CRA Charles River Associates

Value of IP for health and growth

The economic benefits of strengthening the environment for innovation in Brazil

MARCH 2020

CONTENTS

1. Project objectives and methodology

PROJECT OBJECTIVES

- INTERPAT asked Charles River Associates (CRA) to identify and quantify the economic benefits from strengthening the environment for innovation in Brazil.
- The objective of the study is to:
  - Set out the policy framework for supporting innovation in Brazil and the current state of innovative activity.
  - Undertake a case study analysis on countries, outside the Lat Am region, with potential lessons for Brazil on how policies can improve innovation and related activities in countries.
  - Develop scenarios as to how innovative activity could change in Brazil, if policies adopted in other countries were pursued.
- The approach builds on a similar analysis applied to Argentina in 2018.

RESEARCH STEPS

1

THE BRAZILIAN INNOVATION ENVIRONMENT

- Review the current IP framework in Brazil,
  - The current rules and regulations.
  - Academic, grey literature on how it works in practice.
  - The existing policy debate.

Collection of statistics in terms:

- R&D Investment/FDI/ Clinical trials/Patents.

2

EXPERT VIEW OF THE CURRENT IP ENVIRONMENT

- Interviews/survey with INTERPAT members on investment decisions in Latin America and current perception of Brazil.
- Interviews with policymakers, academics, SMEs, CROs.

3

COMPARISON TO PEERS IN LAT AM AND BEST PRACTICE

- Develop comparable country case studies.
  - Development of metrics and recent changes.
- Development of scenarios.
  - Application to Brazil.

4

DEVELOPMENT OF PEER REVIEWED PAPER

- Develop peer-reviewed paper for publication.
- Participate in Lat Am workshops to disseminate findings.

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

- We have reviewed more than 60 international and local publications on the current challenges in the IP regime and innovation policy environment in Brazil as well as its innovative performance, with a focus on the pharmaceutical industry:

ACADEMIC PUBLICATIONS

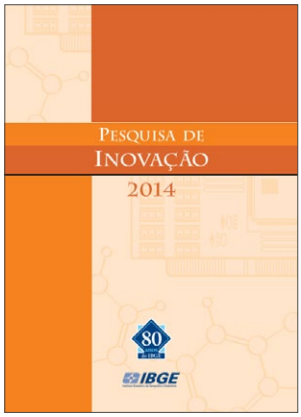
International and local academic literature including Vasconcelos & Silva (2019), De Negri & Rauen (2018), Vieira et al. 2017, Mazzucato & Penna (2016).

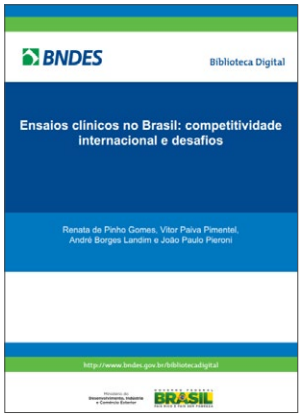
INSTITUTIONAL REPORTS

A review of institutional websites, including reports by INPI, BNDES, IPEA, UNICAMP, Interfarma, OECD, Wilson Center Latin American Program and WIPO.

GREY LITERATURE

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





CASE STUDIES

THE OBJECTIVES OF A CASE STUDY APPROACH ARE TO:

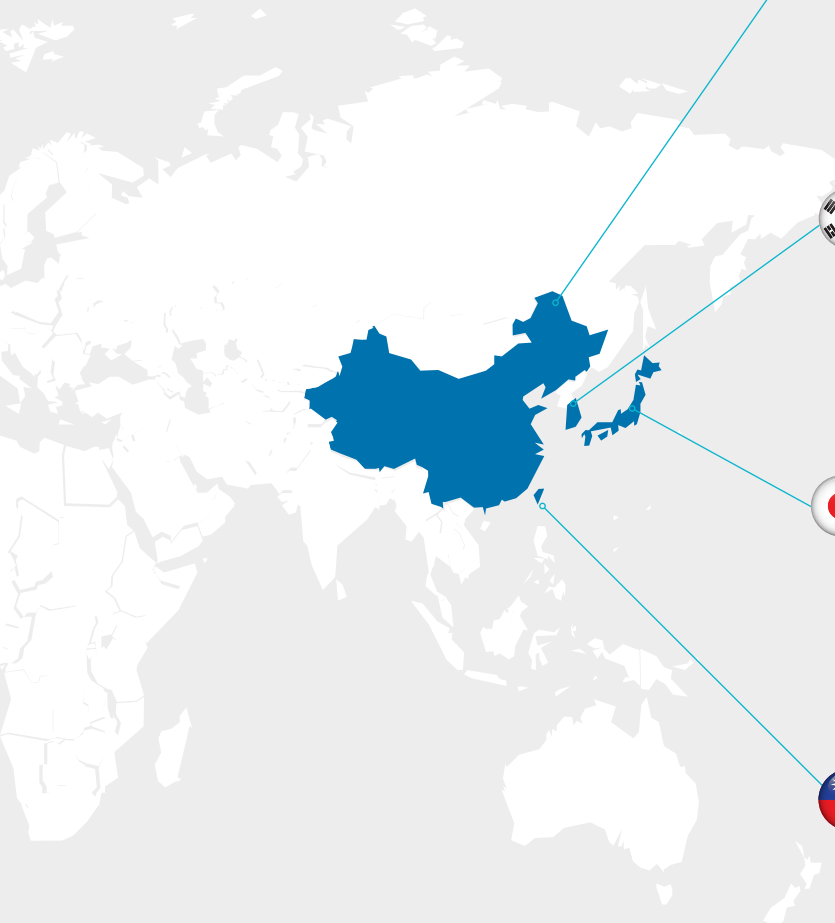
- **Quantify the impact of policies** to strengthen innovation environment.
- Develop **understanding of the context**, to better understand the success of innovation policy change.
- To understand the **policy process to fostering pharmaceutical innovation** in an emerging economy.

Case study markets

Brazil	
Population	209.3 million
GDP per capita	$9,821
Economy	Upper-middle-income

THE SELECTION CRITERIA FOR OUR CASE STUDY MARKETS SUGGESTS FOUR ASIAN MARKETS TO INVESTIGATE:

1. Have shown a **focus on strengthening innovative environment**, particularly the IP protection.
2. Placed **broadly in the same income, size and development category as Brazil** when started focusing on innovation.
3. Show an observable impact on **innovative activity.**



China	
Population	1,386 million
GDP per capita	$8,826
Economy	Upper-middle-income

South Korea	
Population	51.4 million
GDP per capita	$29,472
Economy	High-Income

Japan	
Population	126.5 million
GDP per capita	$39,293
Economy	High-Income

Taiwan	
Population	23.8 million
GDP per capita	$24,557
Economy	High-Income

TO UNDERSTAND BRAZIL'S INNOVATION ENVIRONMENT, WE UNDERTOOK A COMPREHENSIVE INTERVIEW PROGRAMME

- **INTERVIEWS WITH 7 INTERNAL EXPERTS** were used to provide industry view of Brazil's IP policy and innovation environment and remaining key gaps and challenges
  - Pfizer; UCB; Novartis; Janssen; Grünenthal
  - INTERFARMA
- Local/regional teams could provide context and validation of findings identified through literature.

- **7 EXTERNAL INTERVIEWS** with policymakers, academics, local CROs and bio-techs, and influencers of the current innovation environment were used to develop understanding of the broader innovation policy in Brazil
  - INPI
  - IPEA
  - CIPD
  - Aché
- 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 were also requested.

Rio de Janeiro, Brazil, shutterstock.com/marchello74

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

THE FOLLOWING INDICATORS WERE ASSESSED TO UNDERSTAND THE OVERALL INNOVATIVE ENVIRONMENT

POLICY ENVIRONMENT → RESOURCES FOR INNOVATION

OVERALL INNOVATION SUPPORT

- National innovation plans.
- Targeted initiatives e.g. the Brazilian Initiative on Precision Medicine (BIPMed).

RULES FOR INNOVATION PROTECTION

- IP rules and patentability criteria.
- Patent filing and granting process.
- Regulatory data protection.
- Preliminary injunction process.

INCENTIVES FOR INNOVATION

- R&D tax credits.

FUNDING FOR INNOVATION

- Public and private funding for research.
- Foreign Direct Investment (FDI).

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.

TAXES

- Tax revenues from pharma and biotech.

TRADE

- Imports vs exports in pharma and biotech.

INNOVATION POLICIES IN BRAZIL

NATIONAL POLICY ON INDUSTRIAL, TECHNOLOGICAL AND FOREIGN TRADE (PITCE), 2003-2006

Aimed to grow exports, promote innovation capacity in firms, regional development, and capital goods; targets specific priority areas including pharma, by defining innovation as a core dimension of the manufacturing and foreign trade policy.

NATIONAL POLICY FOR SCIENCE, TECHNOLOGY AND INNOVATION IN HEALTH, PNCTIS, 2004

Defines that health innovation should be supported by the production of technical and scientific knowledge adjusted to the economic, social, cultural and political needs of the country.

INNOVATION LAW (LAW 10.973/2004) 2004

Provides incentives to increase the cooperative links between public scientific and technological institutions (STI) and enterprises and also regulate the IP generated from these collaborative activities.

R&D TAX INCENTIVES (LAW 11.196/2005) 2005

Provides an R&D tax allowance of up to 80% of overall R&D expenditures and up to 20% of expenditures on developing patented technologies.

ACTION PLAN FOR SCIENCE, TECHNOLOGY AND INNOVATION, PACTI, 2007-2010

Coordination of national innovation system and increase private R&D spending.

PRODUCT DEVELOPMENT POLICY, 2008-2010

Aimed to improve the competitiveness of various sectors of economy, by promoting investment and partnerships between businesses and universities.

LEGAL FRAMEWORK ON SCIENCE, TECHNOLOGY & INNOVATION (LAW 13.243) 2016

Governing stimulus to scientific development, research, and the development of capabilities in science, technology and innovation. Encourages ties between industry and public scientific institutions by allowing, e.g., university researchers to work for a limited period in private R&D firms, and allowing public institutions to buy minority stakes in start-ups, with the aim of encouraging technological spillover to the market.

NATIONAL STRATEGY FOR SCIENCE, TECHNOLOGY AND INNOVATION (ENCTI) 2012-2015; 2016-2022

Established by the Ministry of Science, Technology and Innovation (MCTI), and sets out plan to address challenges in the S&T framework, including gaps in basic and technological scientific research; STI infrastructure; qualification of human resources; technological innovation in firms; basic sciences (STEM skills).

STEM – Science, Technology, Engineering and Mathematics

RULES FOR PROTECTION AND OTHER INCENTIVES

ANVISA'S PRIOR CONSENT - INPI/ANVISA JOINT ORDINANCE 01/2017

It defined the roles of INPI and ANVISA, in relation to the exam of patents for pharmaceutical products and processes, which depend on Anvisa's Prior Consent, under the terms of Article 229-C of the IP Law and enabled the analysis of these applications.

PATENT PROSECUTION HIGHWAY (PPH) 2016; 2018; 252/2019

Launched with the objective of helping to tackle the patent backlog, the PPH acts to speed up the process of granting patents recognized in selected partner-countries (by Mar/2020, 20 countries are already partners, including USA, UK, Japan and China). Resolution No. 252/2019 merged and simplified the PPH/INPI and extended the possibility of PPH to any technological field, including pharmaceutical.

RESOLUTION NO. 218 (FAST TRACK EXAMINATION), 2018 AND 239/2019

Unifies and establishes the rules for the fast-track of patent applications, including for pharmaceutical products and processes related to the diagnosis, prophylaxis or treatment of HIV, Cancer, Rare and Neglected Diseases. Resolution No. 239/2019 also aims to address the patent backlog.

PLAN TO TACKLE PATENT BACKLOG - RULE #240/2019 AND RULE #241/2019

Establish the rules for the operationalization of the Plan to Tackle Patent Backlog, which aims to reduce the number of patent application pending decision by 80% by 2021 and to reduce the average term until decision to approximately 2 years, from the exam request.

MERCOSUR AND THE EUROPEAN UNION ACCORD, 2019

Involves several commercial aspects mainly aiming at tax reduction to foster commercialization and trade between signatories of the agreement.

MADRID PROTOCOL AGREEMENT, 2019

An international system for requesting trademark protection in several countries at the same time - simplifying the bureaucratic process and reducing costs for obtaining trademark registration. Brazil joins 120 other countries in the Agreement, which represent 80% of world trade.

NO TERM FOR REGULATORY DATA PROTECTION

In Brazil, there is no RDP term established for pharmaceutical products for human use. The RDP includes information on the development of the drug - quality, safety and efficacy, submitted to the health authority - Anvisa, to obtain the marketing authorisation.

INCREASING EFFORTS TO REDUCE PATENT BACKLOG

In 2018 there was a backlog of 208,341 patent applications (all technological fields), with the average decision time of 13 years for a patent applications in the pharmaceutical sector. In Feb/2020, the backlog was of approximately 118.000 patent applications (all technological fields).

Key

○ Areas for improvement in innovation policy.

○ Pro-innovation policies/agreements.

RDP – Regulatory Data Protection

OTHER RECENT PRO-INNOVATION INITIATIVES

Research and interviews with experts have revealed that the new national government of 2018 has ushered in a new focus on innovation policy reform which is expected to benefit pharma innovation going forward*.

- A 2017 Joint Agreement between ANVISA and INPI established their role in relation to the exam of patents for pharmaceutical products and processes, which depend on Anvisa's Prior Consent, under the terms of Article 229-C of the IP Law and enabled the analysis of these applications. This is seen as a workable **solution to the dual patent examination problem**, although the ideal would be the analysis of patent applications for pharmaceutical products to pass only through the patent office, as in other countries.
- A new Inter-ministerial Group of Intellectual Property Committee (GIPI) has been established, with aims to **focus on pharmaceutical issues**.
- The INPI have established targets and a **strategy to reduce the patent backlog**, with accompanying Rules to ensure enforcement. INPI continue to draw lessons from the Japan's JPO.
- The **mailbox patent problem has been largely resolved** through the higher courts system.
- The **tax reform debate has progressed** recently and is expected to advance in 2020.

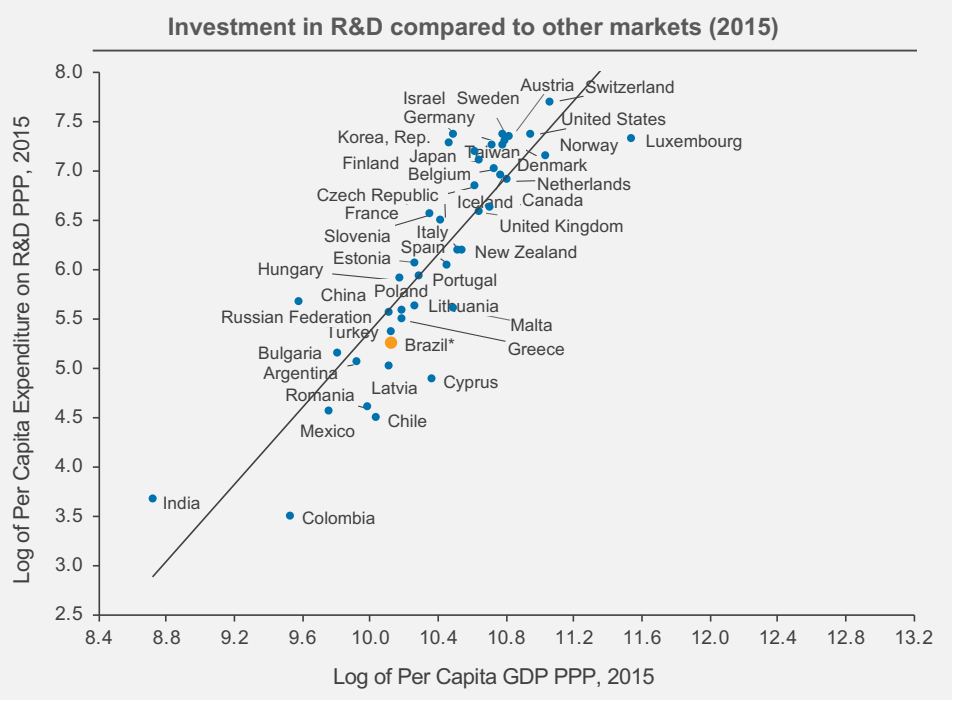
However, Brazil's innovation capacity continues to be limited by the economic effects of the 2014 – 2016 recession.

→ **An ongoing significant constraint is the discontinuity in public policies and research funding, particularly since the onset of the recession, which undermines the country's scientific infrastructure and expertise.**

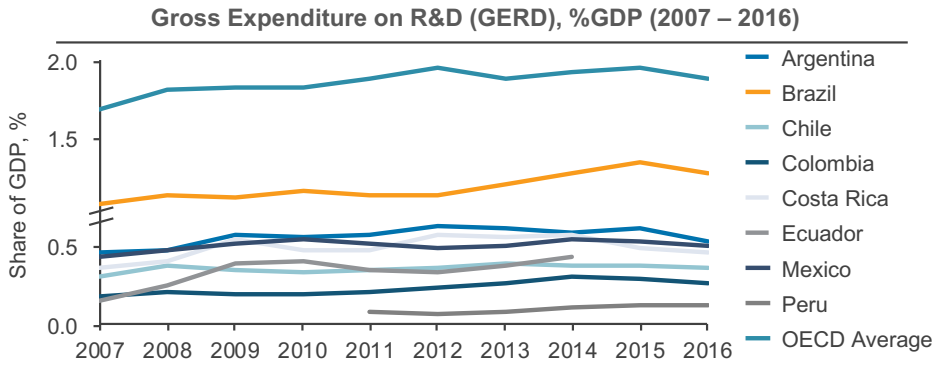
***** Insights from CRA External interview programme.

RESOURCES FOR INNOVATION:
INVESTMENT IN INNOVATION & R&D

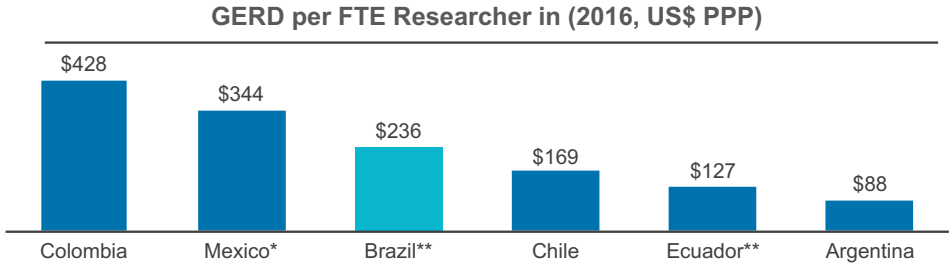
- Despite a number of government initiatives targeted at innovation, Brazil would need to improve R&D investment relative to GDP levels 0.6 percentage points (2016) to reach the OECD average, but is a leader in the LatAm region with 1.3% of GDP spent on R&D in 2016.
- Funding for academics is lower than in other LatAm countries and was identified by 3 local interviewees as a key issue particularly since 2014, causing "brain drain" to the private sector, gaps in qualified staff & obsolescence of equipment and laboratories.[1,2]



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.



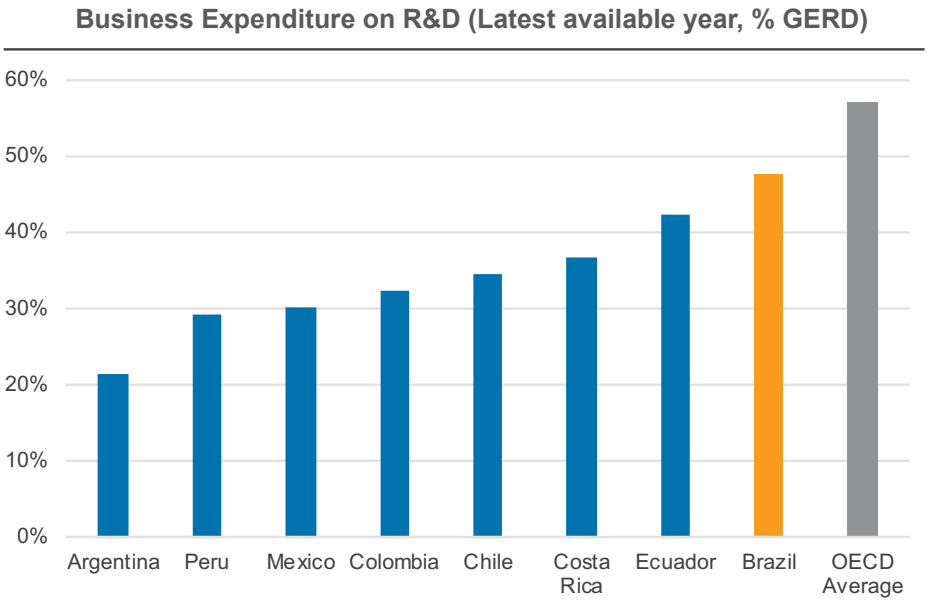
Source: Ibero-American Network, Science and Technology Indicators (2019); OECD Main Science and Technology Indicators (2019); Brazil Ministry of Science, Technology, Innovations and Communications Indicators (2019).



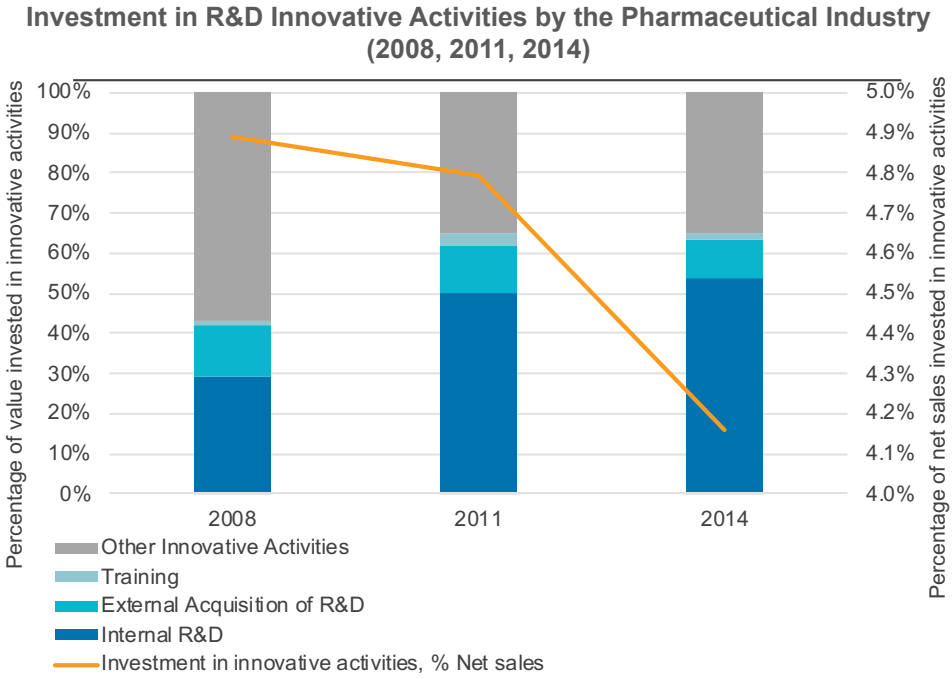
Ibero-American Network, Science and Technology Indicators 2018; OECD Main Science and Technology Indicators (2019). Note: * Latest data from 2013, ** Latest data from 2014.

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

- Private investment in R&D as a percentage of GERD in Brazil exceeds that of other LatAm markets but falls short of the OECD average.
- Specifically, Brazilian pharmaceutical companies invested a lower percentage of their net sales in R&D than the average 15-20% spent by leading global companies[3,4,5,6] but spent more than the 2.3% of net sales on average by pharmaceutical companies in Argentina in 2007-2013.[7]
- Access to funding for R&D and commercial activities of local SMEs through venture capital or government loans (BNDES) is a challenge hampering innovative activities according to an interview with a local CEO.



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.

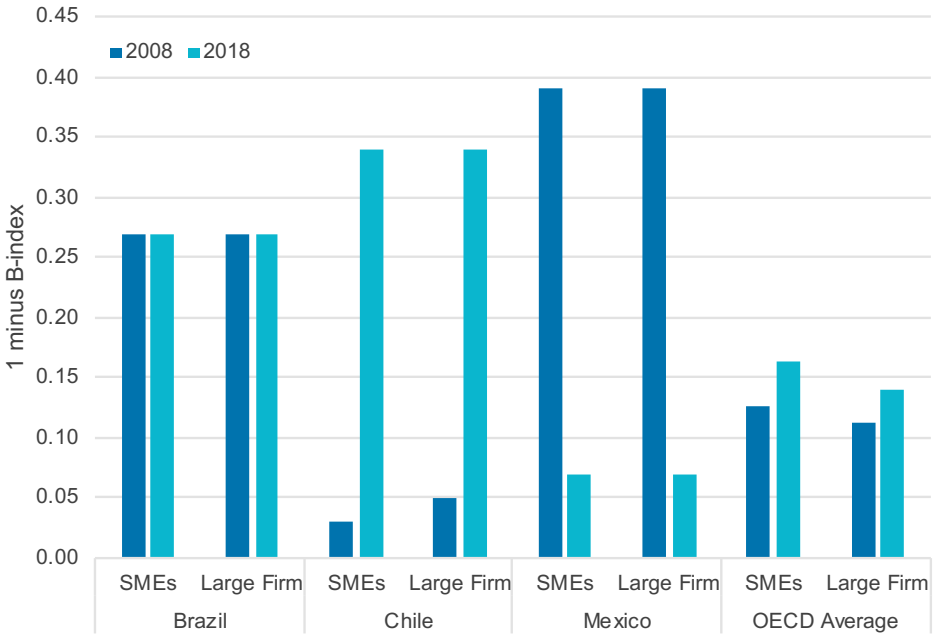


Source: based on data from Survey on Industrial Technological Innovation (PINTEC), 2008, 2011, 2014.

RESOURCES FOR INNOVATION:
R&D TAX INCENTIVES

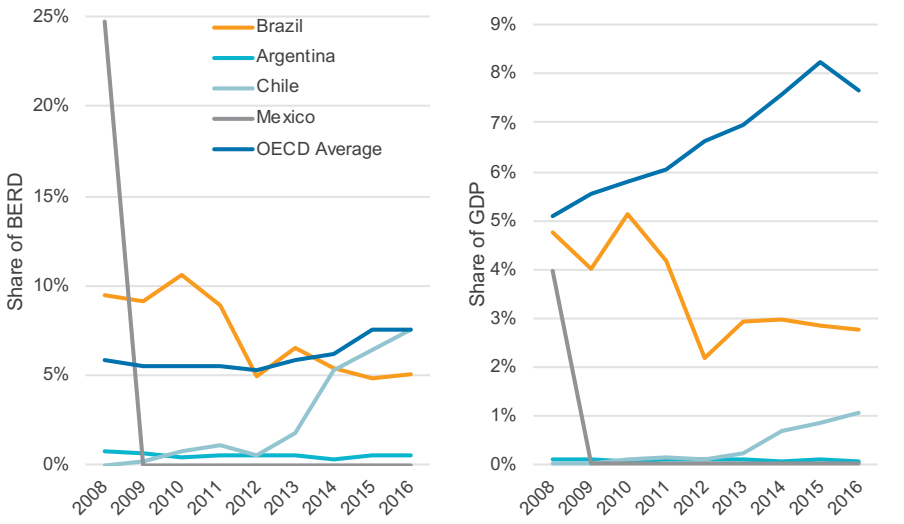
- Law No. 11.196 adopted in 2005 established an R&D tax allowance of up to 80% of overall R&D expenditures and up to 20% of expenditures on developing patented technologies.[8]
- According to an interview and the broader literature, the federal government considers that the law has not made Brazil sufficiently competitive and has not lead to increased innovative productivity. As such, the government is currently reviewing the law.[9]

Implied tax subsidy rates on R&D expenditures (2008 and 2018)



OECD R&D tax subsidy (RDTAXSUB) dataset 2018/2.

Indirect government funding through R&D tax incentives (2008 – 2016)

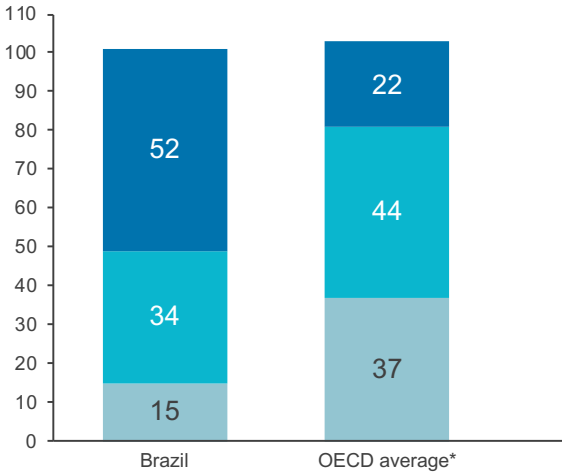


OECD R&D tax subsidy (RDTAXSUB) dataset 2018/2.

RESOURCES FOR INNOVATION: AVAILABILITY AND STRENGTH OF RESOURCES AND EDUCATION

- The proportion of 25-64 year olds in Brazil with tertiary education falls short of the OECD average and amongst graduates with tertiary level education, Brazil has a smaller proportion of STEM graduates when compared to other LatAm countries.
- PISA Science scores in Brazil lags behind other LatAm countries and the OECD average however, interviewees noted the apparent disparity across the regions in Brazil, with the most developed infrastructure and capabilities in the wealthy regions in the South and Southeast.

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

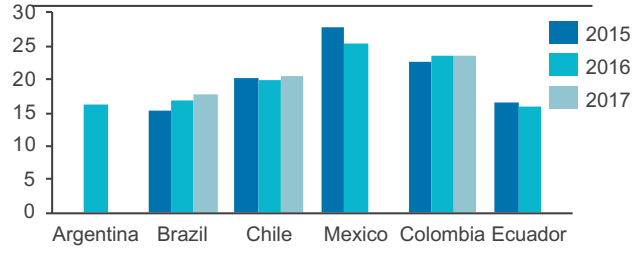


Source: OECD Data, 2018

*Due to averaging, OECD average does not total to 100%

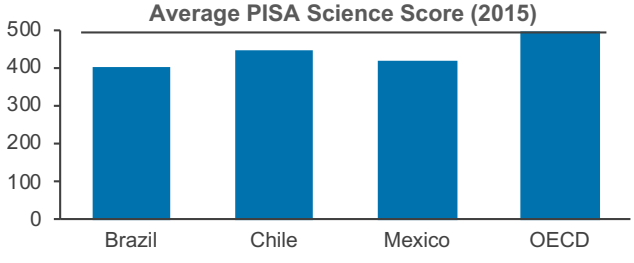
Source: OECD Data, 2018.

Graduates from STEM degrees in tertiary education (%)



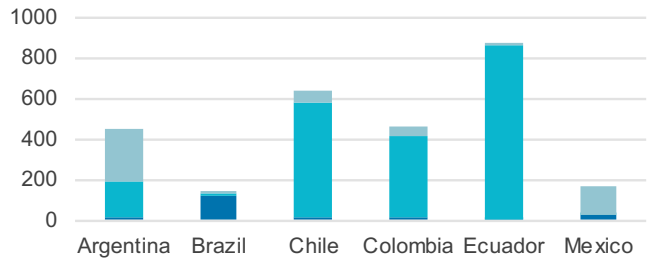
Source: UNESCO UIS.Stat, 2015-2017.

Average PISA Science Score (2015)



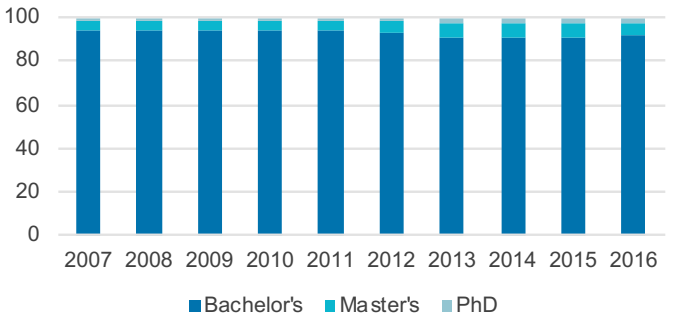
Source: OECD Data, 2015.

Number of medical science graduates by grade (2014)



Source: RICYT, 2014

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

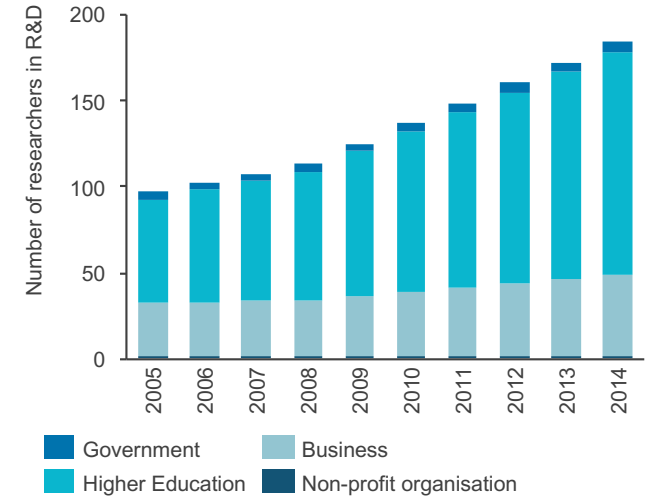


Source: OECD Data.

