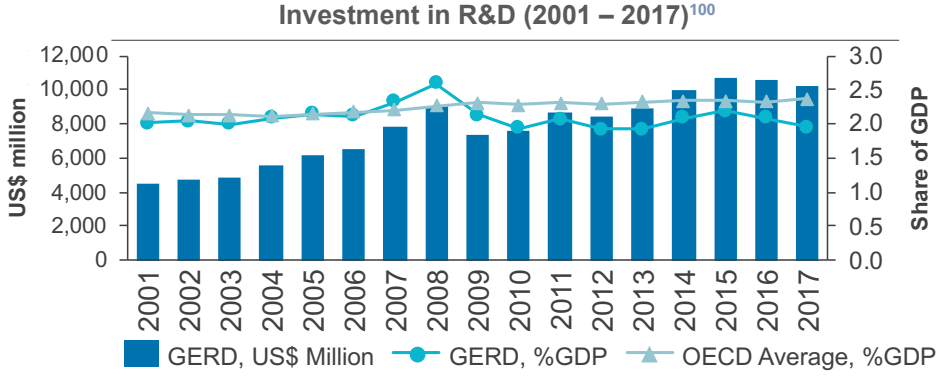
Pharmaceutical BERD (2012 – 2017, US$ Million, PPP)[99]



FDI Inflow in the Industry of Pharmaceutical & Biological Products (1998 – 2018, Millions of Singaporean Dollars)[101]



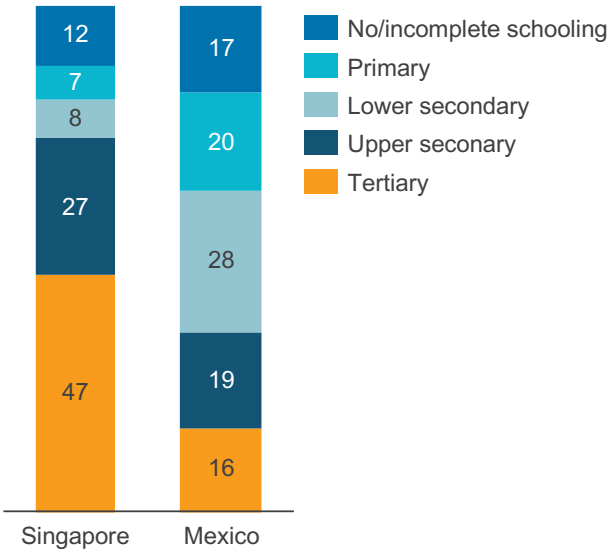
Investment in R&D (2001 – 2017)[100]



UNIVERSITIES AND QUALITY OF EDUCATION

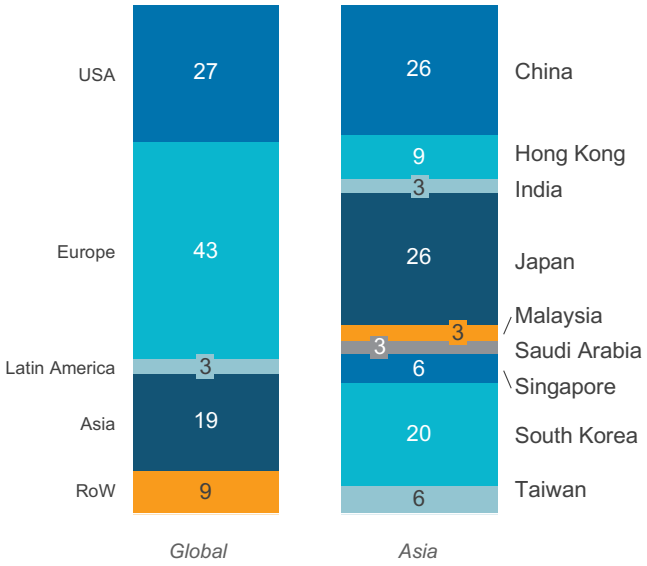
- Nearly half of the Singaporean population has attained tertiary level education and just over a quarter have at most, upper secondary education.
- Singapore makes up 6% of the Asian universities to be ranked in the top 200 for biological sciences in the world, comparable to Taiwan whilst Singapore is ranked 2nd in the world for the average PISA scores in science at 551, 62 points above the OECD average.

Educational attainment of 25+ yo, % of total population



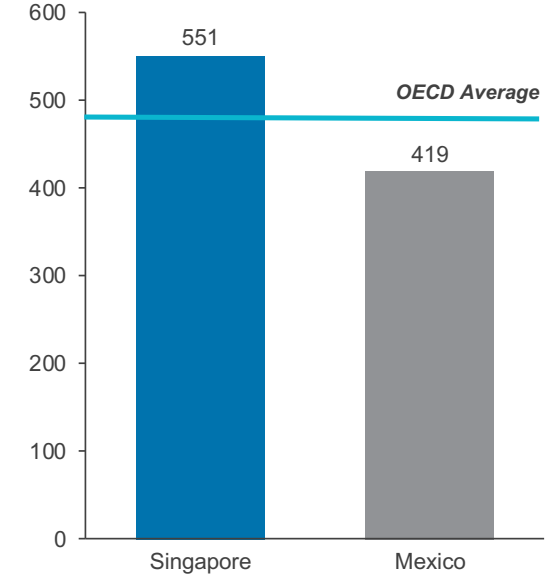
Source: OECD Data, 2018.

Universities in Top 200 Universities for Biological Sciences (2020, %)



Source: Top Universities, 2020.

Average PISA Score in Science (2018)



Source: OECD Data, 2018.

COLLABORATION AND INFRASTRUCTURE FOR RESEARCH

- Biopolis is the largest biomedical sciences cluster based in Singapore and was opened in October 2003. It is driven by 3 agencies Agency for Science, Technology & Research responsible for funding the public sector and academic research, Economic Development Board responsible for industry development plans and attracting international companies and Bio*One Capital responsible for strategic investments in companies to generate spin-offs.[106]
  - The 'plug and play' infrastructure gives companies access to advanced scientific equipment and also access to a centralised laboratory support service such as media preparation, lab supplies etc cutting R&D costs.
  - Within 2 years of opening, 90% of the space was occupied.
  - The Biolopis is also connected with the Academic Medical Centres to transfer knowledge from the bench to the bedside with phase 5 of the development completed in 2014 dedicated to pre-clinical trials.

Map of biotech/biomedical clusters

Source: Asia Pacific Biotech News.[106]

Pharmaceutical and biotech companies within Biopolis

International companies based in Biopolis (non-exhaustive)

