FOSTERING INTELLECTUAL PROPERTY & INNOVATION FOR BIOPHARMACEUTICALS

Recognising R&D investment as part of Singapore's Patent Term Extension (PTE) regime

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SINGAPORE ASSOCIATION OF PHARMACEUTICAL INDUSTRIES

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SECTION 1: EXECUTIVE SUMMARY

Singapore is a regional hub for many pharmaceutical multinationals. The biopharmaceutical industry forms the core pillar of Singapore's manufacturing sector, contributing to 3% of the country's GDP or SGD 26Bn of manufacturing output. The country hosts more than 50 manufacturing plants, over 50 R&D Centres and over 30 regional headquarters of biopharmaceutical companies. Thus, sustaining investments and growth in this industry is crucial to maintaining an innovative ecosystem in Singapore.

This position paper sets out the Singapore pharmaceutical industry's proposal for a review of patent term extension (PTE) provisions under the Singapore Patents Act and other related patents legislations within the US-Singapore Free Trade Agreement (USSFTA) and European Union-Singapore Free Trade Agreement (EUSFTA). It is noted that existing patent system in Singapore is not aligned with developed patent systems such as the United States (US) and European Union (EU). The latter systems compensate patentees for the delay resulting from the clinical development phase, which is a necessary step to acquire marketing approval for any new pharmaceutical product, when certain conditions are met. However, Singapore does not do so and only considers compensating patentees for the delays resulting from the regulatory administrative process for obtaining marketing approval.

A well-designed and effective PTE system can propel Singapore's vision to become a global intellectual property (IP) hub, a regional hub for biotechnology as well as a centre for world-class clinical research and development.

SECTION 2: BACKGROUND ON PATENT TERM EXTENSION OVERVIEW

2.1 Background on SAPI's position on review of current patent term extension regime in Singapore

Patents are a core component of a strong IP system to protect and encourage investments by pharmaceutical companies. Companies apply for patent protection as the research and development progresses, thereby, granting exclusive rights to inventors for a certain period in exchange for the investments made to develop new medicines and fund future research. As part of IP protection, many countries have in place patent term extension (PTE) help to compensate pharmaceutical companies for the delays while obtaining marketing approval for a new drug and the clinical development time to prove the safety and efficacy of the drug. These countries recognise that when applying for marketing approval of a new drug, the clinical development data analysis and results often need to be provided to regulatory authorities.

The Singapore Association of Pharmaceutical Industries (SAPI) had recent consultations with the Singapore government to propose a review of the existing PTE systems. The industry notes that Singapore's PTE conditions and calculations are not in line with international standards today. In turn, this undermines Singapore's efforts to become a centre of excellence for innovation, as well as a competitive regional biopharmaceutical hub and global IP hub.

As a follow-up to the consultations, SAPI has received some queries from the Singapore Ministry of Law (MinLaw), who is the policy owner of the patents legislation under the Singapore Patents Act and the respective US-Singapore Free Trade Agreement (USSFTA) and European Union-Singapore Free Trade Agreement (EUSFTA). The industry views that the existing patent laws is not in line with the spirit of reciprocity in the two FTAs. This position paper aims to address MinLaw's queries on behalf of SAPI, in order for relevant stakeholders to make an informed decision on the next steps to pursue change. Various pharmaceutical industry stakeholders were consulted to address MinLaw's queries. Their views are reflected in various sections of this paper.

2.2 Overview of patent and exclusivity provisions of existing legislations

Generally, patents for pharmaceutical products are governed as an intellectual property protection, under which there are two components:

a. **Basic patent term protection:** lasts up to 20 years from the date of the filing of the patent (as mentioned under section 36(1), Singapore Patents Act) and is subject to payment of renewal fees annually.

b. **Patent term extension (PTE):** extends the term of a patent covering a pharmaceutical product that undergoes regulatory review in order to obtain marketing approval. Patents with extended terms have limited patent rights. The scope of protection will only be limited to the claims directed to the pharmaceutical product and not to the entire patent. Further details about PTE is found in Section 2.3 and 2.4.

In addition to patent protection, exclusivity can separately apply for a pharmaceutical drug as a regulatory provision. There are two components relating to exclusivity:

c. **Data protection/ exclusivity** refers to a period of data protection of a drug clinical test data that is provided by an innovator company to a regulatory agency to prove the safety and efficacy of a new drug. During this period of data protection, which is five years in Singapore's context from the submission date of a marketing approval dossier, a competitor cannot rely on the innovator's clinical data when seeking approval of a generic version of the same drug to the same regulatory agency. New clinical data must be generated by the competitor.

d. **Registration exclusivity** is a right granted to ensure that the product cannot be copied or marketed for a period after marketing approval is granted. This period is typically less than 5 years in Singapore and allow first-mover advantage for the product that is filed and approved first.