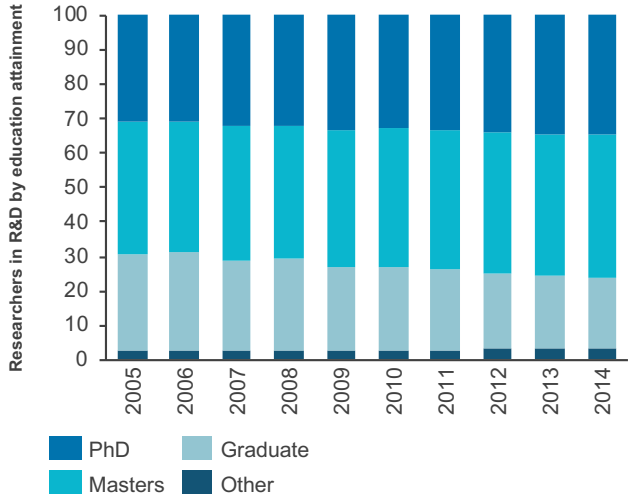
RESOURCES FOR INNOVATION: AVAILABILITY AND STRENGTH OF RESEARCHERS

- The number of R&D researchers in Brazil has increased in the past decade with the most significant growth in researchers working in academia/higher education. In general, the sentiment of the interviewees were that Brazil has qualified researchers with PhD degrees.
- Despite overall growth in the number of researchers, the share at each level of education attainment (undergraduate, master's, PhDs) has remained fairly constant.
- Although LatAm does not fare well in the Global Top 500 Universities with most cited Life Sciences research, two of the four South American universities included in the list are located in Brazil.

Number of researchers in R&D by institution (2005-2014, thousands)

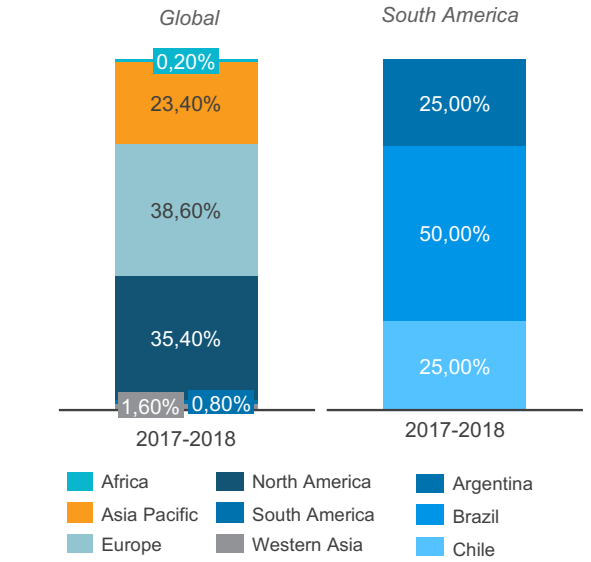


Researchers in R&D by education attainment (2005-2014, %)



Source: Ministry of Science, Technology, Innovations and Communications (MCTIC), 2005-2014.

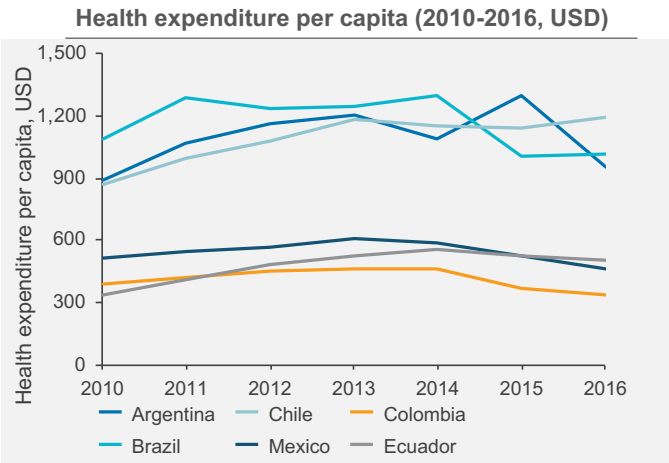
Proportion of top 500 Nature-ranked Universities in Life Sciences research (2017-2018, %)



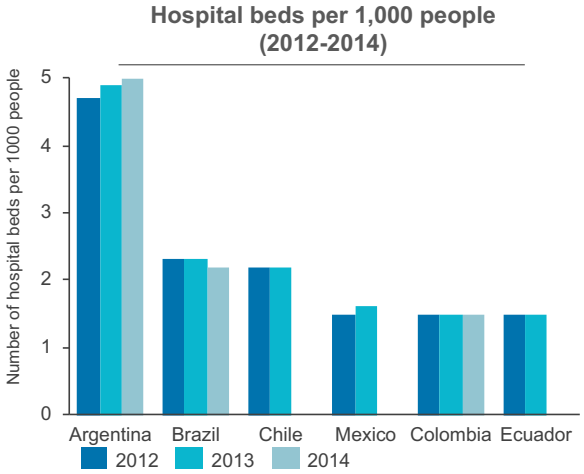
Source: Nature Publishing, 2018.

RESOURCES FOR INNOVATION:
HEALTH BUDGET AND INFRASTRUCTURE

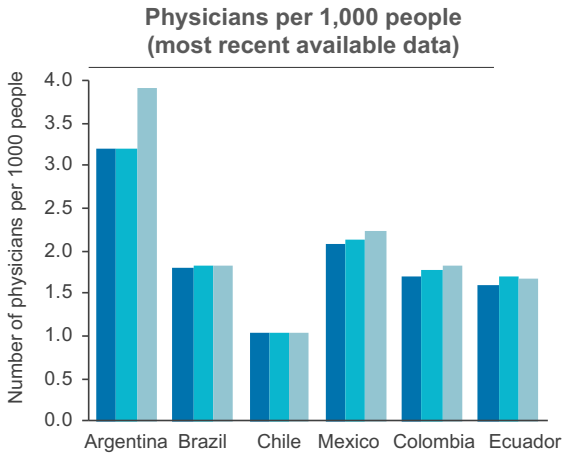
- Between 2010 and 2015 , Brazil had the highest health expenditure per capita within the LatAm region. From 2015 onwards, expenditure per capita has fallen although Brazil remains among the high spenders in the region.
- In terms of infrastructure and healthcare professionals, Brazil performs moderately in the LatAm region.
- Despite this, various interviewees have stated that Brazil has the groundwork to support clinical trials in terms of available research sites.



Source: World Bank, 2018.



Sources: World Bank Data 2018.



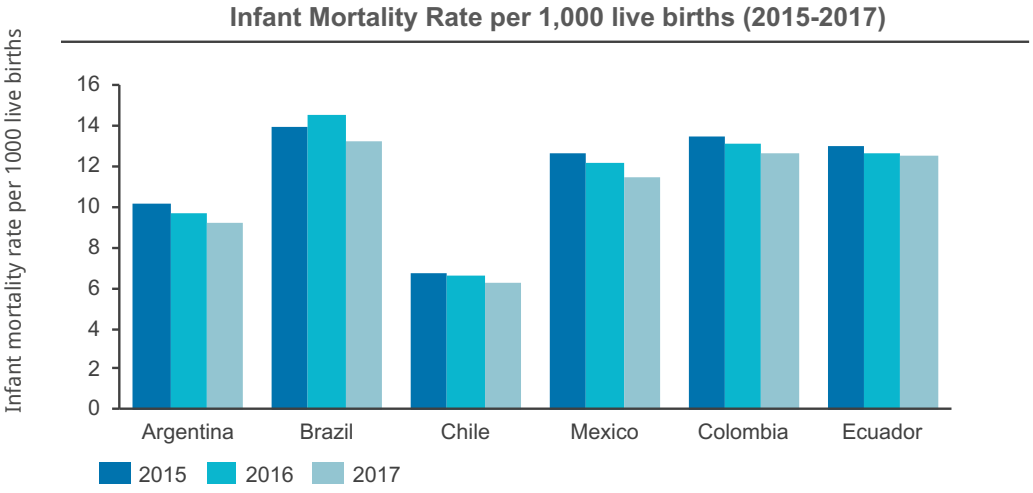
Sources: World Bank Data 2018;

*Most recent available data, clarification in notes.

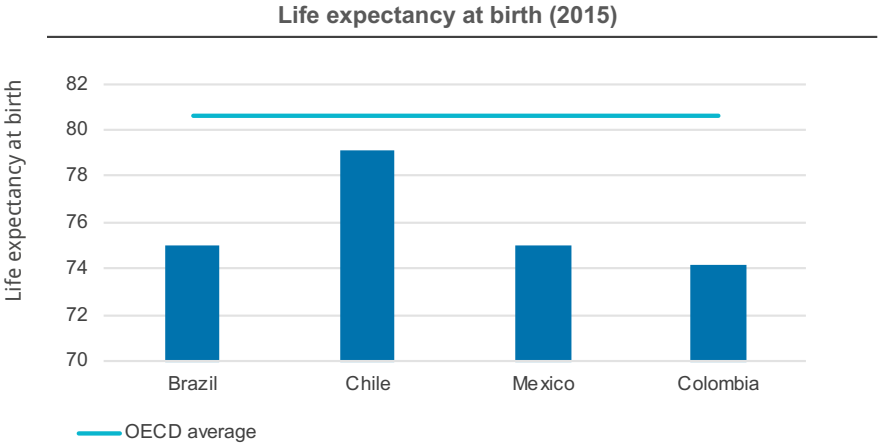
Note the years for Physicians (per 1,000 people): Argentina: 2005, 2010, 2013; Brazil: 2010, 2012, 2013; Chile: 2007-2009; Mexico: 2013-2015; Colombia: 2012-2014; Ecuador: 2009-2011

RESOURCES FOR INNOVATION:
HEALTHCARE SYSTEM AND CARE

- In general, the coverage from both public and private insurance has increased over the years.[10]
  - However, public spending as a share of total health expenditure is remains low in Brazil (46%) in comparison to LatAm region (average of 51.28%) and OECD (average of 62.2%) in 2014.
  - Private insurance coverage has increased from 17.6 to 24.8% of population between the years 2000 to 2014 with nearly 50% coming from out of pocket expenditures.
- In terms of provision of care, Brazil lags behind its neighbouring countries in LatAm, having one of the highest infant mortality rates per 1,000 live births.
- Moreover, Brazil performs moderately in the LatAm region when comparing life expectancy at birth and falls short of the OECD average.



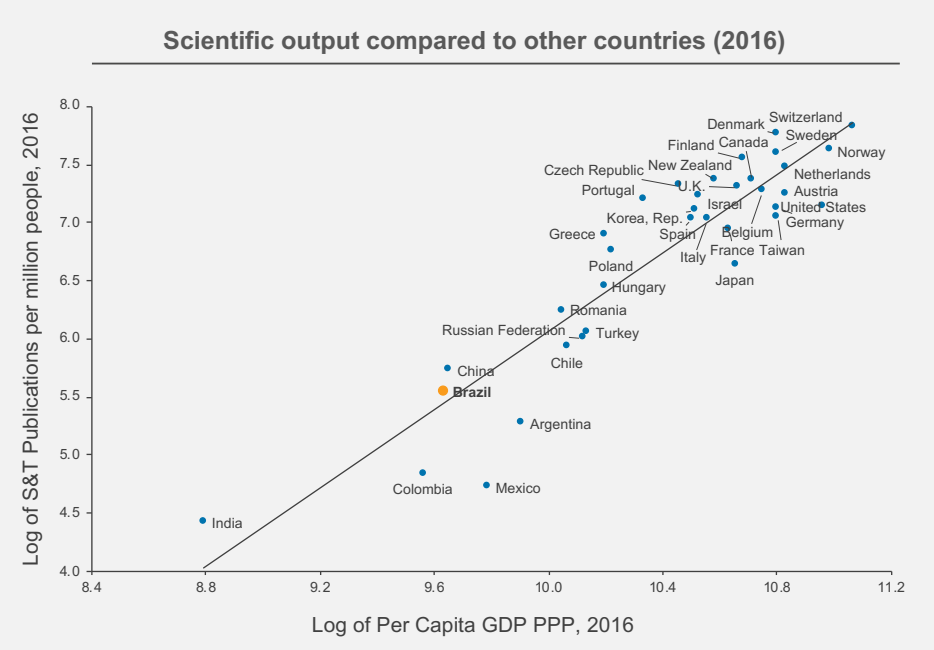
Source: World Bank, 2015-2017.



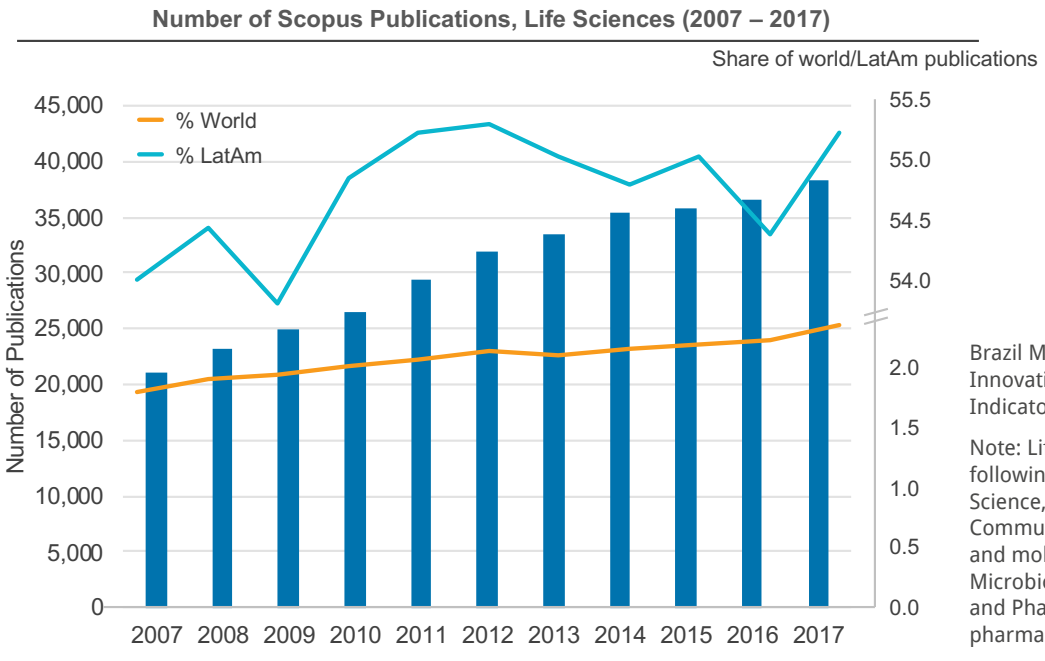
Source: OECD data, 2015.

INNOVATIVE ACTIVITY:
BASIC RESEARCH OUTPUT

- Basic research output in Brazil in terms of publications is on track compared to GDP per capita. Overall output of Science and Technology (S&T) tripled in 2005 compared to the early 1990s and in 2013 Brazil ranked 13th worldwide in the Scopus database.[11,12] The number of publications continues to grow and was identified as an area of strong performance by a local academic.
- In terms of the absolute number of publication in Life Sciences, Brazil accounts for more than half of the total output in the LatAm region and the world share of those has grown by 0.5% in the past 10 years.



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.



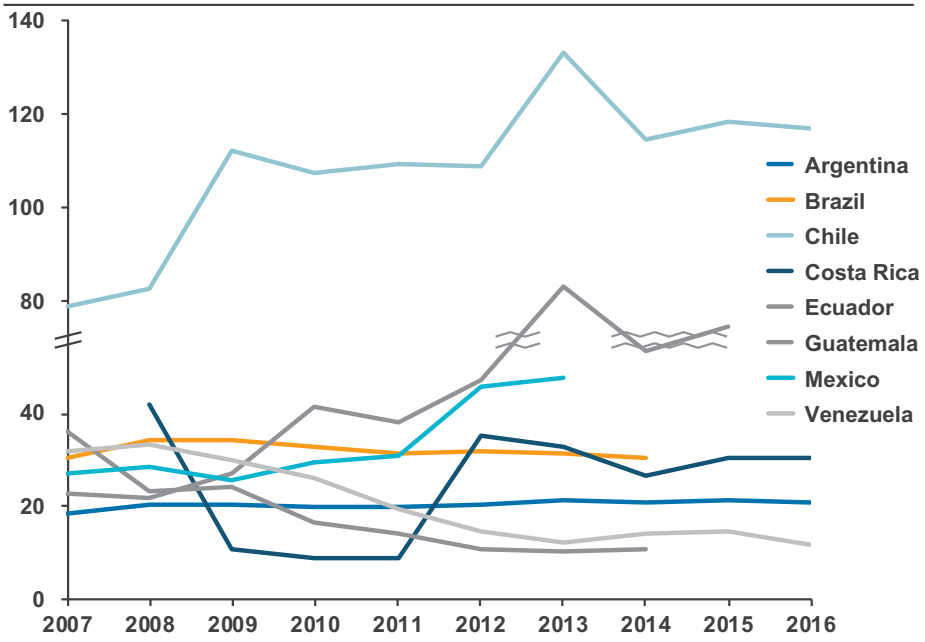
Brazil Ministry of Science, Technology, Innovations and Communications Indicators (2019)

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

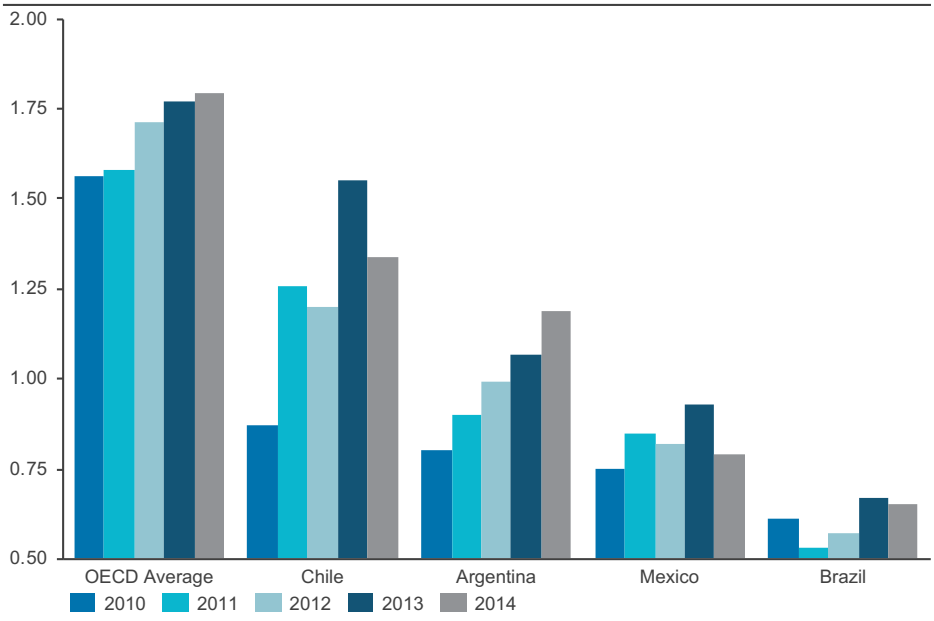
- However, in terms of research productivity, the number of S&T publications per 100 FTE researchers, Brazil falls behind other LatAm countries. Whilst Brazil has improved from 2010 to 2014, the impact of its scientific research, as measured by share of top 1% most cited articles in Scopus, is also lagging behind other LatAm and OECD countries. One contributing factor could be that much of the research output is in Portuguese rather than in English.
- 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)



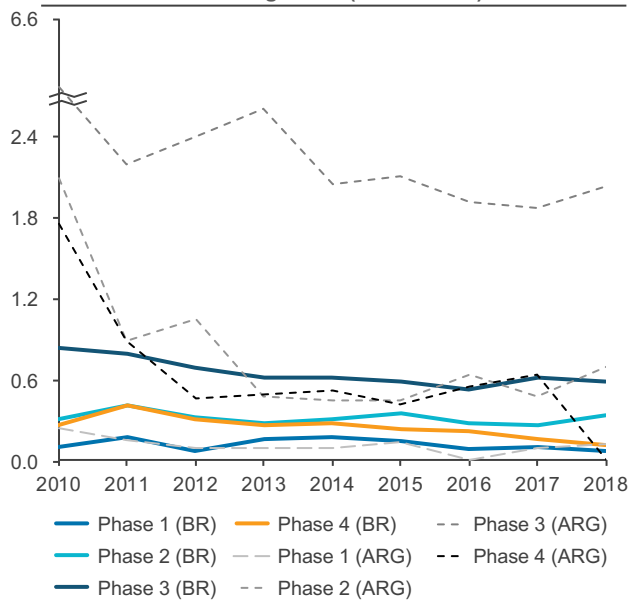
National Science Foundation Survey 2018.

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

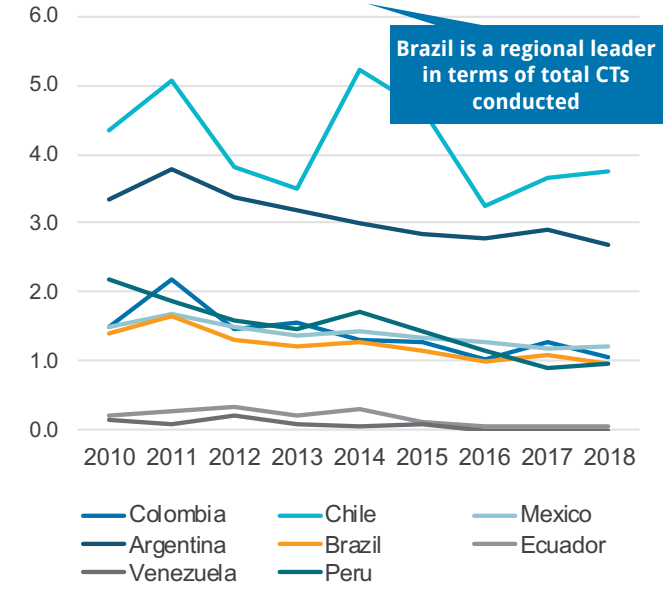
- In terms of the total number of clinical trials per million people, Brazil stands in line with the LatAm average but falls short of Argentina & Chile. Furthermore, the number of phase 3 trials per million people in Brazil is significantly lower than that in Argentina.
- The lack of RDP term as well as the lengthy and bureaucratic process to approving a CT are barriers to local and foreign innovators. For example, it takes an average of 115 days in Brazil (2018) to obtain CT approval as compared to 30 days in the US (4 times as less time).[13]
- According to local SMEs and CROs, whilst RDP is important, improving current CT regulations will have a more significant impact on the number of CTs conducted both by foreign and local companies. For example, dual examination and undetermined post-trial access are additional limitations to conducting CTs effectively. The opportunity for further gains from regulatory improvement is highlighted by the lower cost of conducting CTs in Brazil relative to the US.[14]

Number of Clinical Trials per 1M People by Phase in Brazil & Argentina (2010 – 2018)



CRA Analysis of Clinicaltrials.gov.

Number of Clinical Trials per 1M People in LatAm Region (2010 – 2018)



CRA Analysis of Clinicaltrials.gov.

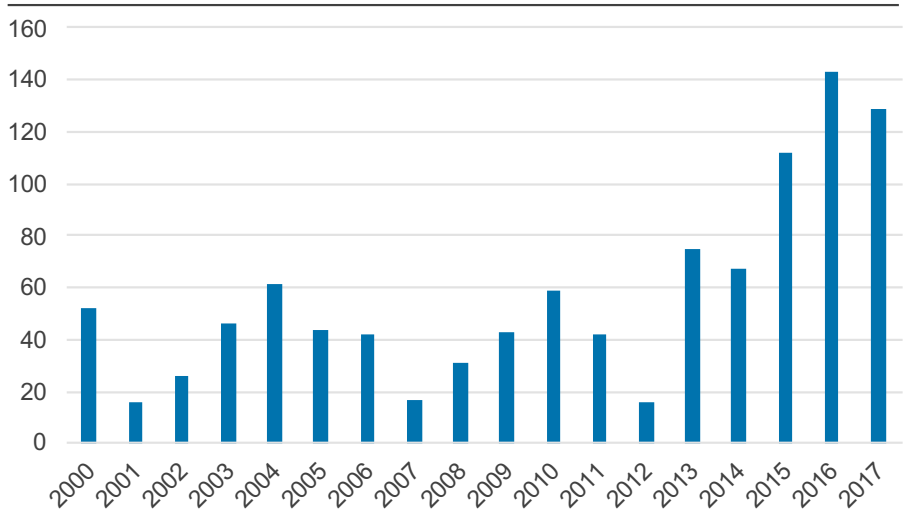
Average cost of conducting clinical trials in Brazil vs. the US

Koster, I. (2010) Clinical Trials in Brazil: trends and experiences and ASPE (2014).

INNOVATIVE ACTIVITY:
PATENTS (INPI)

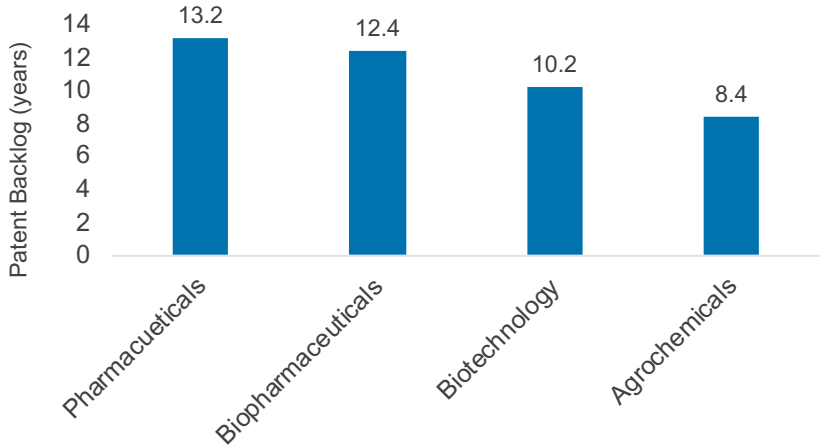
- The patent examination backlog has contributed to higher risk and uncertainty for both local and multi-national pharma companies. Local SMEs highlight this to be a barrier in patenting their invention and securing investment for further development and commercialisation.
- Positive policies to reduce the patent backlog, including and a 25% increase in INPI's staff, have reduced the number of all pending patent applications by 15% compared to the peak in 2016. Still, the average decision time for applications in the pharma field (13.2 years - 2018) remains an opportunity for further improvement in Brazil.[15]
- In an effort to harmonise and accelerate the examination of patent applications, INPI refers to decisions already published by other jurisdictions through the patent prosecution highway (PPH) programmes and applies priority review, through the Fast Track Program, to applications in cancer, AIDS and neglected or rare diseases, upon request.

Number of Pharmaceutical Patents Granted by INPI (2000 – 2017)



Ministry of Science, Technology, Innovation and Communications, 2019.

INPI's Patent Examination Backlog (2018, years)

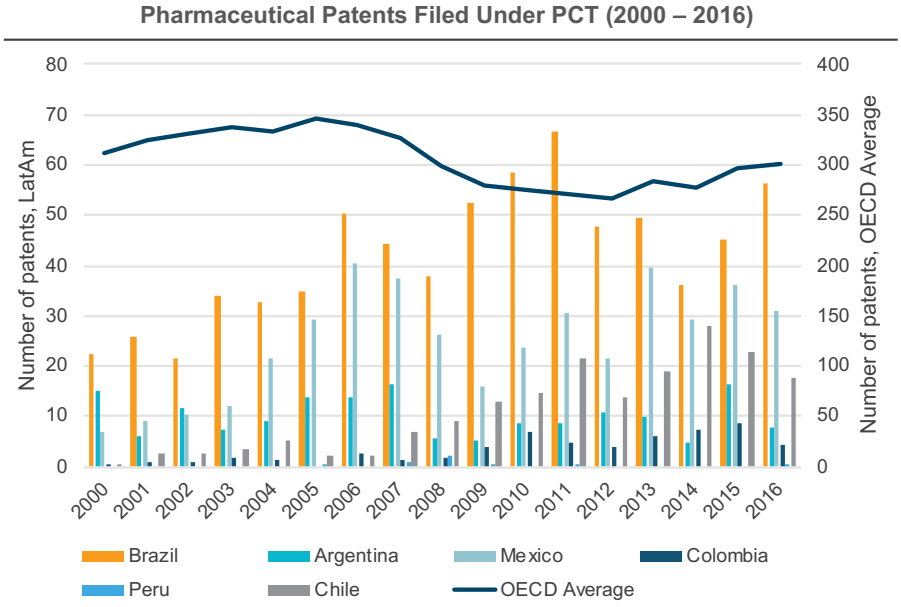


INPI Activity Report 2018.

INNOVATIVE ACTIVITY:
PATENTS (PCT & USPTO)

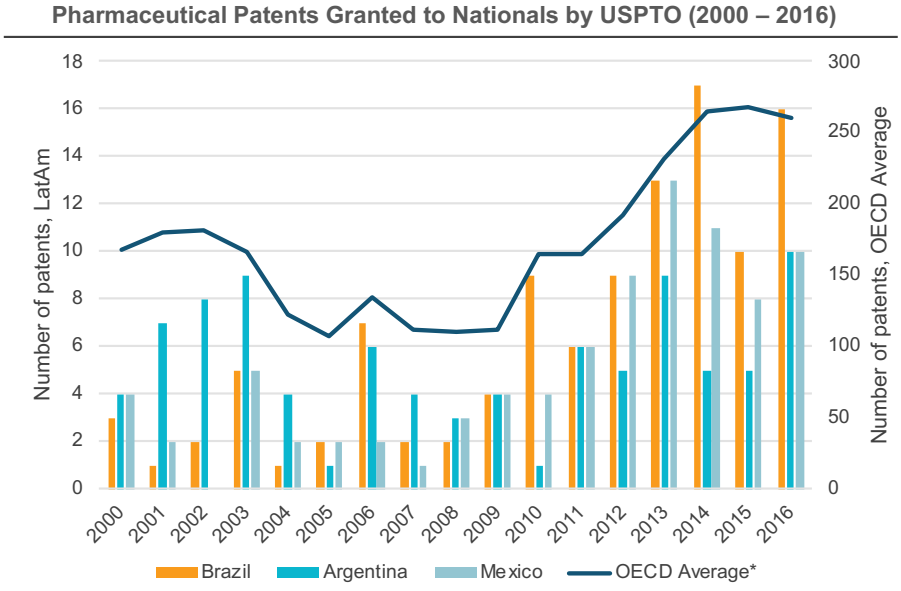
- In terms of the absolute number of pharmaceutical patent applications under the Patent Cooperation Treaty (PCT) and patents granted to Brazilian nationals by the U.S. Patent and Trademark Office (USPTO), Brazil is ahead of other countries in the LatAm region but lags far behind the OECD Average.
- Brazilian universities have historically received the significant government R&D investment and are thus seen as the powerhouse for generating IP. However, a challenge is forming collaborations with the private sector to commercialise this early stage research.[2,16]
- Small innovative companies are also facing difficulties in obtaining funding to develop their IP. In the case of foreign investors this is due to the delay and uncertainty in obtaining a patent.[16] Incentives such as public funding for academics to sustain the development of research projects and platforms to encourage information sharing, may support improve academic- industry collaboration.[16]

OECD Patents by Technology, 2019.



National Science Foundation Survey, Science and Engineering Indicators 2018.

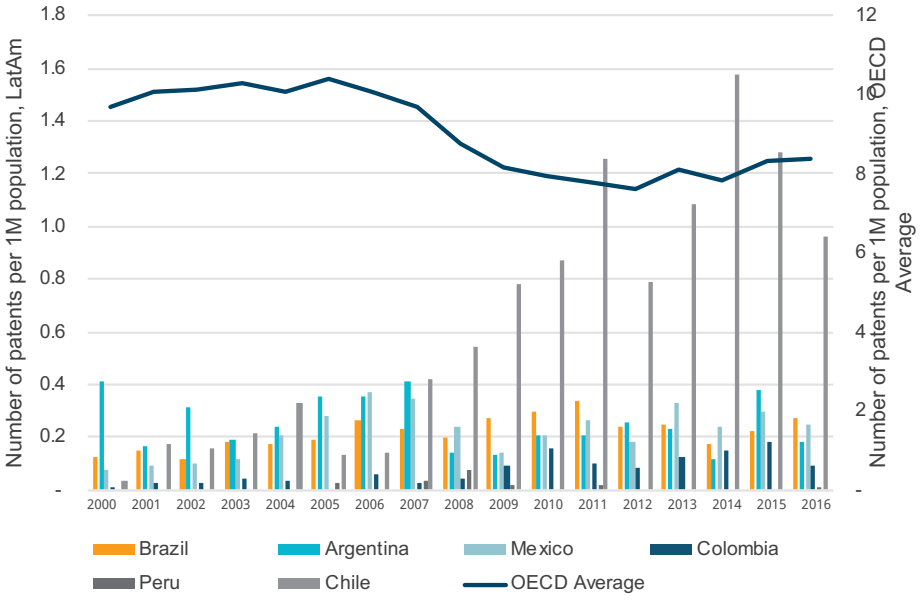
*Selected countries with available information.



[16] Insights from CRA External interview programme.