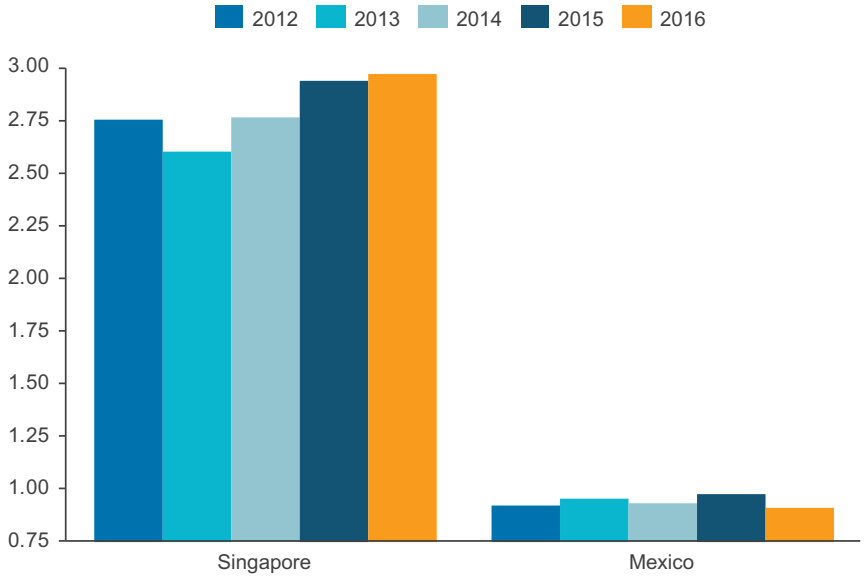
gsk NOVARTIS ES CELL INTERNATIONAL

Abbott Roche CHUGAI

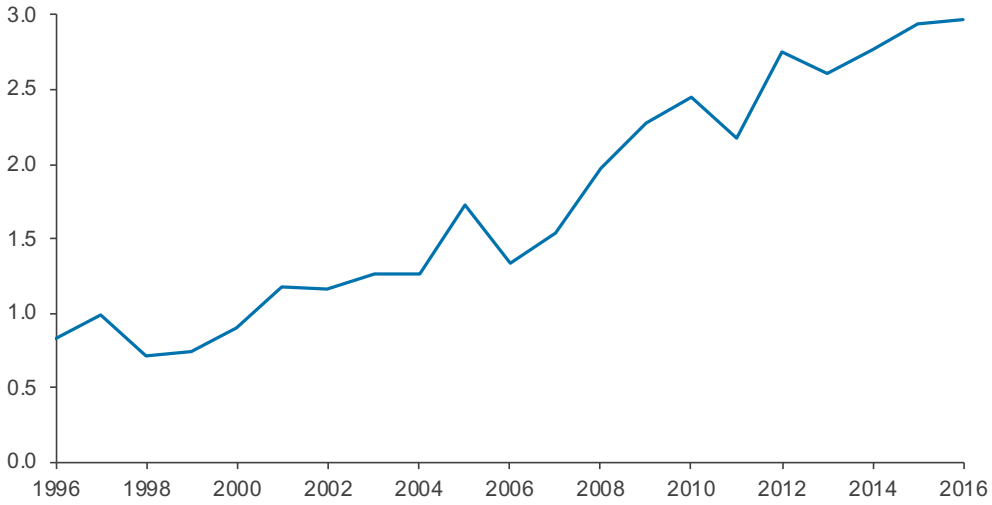
INNOVATIVE ACTIVITY: PUBLICATIONS

- The strength and influence of Singaporean publications have grown significantly and steadily, its share of Science and Engineering (S&E) publications in the top 1% most-cited articles in the Scopus database has tripled between 1996 and 2016.
- Singapore has been noted by the National Science Board as one of the 4 countries outside of the US and EU which has significantly grown its S&E publication output since 2006.[107]

Share of top 1% Most Cited S&E Publications in Scopus* (2012 – 2016)



Share of Singapore S&E publications in the top 1% most-cited in the Scopus database (1996 – 2016)

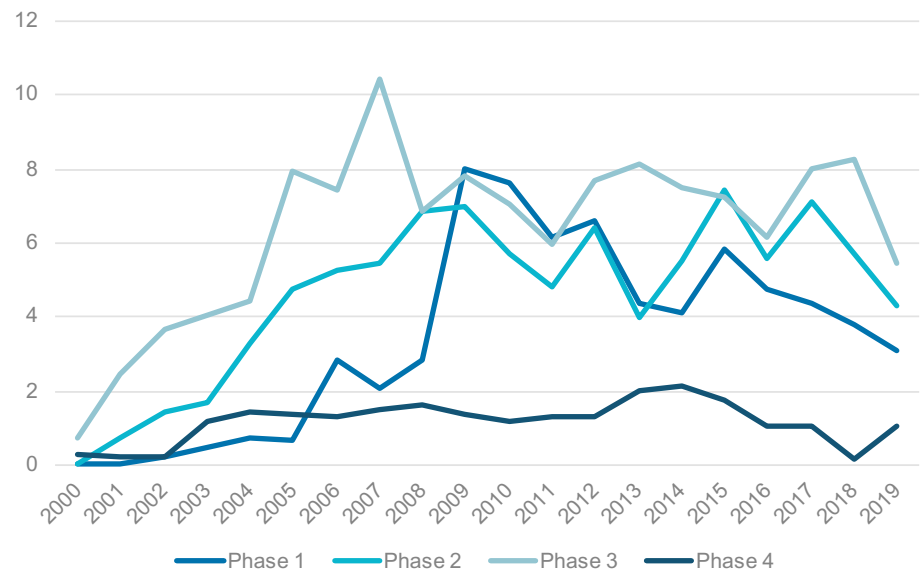


Sources: Scopus database; National Science Foundation Survey 2020.

INNOVATIVE ACTIVITY: CLINICAL TRIALS

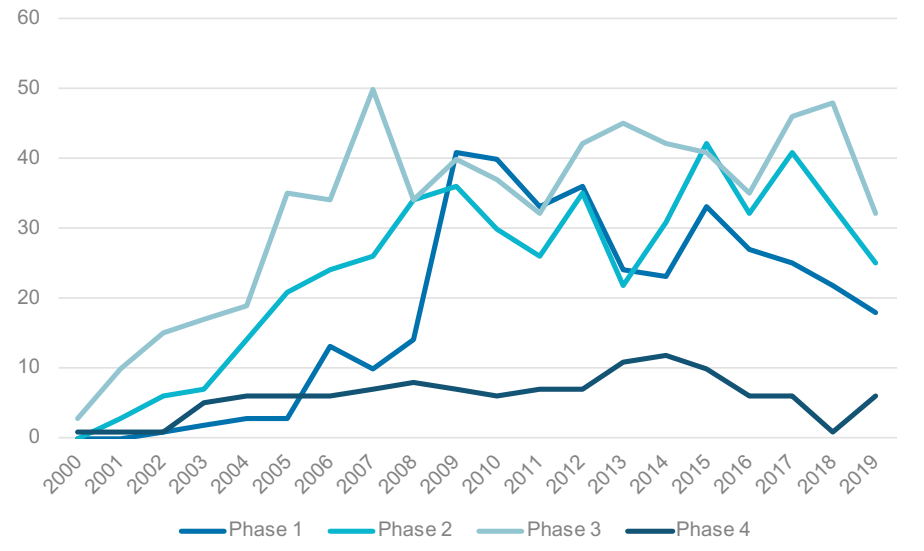
- The level of clinical trial activity has been fairly constant in Singapore since 2009. A significant growth in Phase 1 trials occurred between 2008 and 2009, whilst gradual growth in phase 3 trials occurred from 2000 to 2008.
- Singapore has the 2nd highest enrolled patients per population in Asia (1.20%) behind South Korea (2.30%), and the IP rights index has consistently ranked Singapore in the top 10 and the legal requirements in recruiting patients for clinical trials are minimal.[108]

Number of New Clinical Trials per 1M Population (2000 – 2019)



Source: Clinicaltrials.gov.

Absolute Number of New Clinical Trials (2000 – 2019)

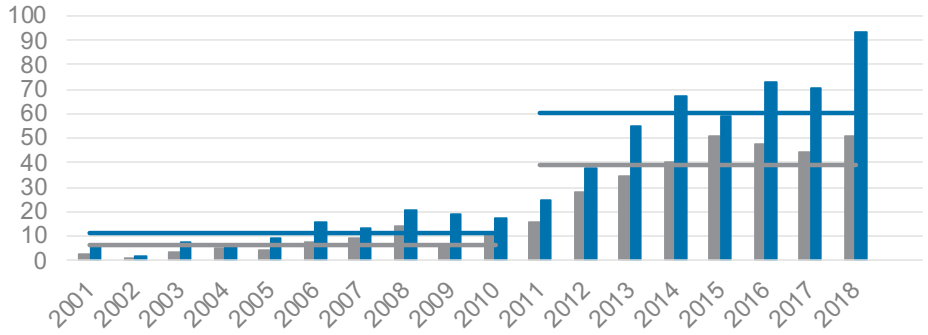


Source: Clinicaltrials.gov.