The remaining differences between patents and exclusivity can be summarised as follows[1]:

- Patents protection and (data and market) exclusivity apply to drugs in different ways, may or may not cover the same aspects of the drug product, and can run in parallel.
- Patents can be issued or expire at any time regardless of the drug's approval status. Exclusivity attaches upon approval of a drug product if the statutory requirements are met.
- Some drugs have both patent and exclusivity protection while others have just one or neither.

2.3 Current Patent Term Extension Legislation in Singapore[2]

The grounds on which PTE may be granted under section 36A of the Singapore Patents Act can be summarised as follows:

a. there was an unreasonable delay by the Registrar in granting the patent[3];

b. there was an unreasonable delay caused by a foreign patent office in the issuance of the patent relating to a corresponding application and the foreign patent office has extended the term of the corresponding patent on the basis of such delay[4];

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[1] https://www.fda.gov/drugs/developmentapprovalprocess/ucm079031.htm#What_is_the_difference_between_patents_a

[2] https://www.ipos.gov.sg/docs/default-source/resources-library/patents/infopacks/patents-infopack-(final)_25042017.pdf

[3] PTE can be requested if the delay exceeds four (4) years from the filing date of the patent application to the date of grant of the patent or two (2) years from the date of request for examination to the date of the grant of the patent. However, the time period excludes any time spent by the applicant responding to Office Actions issued by the examiner. It is therefore impossible to apply for PTE in Singapore on this basis given the maximum 18-month substantive examination proceedings rule set by IPOS.

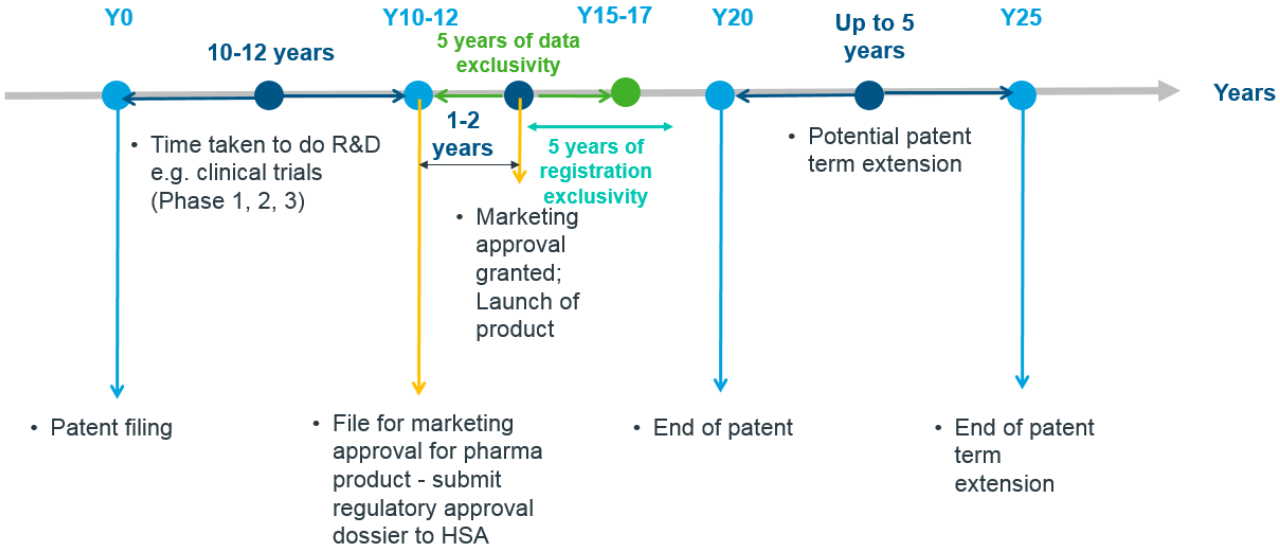
[4] Currently, a request for grant of a patent in Singapore may rely upon an allowed/granted patent in Australia, Canada, EU, Japan, New Zealand, Korea, the UK, or the US. Thus, the available options to

c. there was unreasonable curtailment of the opportunity to exploit the patent caused by the process of obtaining marketing approval for a pharmaceutical product, being the first pharmaceutical product to obtain marketing approval which uses a substance (which is included as part of the patent) as active ingredient; and the term of the patent has not previously been extended on this ground. In particular, the time between the date of application for marketing approval and the date marketing approval was obtained, excluding any period attributable to an act or omission of the applicant for marketing approval, must exceed two years.