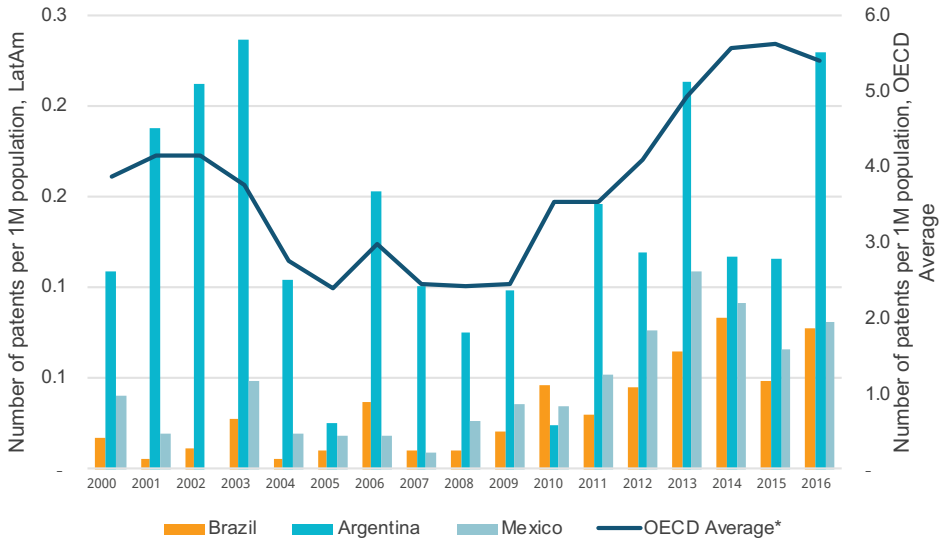
- In terms of the number of pharmaceutical patents filed under PCT and those granted to Brazilian nationals by USPTO on a per million of population basis, Brazil lags behind others LatAm and OECD countries. Particularly, since 2010 Brazil has the lowest number of pharmaceutical patent grants per million people out of Mexico and Argentina.
- This highlights the observation made by an interviewee that whilst strong local capabilities for innovation exist these are concentrated in the South and South East of Brazil in line with the location of key research universities. There is a tremendous potential for training of local manpower and improving existing infrastructure, which can in turn lead to IP being generated, but this would be possible by making Brazil attractive to more investment.[17]

Pharmaceutical Patents Filed Under PCT per 1M People (2000 – 2016)



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.

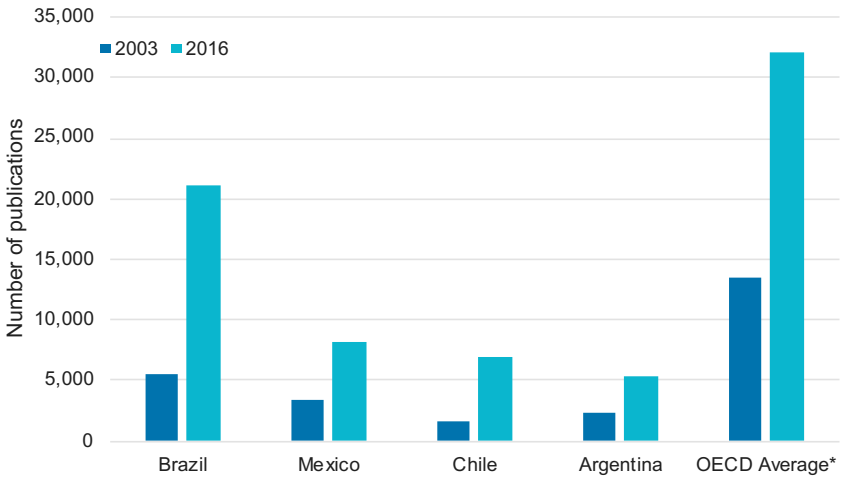
*Selected countries with available information.

[17] Insights from CRA External interview programme.

INNOVATIVE ACTIVITY:
CLUSTERS & COLLABORATIONS

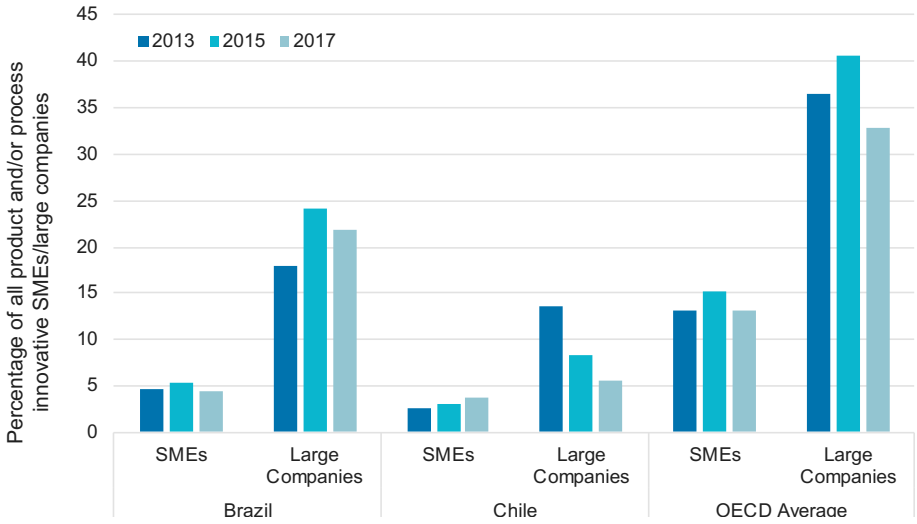
- Brazil's participation in international knowledge networks is seen as limited by local institutions and funding agencies. Current efforts are focused on boosting partnerships between Brazilian and foreign researchers.[18]
- Innovative companies in Brazil collaborate to a lesser extent with academic and government institutions than those in OECD countries. In 2016, less than 9% of new discoveries in the public sector were licensed out to companies, according to Brazil's tech-transfer office.[19]
- A significant challenge is forming public-private partnerships, which is particularly important for the commercialisation of early stage molecules. Policies such as those requiring tendering to form commercial partnerships with academia are seen as a key barrier.[2,16] The Product Development Policy (2008) has failed to address this challenge due to its too narrow on manufacturing instead of R&D.[16]

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



National Science Foundation Survey 2018.
Note: Selected OECD Countries (n=27).

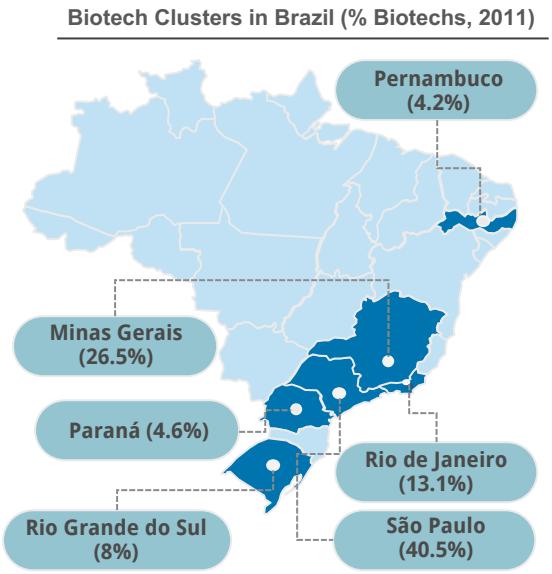
Firms collaborating with higher education or government institutions (2013, 2015, 2017)



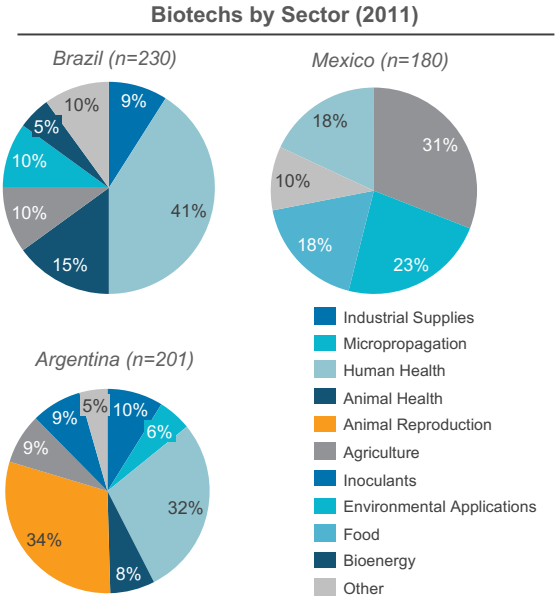
OECD Innovation Indicators 2013, 2015 & 2017.

ECONOMIC ACTIVITY:
CLUSTERS & COLLABORATIONS

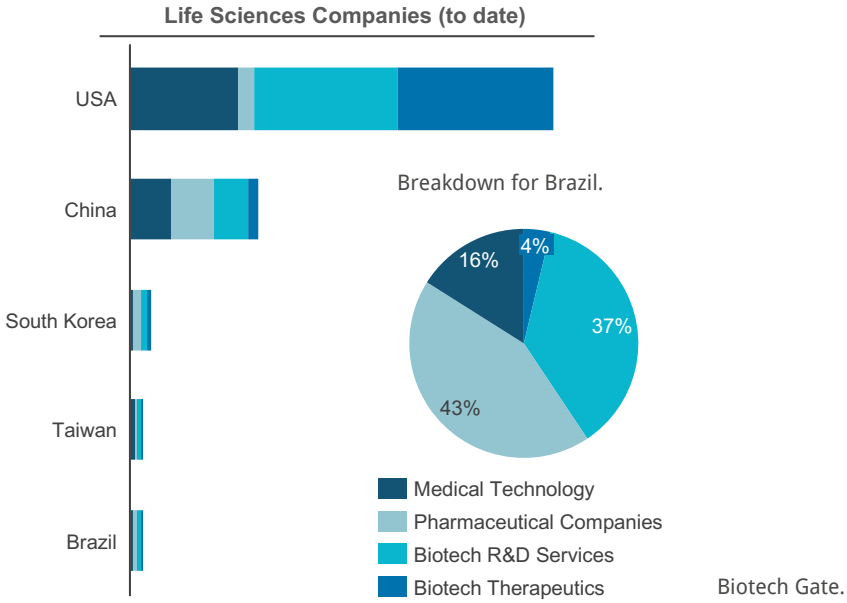
- Business incubators and science parks have played an important role in fostering a growing biotech sector.[20] 95% of the Biotechs are understood to form partnerships with universities and research centres to co-develop products or processes, to use infrastructure, to hire services or to train personnel.[20,21] Less bureaucracy and regulation in setting up a business can encourage entrepreneurship.[22]
- Despite lack of continuous government policies that encourage innovation,[2,23] the National Confederation of Industry–Brazil (CNI), Social Service of Industry (SESI), National Service for Industrial Training (SENAI), Euvaldo Lodi Institute (IEL), and the Brazilian Micro and Small Business Support Service (SEBRAE) play an important role in shaping the future of health innovation.[2]



Brazilian Biotech Map.



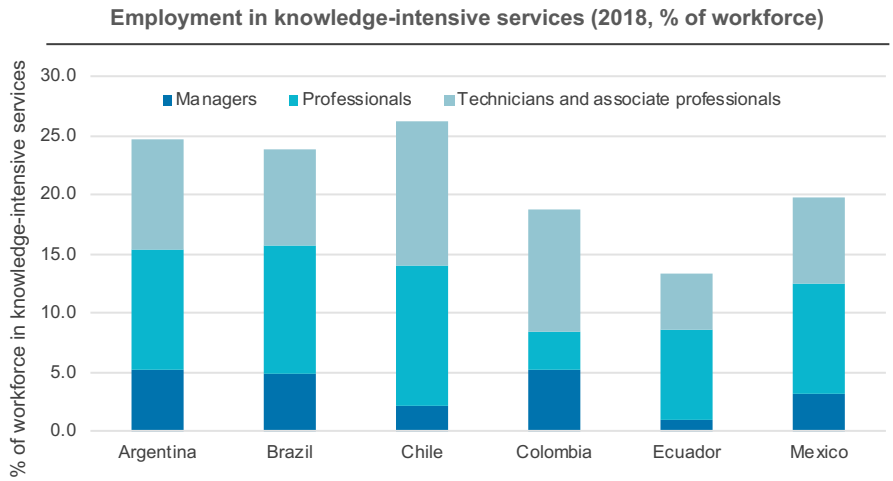
Sources: Ministry of Science, Technology and Innovation; Haar, J., Wilson Center Latin American Program.



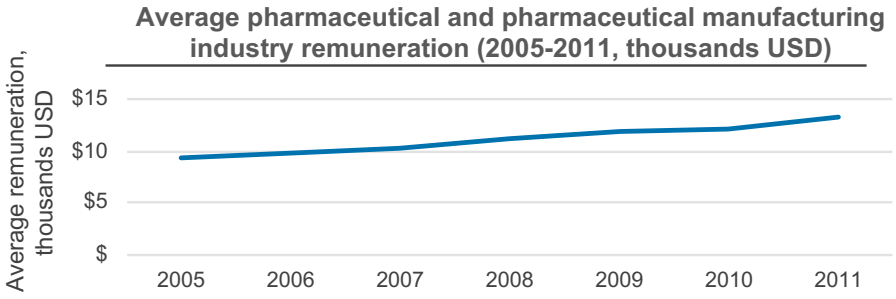
Biotech Gate.

ECONOMIC ACTIVITY
EMPLOYMENT

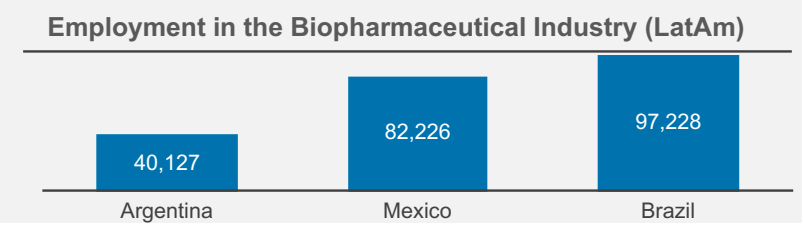
- The proportion of the workforce employed in knowledge intensive services in Brazil is on the upper end within the LatAm region.
  - In general, interviewees noted a movement from a generic led industry towards more research intensive and innovative activity in the local industry in Brazil.
- More specifically, Brazil has the highest level of employment in the biopharmaceutical industry in absolute terms when compared to Argentina and Mexico.
- However, the salary in the pharmaceutical industry has remained fairly stagnant between the years 2005-2011.



Source: International Labour Organisation, 2018.



Source: PINTEC, 2005-2011.

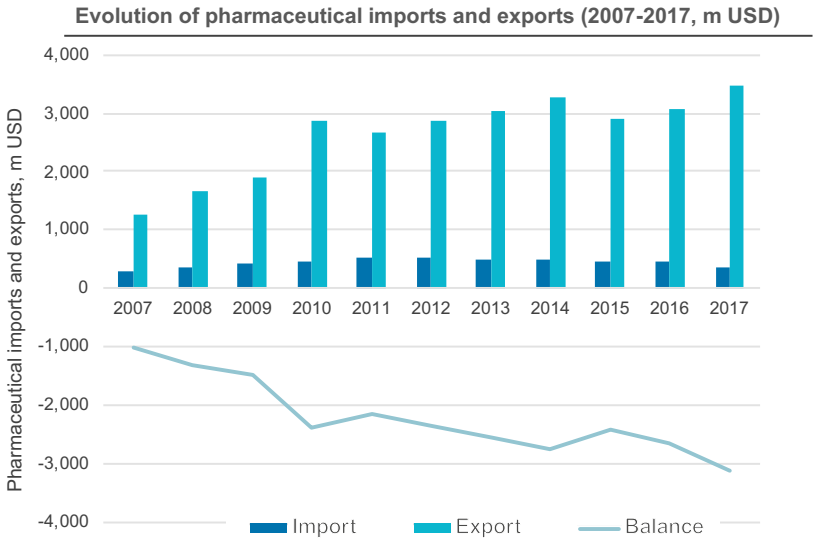


Sources: OEDE-MTEySS; INADEM Mexico; SINDUSFARMA, latest data available*.

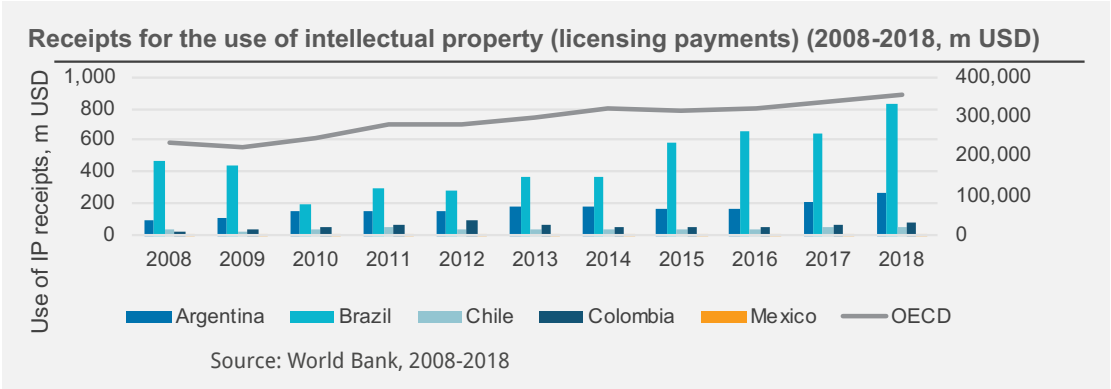
*2014 data for Argentina and Mexico, 2016 data for Brazil.

OTHER ECONOMIC ACTIVITY LINKED TO THE PHARMA SECTOR

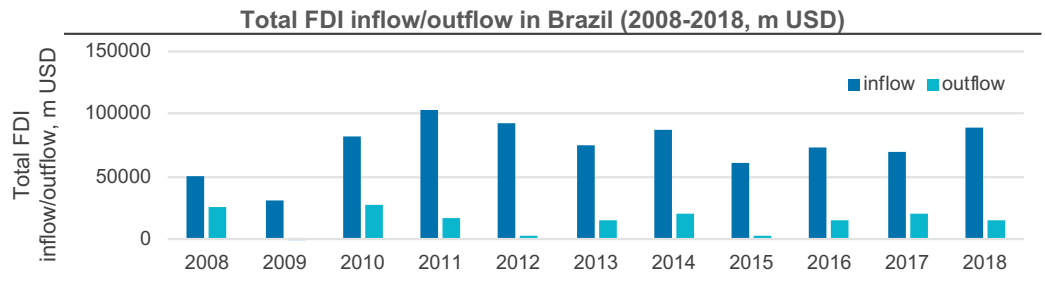
- Within the past decade, Brazil has had an increasing trade deficit in pharmaceutical goods though interviewees have noted recently, there has been an increase in importation of generic drugs.
- The level of FDI inflow into Brazil has remained high (compared to the level of FDI outflow).
- Moreover, as of recent years, Brazil has received growing levels of payments from licensing intellectual property, suggesting that there are a number of innovative products produced locally.



Source: UNCTADstat, 2007-2017.



Source: World Bank, 2008-2018



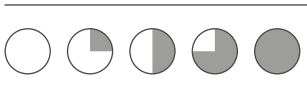
Source: World Bank, 2008-2018

BRASIL:
ASSESSMENT OF PERFORMANCE

- Brazil is an innovation leader in the LatAm region, with comparatively strong human resources, R&D investment and early stage innovative activity. However gaps remain in terms of healthcare infrastructure investment and patent system strength.
- Despite long-standing aspirations of economic growth, there remains opportunity for Brazil's innovation environment to grow to match OECD counterparts. This suggests that Brazil should ensure an environment that supports the development of local human resources and investment in infrastructure to encourage R&D investment.
- Reforms to strengthen the IP environment could drive patent applications and pharma confidence to conduct local clinical trials and licensing 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 average.

Aerial View of Amazon Rainforest in Brazil, shutterstock.com/worldclassphoto

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 Brazil (drawing from regions outside of Latin America).

Choice of case studies: We chose to focus on four markets that:

1. **Have shown a focus on strengthening innovative environment, particularly the IP protection**
   - Have made a significant commitment to focusing on innovation policy.
   - Implementation of regulatory data protection.
   - Focus on reducing patent backlog.

2. **Placed broadly in the same income, size and development category as Brazil when started focusing on innovation**
   - Drawing on case studies developed for pilot study in Argentina.
   - Classified as upper middle income to high income country.
   - Opting for membership in key international groups and organisations e.g. OECD.

3. **Show an observable impact on innovative activity**
   - Demonstrate good data availability.

WE USE CASES 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.

CASE STUDY ANALYSIS AND SCENARIOS: FOCUSING ON JAPAN, SOUTH KOREA, CHINA AND TAIWAN

CASE STUDY SELECTION:

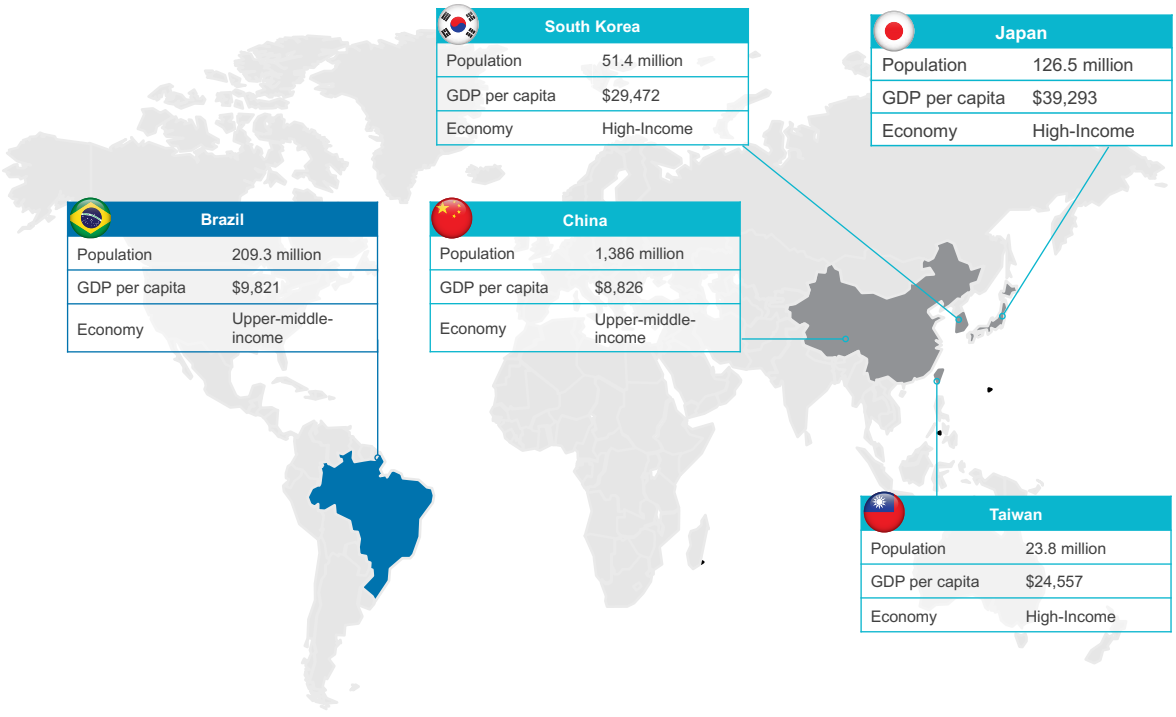
Our research and interview insights reveal that Brazil's key innovation policy gaps are:

- Lack of term for RDP.
- Patent backlog.
- Prior focus on pro "manufacturing" rather than "innovation" by some academics and local companies*.

Our criteria suggests four countries that Brazil could learn from

- Lessons from South Korea and Taiwan were applicable to Argentina. However, they remain relevant for Brazil. In addition, we examine two new countries: China and Japan.
- **Implementation of RDP:** Japan; South Korea.
- **Reduction of patent backlog:** Taiwan; Japan.

  We note that Brazil's economic size and therefore potential for innovation capacity is much larger than South Korea and Taiwan.
- **Comparable economy, increasingly pro-innovation:** China.



* CRA External Interview Program.

RDP – Regulatory Data Protection.

CASE STUDY:
SOUTH KOREA AND JAPAN

Changes in the policy regime to support innovation

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.[24]
- 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.[24]

The increased term of RDP for pharmaceuticals in Japan

- Japan also provides de facto RDP through PMS. Originally introduced in 2000 with 6 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).[25]
- 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.[25]

Impact of changes in the policy regime on innovation activity

- RDP aims to address the distortion in research incentives that is associated with fixed patent terms: the longer a drug spends in development, the less the remaining patent term, shifting incentives towards products for which clinical development is shorter.[26]
- 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."
- 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.[27]
- 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.[28]
- 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.[29]
- 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 [30] and at least 26 drugs with novel active compounds were launched between 1986- 2014, protected by this Act rather than a patent.[31]
- RDP provides an incentive for the introduction o new innovations and once period exclusivity ends, a growth in generic medicines.[32]
- 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.[33]
- Examination of orphan drug clinical trials highlights a significant increase in trials after the extension of de facto RDP in Japan in 2007.[34]

Main expected effects of policy change

- Implementation of RDP leads to increased clinical trials and product development since innovators feel secure that their R&D efforts are protected.

CASE STUDY: TAIWAN

Impact of changes in the policy regime on innovation activity

Impact of reduction of patent backlog in Taiwan

- By the end of 2017, a total of 431,255 patent cases were examined and closed, exceeding the original target of 413,316. In addition, the backlog of pending invention patent applications had dropped to about 44,000 – far less than the 160,000 cases pending in 2011.[35]
- In 2011, on the average, each examiner concluded 110 applications in 2011, an increase from 99 and 105 applications respectively from 2009 and 2010.
- Based on the statistics of the TIPO, the average examination decision period without requesting the AEP or PPH is 43 months for invention patent application in the year of 2012. The statistics until January of 2015 released by the TIPO show that the average examination decision period is from 72.6 to 141.6 days.[36]
- TIPO reports that by training examiners to help reduce backlogs during their services at TIPO, they will be able to take their skills to other businesses after the project is closed, allowing them to continue providing patent-related professional services. In other words, the project has also helped cultivate professional talents specializing in patents.[37]
- Reduction in the patent backlog also bears implications for patient access to medicines. For example, while the patent backlog diminished between 2011 and 2017 the number of novel medicines approved in Taiwan increased from 63 to 140, representing an increase of 122%, whereby the number of those domestically produced increased from 17 to 20 (representing an increase of 18%).[38] The number of generic products approved for the same period increased from 272 to 286, representing an increase of 5%, whereby more than half are domestically produced.[38]

Main expected effects of policy change

- Efforts to decrease the patent backlog will lead to increased patent applications in the short-term. In the medium-term, we would expect increases in R&D investment and employment.

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).[39] 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.[40] Literature notes that the National IP Strategy was significant in increasing the priority of IP on the national agenda.[41]
- 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.[42] 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.[43]
- 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.[44]

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.[45] Fang et al. (2015) also find that strengthening IP protection in China has led to increased private R&D investment.[46]
- 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.[47] 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.[48]

Main expected effects of policy change

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

DESPITE EFFORTS TO IMPROVE, GAPS IN THE IP REGIME REMAIN IN CHINA, SOUTH KOREA AND TAIWAN

Taiwan

Some gaps were addressed with the amendment of the Pharmaceutical Act in 2017:

- RDP did not cover additional new indications.
- RDP is limited to registrations filed within three years from the first approval granted anywhere in the world for a product based on that new chemical entity.
- Lack of systems to effectively prevent marketing of patent-infringing pharmaceutical products (in 2012 at least 58 patent-infringing drugs were approved in Taiwan, and most of them were included on the reimbursement lists).

The remaining gaps in the IP regime are mainly around enforcement:

Enforcement of the Patent Linkage System:

Particularly, when applying for market approval, the Abbreviated New Drug Application (ANDA) filer is allowed to reference the data of the approved originator. On the day following the 5-year RDP period, the generic manufacturer can launch its product. However, when applying for marketing authorisation, the ANDA filer is obligated to declare that the generic drug does not infringe any IPRs of the reference drug. Despite this the TFDA may approve it for the market regardless of whether the declaration is correct or false, and whether or not the reference drug is protected by patents.

Enforcement of Preliminary Injunction:

The ANDA filer is not required to notify the branded manufacturer, who will only become aware once the generic is launched on the market and be in a position to file a lawsuit. Due to Taiwan's double-track system of administrative law and civil law, civil action and has no influence on the grant of market approval, which is an administrative matter. Thus, a preliminary injunction ordered by a civil court neither prevents the TFDA from granting market approval nor does it prevent the National Health Insurance Administration (NHIA) from including the infringing pharmaceuticals on reimbursement lists.

China

Literature generally agrees that despite progress IPR protection reform by China, there remains room for improvement. Cavazos Cepeda et al. agree that China has made progress in strengthening IPR over the past two decades, measured by literature through indicators such as the Patent Rights Index. However, the authors emphasise that uncertainty around the protection of IPR remains an important deterrent for foreign as well as domestic firms engaging in R&D and innovation.[51]

Key weaknesses that remain, include:

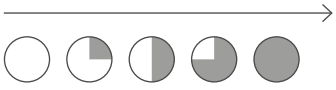
- **Weak patent enforcement:** Transparent mechanisms are needed in China to ensure parties are afforded the opportunity to resolve patent disputes before potentially infringing pharmaceutical products are launched in the market.[52] It remains unclear whether, recent reforms to facilitate the availability of preliminary injunctions in trade secrets and other IP disputes will, in practice, enable right holders to obtain timely preliminary injunctions against all categories of trade secret misappropriation.[53]
  - Specifically the USPTO report that:[53] "...Pharmaceutical innovators are not permitted to rely on supplemental data on a consistent basis to satisfy relevant requirements for patentability during patent examination proceedings, patent review proceedings, and judicial proceedings. This practice leads to application denials, or the invalidation of existing patents, even when counterpart patents are granted by other major patenting offices.
  - China also continues to impose unfair and discriminatory conditions on the effective protection against unfair commercial use, as well as unauthorized disclosure, of test or other data generated to obtain marketing approval for pharmaceutical products. China provides such protection only if the drug in question has not previously received marketing authorization outside China, which is an unfair and discriminatory condition that is unrelated to the purpose of such protection."
- **Loss of Patent Term Due to Regulatory Delay:** [52] Lengthy regulatory approval processes for pharmaceutical products results in a significant loss of effective patent term for such products. China fails to provide patent term extensions to compensate for unreasonable delays that occur in granting a patent.
- **Restrictive patentability criteria:** Certain therapeutic methods of a known indication e.g. new dosage regimens, treatment of new subgroups of patients or new routes of administration cannot be protected by patents in China. As a result, China's patentability criteria fails to capture the significant benefits that innovations through such methods bring to patient. The inability to obtain patents on these inventions undermines the incentives to invest in them, particularly to the extent they are targeted at particular medical and health problems in China.

IMPACT ATTRIBUTABLE TO THE CHANGE IN REGULATION IN A 5-YEAR PERIOD: SUMMARY

	SOUTH KOREA	TAIWAN	CHINA	JAPAN
KEY INNOVATION POLICY CHANGES	"Bio-Vision 2016" Plan of 2007. "577 Initiative" of 2008.	Biotech and New Pharmaceutical Development Act (2007).	Program for Science and Technology Development (2006).	Science & Technology Basic Plan (1996 – 2016).
KEY IP REGULATION CHANGES	Pharmaceutical Affairs Act of 2007: Grant of RDP	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	Growth	Attributable to regulation
Innovative Activity	BERD	11%		14%		26%		4%	
	Early research (publications)	4%		4%		12%		-1%	N/A
	Clinical trials (All)	7%		17%		16%		-3%	N/A
	Patents (local residents)	25%		23%		35%		0.6%	
	Patents (local non-residents)	16%		11%					
	Patents (USPTO)	29%		20%		-2%	N/A	-31%	N/A
Economic Activity	Employment in biopharmaceuticals	7%		8%		17%		-1%	N/A

Impact of the regulation



RDP – Regulatory Data Protection.

Chapada dos Guimarães National Park, Mato Grosso, Brazil, shutterstock.com/Uwe Bergwitz

4.