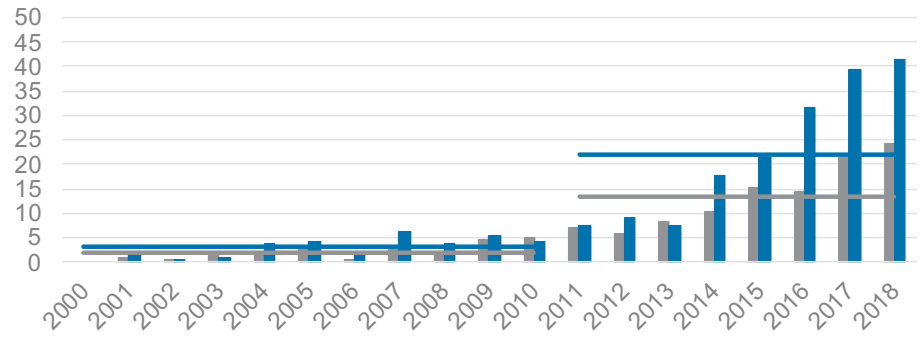
INNOVATIVE ACTIVITY: PATENTS

- Between 2006-2015, the percentage of annual filed patents applications with a Singaporean resident filed with Intellectual Property Office of Singapore increase from ~8 to ~14%.[110] However, in 2019 the number of local patent application was 12%.[111]
- Singapore's IP regime has consistently been ranked as one of the best in the world by international surveys. For example, in the World Economic Forum's Global Competitiveness Report 2017-2018, Singapore was ranked fourth in the world and top in Asia for having the best IP protection.[112]
- The business-friendly IP regime has attracted global pharmaceutical companies to select Singapore as their choice location for investments in business and research and development. Some of these companies have cited Singapore's strong protection of IP rights as one of the factors in their decision.[113]

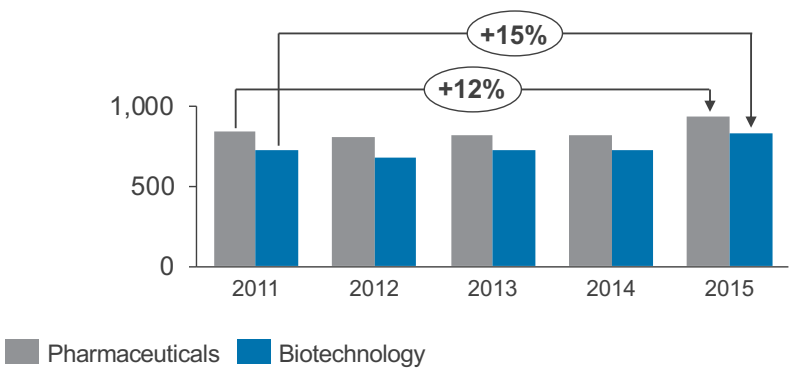
USPTO Pharmaceutical and Biotech patents granted to Singaporeans[109]



EPO Pharmaceutical and Biotech patents granted to Singaporeans[109]



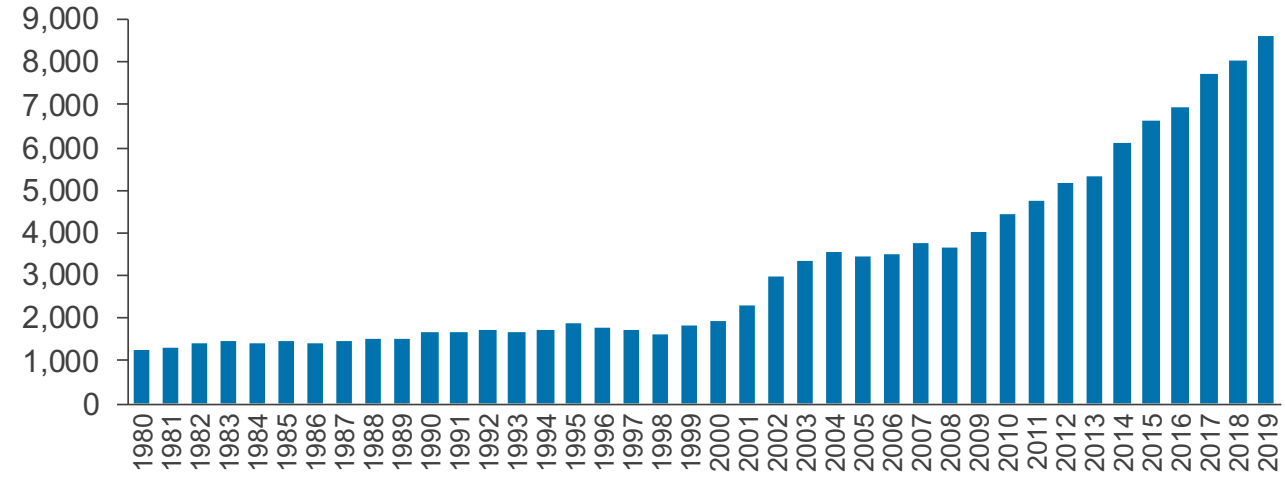
Filed patent applications at IPOS[110]



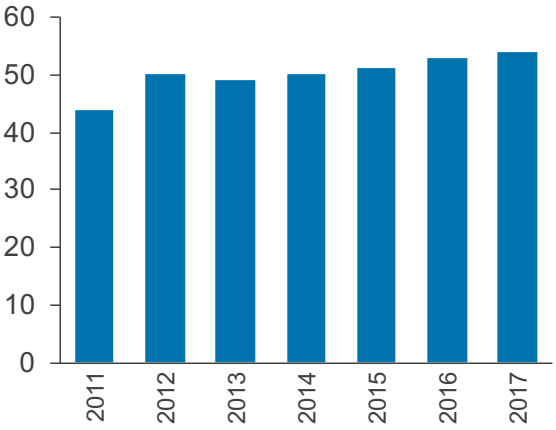
EMPLOYMENT IN THE BIOTECH SECTOR

- Singapore's pharmaceutical manufacturing was primarily imported; GSK established in Singapore in 1972 and in 2006-2007 there was a significant increase in foreign biopharmaceutical investment.[114]
- The number of pharmaceutical and biological manufacturing establishments increased by 23%, from 44 to 54, between 2011 and 2017. More than 6,000 people in the skilled workforce employed in the biopharmaceutical sector, more than double since the early 2000s.[114-116]
- The Attach and Train Programme for Biologics Manufacturing (AnT Biologics) is a manpower talent development programme aims at building up a pipeline of skilled manpower for Singapore's biologics manufacturing industry. This programme is jointly supported by the Workforce Singapore (WSG) and Singapore Polytechnic (SP).[117-119]

Workers in the Pharmaceuticals and Biological Products Manufacturing Industry[120,121]



Pharmaceuticals and Biological manufacturing establishments[120]



Aerial view of the Central Business District, Singapore, shutterstock.com/Travelpixs.

CASE STUDY:
APPLYING LESSONS FROM SINGAPORE TO MEXICO

Changes in the policy regime to support innovation

Enforcement of IP laws.

- After TRIPS, the US-Singapore Free Trade Agreement (USSFTA) has made the greatest impact on Singapore's IP laws.[124]
- The Patent Act and Medicines Act in Singapore was amended in 2004 to reflect the provisions of the USSFTA commitments. This included the introduction of provisions on patent linkage, data exclusivity and patent term extensions.[122]
  - Section 12A established **patent linkage** such that the Singapore Health Sciences Authority (HSA), the licensing authority for medicine products now also licenses pharmaceutical products. The section also provides additional protection to the patent holder as an application from a non-originator applicant triggers a notice period for the patent holder to obtain a court order to block the licencing. If the patent holder fails to obtain a court order in the notice period, then the HAS will grant a licence to the non-originator applicant.[123] This mimics the Hatch-Waxman amendment in the US patent system.
  - Section 12A also establishes **data exclusivity** to the originator in two ways. First, the licencing authority has the obligation to protect the data and second, the authority will not use such information to grant another application. The protection period is 5 years from the date the product application was received by the licencing authority.[123]
  - Section 36A allowed a patent originator proprietor to apply for a **patent term extension** providing that there was unreasonable delay in granting the patent and the patent includes an active ingredient of any pharmaceutical product.[125] However, despite this technical improvement to Singapore's IPR, the PhRMA 301 report does note that the legislation artificially limits the extension to the registration period in Singapore (even if the registration relies on clinical trials outside of Singapore).[126,127]
  - More recently, Singapore passed the IP Dispute Resolution Act to introduce new provisions to facilitate more efficient patent resolutions. This included the implementation of a specialist IP litigation system enabling the High Court to handle all litigation disputes as a fast track option.[128]

Impact of changes in the policy regime on innovation activity

- Since the USSFTA agreement in 2004, pharmaceutical imports from Singapore to the US rose dramatically from $0.09 billion in 2003 to $2.4 billion in 2006. The FTA did not lower the US tariff rate for pharmaceuticals but instead, multinational pharmaceutical companies increased their local footprint and operations in Singapore allowing the country to develop as a regional centre.[129]
- As the regional headquarters for many global pharmaceutical companies, between 2004-2013, pharmaceutical applications made up the largest proportion of patent applications in Singapore.[130]
- Almost 90% of the patent applications filed in Singapore are through foreign applicants. The majority of patents filed between 2009-2013 and the majority were in arthritis disease and cancer contributed by major pharmaceutical companies Merck, Novartis, Roche etc.[130]
- The number of patent publications in the field of pharmaceuticals, biotechnology and medical technology has increased significantly from 4.8% of publications in 2005 to 19.9% in 2015.[130]
- With the reform to the IP Dispute Resolution Act in 2019, it has reinforced Singapore's role as an international hub for arbitration[131] with Singapore consistently ranking highly on global IP rankings including World Economic Forum's Global Competitiveness Report 2019 (2nd in the world).[132]