Innovation policy implications for Brazil

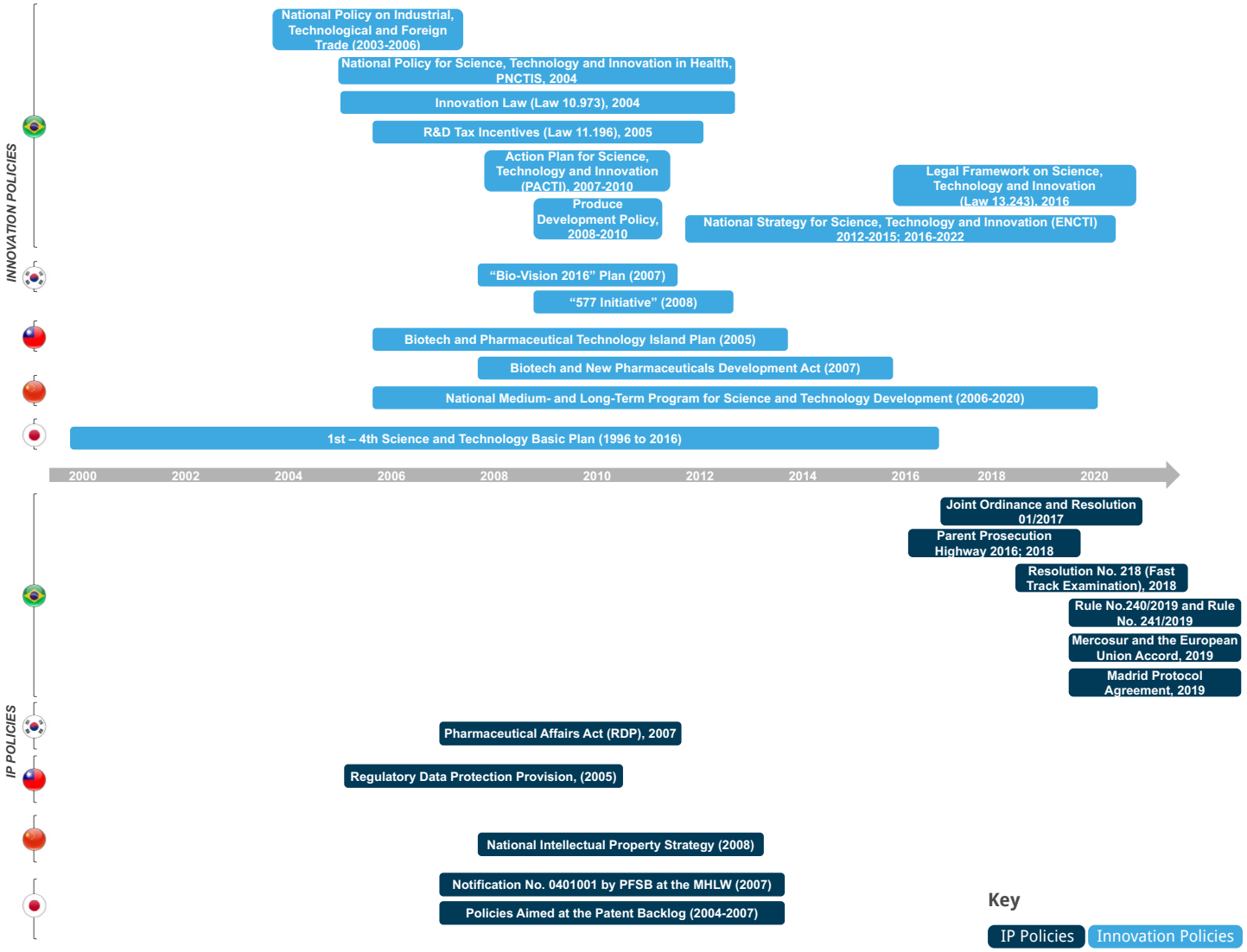
WHAT IF BRAZIL CONTINUES ON A POSITIVE TRAJECTORY OF INNOVATION FRIENDLY ENVIRONMENT?

1. Support for IP and innovation in biopharma:

- Brazil has recently instituted policies that are more favourable to the growth of the local biopharmaceutical industry.
- Brazil has also improved the issue of priori consent by ANVISA and has introduced Joint Ordinance n. 01/2017. Thus, this is seen as a workable **solution to the dual patent examination problem,** although the ideal would be the analysis of patent applications for pharmaceutical products to pass only through the patent office, as in other countries.
- The patent backlog is also being addressed through resolution and various instrument to speed up examination.

Additional support for IP:

- However, compared to other case study markets, Brazil lags behind on IP.
  - IP protection is weaker due to the lack of RDP term pharmaceutical products for human use.
  - If the efforts to reducing approval timelines for patents are sustained then that would ensure sufficient predictability for local and foreign innovators in obtaining a patent on their invention and make Brazil equally attractive as other countries.



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 Brazil for the latest available year, assuming Brazil 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.

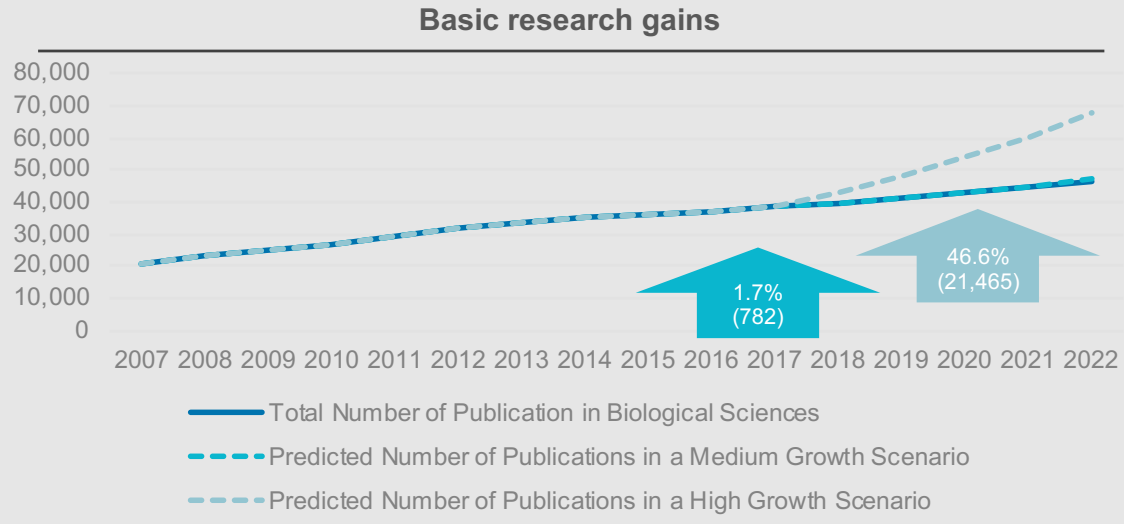
SCENARIOS: DEVELOPING SCENARIOS ON IMPACT ON STRENGTHENING IP REGIME AND INNOVATION POLICY

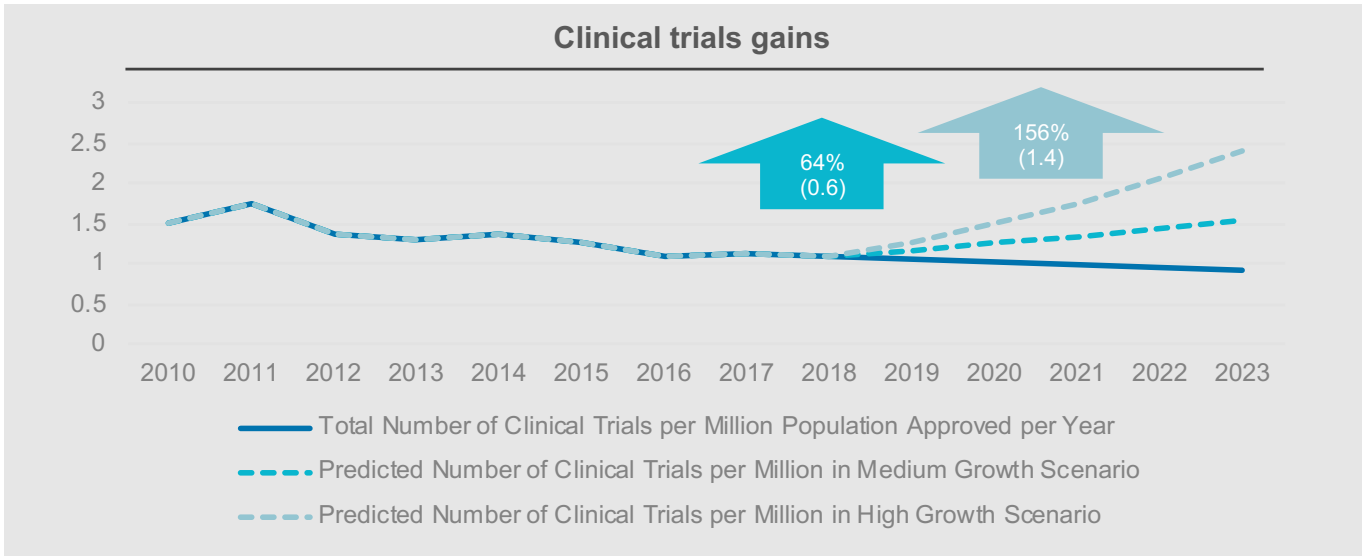
Drawing from the case study analysis and the statistical analysis, we establish two scenarios:

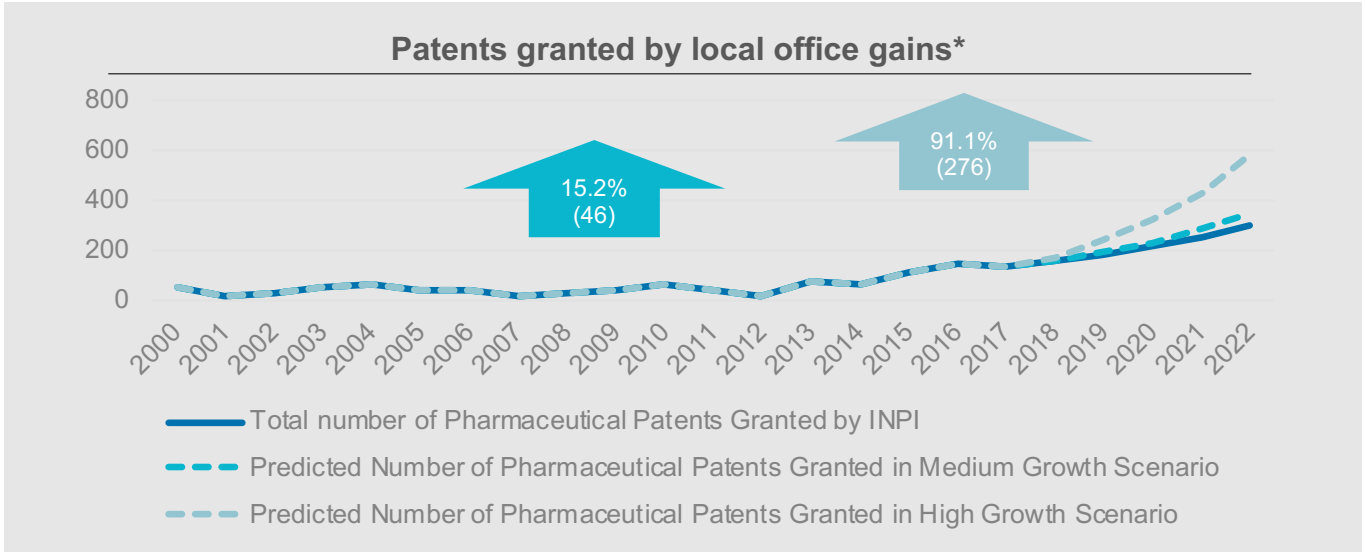
- A scenario assuming an IP regime change in conjunction with other innovation policies (medium growth due to limited implementation).
- A scenario assuming an IP regime change in conjunction with other innovation policies (high growth with good policy implementation).

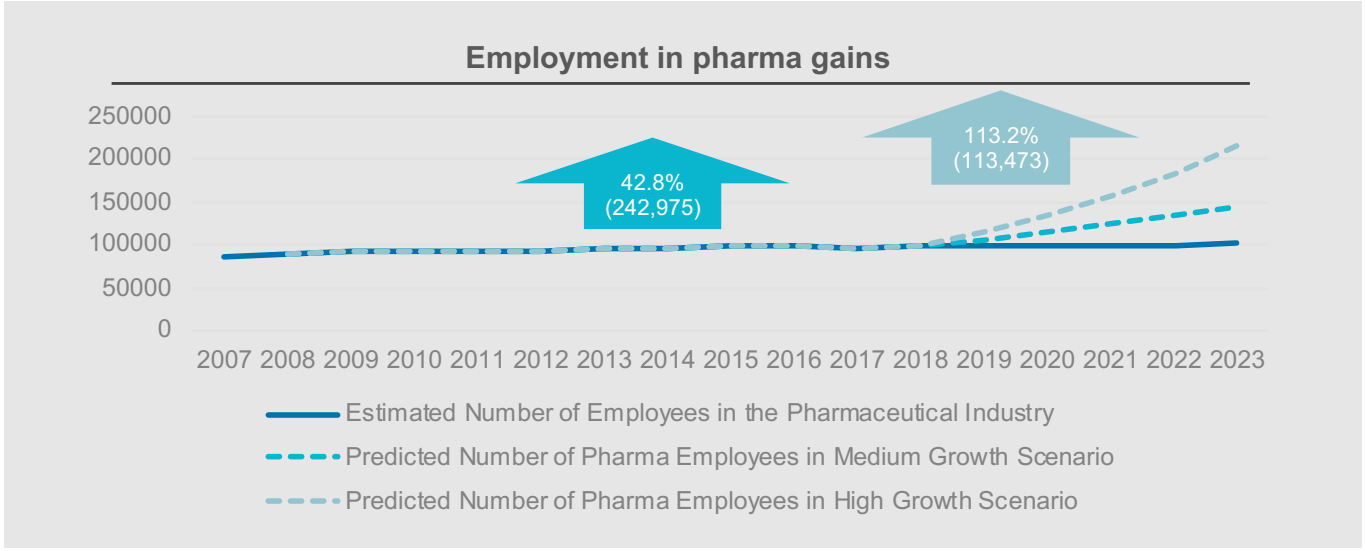
	SCENARIO DETAILS	BASIC RESEARCH	CLINICAL TRIALS	PATENTS	EMPLOYMENT
IP REGIME AND INNOVATION POLICY – MID GROWTH	Paced growth scenario based on an improvement of the IP regime (by introduction of RDP and tackling the patent backlog) and other innovation incentives but with limitations in implementation (based on case study markets analysis).	Average annual year on year growth of scientific publications in the biological sciences of 4%.	Average annual number of clinical trials of 7%.	Average annual year on year growth in pharmaceutical patents of 22%.	Average annual year on year growth in employment in the biopharmaceutical industry 8%.
IP REGIME AND INNOVATION POLICY – HIGH GROWTH	Escalated growth scenario based on an improvement of the IP regime (by introduction of RDP and tackling the patent backlog) and other innovation incentives with good implementation (based on case study markets analysis).	Average annual year on year growth of scientific publications in the biological sciences of 12%.	Average annual number of clinical trials of 17%.	Average annual year on year growth in pharmaceutical patents of 35%.	Average annual year on year growth in employment in the biopharmaceutical industry 17%.

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







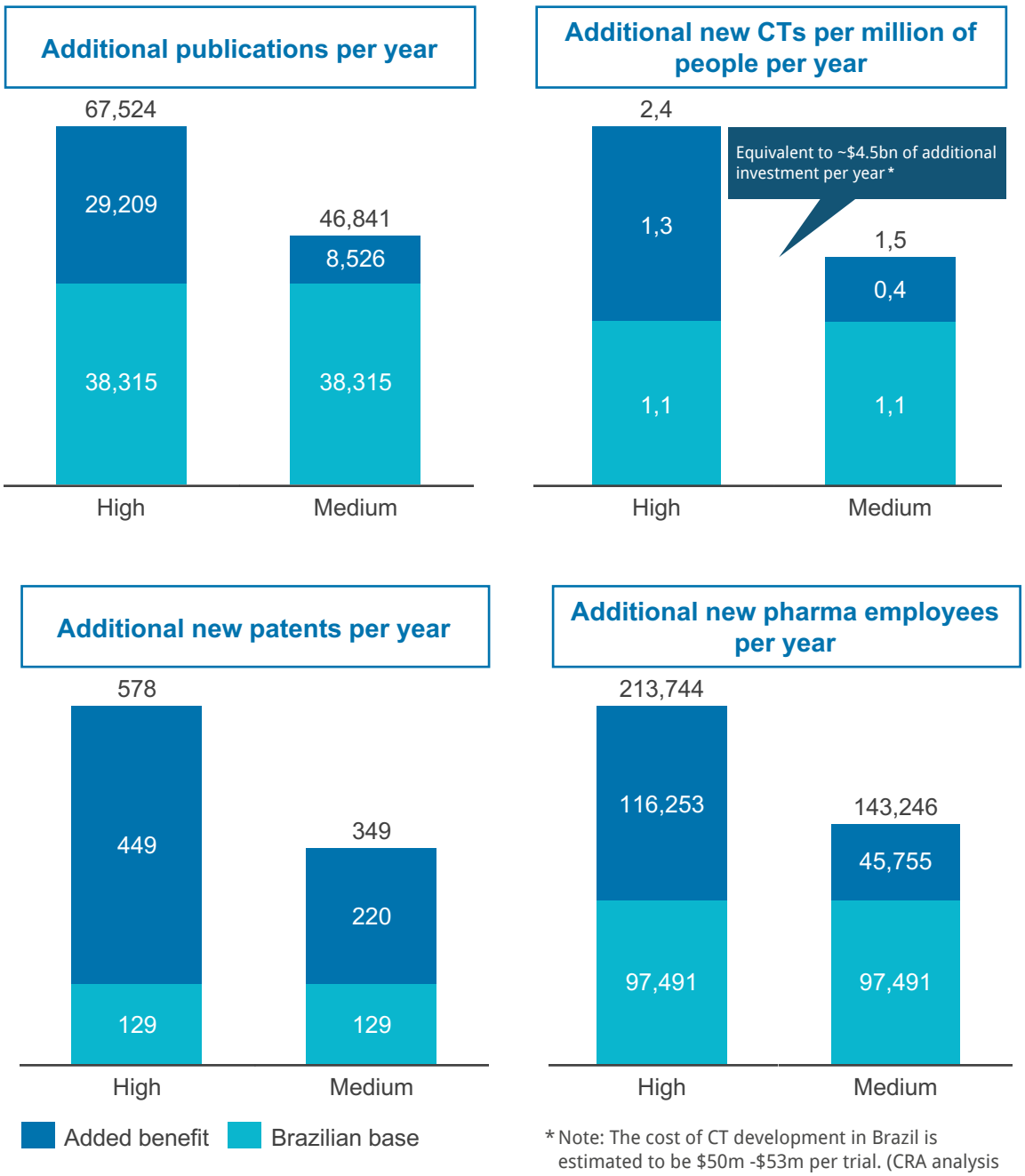


Note: the number of employees in the pharmaceutical industry was estimated based on ILO data for the number of employees in knowledge intensive industries and the number of pharmaceutical industry employees in 2016. The employment ratio of pharmaceutical to total knowledge intensive industries is assumed constant throughout the years.

ILLUSTRATION OF GAINS FOR BRAZIL (ABSOLUTE GAINS)

Drawing from the findings in the analysis, strengthening the IP environment in Brazil 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 (which Brazil already performs well on and are expected to be indirectly impacted by IP and Innovation regime changes).



* Note: The cost of CT development in Brazil is estimated to be $50m -$53m per trial. (CRA analysis of I. Koster (2010) and ASPE (2014).

ENABLERS OF INNOVATIVE ACTIVITY AND CHALLENGES IN BRAZIL

- 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, Brazil exhibits:
  - Good education base, large and diverse population, strong local biopharmaceutical industry, which increasingly investing in R&D, but
  - Lags behind on investment in technology transfer and collaborations, research, regulatory process, system predictability due to large patent backlog and strength of protection.
- The rest of the analysis focuses on potential gains from improving the enablers and particularly the strength of the IP regime.

	AREAS	DESCRIPTION IN BRAZIL
ENABLERS	**Human capital and expertise**	Good availability of top universities and education attainment to higher degrees and good standards.
	Size and diversity of population	Being highly populated, Brazil represents an attractive market for foreign manufacturers. The heterogeneity of the local population means that Brazil is attractive location for clinical trials.
	Private investment in R&D	The local pharmaceutical is increasingly investing in innovative activities and R&D.
	Technology transfer and collaborations	Whilst Brazil has a strong base of researchers in academia, there are legal barriers to public-private collaborations impeding technology transfer.
	Regulatory methods and process	Though improvements have been made, the process for regulatory approval of clinical trials remains relatively slow and is regarded as inconsistent.
	Predictability of the patenting system	Given the large patent backlog innovators can face substantial risk in obtaining a patent.
	IP protection	Lack of RDP term for pharmaceutical products for human use, on top of the long timelines for approving a patent.

FINDINGS

1. Brazil's current innovation capacity and potential

Brazil leads the LatAm region in many innovation activities

- The innovative potential of Brazil is indicated by the market as a leader in businesses expenditure on R&D and strong educational attainment of the population. In addition, Brazil has fostered a growing number of patent filings and is a region-leader in terms of international S&T collaborative activities.
- Interviews with experts from INPI and local CROs have revealed significant government efforts to strengthen Brazil's innovation environment.

Brazil exhibits room for improvement when compared to OECD and Asia markets in many innovation activities

- Brazil's innovative achievements have occurred despite the relatively low investment in resources for innovation. This is reflected by comparatively low R&D investment and spending on healthcare infrastructure.
- As a consequence, outputs of innovation, as measured by indicators such as scientific publications and clinical trials, remain relatively low in Brazil.
- Analysis suggests that Brazil has the potential to unlock further value from existing resources in undertaking research activities and increasing the levels of investment.
- This is supported by examination of similar markets in Asia, which following positive reforms to innovation policy, have demonstrated significant economic benefits. This suggests the potential for Brazil to achieve comparable growth.

This has led to a less dynamic industry with low and decreasing economic outputs

- A decrease in growth and overall low levels of innovative activity lead to losses in employment, trade and taxes requiring a broader consideration in policy.

2. Lessons from statistical analysis and case studies

Updated statistical analysis shows that IP protection and patent regime leads to a positive impact across innovative and related economic activities

- This in turn, incentivises more overall spend on research activities. Indeed, applying updated data illustrates an even stronger statistical association between IPR and innovative activities such as R&D.

However, case studies show that a broader approach to support innovation is beneficial across activities and particularly clinical trials, patents issued and employees in research

- This entails innovation plans in addition to strong rules on IP protection and economic incentives.

3. Implications for Brazil's innovation and economic policy

Brazil has recently implemented, or is in the process of including, several reforms that aim to strengthen the innovation environment

- Our analysis suggests the potential for further mechanisms to unlock the potential value of strong resources in Brazil and incentivise increased economic activity.

IP regime

- Brazil has made several recent efforts to strengthen it's IP environment and ensure alignment with global standards. However interviews revealed that benefits to innovation have yet to be realised, in part due to limited enforcement. Increasing government accountability will ensure recent reforms will encourage innovation.

Regulatory Data Protection

- Findings from comparable Asian markets reveal the benefits of strong protection for clinical trial test data. Innovators would be able to investment in clinical trials and manufacturing with security that their innovation would be protected.
- Ensuring RDP for pharmaceutical products, in line with countries of similar healthcare development and aspiration for innovation would support local investment in clinical research.

Direct support for research

- Lessons from China highlight the value of targeted programs of investment in the science and technology sector.
- Increase levels of public spending on R&D activities in general and in pharma to provide support to early research and signal an enhanced focus in the sector.

Encourage collaboration between public and private entities in conducting research

- Interviews with external experts revealed Brazil's population's strong skill-set. However these remain under-utilised due to lack of diverse opportunity in Brazil.
- Increase incentives for academics in biomedical sciences to stay or return to Brazil and engage in research activities.

Macro stability

- Brazil has recently grown out of economic recession and has a new government. Government incentives for R&D and ensuring a stable investment environment will signal the aspiration for innovation and economic growth.

5. Appendix:

SOUTH KOREA
INNOVATION AND IP POLICIES

CHANGES IN THE IP REGIME

SUBSTANCE PATENT AMENDMENT 1981

Amendment to the 1961 Patent Law to introduce substance patents.

PATENT LAW STANDARDISATION 2001

The government changed their 'Patent Law' and worked with the World Trade Organisation (WTO) to bring Korea's patent regime in line with international standards. This started in the '80s with the substance patent amendment which opened the government's eyes to R&D.

PHARMACEUTICAL AFFAIRS ACT 2007 ★

The Pharmaceutical Affairs Act (PAA), initially amended in 2007, includes a provision that new drugs and certain prescription drugs benefit from de facto data protection of four to six years.

DOSAGE PATENT DECISION 2015

The South Korean Supreme Court allowed patenting of dosage regime.

ORPHAN DISEASE MANAGEMENT ACT 2016

The Orphan Disease Management Act (ODMA) allowed orphan drugs to benefit from a 10 year re-examination period if the indicated disease does not have therapeutic alternatives.

CHANGES IN INNOVATION POLICY

"BIOTECH 2000" PLAN 1994

National Science and Technology Plan "Biotech 2000" recognising the importance of biotechnology as an emerging sector and shifting national attention to work in that area.

KOREAN HEALTH INDUSTRY DEVELOPMENT INSTITUTE 1999

Establishment of the Korean health Industry Development Institute to improve the national health industry by providing support for programs and strengthen the global competitiveness of the national health industry.

"BIO-VISION 2016" PLAN 2007 ★

National science and technology plan with the intention of expanding Korean R&D infrastructure, globalize the bio industry and raise awareness among the general public.

"577 INITIATIVE" 2008 ★

A science and technology plan that aimed to invest 5% of GDP on R&D, focused on 7 key S&T areas & become one of the major global S&T powers.

Key

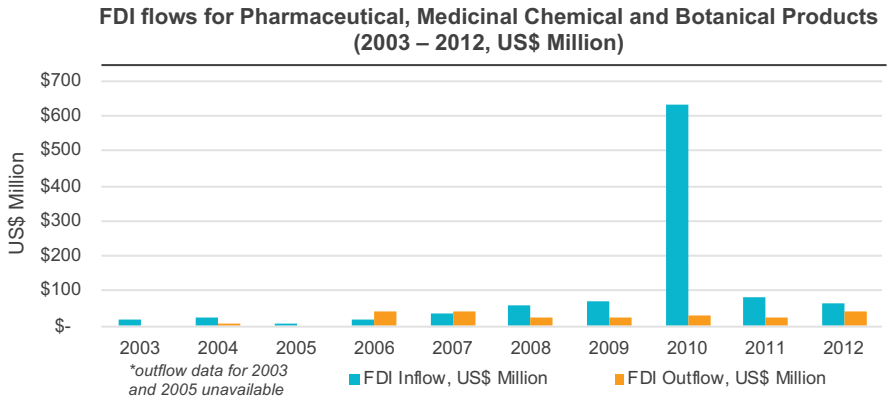
★ Focus of analysis.

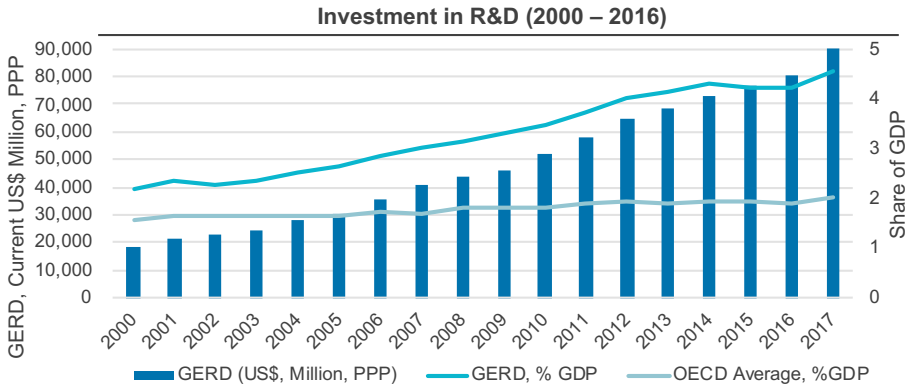
Note: Regulation marked with a star will be used as proxy for change in estimating growth differences.

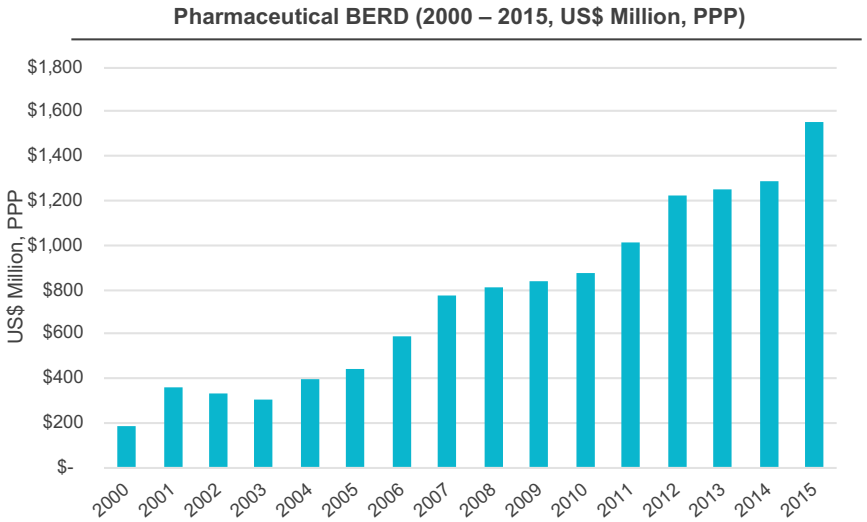
SOUTH KOREA

INVESTMENT IN R&D AND FDI

- With a national focus on biopharma, South Korea has seen a rapid increase in government and private R&D investments and a focus on the pharmaceutical industry.
- South Korea has enjoyed increasing FDI inflows for pharmaceuticals, demonstrating it's ability to attract foreign investment by raising awareness of the strength of the national industry.







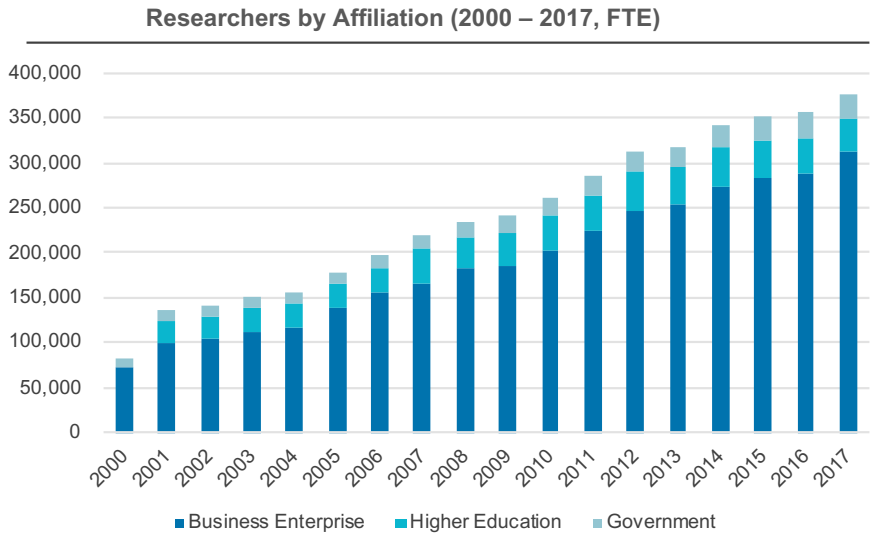
GERD = gross expenditure on R&D, BERD = business expenditure on R&D, FDI = foreign direct investment, OECD = organisation for economic cooperation and development, KOTRA = Korean Trade-Investment Promotion Agency.

Sources: OECD Statistics, KOTRA 'Invest Korea Annual Report 2010'.

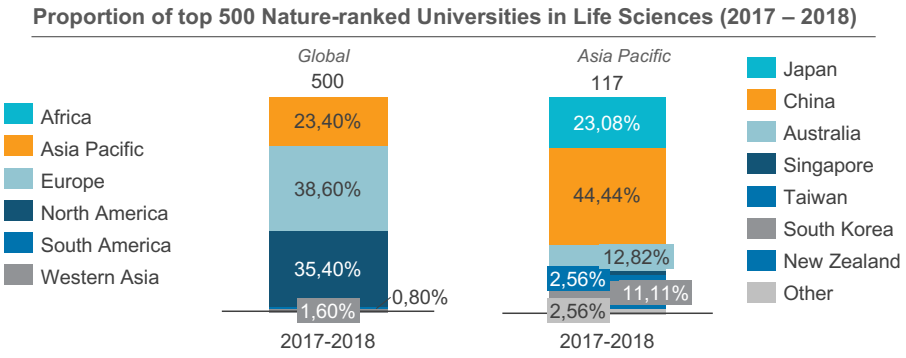
SOUTH KOREA

UNIVERSITIES AND QUALITY OF EDUCATION

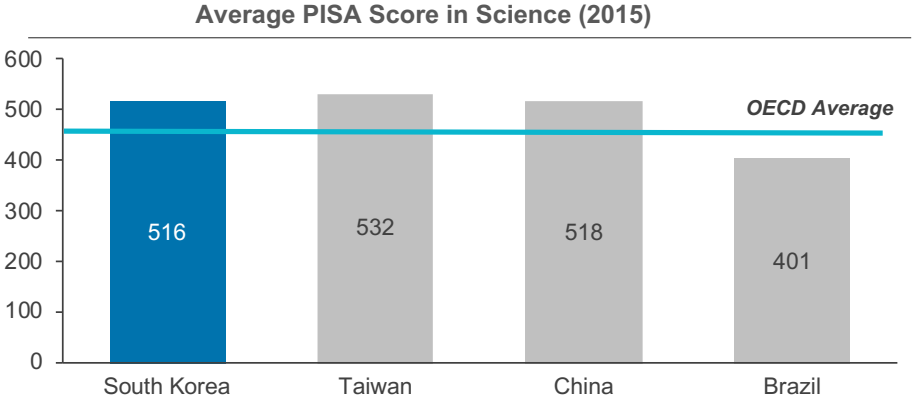
- South Korea's shift in national mentality to focus on becoming a leading biotechnology powerhouse has also been seen by the spill over effects in higher education.
- South Korean universities regularly appear in top 200 universities in the world for a variety of biomedical subjects and the general trend of focus on science and technology have put Korea as the 2nd largest Asian nation (on par with China) to be represented in the best universities in the world.



Sources: OECD Statistics, Top Universities (QS Rankings) 2018/2019.



Source: Nature Publishing (2018).



Source: National Center for Education Statistics, https://nces.ed.gov/surveys/pisa/pisa2015/pisa2015highlights_3.asp.

SOUTH KOREA

COLLABORATION AND INFRASTRUCTURE FOR RESEARCH

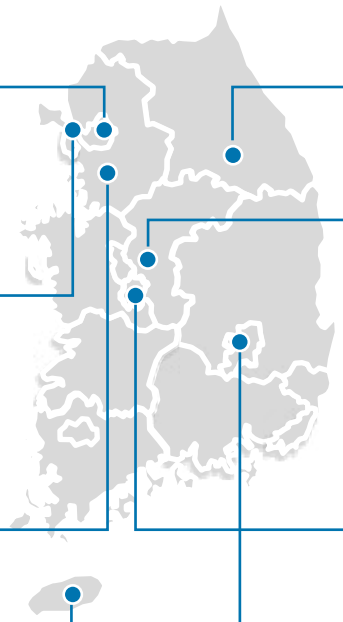
- South Korea has spurred the creation of bio clusters that vary in activity (from R&D to production) and industry (from pharmaceuticals to medical devices) aiming to gain both vertical and horizontal integration opportunities.
- This push towards an innovative environment throughout the nation has attracted numerous international companies, government-funded research centres and universities of upmost academic excellence. By being in close proximity to each other, the simplification of process is possible with companies able to seek regulatory and government help by having agencies near them or being able to hire the brightest academic talents.

Seoul
(4.7k employees, 185 companies, 239.2 billion KRW output):
- **Hongreung:** startup and commercialization support
- **Medical and pharmaceutical industry:** clinical R&D

Incheon
(3.5k employees, 22 companies, 704 billion KRW output):
- **Songdo:** biopharmaceutical production
- **Bio/medical industry:** R&D and production

Gyeonggi-do
(13.6k employees, 313 companies, 4.2 trillion KRW output):
- **Gwanggyo-Pangyo Technovalley:** academic-industry collaboration, drug analysis support
- **Bio/medical industry:** Production and R&D

Jeju
(200 employees, 14 companies, 3.9 billion KRW output):
- **Technopark, Science Park**



Gangwon-do
(2.3k employees, 55 companies, 214.3 billion KRW output):
- **Wonju**
- **Medical devices:** R&D and production

Chungbuk
(5.6k employees, 72 companies, 1.4 trillion KRW output):
- **Osong Advanced Medical Complex:** bio clinical and non clinic research
- **Biomedicines and medical devices:** R&D

Daejeon
(2.2k employees, 81 companies, 309 billion KRW output):
- **Daedeok Innopolis:** R&D focus, venture firms
- **NT, BT, IT and convergence technology:** R&D

Daegu
(600 employees, 23 companies, 10.1 billion KRW output):
- **Daegu Advanced Medical Complex:** chemical drugs, medical industry
- **IT-based devices, synthetic new drugs:** R&D and production

Sources: Biotechnology in Korea 2018 Report (https://www.kribb.re.kr/eng/file/2018_BIK.pdf).

Daedeok Innopolis

Seoul BIOHUB

Pangyo Technovalley

Daegu-Gyeongbuk Medical Cluster

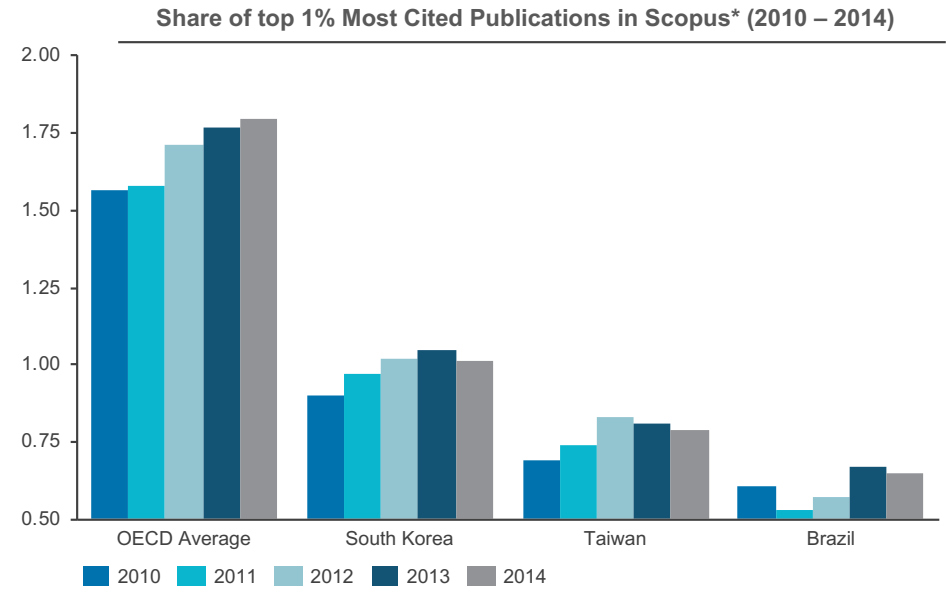
Songdo, Incheon

Osong Advanced Medical Complex

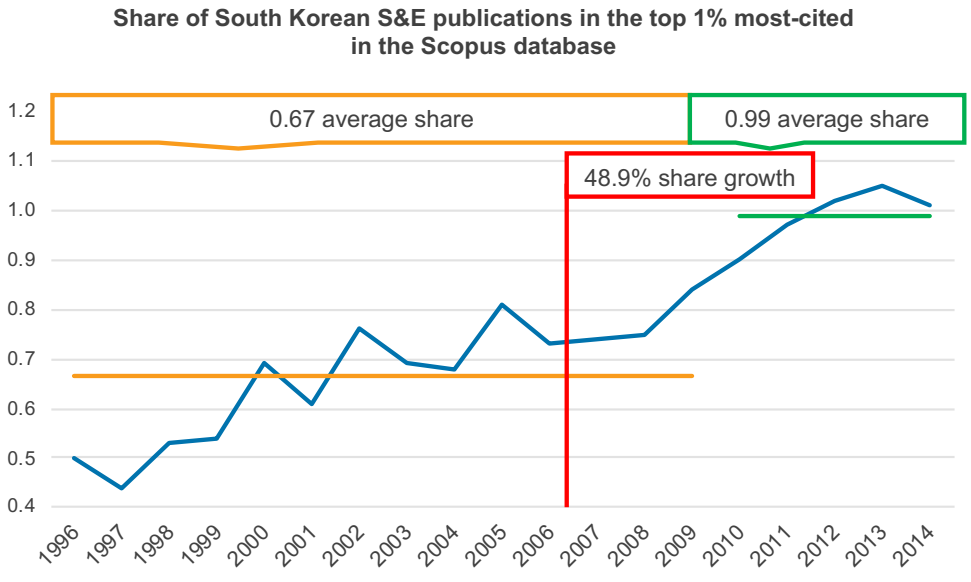
SOUTH KOREA

INNOVATIVE ACTIVITY: PUBLICATIONS

- South Korean publications have grown significantly in impact factor over between 1996 and 2014 as shown by the rapid growth in share of the top 1% of most-cited S&E publications, having more than doubled in those 18 years.
- Whilst lagging behind the US and EU, the share of publications has increased in comparison to other Asian neighbours such as Taiwan.



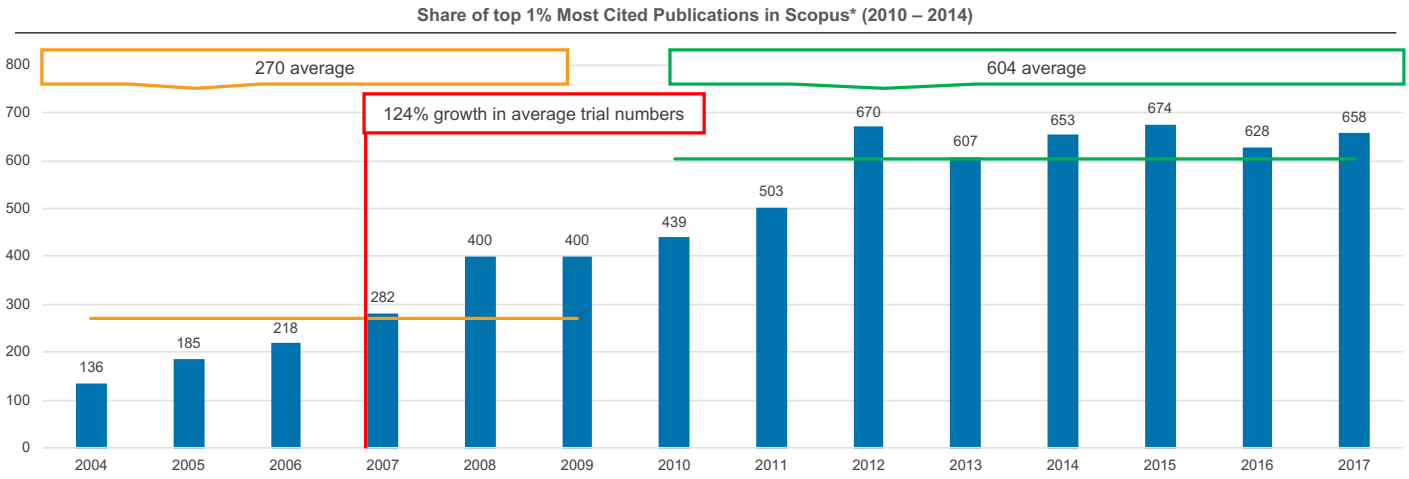
Sources: Scopus database; National Science Foundation Survey 2018.



SOUTH KOREA

INNOVATIVE ACTIVITY: CLINICAL TRIALS

- South Korea has experienced a rapid increase in the number of clinical trials over the last 14 years with the largest jump being between 2011-2012 where an additional 167 trials were conducted.
- The period between 2012-2017 has been relatively stable with only minor occasional decreases in trial numbers but the continual trend of 600+ trials for 5 consecutive years speaks to the reliability of Korea as a clinical study powerhouse.

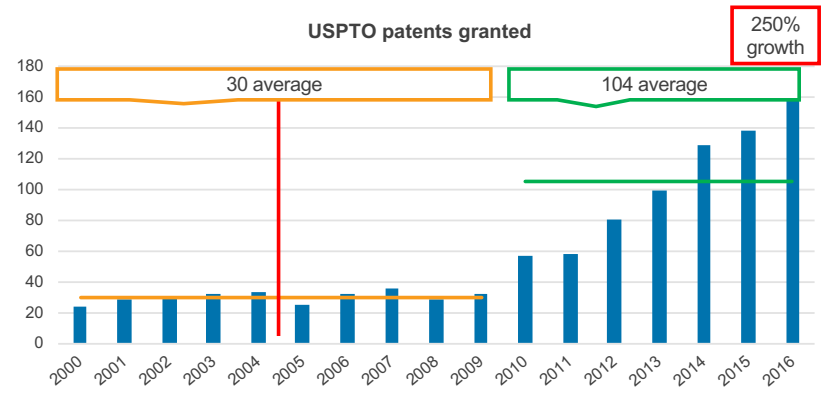


Sources: Ministry of Science and ICT/Biotech Policy Research Center (2018).

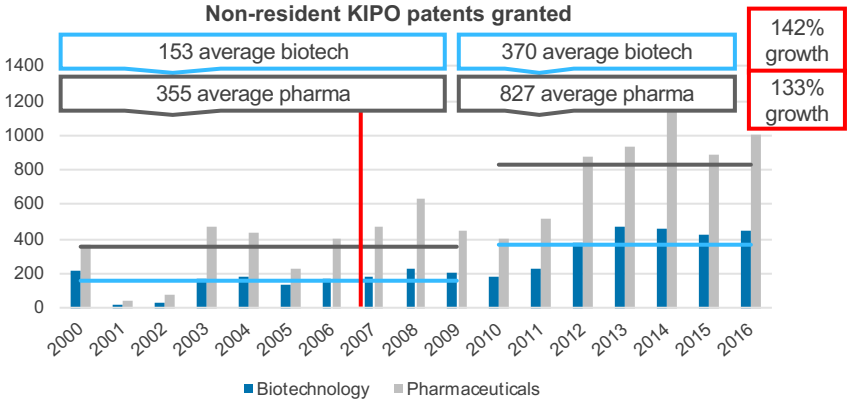
SOUTH KOREA

INNOVATIVE ACTIVITY: PATENTS

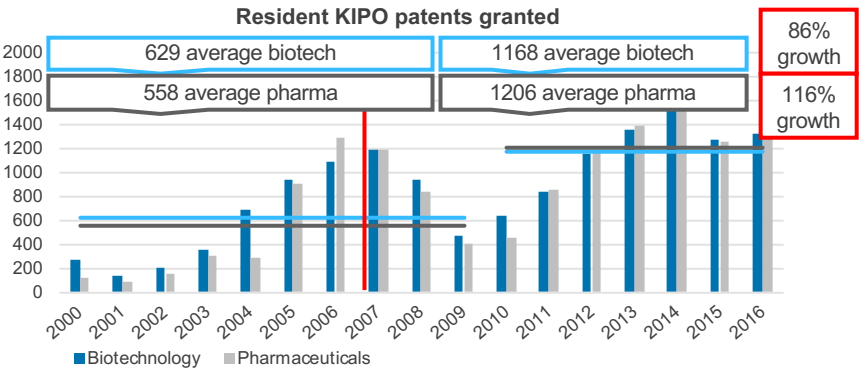
- There has been a sharp growth in USPTO patents granted from 2009 potentially showing the globalisation elements of the '577 Initiative' as more Korean companies expand internationally and seek to patent in the US.
- Additionally, the number of KIPO patents for residents and non-residents has been growing with the largest increase observed for pharmaceutical patents post-2010 for non-residents and post-2004 for residents.
- Resident patents suffered from a decrease between 2008 and 2010 (in line with the 2008 mortgage crisis) but rapidly recovered from 2011 testifying to the resilience of the Korean economy.



Source: USPTO.



Source: KIPO.

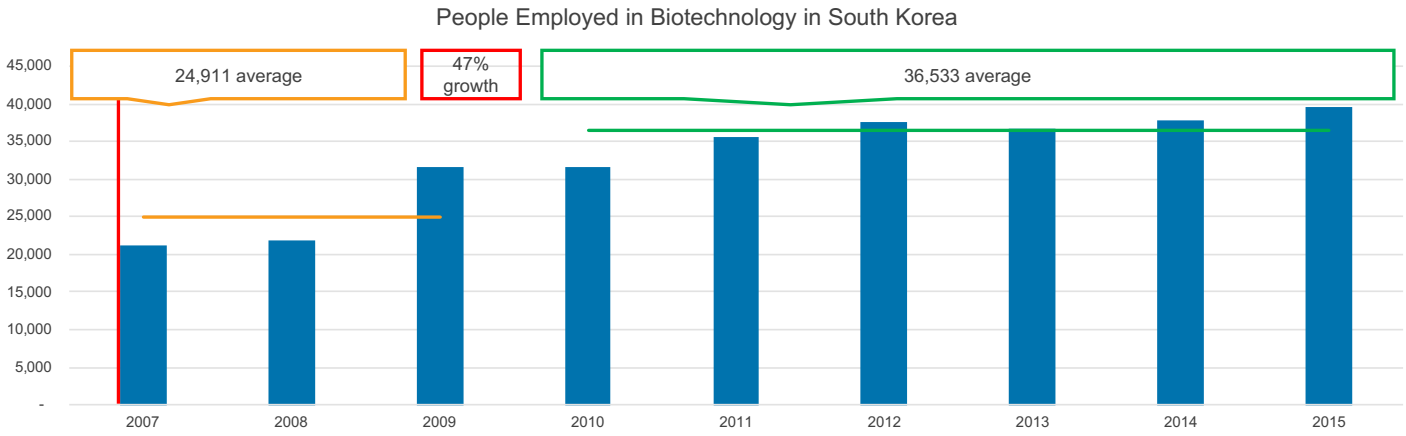


Source: KIPO.

SOUTH KOREA

EMPLOYMENT IN THE BIOTECH SECTOR

- In line with the implementation of ambitious biotechnology and science & technology plans from 2007 (notably the 2007 'Bio-Vision 2016' initiative and the 2008 '577 Initiative') the number of individuals hired in biotechnology has steadily increased since 2007 (with a minor dip in 2013).
- This increase in employees may also testify to the strength and prowess of Korean universities for biological sciences as they produce talented individuals who have the skills and tools to go on and innovate.



Source: Korea Research Institute of Bioscience and Biotechnology, http://www.kribb.re.kr/eng/file/btik/btik_010.html; https://www.kribb.re.kr/eng/file/2018_BIK.pdf.

SOUTH KOREA

IMPACT OF IMPROVED IP REGIME ON INNOVATIVE ACTIVITY

- Innovation policy has long been debated in South Korea and there may be challenges in unpicking the causal factors underlying growth rates in innovation, advances in innovative initiatives or the general progression of the science and technology economy.
- **Prior studies have observed the following**
  - Jae-Hong Baek (2008) notes how strong IP increases market competitiveness. This can be incentivised through government initiatives such as KIPO IP consultations for companies in an effort to nurture high-growth entities.
    - With close to 1000 domestic biotech companies[54], the Korean industry has embraced the culture of nurturing their companies with a focus on IP as shown by the number of USPTO and KIPO patents granted.
    - The size of capable workforce, number of world-renowned universities and creation of numerous bio clusters emphasises the national desire to embrace an entrepreneurial spirit – the ability to do this in a strong and reliable IP environment enables long-term growth and global competitiveness.
  - 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."
    - This departure from a 'copy-cat' economy launched Korea into an innovation spree with 1 national science and technology plan being completed by the turn of the millennium and 2 additional ones planned (1 launched) by 2008.
  - Government support for pharmaceutical R&D has also been a significant contributing factor with investments increasing from 154 billion KRW in 2006 to 294 billion KRW and a commitment to pledge 5% of the GDP towards science and technology R&D (part of the '577 Initiative').
    - This significant increase in R&D expenditure has mainly been concentrated in universities and companies with the former benefiting more. In the United States, government funding indirectly contributed to at least half of new drug approvals (Lichtenberg, 2011) emphasising the role of government funding in bio-pharmaceutical innovation.

Seoul City Skyline, South Korea, shutterstock.com/CJ Nattanai

TAIWAN
INNOVATION AND IP POLICIES

CHANGES IN THE IP REGIME

EXTENSION OF PATENT TERM (1992)

The patent term extended to 20 years (WTO rules).

PATENT EXTENSION (SPC) PROVISION 1997

Amendment to the Patent Act was introduced to allow for the possibility to extend patent by 2-5 years to a maximum of 14-year protection period following the marketing authorisation of the product, with the aim to compensate for regulatory delays.

REGULATORY DATA PROTECTION PROVISION (2005) ★

- Taiwan effectively implemented Article 39.3 of the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and introduced exclusivity for 5 years*.
- The basic framework for patent linkage was introduced – registration of patent owners upon marketing authorisation similar to Orange Book.

RDP AND PATENT LINKAGE PROVISION (2017)

- RDP was expanded to include new indications though lasting for 3 years, which can be extended to 5 years if clinical trials are conducted in Taiwan.
- The Patent Linkage Provision requires generic manufacturers to demonstrate evidence that no patents would be infringed upon grant of marketing authorisation.

CHANGES IN INNOVATION POLICY

BIOTECH AND PHARMACEUTICAL TECHNOLOGY ISLAND PLAN (2005) ★

With an aim to build Taiwan's Biobank database and establish a clinical trial and research system.

BIOTECH AND NEW PHARMACEUTICAL DEVELOPMENT ACT (2007) ★

Incentivised academia-industry collaborations and tech transfer by allowing for publicly-funded researchers to help private companies with R&D & serve as biotech company executives. Introduced R&D tax incentives.

ACTION PLAN FOR BIOTECH TAKE-OFF (2009 AND 2013)

- Key actions included to strengthen Taiwan's technology acquisition capabilities, establish the industry's venture capital, promote the country's incubation system.
- Promote the development of legal, commercialisation and technical services in Taiwan to improve world-wide perception.

LATER PLANS IN 2015 ONWARDS

- Bio-economy Development Plan 2015.
- Five plus Two Innovative Industries for Priority Development, with a specific Biomedical Industry Innovation Program in 2016.

Key

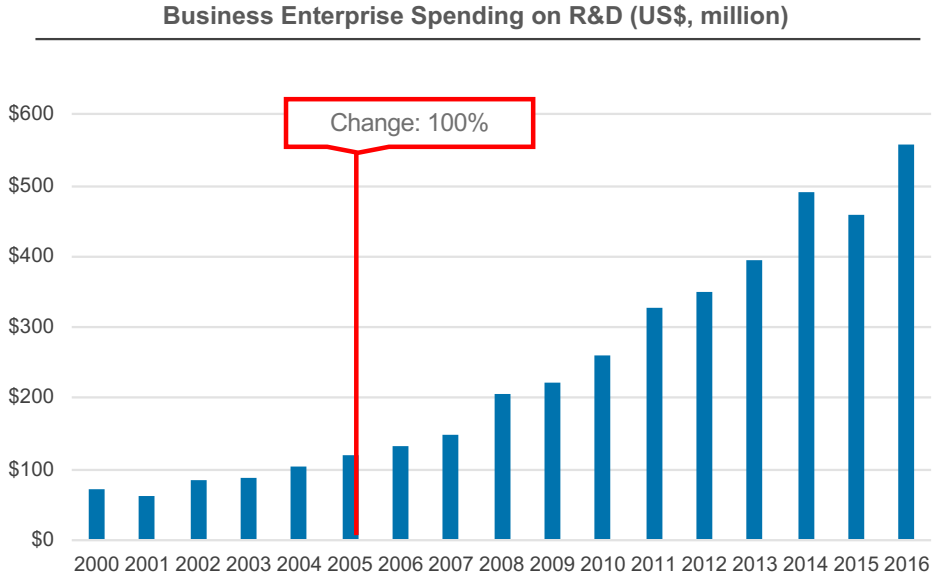
★ Focus of analysis.

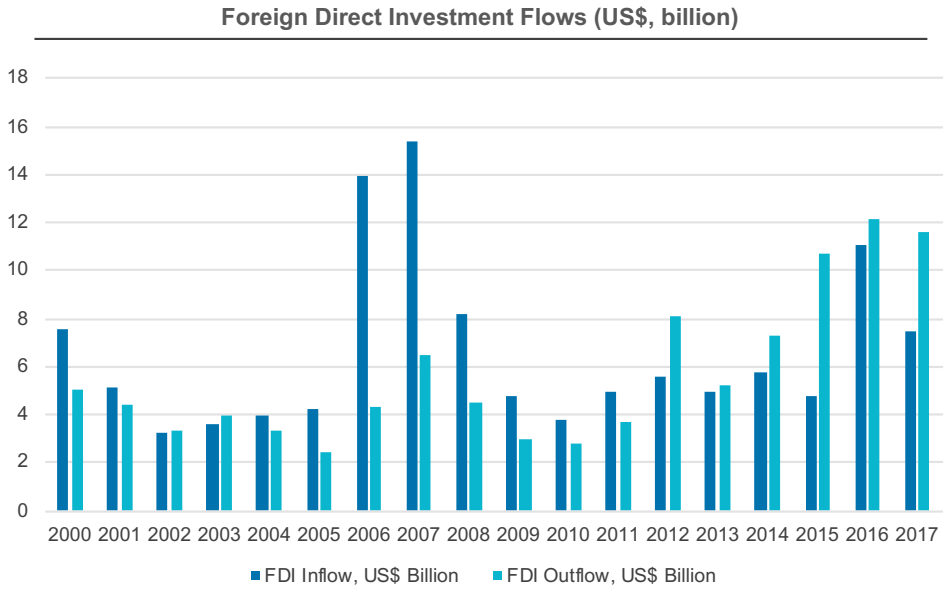
Note: *Data exclusivity did not apply to new dosages, formulations, indications and combinations; Note: Regulation marked with a star will be used as proxy for change in estimating growth differences.

TAIWAN

INVESTMENT IN R&D AND FDI

- With its increasing focus on the innovative knowledge based economy, companies have increased their R&D spending on pharmaceuticals in Taiwan, as both local and multi-national companies have increased their local footprint.
- Taiwan has historically focused on attracting FDI based on its highly educated and productive labour force, which more recently has evolved to attracting FDI in the technology-intensive areas in order to encourage and promote domestic spill over effects.





Source: OECD Indicators 2018

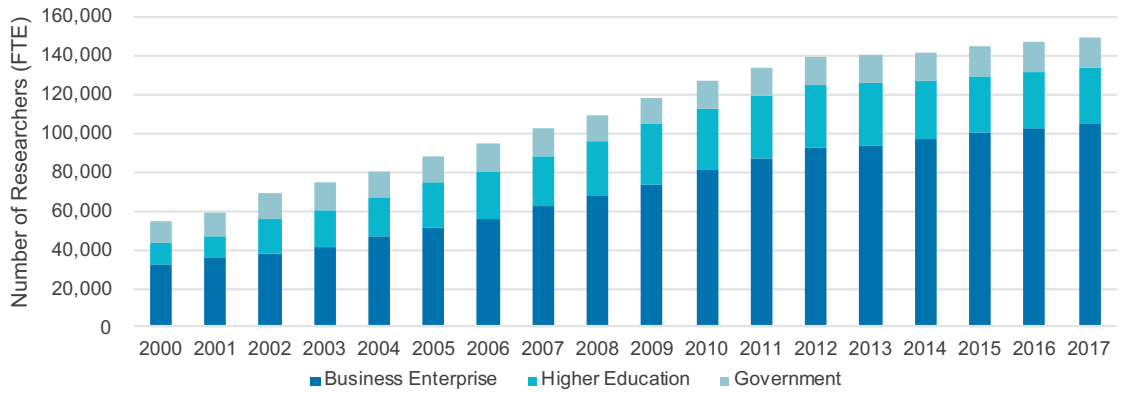
Note: According to Chen 2013 the peaks in FDI Inflows in 2006 and 2007 we due to "several large investments by foreign multinational enterprises (MNEs) such as Phillips, and private equity firms, including the Carlyle Group, Macquarie Bank, MBK Partners, and Newbridge Asia", whilst the drop 2008-2010 is attributed to the global financial crisis.

TAIWAN

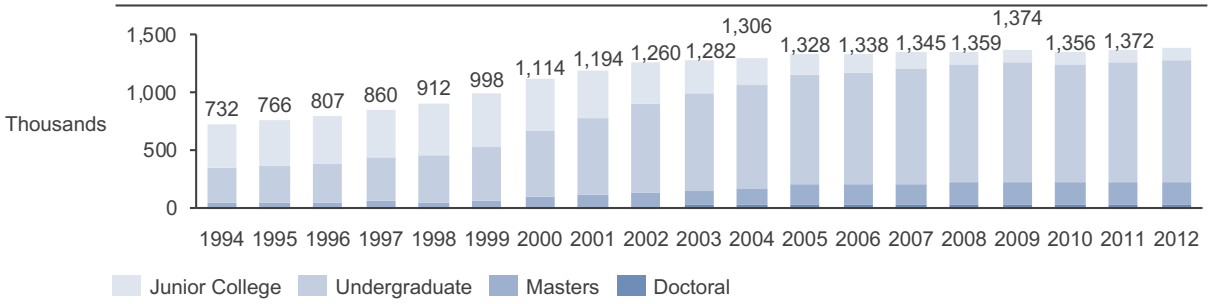
UNIVERSITIES AND EDUCATION QUALITY AND ATTAINMENT

- Higher education has gradually evolved to universal since the 1990s to meet the demands of economic transformation from manufacturing based to an innovation based knowledge economy.

Researcher by Affiliation (2000 – 2017, FTE)

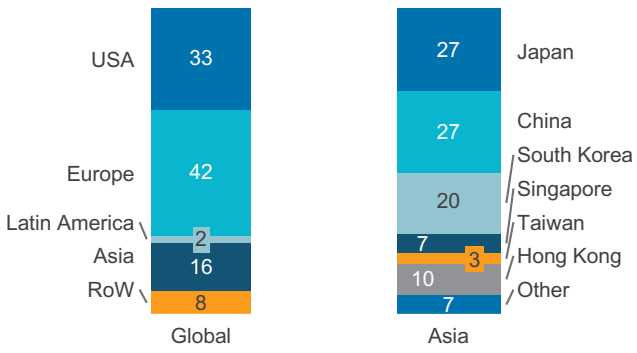


Number of Students in Higher Education by Level (1994 – 2012)



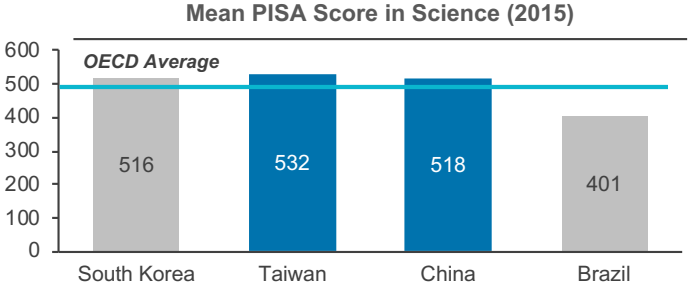
Source: Ministry of Education 2014.

Percentage Universities in Top 200 Universities for Biological Sciences



Source: Top Universities 2018.

Mean PISA Score in Science (2015)



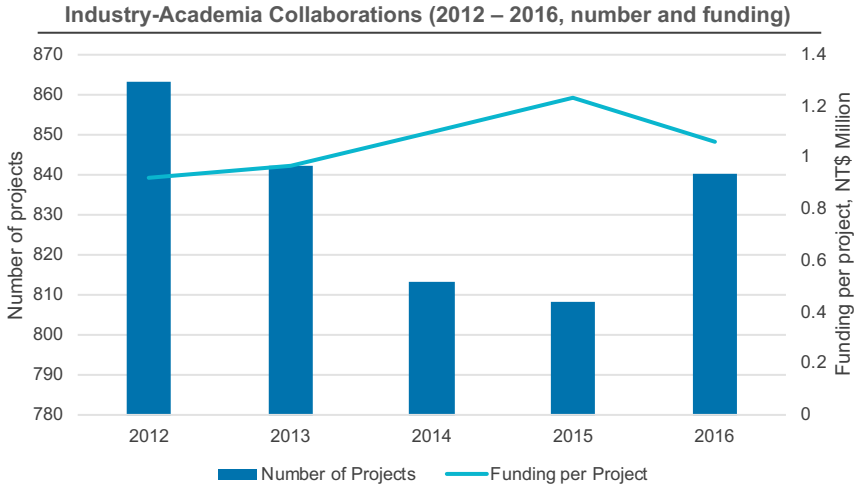
Source: OECD Indicators 2018.

Other sources: Chan and Lin, "Massification of Higher Education in Taiwan: Shifting Pressure from Admission to Employment" 2015.

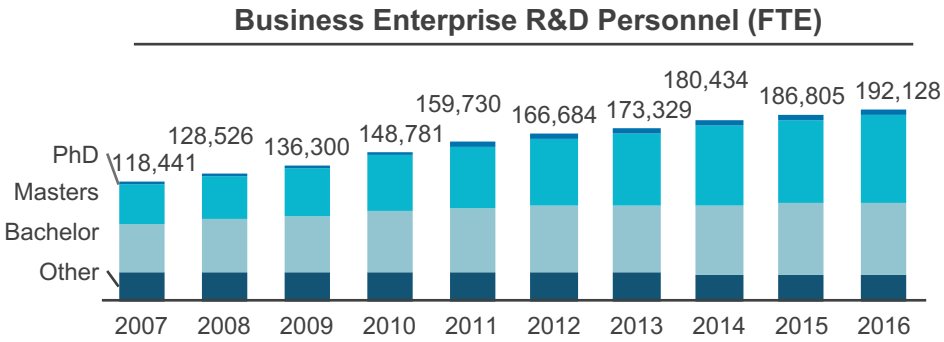
TAIWAN

COLLABORATION AND INFRASTRUCTURE FOR RESEARCH

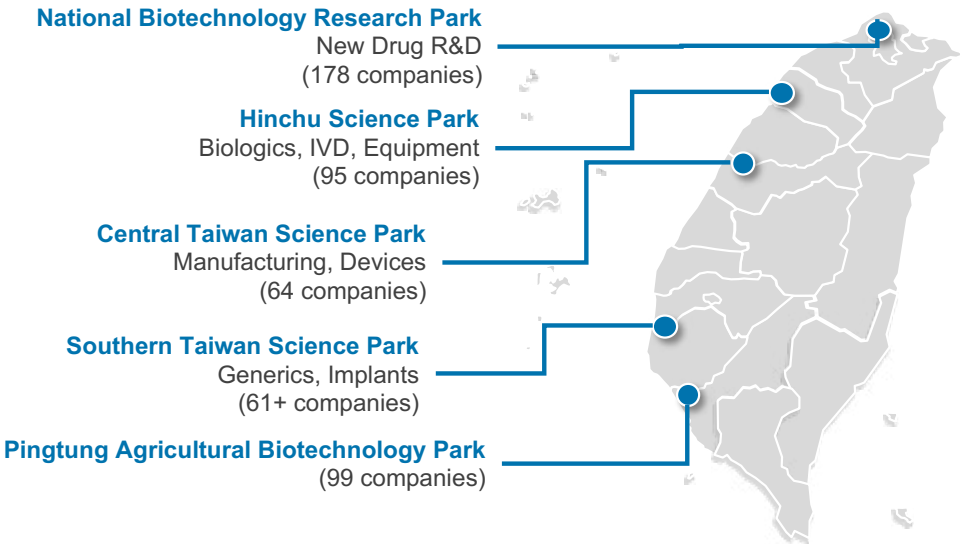
- To build highly skilled base of researchers, with its Bio-Pharmaceutical Innovation Plans, Taiwan has historically focused on encouraging collaboration between the private and public sectors.
- Science clusters are a key element of this.