Main expected effects of policy change

- Following the USSFTA, the Singaporean government implemented provisions in the local law to reflect the FTA provisions including the strengthened patent enforcement and provisions related to data exclusivity. This created assurance for multinational companies to choose Singapore as a location to develop local manufacturing and research centres and developments have been observed in the increase in the number of patents and clinical trials as well as recognition as a global hub for IP arbitration.[130]

IMPACTS ON INNOVATION FROM POLICY CHANGE IN ADDITIONAL ASIAN MARKETS: CHINA, JAPAN, SOUTH KOREA AND TAIWAN

CASE STUDY: CHINA

Changes in the policy regime to support innovation

Pro-innovation policies:

- China's drug R&D evolution can be viewed to have four phases, as: (l) pure imitation (1949 - 1984), (2) innovative imitation(1985 - 1993), (3) imitative innovation (1993 - 2008), and (4) independent innovation (2008-present).[133] In 2008, the Chinese State Council issued "National Intellectual Property Strategy Compendium", asserting that China would be transformed into a country with high level of creating, utilizing, protecting and administrating intellectual properties by 2020. This is the first time the Chinese government included the concept of innovation in its national development strategy.

- This strategy provided a comprehensive plan to improve the protection and management of intellectual property rights while emphasising the need for active development of independent or self-controlled intellectual property.[134] Literature notes that the National IP Strategy was significant in increasing the priority of IP on the national agenda.[135]

- The China Pharmaceutical Innovation and Research Development Association find that where Chinese companies used to focus on generics, they have more recently been building up R&D capabilities to invest in innovative drugs.[136] From 1949 to 2008, less than five domestically developed drugs were approved by Chinese authorities, while from 2008 to 2018, the number increased by about 10 times to about 40.

Impact of changes in the policy regime on innovation activity

Partnerships, local R&D and patents.

- Zhang et al. (2018) link the strengthening of IP in China to the rise of MNCs' R&D activity in China. In addition, the authors find that MNCs in China are moving from coordinating global R&D projects to increasingly focusing on localized product development.[137]
- Hu and Jefferson (2009) find that China's growth in patent applications from the late 1990s was in part driven by amendments to national Patent Law that include mechanisms to better enforce patent rights.[138]

R&D Investment and FDI:

- Park and Lippoldt (2008) showed that stronger IPRs in developing countries including China are associated with an increase of technology-intensive FDI.[139] Fang et al. (2015) also find that strengthening IP protection in China has led to increased private R&D investment.[140]
- Awokuse and Yin (2008) study the relationship of IPR protection in China to FDI inflows, and conclude that IPR reforms in China have had a positive and significant effect on inbound FDI, and this effect is more pronounced in knowledge-intensive sectors such as pharmaceuticals.[141] The authors find that pharmaceutical market expansion in China was more significant in the early 1990s as China began to strengthen it's patent laws. Separately, Maskus (2001) finds that the strengthening of IP following China's recognition of TRIPS Agreement led to increased high-tech imports and FDI.[142]

Main expected effects of policy change

- Pro-innovation policies are expected to lead to increased patent applications, R&D investment and partnerships.

CASE STUDY:
JAPAN AND SOUTH KOREA

Changes in the policy regime to support innovation

RDP for pharmaceuticals in Japan

- Japan also provides de facto RDP through PMS. Originally introduced in 1979 with only 2 years, data exclusivity was most recently extended to 8 years for new medicines in 2007 by the Pharmaceutical and Food Safety Bureau (PFSB) at the Ministry of Health, Labour and Welfare (MHLW).[144]
- When a novel drug is approved, it is subject to re-examination. This re-examination period or PMS period of 8 years prevents any applicant of a generic product from relying on the originator's clinical trial data and applying to marketing authorisation, until the re-examination period for the original (innovator) drug expires. This has an equivalent effect to RDP.[144]

RDP for pharmaceuticals in South Korea

- The Korean Pharmaceutical Affairs Act was amended in 1995 to provide a de-factor 4 or 6 year data protection for new drugs and certain prescription drugs.[143]
- Although not officially RDP, this Amendment provides data exclusivity through Post-Marketing Surveillance (PMS). Before the expiry of the PMS period, no generic applicant can rely on the clinical trial data of the reference product unless data is significantly different or exceeds the scope of data submitted first approval.[143]
- This was to meet the requests from the United States, EU, and Japan to extend the patent for 'pipeline' products.[143]

Patent Linkage in South Korea

- Between 2012 and 2015, the South Korean Patent-Approval Linkage System was introduced and implemented in response to Article 18.9 of Korea-US Free Trade Agreement.
- The South Korean patent linkage system was built based on that under the US Hatch-Waxman Act. For example, the Ministry of Food and Drug Safety constructed a patent database called the Green List, similar to the Orange Book in the US.
- However, the South Korean system further modified other patent linkage provisions of Hatch–Waxman to promote generic pharmaceutical competition.

Impact of changes in the policy regime on innovation activity

Impact of RDP provisions.

- Kyle et al (2015) observe that changes to this national focus on IP started well before the new millennium.
- "Once the Korean government began to recognize and grant patents on substances in 1987, pharmaceutical companies could no longer produce active substances without patent permissions. This situation led them to realize that the key to survival was the development of new drugs, which in turn opened their eyes to the central importance of R&D investment."[145]
- This departure from a 'copy-cat' economy launched Korea into an innovation spree with one national science and technology plan being completed by the turn of the millennium and two additional planned (one launched) by 2008. Between 2007 and 2017, the Korean pharmaceutical industry developed and successfully launched 17 innovative drugs. In addition, South Korea demonstrated a 14% increase in the number of trials over the second time period (2011–2012) while exhibiting a decline in site numbers, suggesting an improvement in efficiency, as new medicines were increasingly trialled.[146]
- In Japan, the number of new drug approvals by PDMA declined by 13% in 2000-2008. Whereby RDP was introduced in 2007, the number of new drug approvals grew by 37% between 2009-2018.[147]
- Diminished patent protection will reduce innovative desire to develop new and potentially better drugs and treatments, which in turn could result in the use of more expensive treatments. This effect could be exacerbated by increasing research costs.[148]
- In the US, the Hatch-Waxman Act which first established RDP, was found to lead to increased pharmaceutical R&D funding and R&D intensity[149] and at least 26 drugs with novel active compounds were launched between 1986- 2014, protected by this Act rather than a patent.[150]
- RDP provides an incentive for the introduction o new innovations and once period exclusivity ends, a growth in generic medicines.
- **Analysis of OECD data from Japan (and Canada) find that pharmaceutical spending as a share of GDP did not increase following extensions to local RDP provisions.**
- **Examination of orphan drug clinical trials highlights a significant increase in trials after the extension of de facto RDP in Japan in 2007.**

Impact of changes in the policy regime on innovation activity

Impact of patent linkage system

- The patent linkage system in South Korea was implemented to encourage drug development and R&D investment in order to facilitate South Korean companies to gain a foothold in the world market.[151] Following the implementation of the patent linkage system in 2015, patent litigations occurred much sooner and studies suggest the linkage system encouraged patent challenges without reducing the effective market exclusivity of patented products.[152]
- It was also expected that the linkage system will lead to greater predictability in terms of how drugs are approved and sold, and that more and earlier information will be provided to patentees about prospective generics companies and their patent challenges for more efficient strategy planning. Greater harmonisation with international standards should lead to greater predictability for foreign pharmaceutical companies seeking to pursue IP rights in South Korea.[153]

Main expected effects of policy change

- Implementation of RDP leads increased clinical trials and product development since innovators feel secure that their R&D efforts are protected without increasing pharmaceutical spending and hindering efforts towards universal access to medicines.

CASE STUDY: TAIWAN

Changes in the policy regime to support innovation

Impact of patent linkage system and RDP enforcement.