Sources: Ministry of Science and Technology.



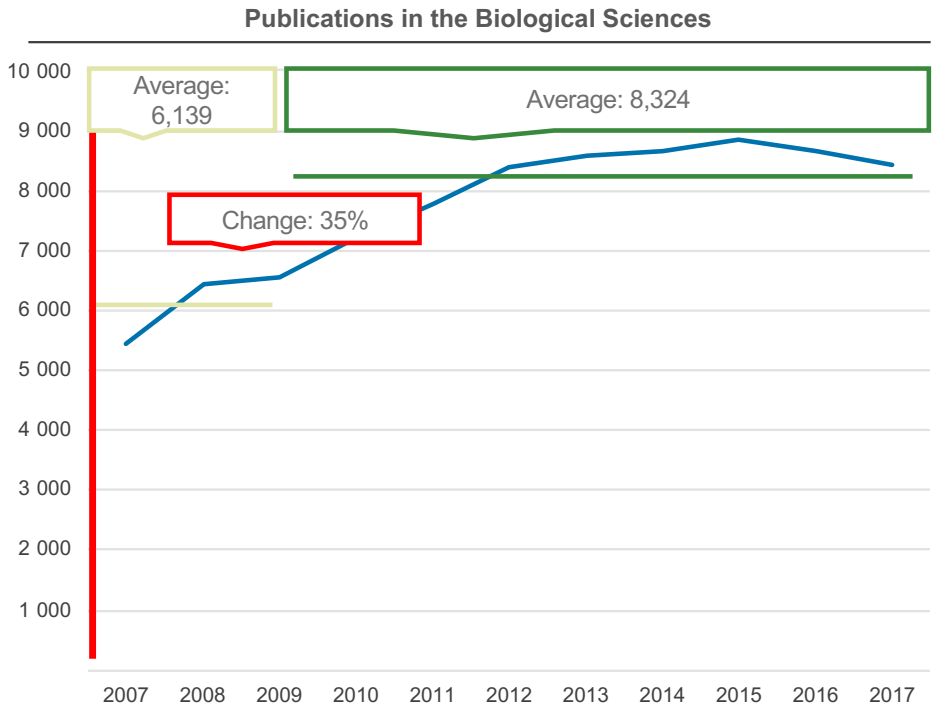
Source: Ministry of Science and Technology Indicators.



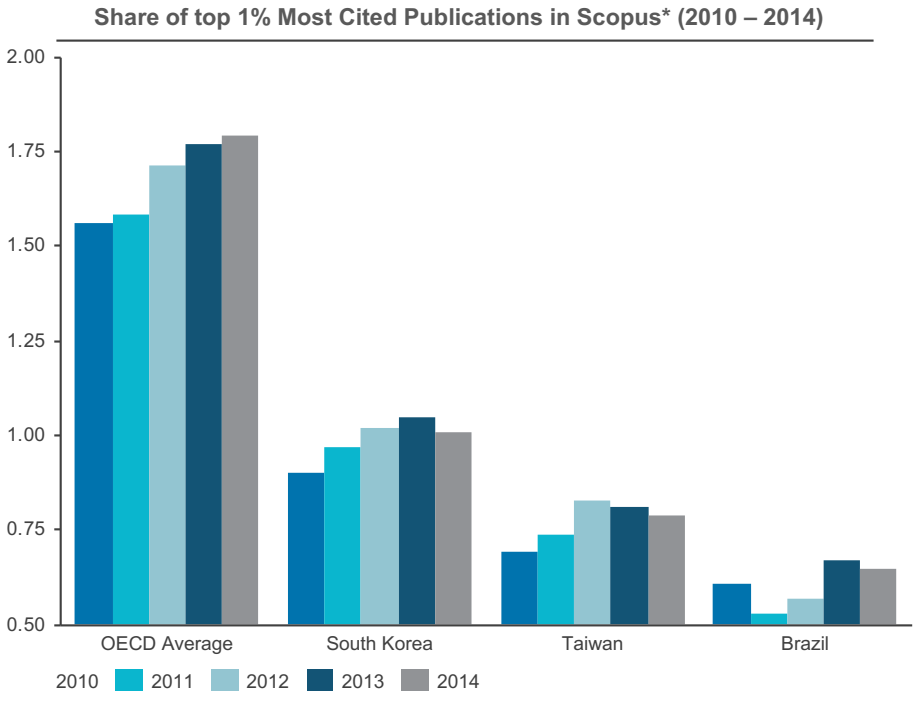
TAIWAN

INNOVATIVE ACTIVITY: PUBLICATIONS

- The number of Biological Sciences publications has more than tripled in recent years. However, Taiwan underperforms in terms of impact of its publications in comparison to peers.
- Funding per collaborative project has grown, offset by a decrease in the number of projects.



Source: Ministry of Science and Technology.

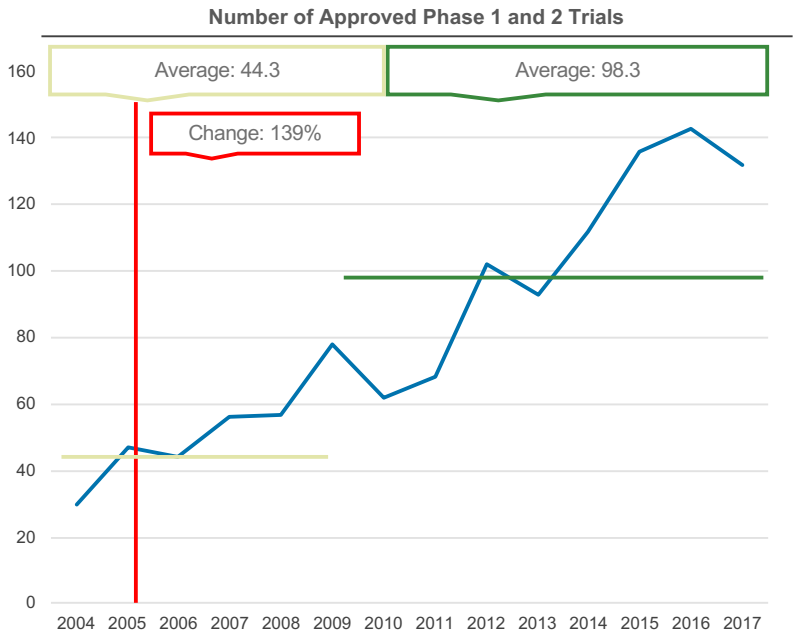


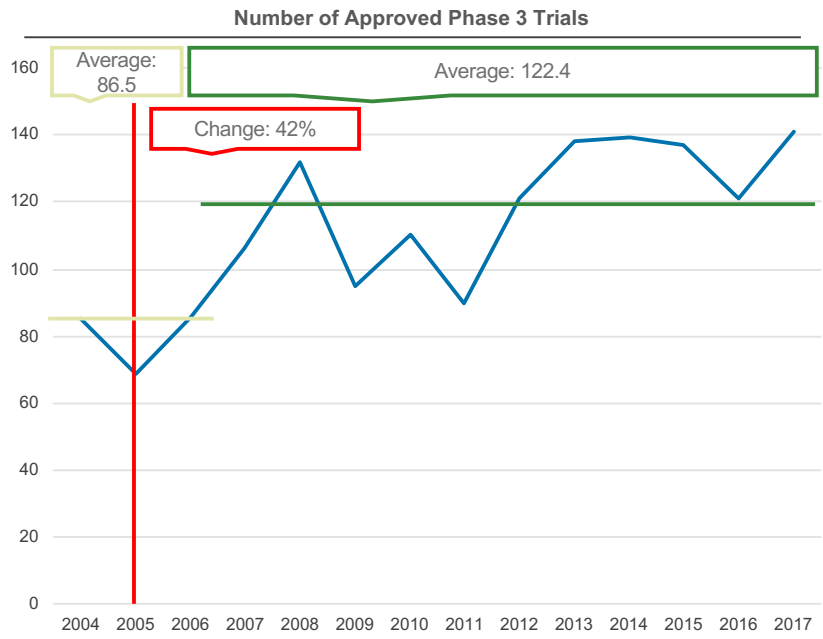
Source: National Science Foundation Survey 2018.

TAIWAN

INNOVATIVE ACTIVITY: CLINICAL TRIALS

- There has been a steady growth in the number of phase 1, 2 and 3 clinical trials in Taiwan with a significant jump in 2008 and later in 2012, potentially reflecting the strengthening of RDP from 2005 and the effects of the earlier Bio-Pharmaceutical Innovation plans.
- Over the past year, Taiwan's FDA has taken action to reduce the review process for new drugs. In October 2017, Taiwan shortened the average review time for approval of investigational new drugs, increasing the incentive for researchers to work on a wider range of new therapies. Shortly thereafter, it reduced its review timelines for first-in-human (FIH) clinical trial applications from 120 days to 30 days.[55]



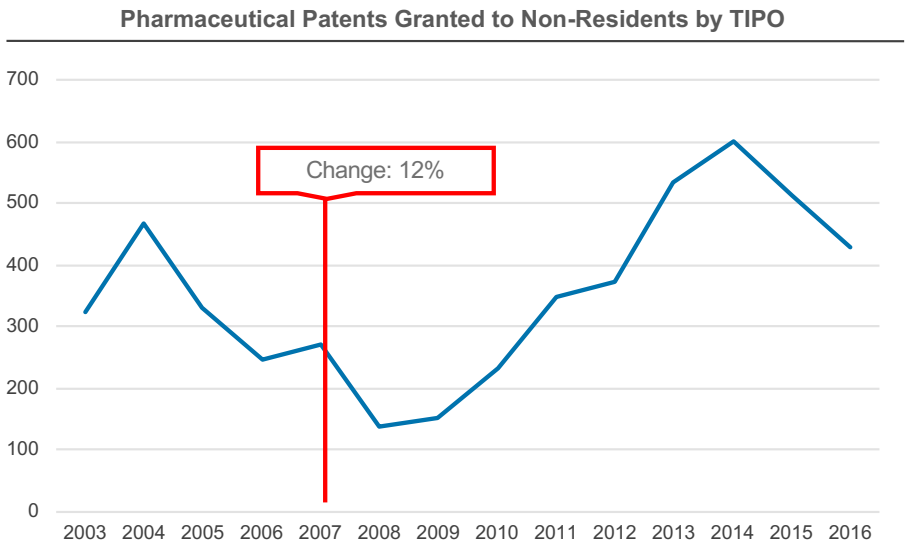


Source: TFDA.

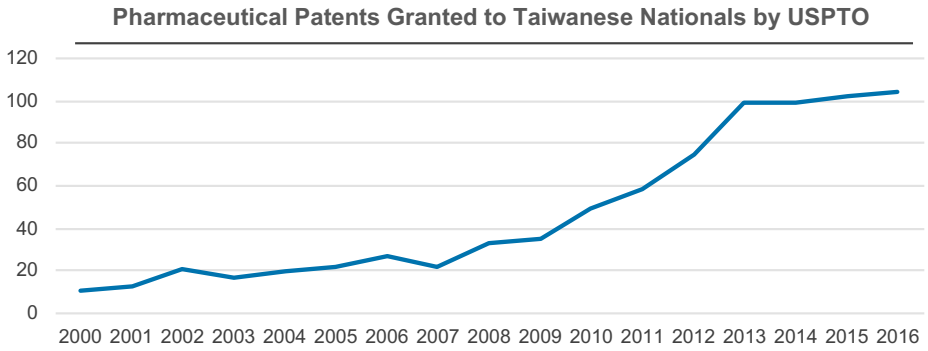
TAIWAN

INNOVATIVE ACTIVITY: PATENTS

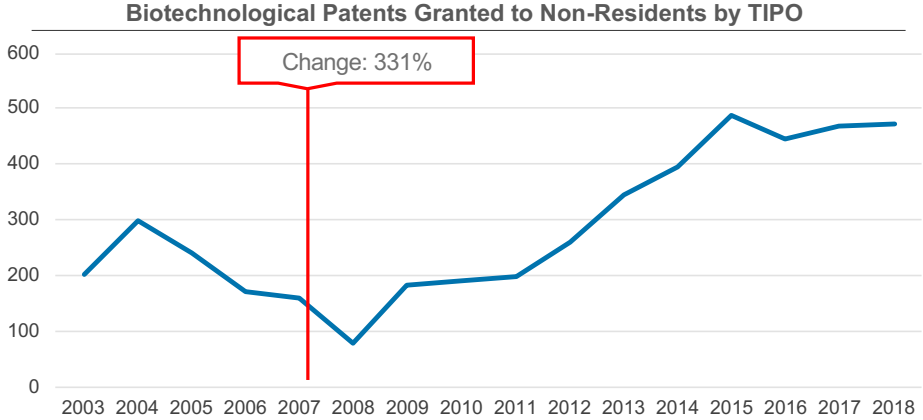
- Innovation patent indicators that experienced significant growth in recent years include the patents granted to Taiwanese nationals by USPTO, as well as the patents granted by TIPO to Non-Residents in the pharmaceutical and biotechnology industries.
- Whilst the number of TIPO patents to residents has grown over time, the change growth rate is less pronounced.



Sources: Taiwan Patent Office.



Sources: National Science Foundation Report 2018.

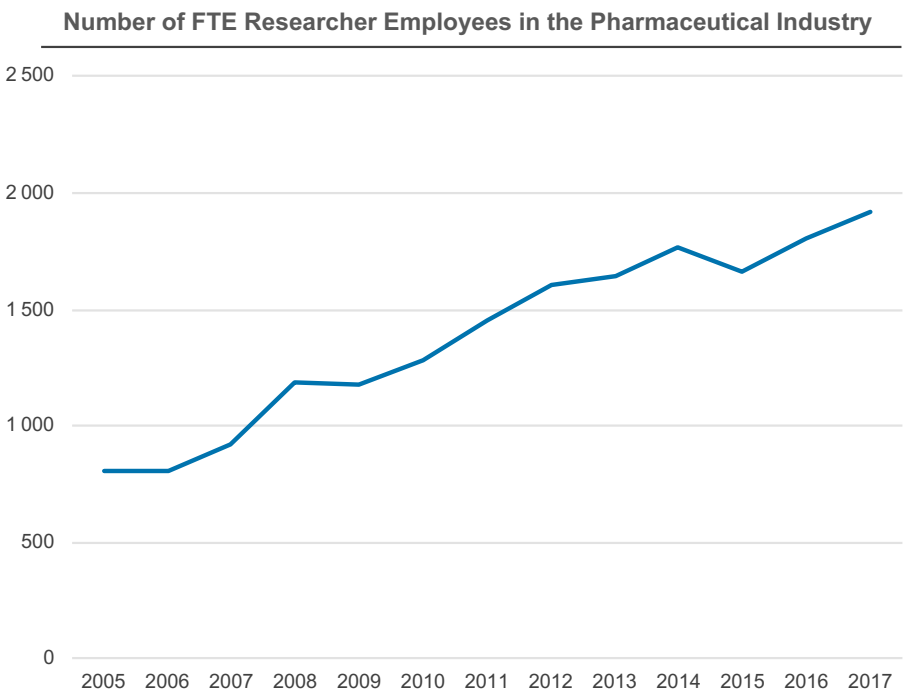


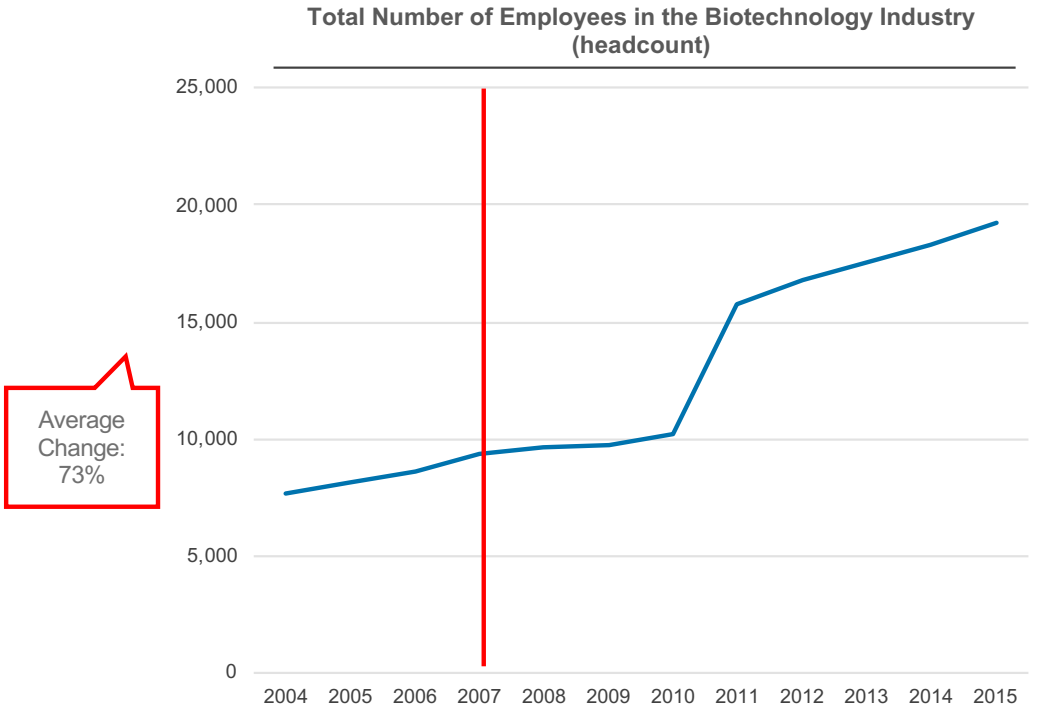
Sources: Taiwan Patent Office.

TAIWAN

EMPLOYMENT IN RESEARCH IN PHARMA AND BIOTECH

- The number of researchers employed in the pharmaceutical industry and the overall number of employees in the biotechnology has grown significantly compared to growth prior to the 2005 change.
  - The biotechnology has benefited more than the pharmaceutical industry in terms of revenue and workforce size.





Sources: Ministry of Economic Affairs.

TAIWAN

IMPACT OF IMPROVED IP REGIME ON INNOVATIVE ACTIVITY

- Taiwan has incrementally improved the IP regime for pharmaceuticals in line with WTO standards and deficiencies set out in the 2013-2015 PhRMA 301 Special Reports. To date there are no studies that have tried to examine the impact of the introduced changes in the IP regulatory as a result. However, past studies exist measuring effects on innovation across developed countries and past regulatory changes:
  - For example, Lo (2011) found that the introduction of longer lasting patent rights in 1986 led to a long-lasting increase in innovation measured in terms of R&D spending and patents filed in the U.S.
- **Domestic Innovation:** Taiwan is widely recognised to have taken long-term strategic steps to the improve the IP regime more widely and reinvented itself as focusing on IP and innovation. As a result, in 2014 Taiwan had the highest number of patents per population, and per R&D expenditure in the world according to Bloomberg, additional contribution was the availability of the strong skills base of the population.
- In terms of wider innovation studies, there is lack of clear consensus in the literature as to whether stronger domestic IP regime leads to improved local innovation (measured by the number of pharmaceutical patents granted by USPTO):
  - Some studies (Allred and Park 2007) find a "U" shaped relationship between patent protection and foreign patent filings. Similar relationship has been found in other studies (Chen and Puttitanun 2005) between IP rights and the economic development of a country.
  - Gamba finds a positive correlation between local Pharmaceutical Patent Index strength and the innovative activity of a country as measured by patent applications to EPO. Furthermore, similar to Taiwan's approach, it is concluded that gradual implementation of reforms that slightly increase the level of protection rather than rare reforms that greatly alter it will render the strongest effect.
- **Clinical trial activity:** Berndt, Cockburn, and Thiers (2006) find the rising trend of clinical trials in emerging economies at the beginning of the century to be due to changes in the strength of patent protection for biomedical inventions. This activity is primarily driven by Phase III clinical trials.
- **Number of employees:** Kumar (1995) finds that whilst the available infrastructure and local capabilities influence the probability of attracting R&D investments from multi-national companies (MNCs), the overall strength of the intellectual property protection also contributes to attracting foreign R&D investments in a sample of industrialised countries including Taiwan.

Xinyi District, Taipei, Taiwan, shutterstock.com/FenlioQ

CHINA
INNOVATION AND IP POLICIES

CHANGES IN THE IP REGIME [61-66]

CONSTITUTION OF THE PEOPLE'S REPUBLIC OF CHINA AT THE FIFTH SESSION OF THE FIFTH NATIONAL PEOPLE'S CONGRESS (1982)

Established the first substantive laws covering intellectual property rights.

PATENT LAW ESTABLISHMENT (1984) AND STANDARDISATION (2001)

China amended the 1984 Patent Law which established patent rights, to become more aligned with the World Trade Organisation (WTO) and TRIPS. China proceeded to do the same with the Copyright Law and the Trademark Law during the same year.

REGULATORY DATA PROTECTION (RDP) (2001)

As part of its accession to the WTO, China committed to introduce RDP of at least 6 years for new chemical entities for pharmaceutical products. This was achieved through the Pharmaceutical Administration Law and the Provisions for Drug Registration Law.

NATIONAL INTELLECTUAL PROPERTY STRATEGY (2008) ★

Aimed to promote national 'capacity in creation, utilisation, protection and administration of intellectual property' by 2020 and thereby 'improve China's capacity for independent innovation'.[61]

"REFORM OPINION" (INNOVATION OPINION AND CIRCULAR NO. 55) (2017-2018)

The Chinese government issued three opinions on drug patent protection policies, proposing the establishment of drug patent link systems, piloting drug patent term compensation systems, and improving and implementing test data protection systems beyond the current 6-year period for orphan medicinal products, paediatric, medicinal products, biologic products and first generic product.

CHANGES IN INNOVATION POLICY [61-66]

NATIONAL HIGH TECHNOLOGY DEVELOPMENT PROGRAM (863 PROGRAM) (1986)

Funded both basic and applied research on marketable high-end technologies.[62,63]

NATIONAL BASIC RESEARCH PROGRAM (973 PROGRAM) (1993)

Funded multi-disciplinary basic research in "cutting-edge" technology, and promotes promising scientists. Most of its projects involve some form of international cooperative research.[62,63]

NATIONAL MEDIUM- AND LONG-TERM PROGRAM FOR CIENCE AND TECHNOLOGY DEVELOPMENT (2006–2020) ★

Established the framework for Chinese research and technology policy up to 2020. Specific targets involve an increase in R&D expenditure to at least 2.5% of GDP and raise the R&D contribution to economic growth to at least 60% of GDP.[62]

THE 12TH FIVE-YEAR PLAN (2011–2015)

Sets out the goals for the National Medium- and Long-Term Program and describes measures and the enabling conditions required to promote research and technological innovation, and for the expansion of the innovation system.[62]

Key

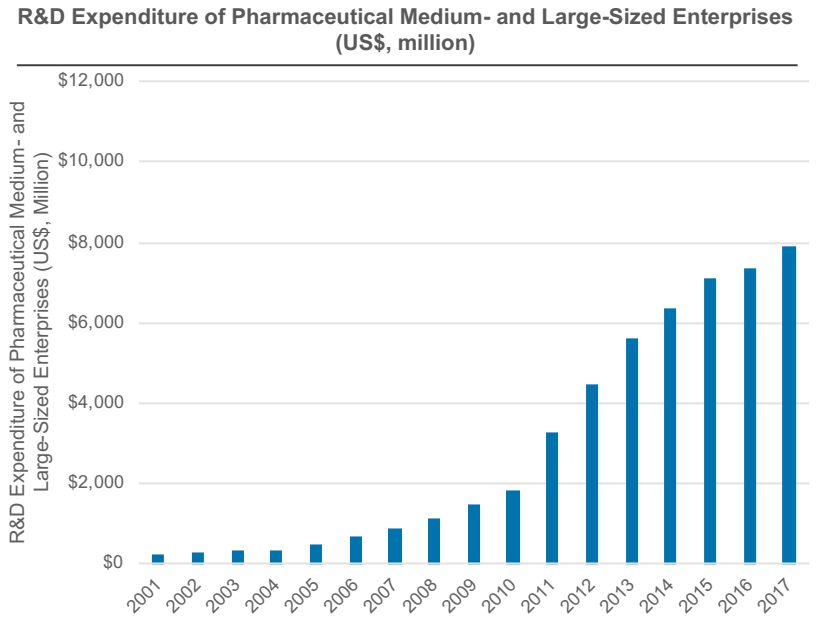
★ Focus of analysis.

Note: Regulation marked with a star will be used as proxy for change in estimating growth differences.

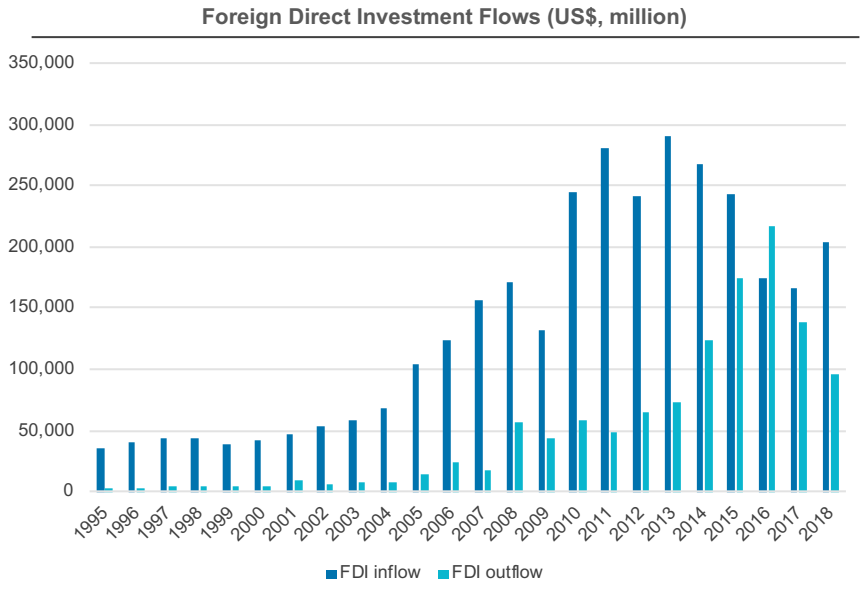
CHINA

INVESTMENT IN R&D AND FDI

- Pharmaceutical R&D expenditure from medium- and large- sized enterprises have grown rapidly since the year 2010. In 2017, China's total R&D spending represented 20% of the world's R&D expenditure with the rate of growth significantly exceeding that of the US and EU.[67]
- Increase in FDI inflow has been matched by an increase in FDI outflow, albeit with a lag of ten years.



Source: China Statistical Yearbook Series 2000 – 2018.

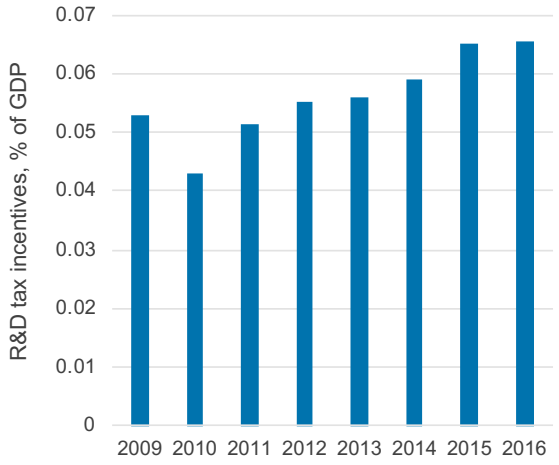


Source: World Bank, 1995-2018.

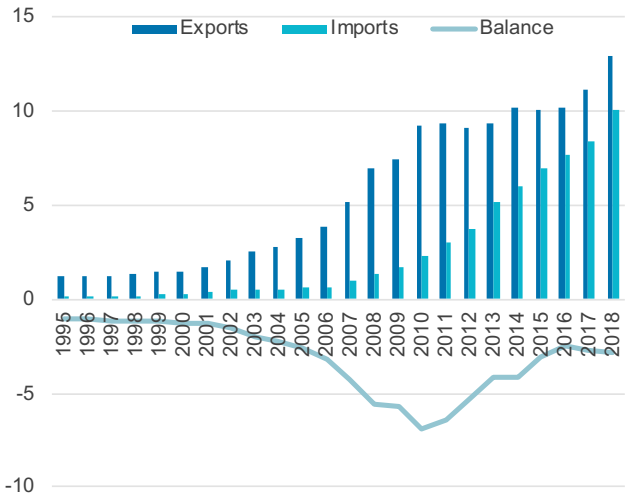
CHINA
TAXES & TRADE

- There has been increasing levels of indirect government support through R&D tax incentives since 2010.
  - More specifically, pharmaceutical firms are eligible for exemption of income and sales tax for their R&D expenses.[68]
- China has maintained a steady trade balance as levels of both pharmaceutical imports and exports have increased rapidly with a significant increase in the value of new medical and pharmaceutical exports.

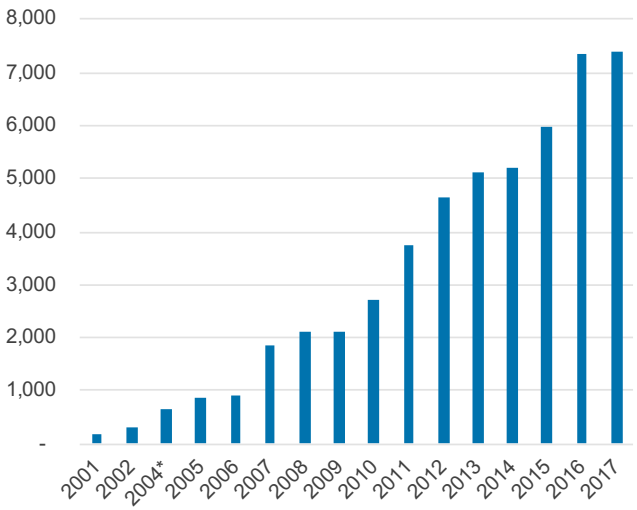
1. R&D tax incentives, % of GDP (2009-2016)



2. Evolution of pharmaceutical imports and exports (1995-2018, m USD)



3. New medical and pharmaceutical product exports, m USD (2001-2017)



1. Source: OECD 2009-2016.

2. Source: UNCTADstat, 1995-2018.

3. Source: China Statistical Yearbook Series 2001 – 2017.
Note: *No data available for 2003.

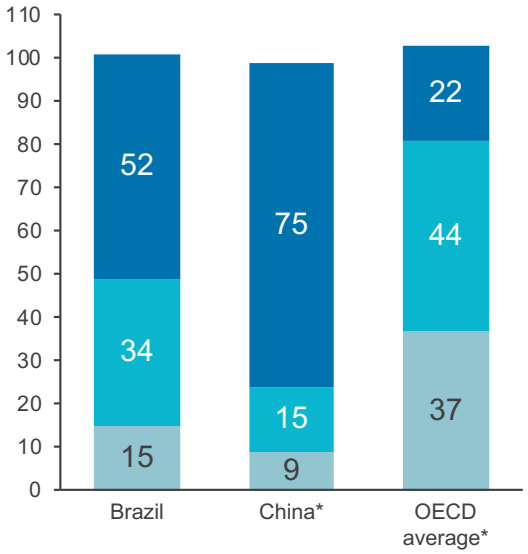
Life Science Park, Zhongguancun, shutterstock.com/HelloRF Zcool

CHINA

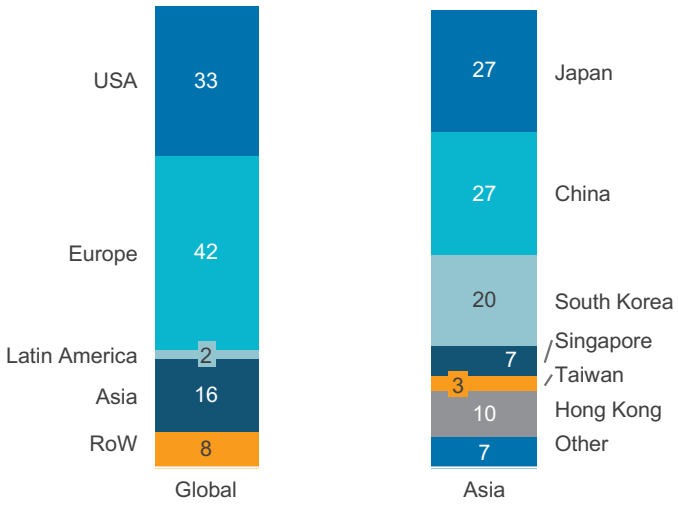
UNIVERSITIES AND EDUCATION QUALITY AND ATTAINMENT

- Despite 75% of the 25-64 year old population with an education level below upper secondary, China scores above the OECD average on the mean PISA scores in Science.
- Moreover, within the APAC region, Chinese universities have the highest representation within the top 200 universities in Biological Sciences.

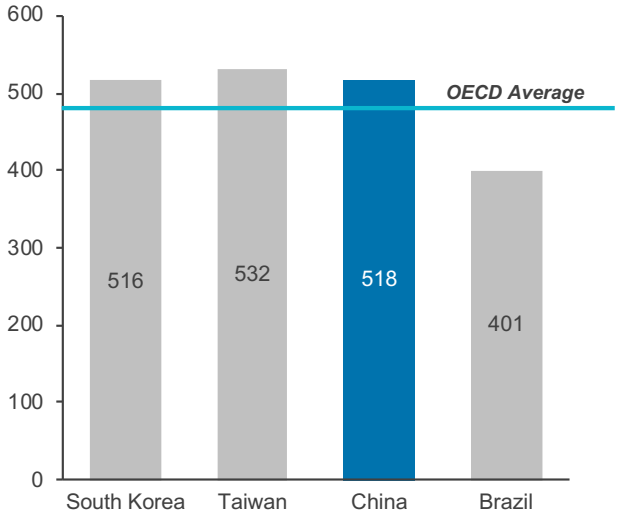
1. Educational attainment of 25-64 year olds (2017, %)

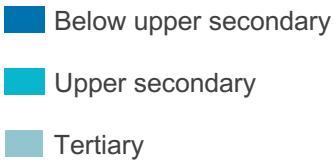


2. Percentage Universities in Top 200 Universities for Biological Sciences



3. Mean PISA Score in Science (2015)





*Due to averaging, values do not total to 100%.