- The Pharmaceutical Affairs Act was amended in 2017 to harmonise the generic approval process with international norms including data exclusivity and patent linkage. The system is very similar to the Hatch-Watchman Act governing US generic approvals.[154] Taiwan recognised that
  - 5 years of data exclusivity for drug approvals containing new ingredients and 3 years for drug approvals of new indications was enacted in 2018.[155]
  - A patent linkage system was established in 2019 for resolving disputes related to listed patents between the generic applicant and original marketing approval holder.[154]
- Efforts towards establishing the patent linkage system stems from the governments willingness to participate in international trade agreements but also secure future growth by fostering innovation-intensive industry including biopharmaceuticals.[156]

Impact of changes in the policy regime on innovation activity

- President Ing-Wen's has expressed a clear vision of developing Taiwan as a biotech research hub in Asia. The number of clinical trials and also biopharma companies have steadily increased. The sector grew from US$6 billion in 2009 to 22 billion in 2015.[157]
- Between 2003 and 2016, there were growing numbers of domestic patent assignees highlighting that the local industry has increasing awareness on the importance of IP protection.[158]

Main expected effects of policy change

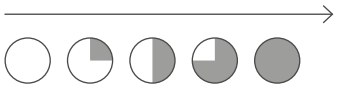
- It may be too early to observe the impact of the amendments to the Pharmaceutical Affairs Act, as the patent linkage system only came into effect in August 2019 and the includes biological drugs.[159] This is likely to have an impact on the number of patents filed in Taiwan, particularly for innovative medicines particularly when the amendment to data exclusivity now includes protection for new indications.

IMPACT ATTRIBUTABLE TO THE CHANGE IN REGULATION IN A 5-YEAR PERIOD: SUMMARY (2/1)

	DENMARK	SINGAPORE	SOUTH KOREA
KEY INNOVATION POLICY CHANGES	Globalization Strategy, "Denmark – Building on Tradition" 2006.	Biomedical Sciences Initiative, 2000.	"Bio-Vision 2016" Plan of 2007 "577 Initiative" of 2008.
KEY IP REGULATION CHANGES	Act on Inventions at Public Research Institutions, 2000.	Singapore-US Free Trade agreement, 2004.	Pharmaceutical Affairs Act of 2007: Grant of RDP.
OTHER KEY REGULATION CHANGES	Technology Transfer Offices, 2000.	Establishment of IP courts, 2002.	Dosage patent decision 2015.

		Growth	Attributable to regulation	Growth	Attributable to regulation	Growth	Attributable to regulation
Innovative Activity	BERD / GERD	3%		70%		11%	
	Early research (publications)	7%		4%		4%	
	Clinical trials (All)	4%		7%		7%	
	Patents (local residents)	0%		4%		25%	
	Patents (local non-residents)					16%	
	Patents (USPTO)	17%		22%		29%	
Economic Activity	Employment in biopharma-ceuticals	3%		6%		7%	

Impact of the regulation



IMPACT ATTRIBUTABLE TO THE CHANGE IN REGULATION IN A 5-YEAR PERIOD: SUMMARY (2/2)

	TAIWAN	CHINA	JAPAN
KEY INNOVATION POLICY CHANGES	Biotech and New Pharmaceutical Development Act (2007).	Program for Science and Technology Development (2006).	Science & Technology Basic Plan (1996 – 2016).
KEY IP REGULATION CHANGES	Revision of Pharmaceutical Affairs Law (2005): Grant of RDP.	Regulatory Data Protection (RDP) (2001).	Notice extending the RDP term (2007).
OTHER KEY REGULATION CHANGES	Backlog Reduction Program, 2010-2017.	National Intellectual Property Strategy (2008).	Policies targeted at the patent backlog (2004 – 2007).

		Growth	Attributable to regulation	Growth	Attributable to regulation	Growth	Attributable to regulation
Innovative Activity	BERD	14%		26%		4%	
	Early research (publications)	4%		12%		-1%	N/A
	Clinical trials (All)	17%		16%		-3%	N/A
	Patents (local residents)	23%		35%		0.6%	
	Patents (local non-residents)	11%					
	Patents (USPTO)	20%		-2%	N/A	-31%	N/A
Economic Activity	Employment in biopharma-ceuticals	8%		17%		-1%	N/A

Impact of the regulation →

4.

Innovation policy implications for Mexico

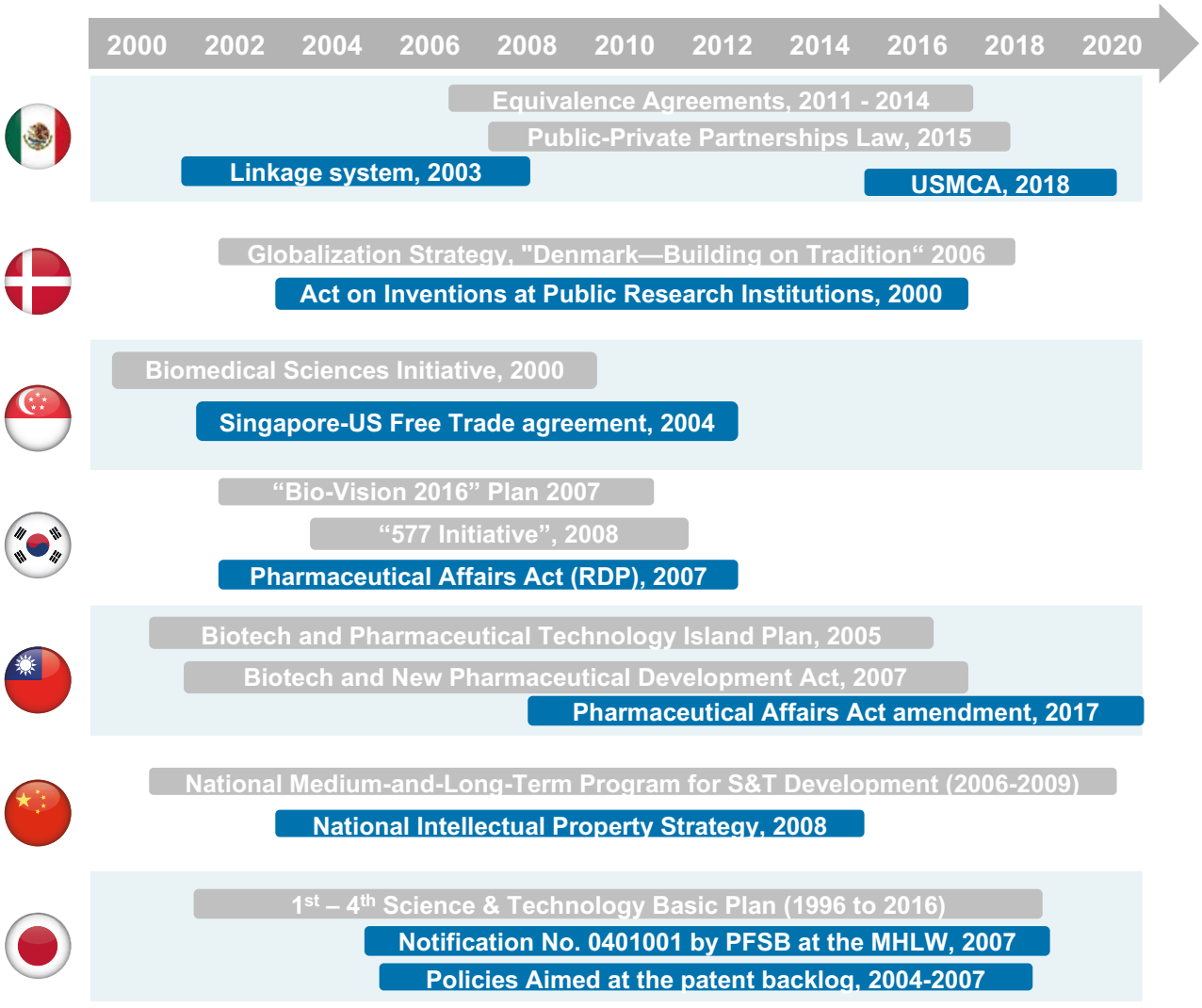
WHAT IF MEXICO CONTINUES ON A POSITIVE TRAJECTORY OF INNOVATION FRIENDLY ENVIRONMENT?

Support for IP and innovation in biopharma:

- Mexico has recently instituted policies that are more favourable to the growth of the local biopharmaceutical industry, particularly the enactment of the USMCA and the new Industrial Property Law.
- Through the **new Industrial Property Law**, which was approved by the Senate in June 2020:
  - The IP infringement resolutions will be improved.
  - Patent term adjustment will be introduced.
  - Regulatory data protection will be extended.
  - The Linkage system will be improved further.

Additional support for IP :

- However, compared to other case study markets, Mexico lags behind on proper enforcement of legislation and in fostering private-public partnerships.



APPROACH TO DEVELOPING GAINS IN THE FOUR SCENARIOS

- In order to assess potential gains from an improvement in the enablers of innovation we apply the following approach:
  - ***Step 1,*** we take as baseline the level of innovative activity per indicator Mexico for the latest available year, assuming Mexico remained on the positive path and improved IP and innovation policy changes.
  - ***Step 2,*** we apply the average growth rates for the 5 year period prior to the baseline year assuming constant growth.
  - ***Step 3,*** finally, we apply growth scenarios from case study countries, where positive changes in the IP and innovation regime were introduced.
- We apply the methodology to four indicators of innovative and economic activity including: publications, clinical trials, patents, employment in the biopharmaceutical sector.

SCENARIOS: DEVELOPING SCENARIOS ON IMPACT ON STRENGTHENING IP REGIME AND INNOVATION POLICY

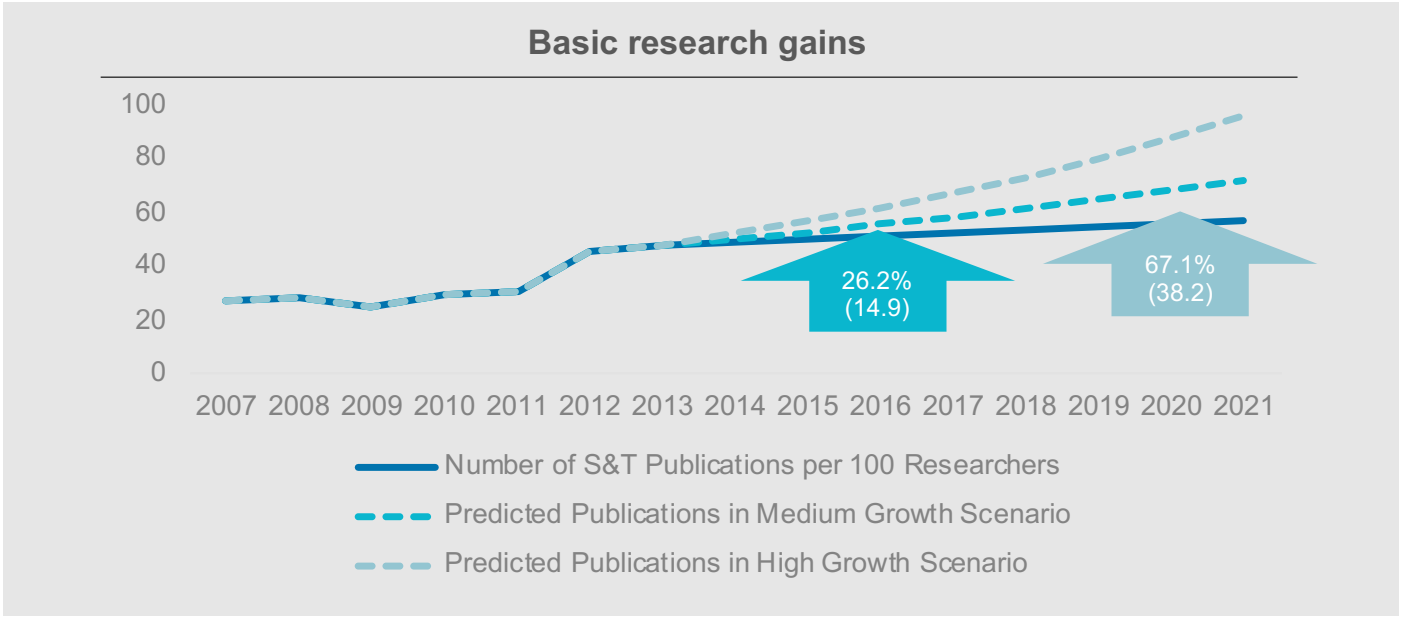
Drawing from the case study analysis and the statistical analysis, we establish two scenarios:

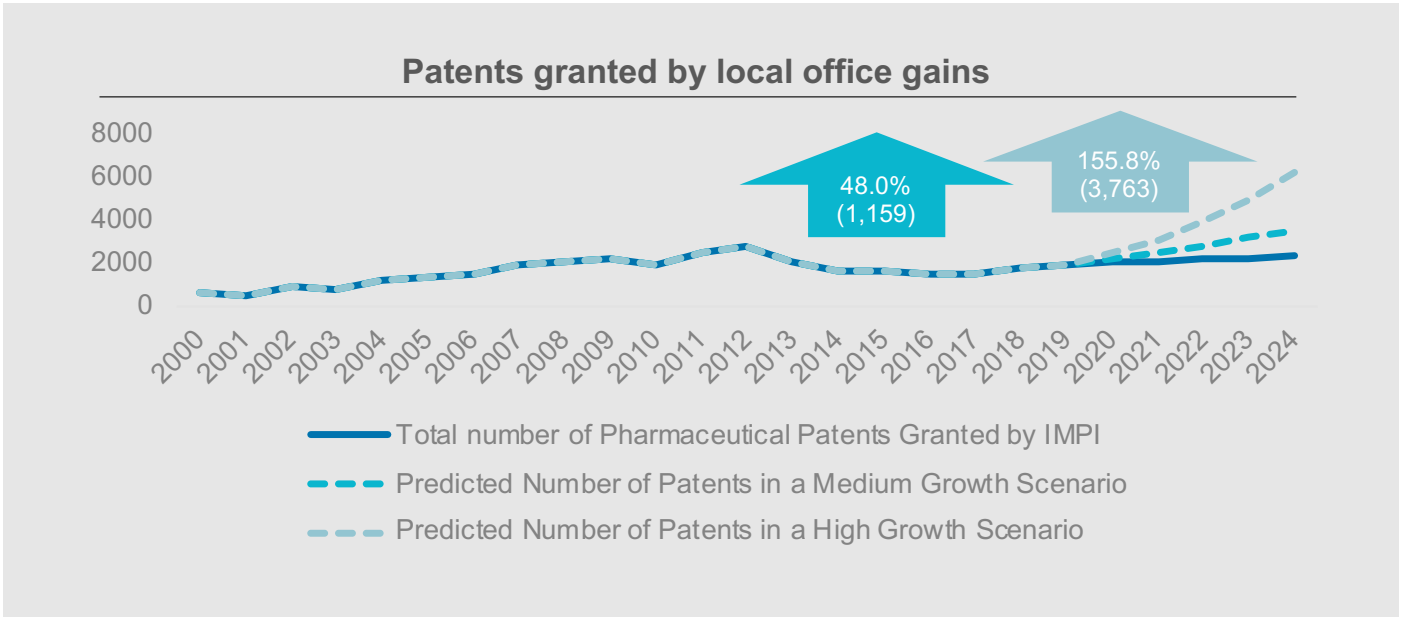
- A scenario assuming an IP regime change in conjunction with other innovation policies (medium growth due to limited implementation).
- A scenario assuming an IP regime change in conjunction with other innovation policies (high growth with good policy implementation).