1. Source: OECD Data, 2017.

2. Source: Top Universities 2018.

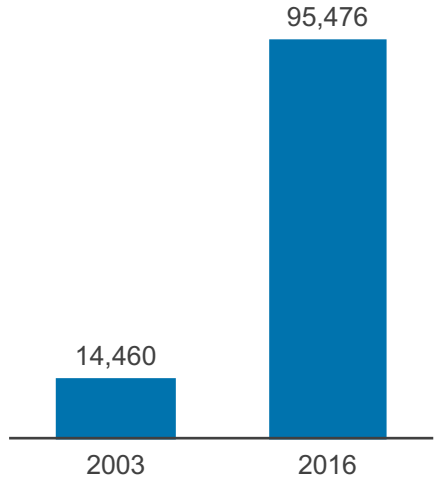
3. Source: OECD Indicators 2018.

CHINA

COLLABORATION AND INFRASTRUCTURE FOR RESEARCH

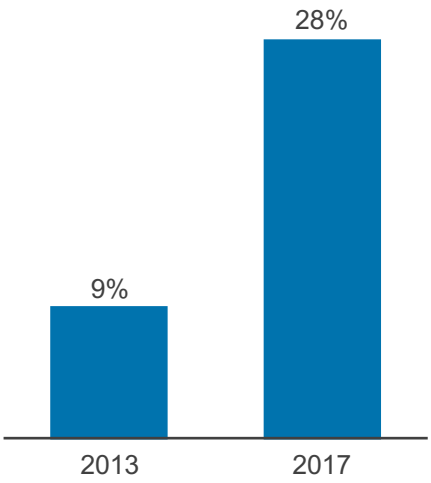
- The first China high-tech zone was established in Beijing in 1988 at Zhongguancun Life Sciences Science Park and since then there are 169 zones across 31 provinces.[69]
- China has a large pool of well-trained scientists and workers, with over 100 000 skilled workers that are involved in biotech research and exploration, and an estimated 30 000 undergraduate and graduate students graduating from Chinese universities and academic institutions annually.[70]
- Increasingly MNCs are conducting R&D activities and establishing partnerships with domestic firms and research institutes.[2]

Internationally co-authored S&E publications (2013 & 2016)



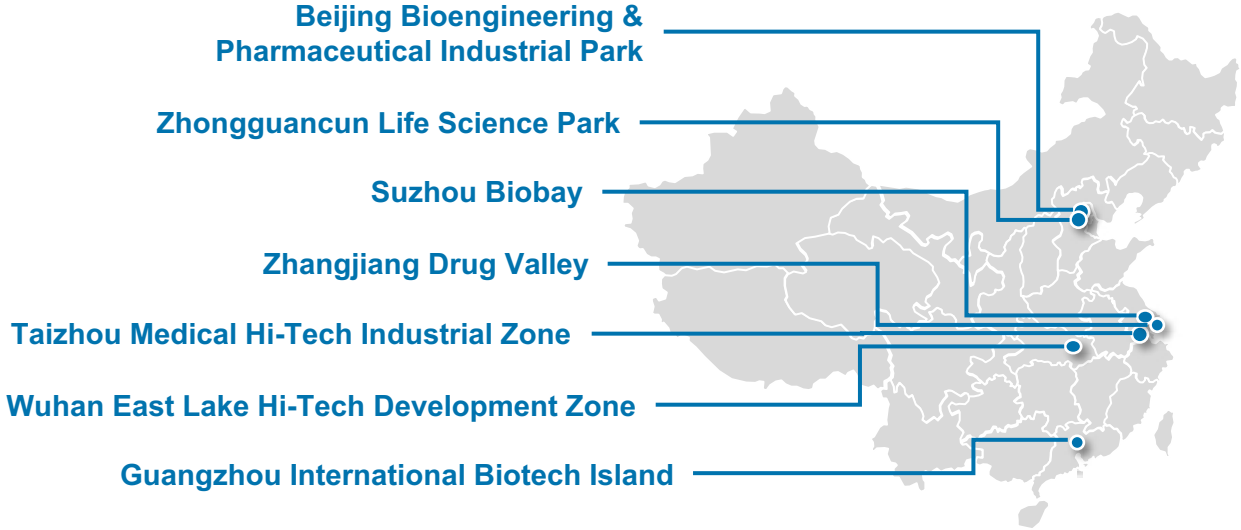
Source: National Science Foundation Survey.

Firms collaborating with academic or government institutions (2013 & 2017, % of all innovative firms)



Source: OECD.

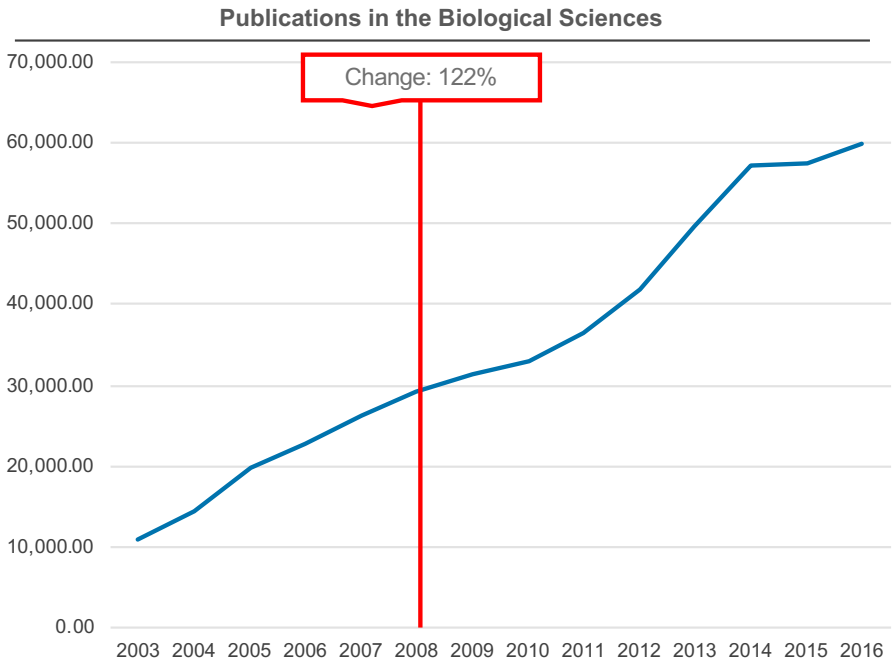
Biomedical Science Parks



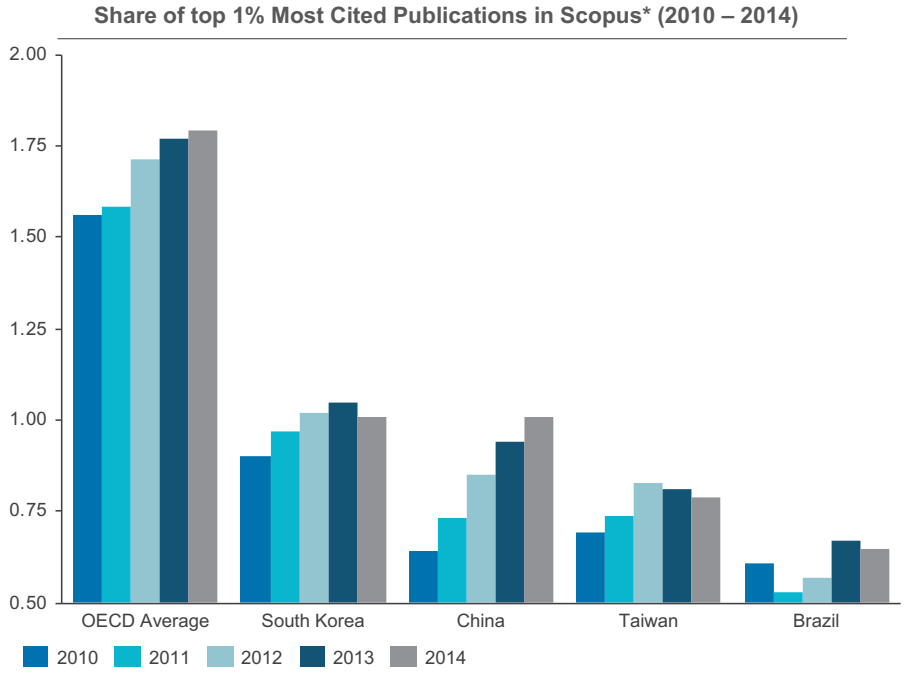
CHINA

INNOVATIVE ACTIVITY: PUBLICATIONS

- China's basic research output in the biological sciences as measured by the number of publications each year has increased from around 10,000 in 2003 to 60,000 in 2016 with an average growth of just below 4,000 new publications each year.
- Whilst the impact of China's publications, as measured by the share of top one percent most cited, remained below the OECD Average in 2014, it experienced strong growth between 2010 and 2014, reaching similar levels to that of South Korea in 2014.



Source: Ministry of Science and Technology.

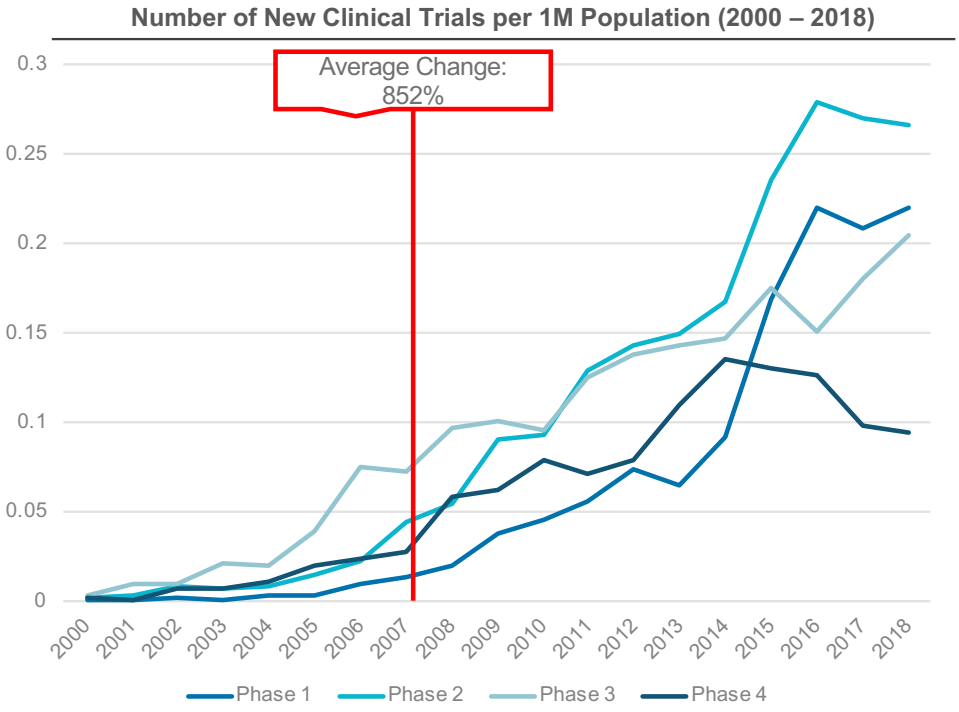


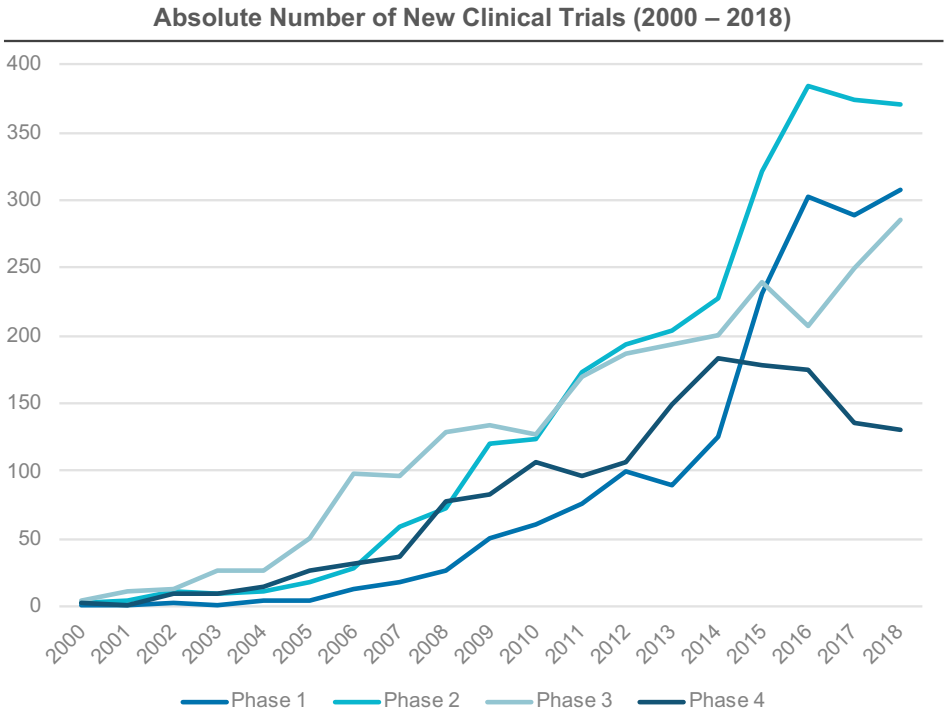
Source: National Science Foundation Survey, 2018.

CHINA

INNOVATIVE ACTIVITY: CLINICAL TRIALS

- The number of all clinical trials increased sharply between 2000 and 2018, but most significantly China gained in phase 1 and 2.
- Phase 3 clinical trials were most abundant up to 2010 and were since overtaken by phase 2 clinical trials. In 2015, the number of new phase 1 clinical trials exceeded that of phase 3 and 4.





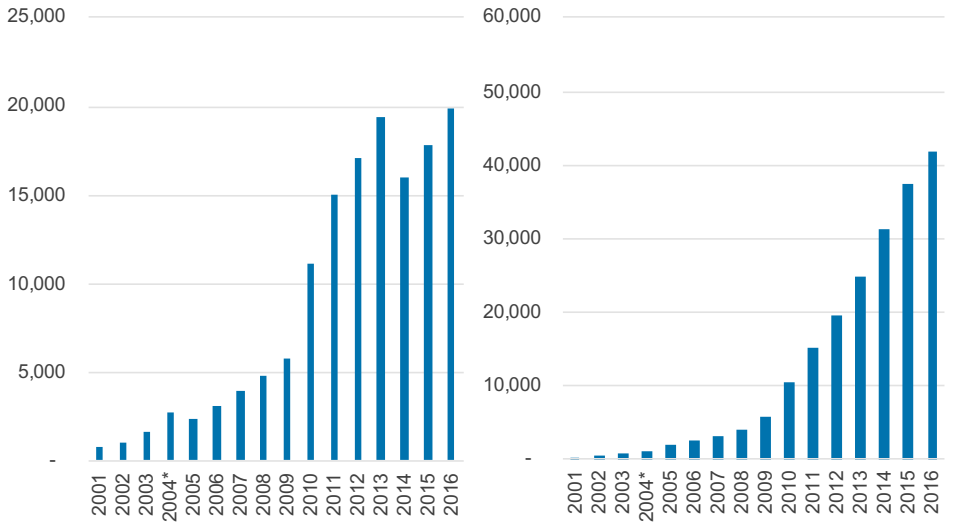
Source: Clinicaltrials.gov.

CHINA

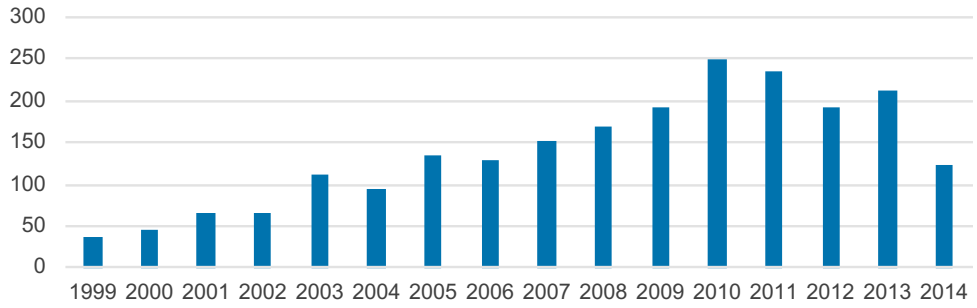
INNOVATIVE ACTIVITY: PATENTS

- Pharmaceutical patent applications and patents granted to medium- and large-sized enterprises by the Chinese patent office, increased steeply between 2010 and 2017. For example, patents granted increased from under 500 in 2001 to over 40,000 in 2017.
- Pharmaceutical patent applications under PCT increased from 120 in 2001 to ~1,500 in 2016, whereas patents granted to Chinese nationals each year by USPTO doubled between 2001 and 2014.

Pharmaceutical Patent Applications and Grants to Medium- and Large-Sized Enterprises

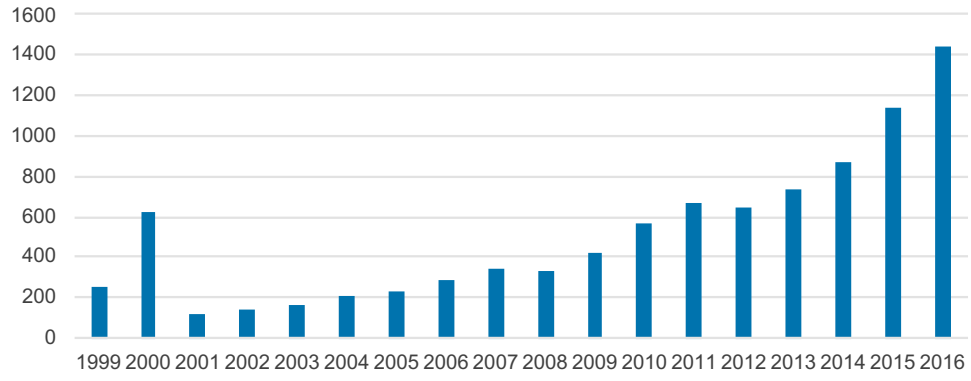


Pharmaceutical Patents Granted to Chinese Nationals by USPTO



Sources: OECD Main Science and Technology Indicators (2019).

Pharmaceutical Patents Filed under PCT by Chinese Residents



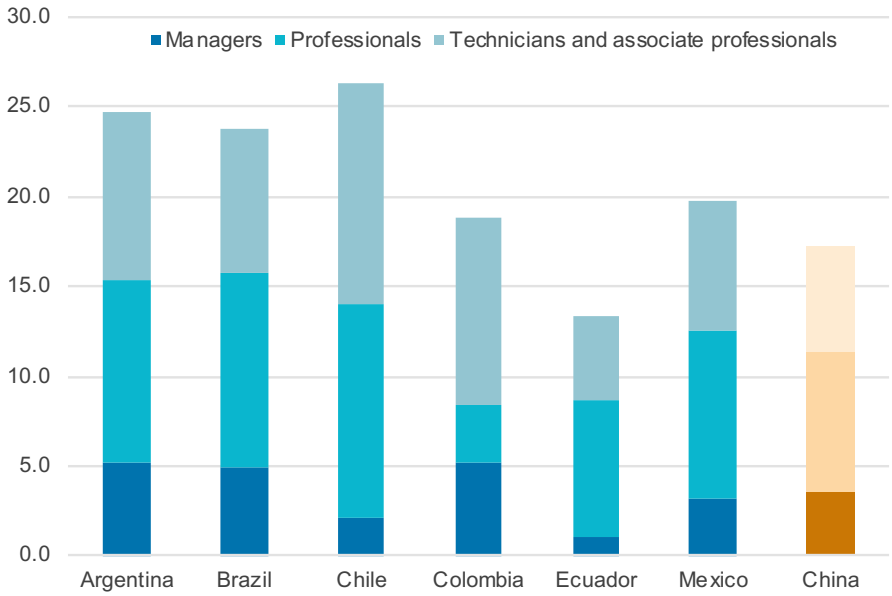
Sources: China Statistical Yearbook Series 2000 – 2018; OECD Main Science and Technology Indicators. Note: No local data for 2003.

CHINA

EMPLOYMENT IN RESEARCH

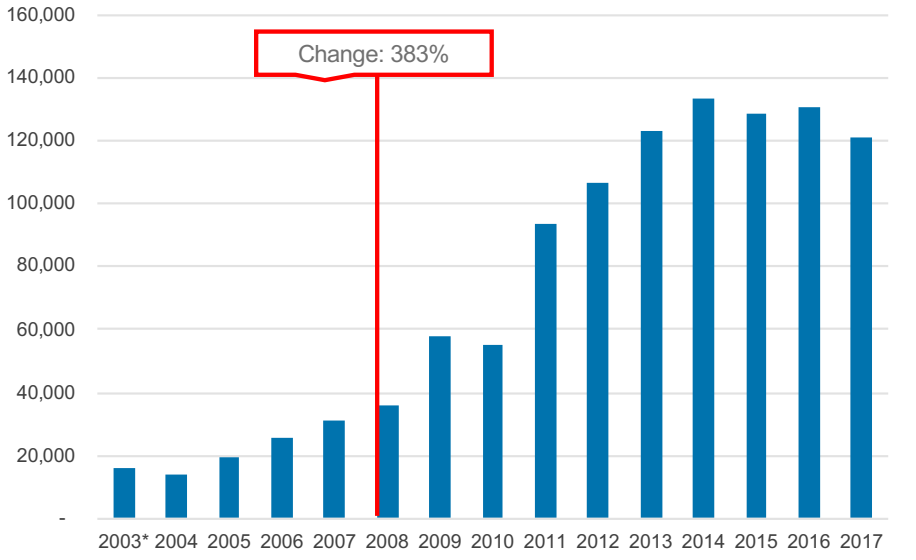
- Less than 20% of the workforce are employed in knowledge-intensive services which is comparatively low against the LatAm region.
- Despite this, the number of R&D personal within medium- and large- sized pharmaceutical enterprises have been on the rise with significant growth since 2011.

Employment in knowledge-intensive services, % of workforce (2018)



Source: International Labour Organisation, 2018.

R&D Personnel (FTE) in Pharmaceutical Medium- and Large-Sized Enterprises (2001-2017)



Source: China Statistical Yearbook Series 2000 – 2018.
Note: *Estimated.

JAPAN
INNOVATION AND IP POLICIES

CHANGES IN THE IP REGIME [71-74]

POST MARKETING SURVEILLANCE (1979)

Necessitates for post marketing surveillance studies and re-examination to be conducted and effectively grants two years of data and marketing exclusivity by preventing generic companies to launch their product.

NOTIFICATION NO. 0401001 BY PFSB AT THE MHLW (2007) ★

The period of marketing exclusivity was increased from six years to eight years for new medicines (and to ten years for orphan drugs).

BASIC INTELLECTUAL PROPERTY LAW (2003)

The IP Strategy Headquarters in the Cabinet began to publish annual strategy programs that charged ministries and agencies, particularly the M.E.T.I. (Ministry of Economy, Trade and Industry) and the J.P.O. (Japan Patent Office), with implementing action plans to enhance patent protection.

POLICIES AIMED AT THE PATENT BACKLOG (2004 – 2007) ★

- In 2004 a law enabled hiring fixed term examiners at JPO and outsourced the initial search for prior art prior to a technical decision.
- In 2007, JPO adopted "Guidelines Concerning the Use of Prior Art Search/Examination Results of Foreign Patent Offices" to facilitate the prior art search based on patents approved by partner patent offices.
- The backlog was reduced from 2.4 years in 2008 to 10.4 months in 2014.

CHANGES IN INNOVATION POLICY [71-74]

SCIENCE AND TECHNOLOGY BASIC LAW IN 1995

Outlined an integrated government policy towards science and technology, introducing successive five-year Science and Technology Basic Plans, each focused on a set of priority fields and important goals.

1ST – 4TH SCIENCE & TECHNOLOGY BASIC PLAN (1996 TO 2016)

- Emphasized not an increase in the budget for research and greater collaboration between universities and industry.
- The period included the adoption of the 1998 Law Promoting Technology Transfer from Universities to Industry.

INNOVATION 25 INITIATIVE (2006)

Aimed to increase the international relevance of Japanese innovation and to connect innovation to changing social values.

JP LAW TO PROMOTE HEALTHCARE AND MEDICAL STRATEGY (2014)

Establish the Office of Healthcare and Medical Strategy Promotion in its Cabinet, which should promote R&D in the healthcare and medical industry by easing regulatory guidelines.

5TH SCIENCE & TECHNOLOGY BASIC PLAN FOR 2016 TO 2020

- Identifies sustainable development, climate change, national security and biodiversity as important areas of research for long term STI strategy.
- Aimed at investing in "Society 5.0": the integration of cyber and physical spaces, using AI, IoT, Robotics, and Big Data.

Key

★ Focus of analysis.

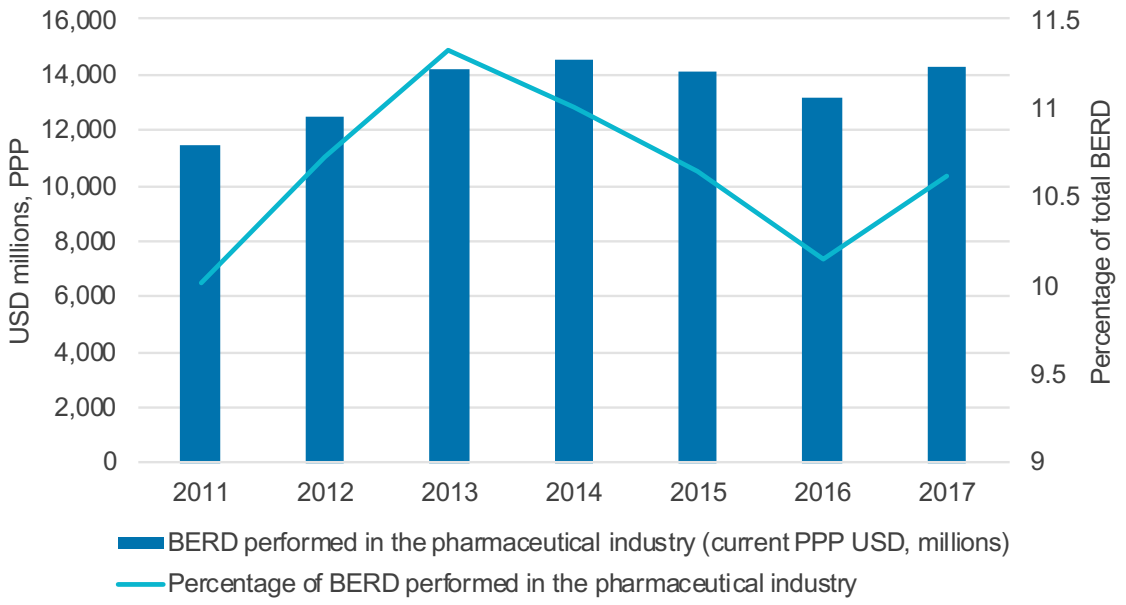
Note: Regulation marked with a star will be used as proxy for change in estimating growth differences.

JAPAN

INVESTMENT IN R&D AND FDI

- Japan has one of the most R&D-intensive economies in the world. In 2016 (latest available data), 3.14% of GDP was invested in gross domestic expenditure on research and development (GERD), while the world average was 2.23% of GDP.[71]
- BERD performed in the pharmaceutical industry has increased from around US$12.5 billion in 2012 to US$14.2 billion in 2013 and since then has remained relatively constant.
- However, the percentage of BERD performed in the pharmaceutical industry compared to other industries peaked at 11.3% in 2013 and overall decreased to 10.6% in 2017.

BERD performed in the pharmaceutical industry

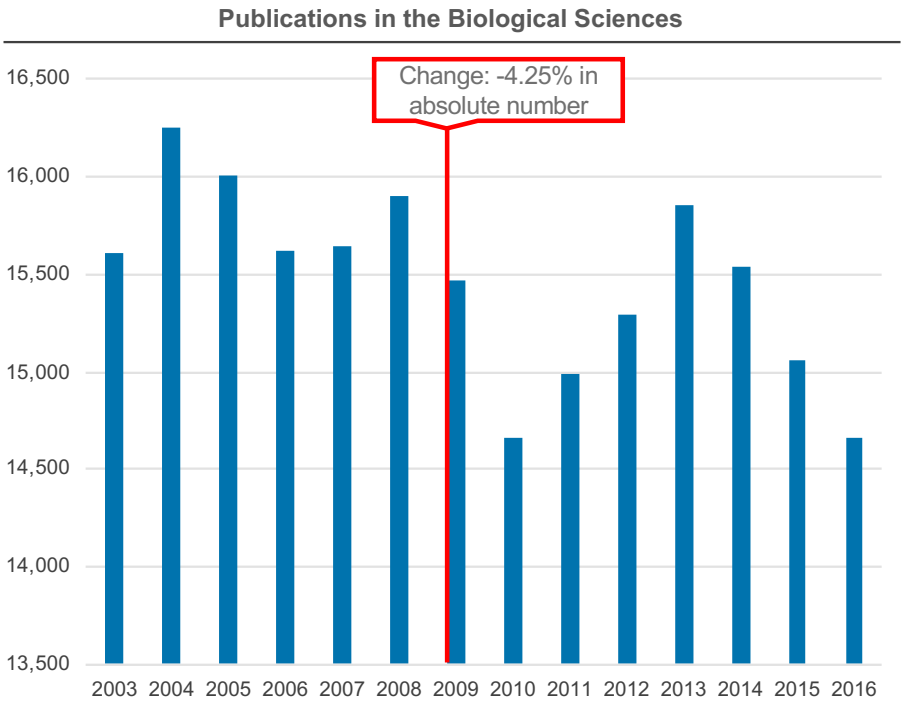


Source: OECD Statistics.

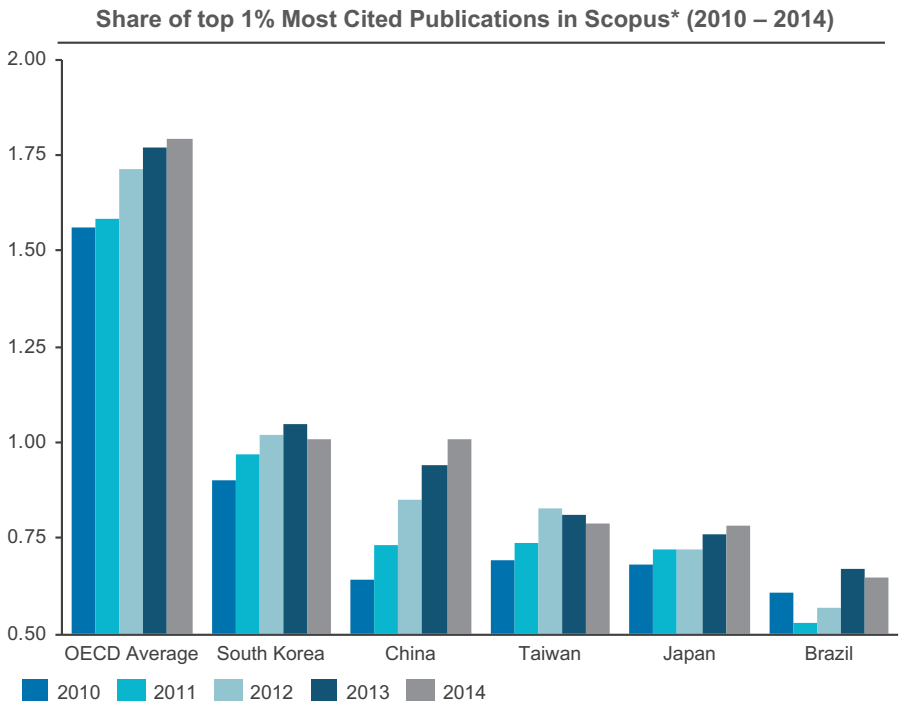
JAPAN

INNOVATIVE ACTIVITY: PUBLICATIONS

- Japan is the world's second largest producer of scientific articles, in absolute terms. However, production of scientific articles on a per capita basis is below the OECD average and well behind that of the leaders, and the level of citations is relatively low.[75]
- In the case of publications in the biological sciences, the number of publications in recent years has been declining – decreasing from 15,859 in 2013 to 14,661 in 2016.



Source: National Science Foundation Survey.