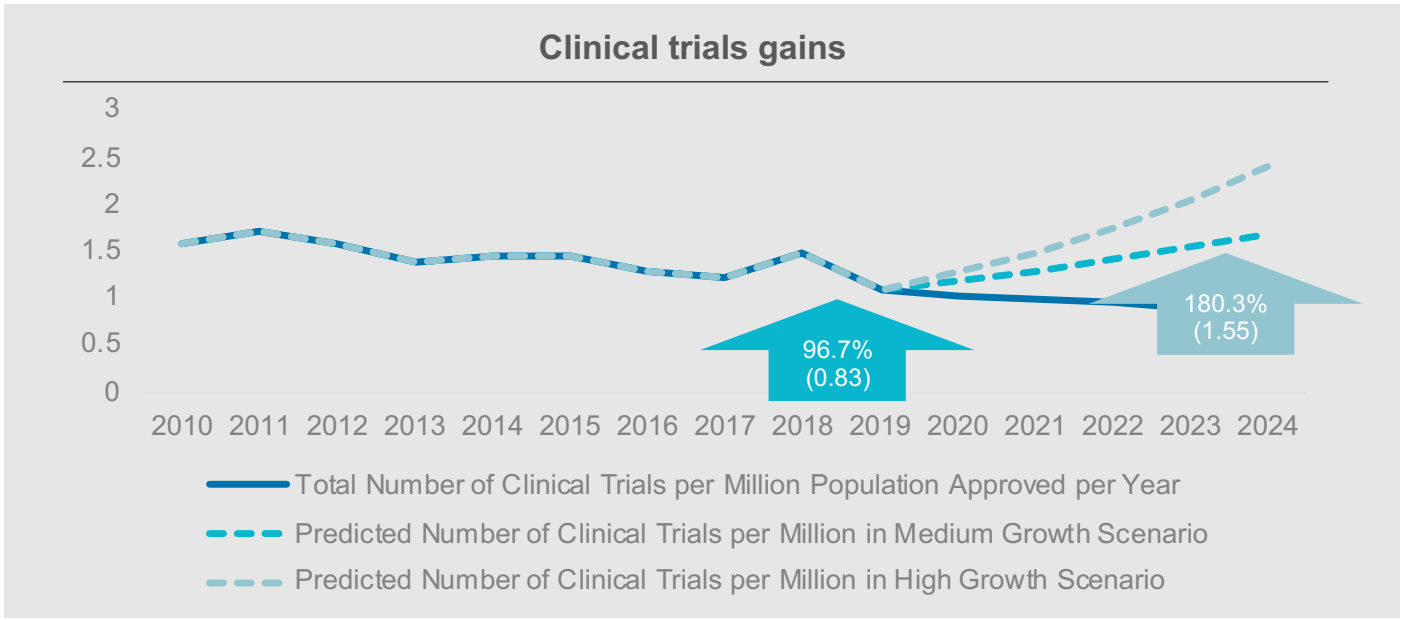
	SCENARIO DETAILS	BASIC RESEARCH	CLINICAL TRIALS	PATENTS	EMPLOYMENT
IP REGIME AND INNOVATION POLICY – MID GROWTH	Paced growth scenario based on an improvement of the IP regime (for example, by improving RDP and patent enforcement) and other innovation incentives but with limitations in implementation (based on case study markets analysis).	Average annual year on year growth of S&E publications in the top 1% most-cited in the Scopus database of 5%.	Average annual number of clinical trials of 9%.	Average annual year on year growth in pharmaceutical patents of 12%.	Average annual year on year growth in employment in the biopharmaceutical industry 7%.
IP REGIME AND INNOVATION POLICY – HIGH GROWTH	Escalated growth scenario based on an improvement of the IP regime (for example, by improving RDP and patent enforcement) and other innovation incentives with good implementation (based on case study markets analysis).	Average annual year on year growth of S&E publications in the top 1% most-cited in the Scopus database of 9% (China).	Average annual number of clinical trials of 17% (Taiwan).	Average annual year on year growth in pharmaceutical patents of 25% (South Korea).	Average annual year on year growth in employment in the biopharmaceutical industry 17% (China).

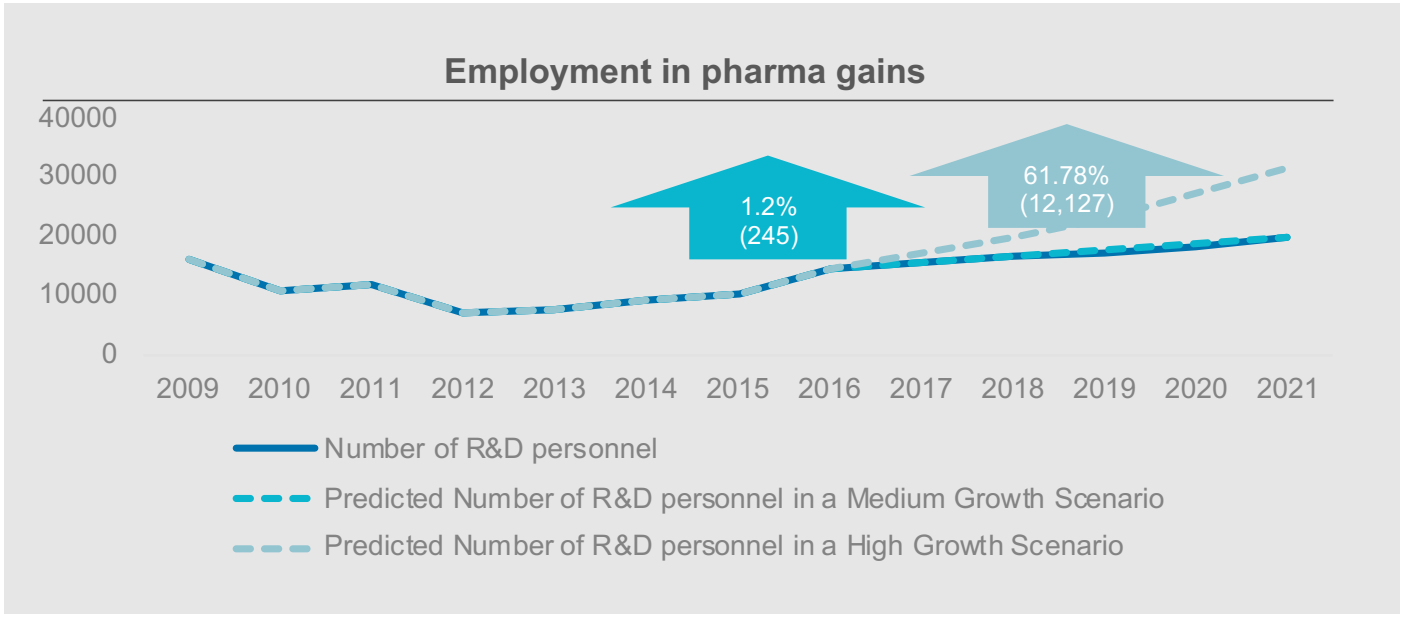
- *Mexico's medium growth scenario represents the average growth scenario of China, Denmark, Japan, Singapore, South Korea and Taiwan
- Mexico's high growth scenario represents the highest growth scenario out of the relevant case studies for the particular metric of innovation output, outlined on page 52:
  - Basic research and Employment, the relevant case study markets are China and Denmark;
  - Clinical trials, the relevant case study markets are Japan, Singapore, South Korea and Taiwan;
  - Patents the relevant case study markets are Singapore, South Korea and Taiwan.

SCENARIO ANALYSIS ACROSS INNOVATIVE AND ECONOMIC ACTIVITY IN MEXICO: ABSOLUTE GAINS AND GROWTH POTENTIAL (ON AVERAGE)







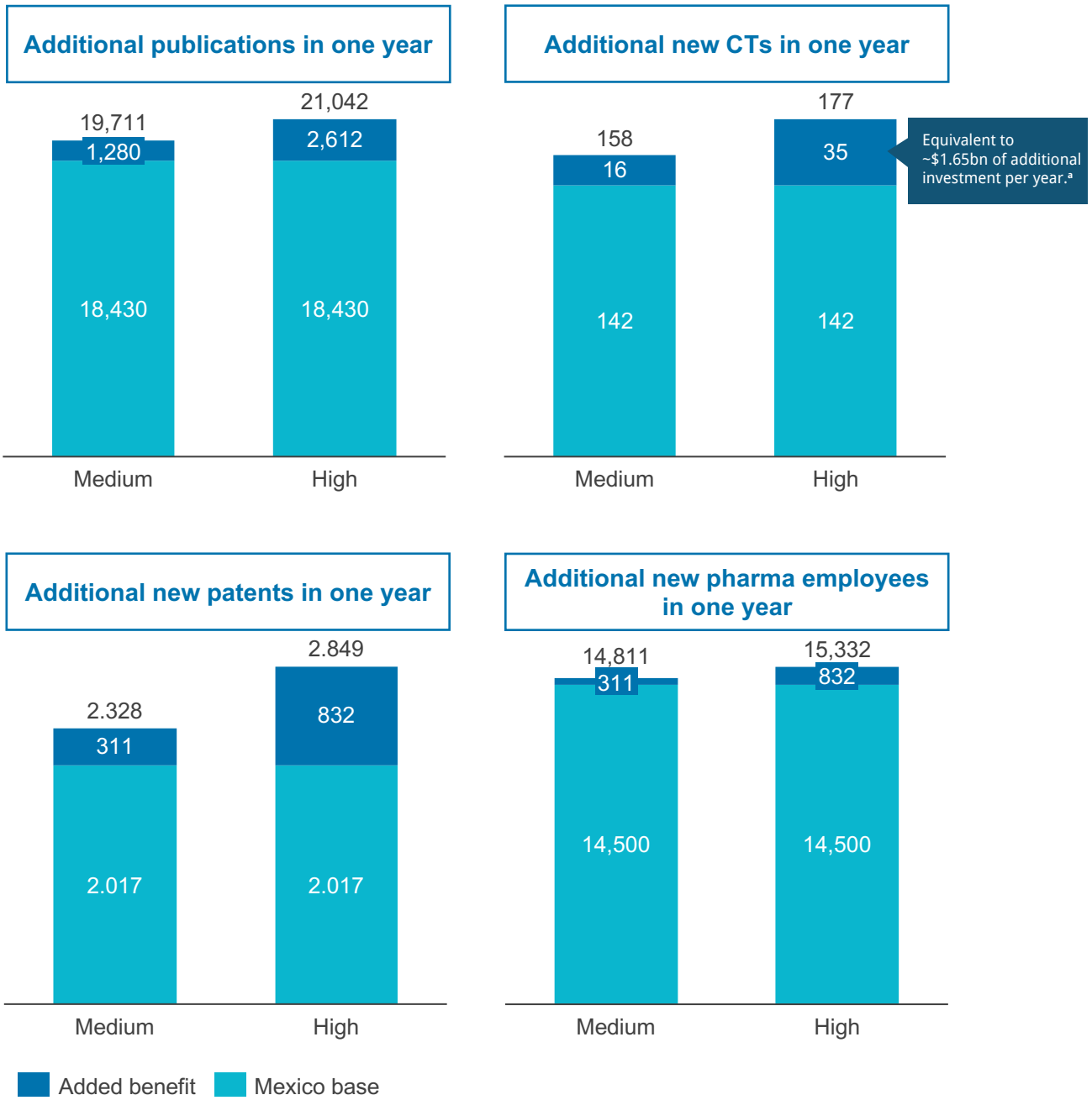


Note:
The number of employees in the pharmaceutical industry was estimated based on the number of R&D personnel.
The employment ratio of pharmaceutical to total knowledge intensive industries is assumed constant throughout the years.

ILLUSTRATION OF GAINS FOR MEXICO (ABSOLUTE GAINS)

Drawing from the findings in the analysis, strengthening the IP environment in Mexico would lead to:

- ***Significant gains*** in areas such as clinical trials (that are strongly impacted by the level of protection of data generated), patents granted (with the most direct impact from IP rules) and employment (with most direct impact from improvement in innovation policies).
- ***Moderate gains*** in biological publications (are expected to be indirectly impacted by IP and Innovation regime changes).



[a] Note: The cost of CT development in Mexico is estimated to be 30% of that of the costs in the US.[160]

FINDINGS

1. Mexico's current innovation capacity and potential.

Mexico has many of the factors required to be successful in encouraging biopharmaceutical innovation.

- This includes: a skilled workforce; a large, treatment-naïve population; strategic placement next to the US and established treaties to attract foreign investment.
- The market has also developed a relatively comprehensive IPR framework, a strong foundation in academic research and several regional innovation clusters.

There is room for improvement however when compared to OECD and Asia markets in many innovation activities.

- There are several weaknesses in Mexico's innovation framework : Weak enforcement of existing IP legislation; the bifurcated IP infringement resolution system; loopholes which allows for IPR infringement to be exploited and create uncertainty for innovative industry.
- Additionally, patent linkage is applied inconsistently and there is a lack of regulatory data protection. Although both of these IP regime limitations have the potential to be addressed through the new Industrial Property Law, the extent to which the Law will be implemented effectively remains unclear.
- Further delay to effective improvement of the IP framework risks Mexico's innovation environment lagging behind other Latin American markets (who are strengthening their IP frameworks).

Gaps in Mexico's innovation framework have constrained innovative activity in Mexico, especially in terms of lower basic research, clinical trial activity, patent filings and employment.

- University regulations prevent researchers from collaborating with the private industry and the private industry is not provided with sufficient incentives to partner with the public industry.
- There is limited research funds available and public funds are not allocated on the basis of commercialisation potential.
- Furthermore, there is a limited number of Technology Transfer Offices across the country, resulting in only a few patents being commercialised.

2. Implications for Mexico's innovation and economic policy.

Immediate need for enforcement of IP laws with a "do no harm" approach.

- Mexico has made several recent efforts to strengthen it's IP environment such as through the USMCA (October 2018) and the new Industrial Property Law (July 2020). However implementing regulations are lacking. Lessons from Singapore highlight how amendments to local law created the assurance for multinational companies to choose Singapore as a location for innovation.
- There is immediate need for Mexico to implement legal rules to enforce it's commitment to the USMCA. The government has already set a precedent for capitalizing on the USMCA's transition period by implementing early provisions related to the Agreement's copyright and trademark commitments. Mexico should avoid repeating the failure to implement RDP following ratification of NAFTA.
- In addition, the government should ensure an informed, "do no harm" approach to implementation and consider the true objectives of the IP law to avoid any negative unintended consequences on the incentives to innovate.

Regulatory Data Protection.

- Since 1994, under NAFTA and now through the UMSCMA Mexico has the legal foundation to provide RDP however COFEPRIS has failed to implement any associated legal instruments. Findings from comparable Asian markets reveal the benefits of strong protection for clinical trial test data. The Singapore-US Free Trade agreement was the impetus for updates to Singapore's IP framework including the implementation of RDP and the enforcement of patient linkage and Bolar exemption through the Patent Act. New pharma investment in Singapore has since been linked to these updates to IPR.
- Mexico should ensure implementing legislation to recognise RDP for biologics and new formulations and indications. Mexico could amend the IP Law or include a provision in the national Health Law, to domestically implement legislative or regulatory measures on RDP.

Encourage system of communication between COFEPRIS, IMPI and industry and implementation of patent linkage.

- Interviews with experts revealed poor communication between COFEPRIS, industry and IMPI have led to delays in clinical trial approval, poor enforcement of patent linkage and sparse communication with industry.
- Lessons from Singapore and Denmark highlight how organisations and platforms which aim to improve communication between innovation stakeholders can facilitate technology transfer. In addition, Taiwan and South Korea implemented local laws to enforce patent linkage and improve communication between the national health and patent authorities.
- In Mexico, the expanded Patent Linkage system, as per the new IP Law, enhances the communication between COFEPRIS and IMPI and will signal to industry that patents are being protected. However secondary implementing regulations are still required to ensure legal certainty and to adopt measures introduced by the USMCA allowing the participation of the involved parties in the Patent Linkage system to provide arguments supporting their interests, trough a non adversarial proceeding.

Creation of an environment that provides legal certainty for collaboration and tech transfer.

- Mexico's population have a strong skill-set however academics lack the opportunity to partner with industry and the incentive (e.g. licensing, royalties) to commercialise patents. However, some universities are starting to recognize the value of innovation e.g. the University of Monterrey. Denmark was once in a similar position. The Danish government made a concerted effort to foster collaboration between industry and academia, and an environment of legal certainty around innovation through incentives, grants and knowledge sharing platforms to support pharma innovation.
- In the same vein, the Mexican Federal government could encourage the amendment of university regulations to foster private-public partnerships, allocate public funds on the basis of the commercial potential of the research and amend the Science and Technology Law to align stakeholders' research objectives and signal government's commitment to innovation.

Government prioritization of innovation.

- The Mexican Federal government's austerity measures from last recession have already reduced federal funding for innovation and future reliance on cost-cutting measures may exacerbate this trend as a result of the COVID-19 pandemic. However some States remain committed to innovation, such as the State of Jalisco, which has been investing in increasing capacity for pharmaceutical innovation and production.
- South Korea and Japan exemplify how long term, concerted prioritisation of innovation can lead to economic growth and high levels of patient access. Singapore facilitated the coordination of public innovation bodies and industry to overcome barriers such as small population size and relatively few comparative advantages, to drive innovation.
- The Mexican Federal government should support the establishment of State-level Ministries of Innovation and more local Technology and Technology Transfer Offices at universities. By strengthening government innovation institutions, the Federal government will also motivate academia and signal to industry it's prioritization of innovation.

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