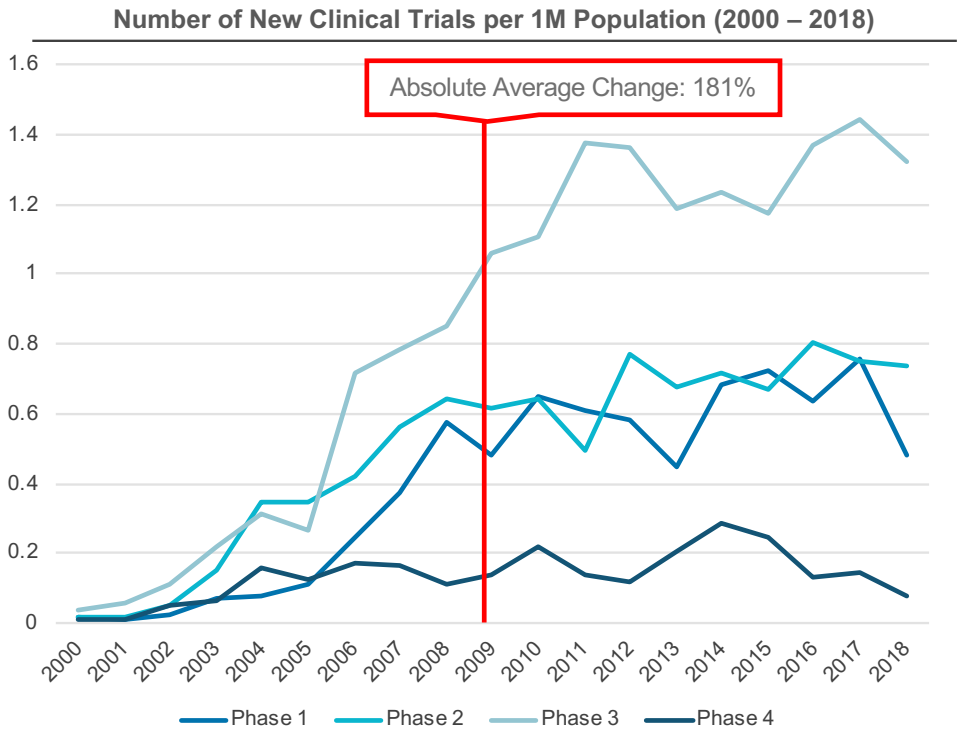


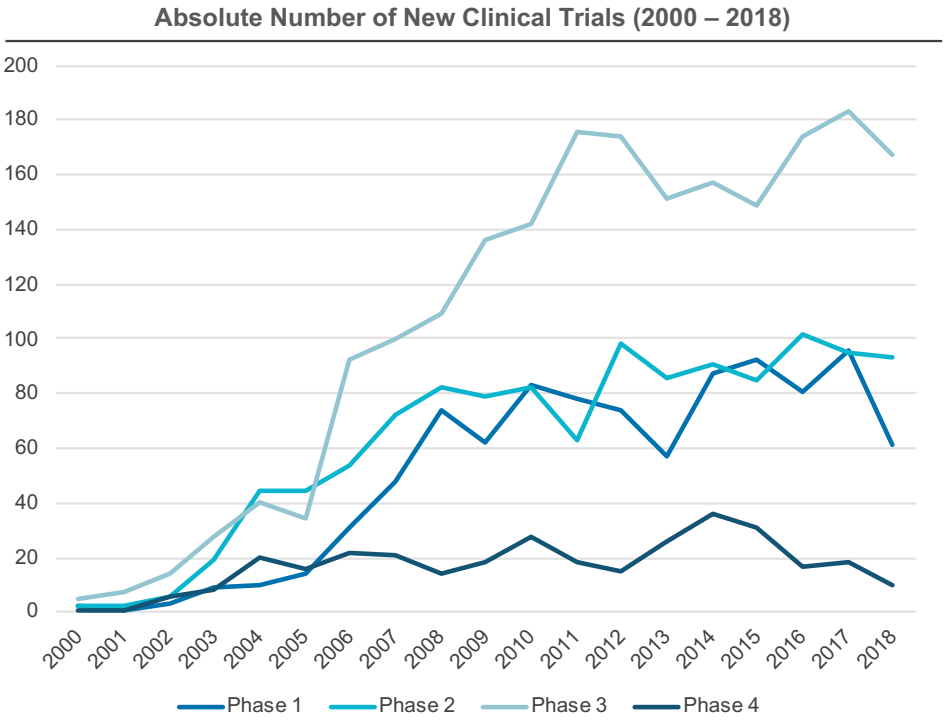
Source: National Science Foundation Survey, 2018.

JAPAN

INNOVATIVE ACTIVITY: CLINICAL TRIALS

- The number of all clinical trials conducted in Japan increased sharply between 2005 and 2010. This was most significant for phase 3 trials. By contrast, phase 4 clinical trials remained relatively stable at around 0.2 trials per million people, on average between 2005-2010.
- Since 2010, the growth in clinical trials was relatively low with an average total number of phase 1 to 4 of 2.8 per million per year.





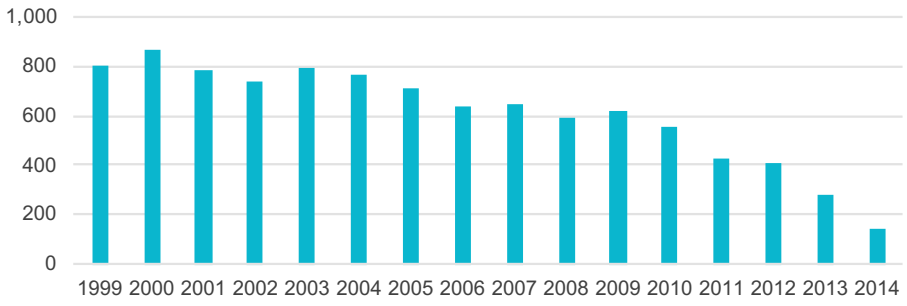
Source: Clinicaltrials.gov.

JAPAN

INNOVATIVE ACTIVITY: PATENTS

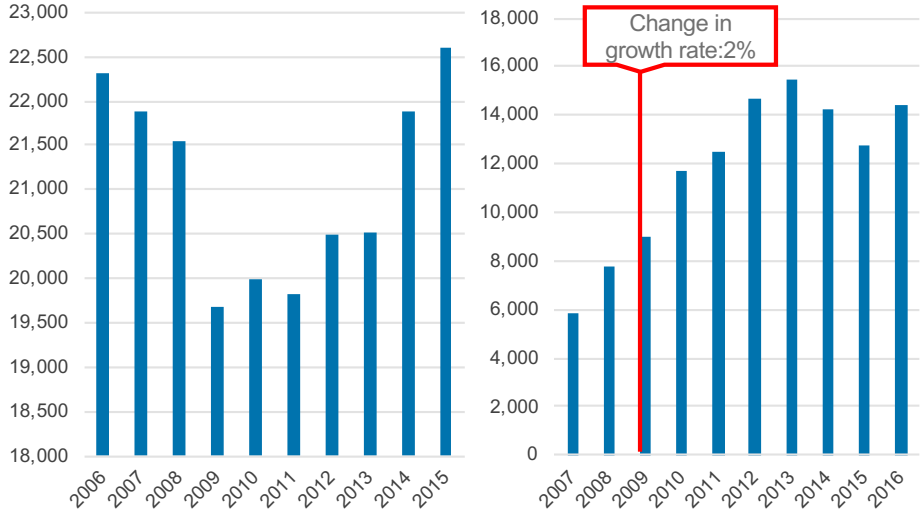
- Pharmaceutical patents granted by the JPO increased steeply between 2007 and 2012. Patent applications decreased from 22,302 in 2006 to 19,684 in 2009 but then recovered to 22,597 in 2015.
- Pharmaceutical patents granted to Japanese nationals by USPTO steadily decreased between 2009 and 2014 from over 600 to 142.
- In recent years (2010-2016), the number of patents filed under PCT has been relatively constant at around 1,000 each year.

Pharmaceutical Patents Granted to Japanese Nationals by USPTO



Sources: OECD Main Science and Technology Indicators (2019).

Pharmaceutical Patent Applications and Grants by the Japanese Patent Office (JPO)



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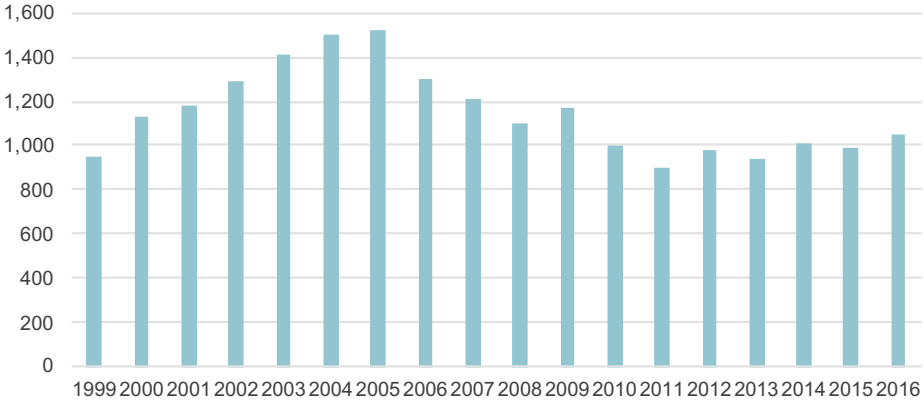


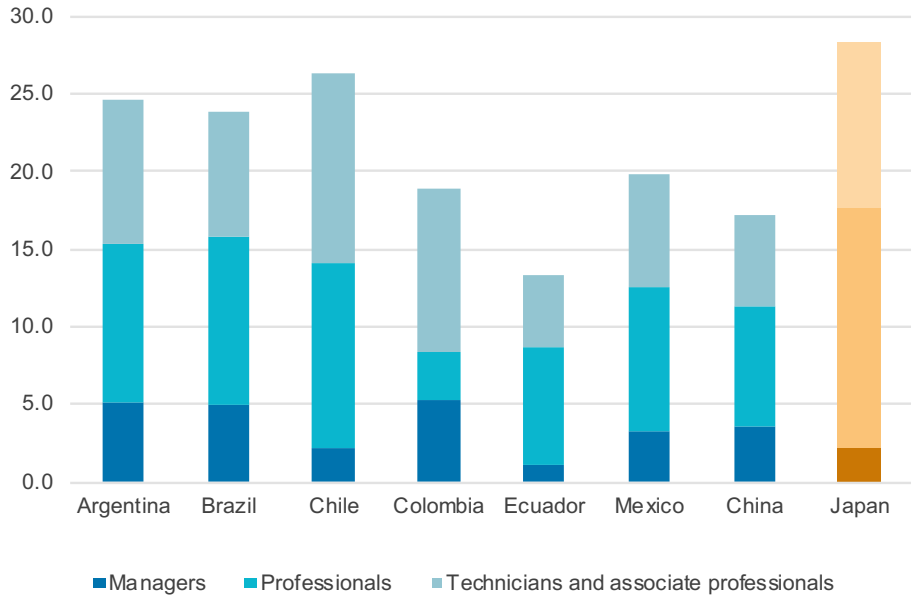
Sources: JPO Website; OECD Main Science and Technology Indicators.
Note: No local data for 2003.

JAPAN

EMPLOYMENT IN THE PHARMACEUTICAL INDUSTRY

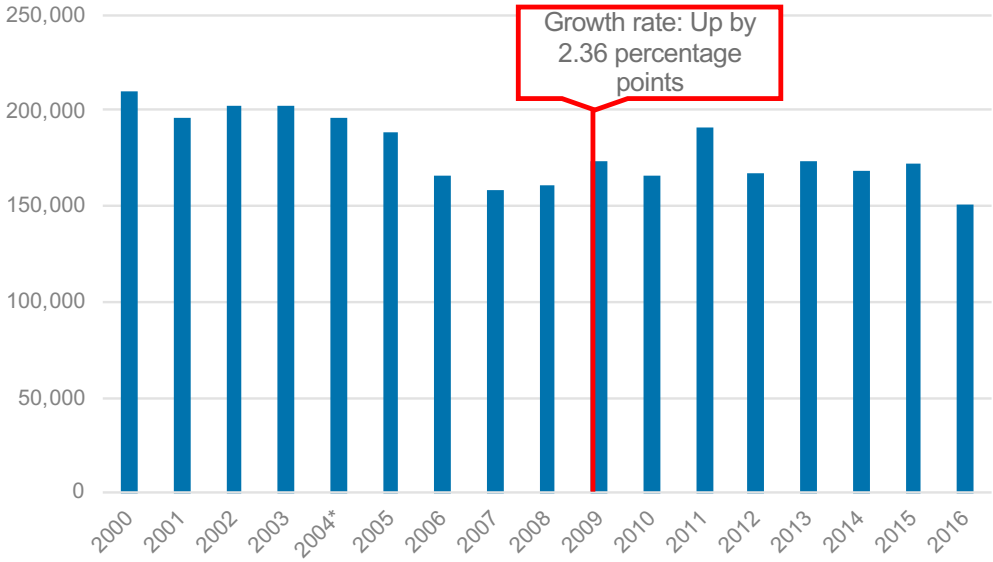
- In the period of 2001 to 2018, Japan has consistently employed between 27% and 28% of its workforce in knowledge-intensive services.
- Although the number of personnel in the pharmaceutical industry has remained stagnant since the year 2000, this is reflective of the overall employment levels in the knowledge-intensive services in Japan which also remained relatively stable.

Employment in knowledge-intensive services, % of workforce (2018)



Source: International Labour Organisation, 2018.

Employment in the pharmaceutical industry (2000-2015)



Source: JPMA Data Book 2017, *2004 estimate.

6. Statistical analysis

UNDERSTANDING THE IMPACT OF **IMPROVING THE IP REGIME:** APPROACH

Aim: In order to establish useful lessons on potential gains from an improved environment, we first need to:

1. Determine relationship and causality between policy and regulation change and impact in innovative activities.
2. Understand the overall magnitude of impact of the IP regime on innovative activities.
3. Create alternative scenarios of impact of broader policy approach including IP regime and other innovation incentives based on the experience of case study markets.

Literature on causality and impact of IP:

- Prior research has shown that patents and other forms of exclusivity for pharma and bio products such as RDP, provide companies with an incentive to invest in innovative activity to deliver new medicines.
  - These studies have found that a 1% change in the strength of a national IP environment (based on a statistical index) is associated with:[1]
    - 2.8% increase in FDI in-flows,
    - 2% increase in service imports, and
    - 0.7% increase in domestic R&D

Determining causality and magnitude of impact:

To assess potential impact and magnitude of gains from an improvement in the IP regime, we apply the following approach:

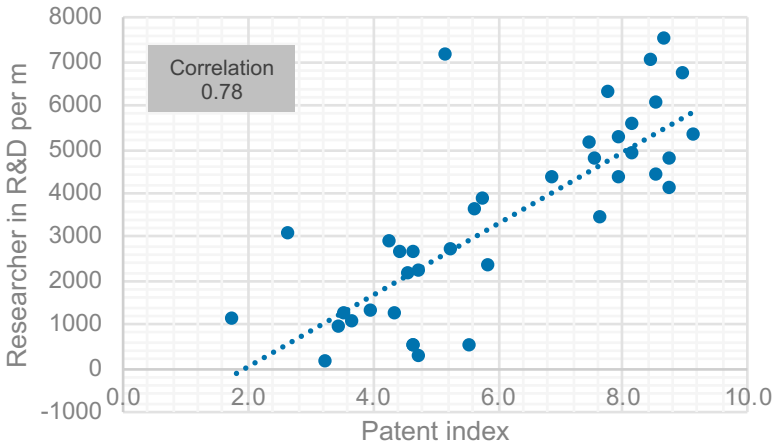
- **Step 1:** we construct a database including the following data:
  - **IP protection** using patent index (by US Chamber of Commerce (n=50)) as a proxy – countries are rated on a scale from 0 (lowest-weakest) to 8 (highest-strongest).
  - **Innovative and economic activity variables:**
    - R&D spending (as % of GDP)
    - Clinical trials (adjusted per population)
    - Patent numbers (adjusted per population)
    - Number of researchers (adjusted per population)
- **Step 2:** we determine whether there is a correlation between each innovative activity variable and IP protection.
- **Step 3:** we ran regressions to analyse if there is a significant impact (causality) of IP protection on innovative activity. The coefficient for each variable will also dictate the direction and magnitude of impact (reported in appendix).

CORRELATION BETWEEN PATENT PROTECTION STRENGTH AND INNOVATIVE ACTIVITY

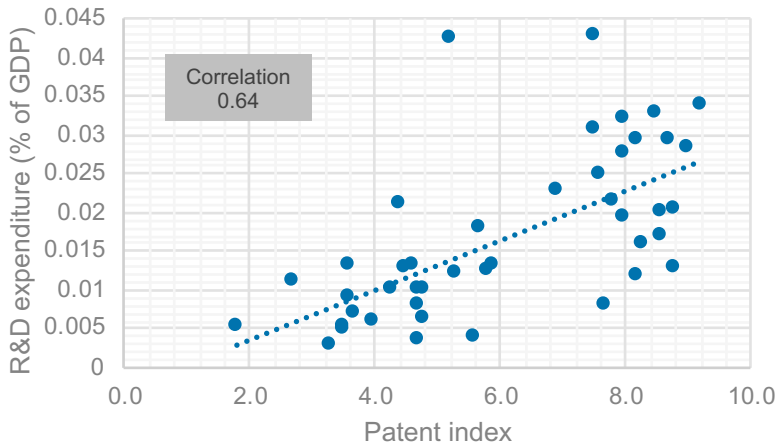
- The correlation between patent system strength and variables on innovative activity namely R&D researchers, R&D expenditure, clinical trials and patents granted was evaluated using updated data.
- A positive correlation was demonstrated i.e. stronger the IP protection was associated with more innovative activity.
- With updated data, we note stronger correlations of IPR and R&D expenditure (0.64) and R&D esearchers (0.79) compared to those found in 2018 Report (0.41 and 0.67 respectively).

- **R&D spend,** the correlation shows high strength which can be attributed to the fact that stronger IP incentivises greater expenditure in R&D due to greater confidence in the system.
- **Researchers employed in R&D,** the correlation shows medium to high strength which can be attributed to the increased incentives for activity in clinical research which in turn increases the demand for researchers.

Correlation between Patent Index and Researchers in R&D

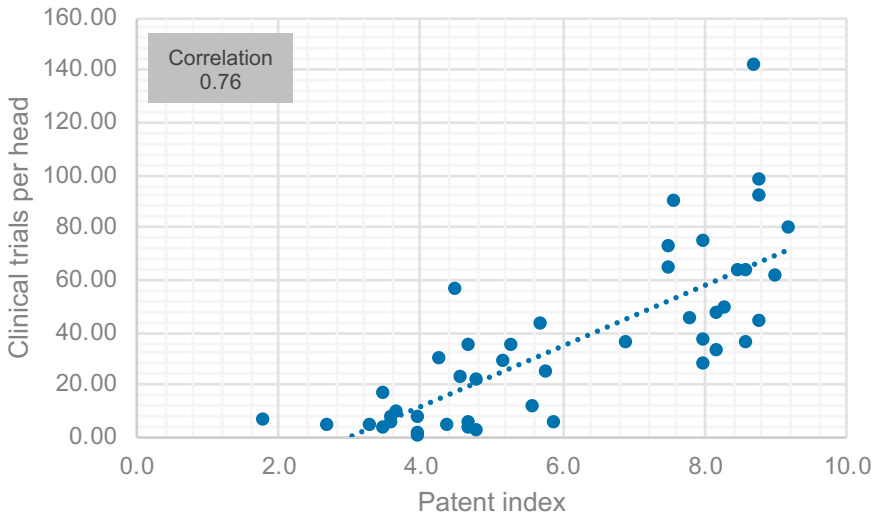


Correlation between Patent Index and R&D spend (%GDP)

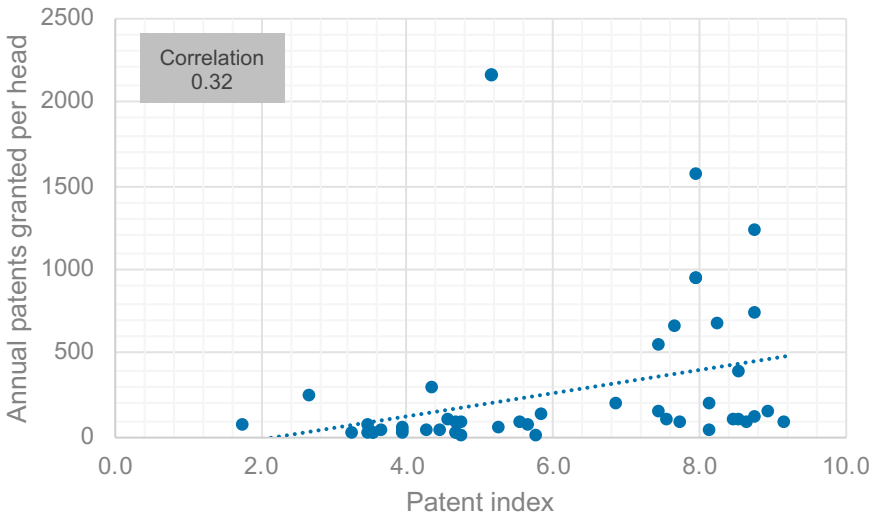


- **Clinical trials,** the identified strong correlation supports evidence that this is one of the indicators of innovation that is most commonly impacted by the strength of the IP protection.
- **Patents granted,** correlation shows medium strength which can be in part attributed to significant outliers (some countries with particularly high number of patents for their size and IP strength – see example in orange).

Correlation between Patent Index and Clinical Trials



Correlation between Patent Index and patents granted



UNDERSTANDING THE IMPACT OF **INTRODUCING RDP:** APPROACH

Aim: In order to establish useful lessons on potential gains from introducing RDP, we first:

1. Conduct literature review to establish hypothesis of how RDP is likely to influence innovative activities.
2. Understand the overall magnitude of impact of introducing RDP on innovative activities, based on the experience of case study markets.
3. Apply findings to the scenario of Brazil.

Literature on causality and impact of RDP:

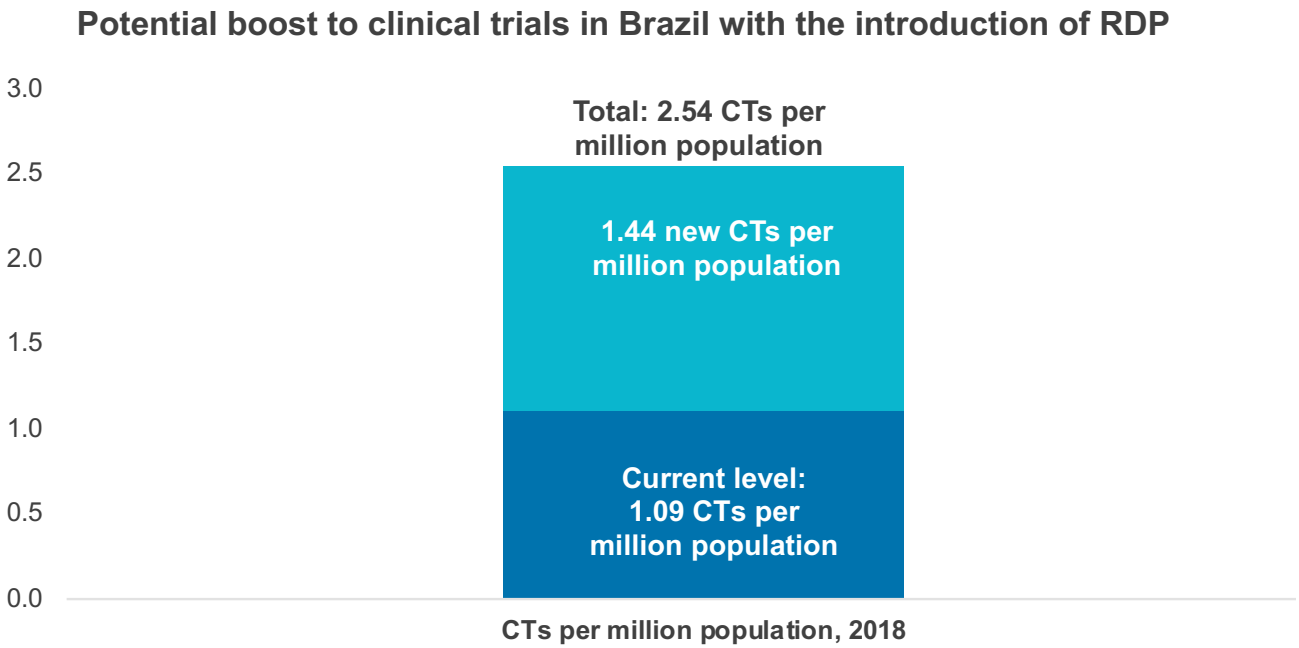
- Grabowski et al. (2011) examine the impact of data exclusivity period on the ability of biologic manufacturers to break-even and therefore cover their innovation investments. The study finds that a 12 year exclusivity period for biologics in the US appropriately balances potential cost savings from price competition from biosimilars with long-term incentives for investment in innovative biologics.[76]
- Goldman et al. (2011) study the impact of longer data exclusivity on revenues and therefore innovation incentives.[77] The analysis finds that extending data exclusivity from 5 years to 12 years in the US would increase lifetime drug revenues by 5%, on average. This would result in 228 extra drug approvals between 2020-2060.
  - The authors also examine the public health effects and find that the population turning fifty-five in 2060 can expect increased life expectancy of 1.44 years as opposed to 1.30 years under the status quo. The 1.7-month difference is a result of innovation in the interceding years, ie. the new medicines brought to market because of lengthier data exclusivity.

Determining causality and magnitude of impact: To assess potential impact and magnitude of gains from an introduction of RDP, we apply the following approach:

- **Step 1:** We construct a database including the following data from our case study markets (South Korea, Taiwan, China and Japan):
  - **RDP binary variable**, where RDP = 1 if RDP was introduced in a certain year and RDP = 0 if the market had no RDP.
  - **Innovative activity variable:** Based on our literature review, we expect revenues and therefore investment in new medicines to increase. We examine the impact on clinical trials per million population.
- **Step 2:** We determine whether there is a correlation between clinical trial activity and RDP.
- **Step 3:** We run regressions to analyse if there is a significant impact (causality) of RDP on innovative activity. The coefficient for the variable dictates the direction and magnitude of impact.

UNDERSTANDING THE IMPACT OF **INTRODUCING RDP:** RESULTS

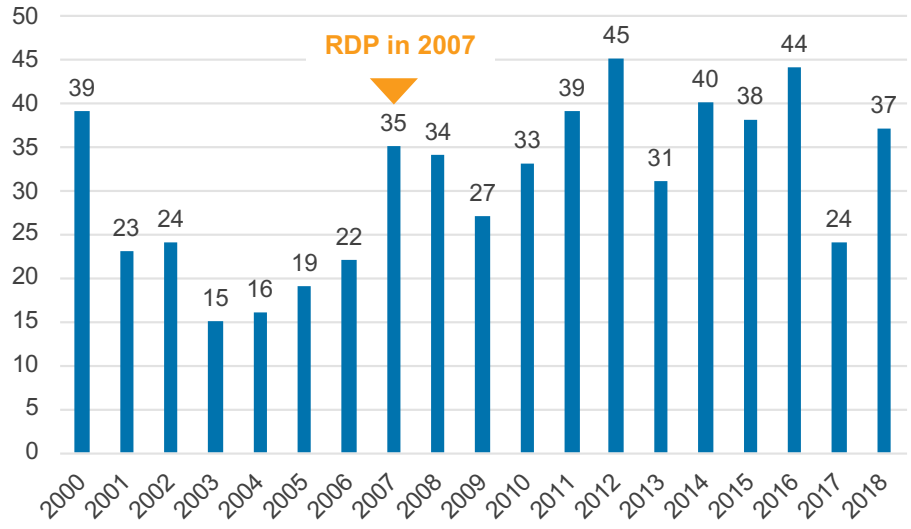
- Controlling for potential pharmaceutical market size (population) and overall economic growth (GDP per capita, PPP terms), we **estimate the relationship between the introduction of RDP on clinical trials per population**.
- Based on our four case study markets, **South Korea, Taiwan, China and Japan,** we estimate that with RDP, clinical trials per million population is expected to be 131% higher on average, per year (statistically significant, at the 10% level), all other things held constant.
- **Applying these findings to Brazil,** we estimate that **1.44 additional clinical trials (CTs)** could have been conducted if there were RDP provisions to incentivise product development.



UNDERSTANDING THE IMPACT OF **INTRODUCING RDP:** MEDICINES ON THE MARKET

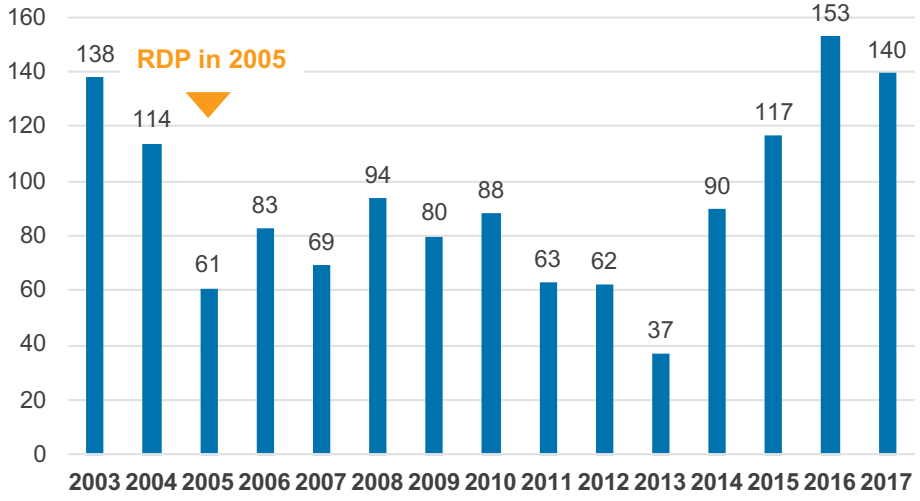
- RDP offers additional protection to a new innovation outside its patent. It is seen as an incentive for the introduction of new innovations, particularly those that require significant investment and are challenging to develop, for example biologics and anti-cancer medicines. [78,79]
- RDP has a part to play in incentivising the launch of new products. For example, since the introduction of RDP in Japan and Taiwan, the number of new product launches has grown at an average of 4.5% and 15.7% year on year in each of the countries respectively.
- RDP indirectly leads to an increase in the number of generic products once the exclusivity period ends.[80] In the case of agrochemicals that benefit from RDP, RDP has not been a barrier to the launch of new and generic products every year. For example, the number of those approved increased from 200 in 2005 to 277 in 2016, 405 in 2017 and 455 in 2018.[81]

Number of new medicine launches in Japan (2000 – 2018)



Source: JPMA.

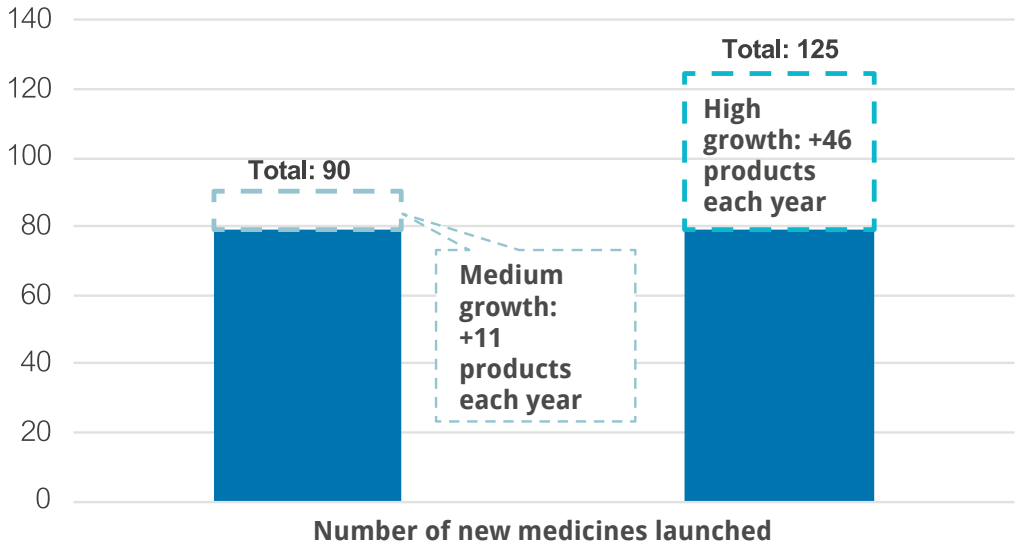
Number of new medicine launches in Taiwan (2007 – 2017)



Source: TFDA.

- RDP confers on the holder of a pharmaceutical marketing approval, for a set period of time, the exclusive right to benefit from the proprietary pre-clinical and clinical data that it generated at significant cost and submitted to the applicable regulatory authority to obtain approval of its product. RDP therefore provides an effective incentive for the introduction of new medicines and vaccines in a given market.
- A positive growth in the **number of new medicines** launched has been observed both in **Japan** and **Taiwan since the introduction of RDP** in 2007 and 2005, respectively.
- The introduction of RDP in Brazil could yield between **2 and 26 new products** in a given year over the period of five years presenting new options in the treatment of patients.

Potential boost to the number of new medicines approved in Brazil with the introduction of RDP



Note: The number of new products launched in Brazil is based on the average number of new products and biologics approved in 2015 and 2016 according to ANVISA – 79 products (DOC_PARTICIPANTE_EVT_4417_1503497954589_K-Comissao-Permanente-CAS-20170823EXT035_parte8338_RESULTADO_1503497954589).

The medium growth scenario applies the growth in cumulative number of drugs approved in Japan since the introduction of RDP in 2007 (timespan 2008 – 2018).

The high growth scenario represents a similar analysis but taking the growth in Taiwan since the introduction of RDP in 2005 (timespan: 2007 – 2017).

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