Thus far, no pharmaceutical products registered in Singapore have received approval for PTE[5].

An illustrative timeline of how patent protection and exclusivity provisions apply in the Singapore context is shown in Figure 1 below.

Figure 1: Illustrative timeline of patent filing to marketing approval and patent term extension in Singapore's context[6]



qualify for this ground is limited to the above-mentioned jurisdictions on the condition that PTE is also permissible and granted in that jurisdiction. Among the prescribed patent offices, only US and Korea allow PTE due to a delay in granting a patent.

[5] Consolidated feedback from IQVIA's internal survey of pharma companies.

[6] Verified by legal experts.

2.4 Marketing approval considerations and Current Patent Term Extension Legislations under USSFTA and EUSFTA

To promote and strengthen IP systems among countries whom Singapore holds strong bilateral relations with, the USSFTA and EUSFTA contains PTE clauses for pharmaceutical products. Both articles under the USSFTA and EUSFTA related to PTE do not specifically mention drug discovery and development time to be taken into consideration as part of the administrative marketing approval process[7]. Yet, applications for marketing approval require the results and data analysis from the entire clinical development program, as well as the earlier preclinical testing and proposals for manufacturing and labelling of the new medicine. Clinical trials are an important phase in drug development. Following the discovery of a new drug or a new treatment for a known drug, the product is put through the lengthy and costly clinical trials to test its efficacy and toxicology. This data, which can take between 10 to 12 years to generate, is needed for the issuance of marketing approval for a new drug to be launched in each country. Not factoring in these regulatory compliance considerations into PTE could prevent the drug inventor from enjoying the benefits of their patent rights.

The USSFTA, which entered into force in January 2004, contains safeguards to strengthen patent protection between the two countries. On PTE, either party shall extend the term of a patent (at the owner's request) to compensate for unreasonable delays that occur in granting the patent. This would include a delay in the issuance of the patent of more than 4 years from the date of filing of the application with the Party, or 2 years after a request for examination of the application has been made, whichever is later. Specifically, for any patented pharmaceutical product, each party shall make available a PTE to compensate the patent owner for unreasonable curtailment of the patent term as a result of the marketing approval process. It is known that Section 36A of the Singapore Patents Act was enacted to fulfil Singapore's obligations under the USSFTA. However, since the signing of the USSFTA, patent laws in the US have evolved. Yet, Singapore's patent laws have not kept up with changes.

The EUSFTA, which concluded negotiations in October 2014, offers a comprehensive, high level of protection and enforcement of IP and ensures reciprocity in IP treatment to maintain competitiveness of both economies. The EUSFTA states that the Parties shall make available PTE to compensate the patent owner for the reduction in the effective patent life as a result of the administrative marketing approval process[8]. The extension of the duration of the rights conferred by the patent protection may not exceed five years[9]. In the case of the EU's patent system, PTE is offered under the Supplementary Protection Certificates (SPC) to compensate

[7] Cited by undisclosed legal expert.

[8] Singapore undertakes to make available an extension of the duration of the rights conferred by patent protection to compensate the patent owner for the reduction in the effective patent life as the result of the administrative marketing approval process to substances for diagnosis or testing and authorised as a medicinal product.

[9] The conditions and procedures for the provision of the extension of the patent term shall be determined by the respective legislations of the Parties. This is without prejudice to a possible extension for paediatric purposes, if provided for by either Party.

pharmaceutical companies for the delays in carrying out the necessary steps (e.g. R&D) to obtain marketing approval for a new drug product. Thus, the industry encourages Singapore to reinterpret the texts of the EUSFTA to account for development time as part of the regulatory administrative process for obtaining marketing approval, similar to the conditions of the SPC.

To date, no pharmaceutical companies have sought PTE under both FTAs. However, as new medicines develop and launch in the Singapore market (e.g. ETC[10]159 and 206), it is likely that more companies will benefit and reinforce reciprocity if Singapore grants the same PTE treatments as in the US and EU today.

2.5 Overview of differences in pharmaceutical patent term extension considerations in Singapore versus other jurisdictions

Today, delivering authentic innovative medicines is more challenging and complex than ever. The time taken to conduct research and development is often long but necessary for gaining regulatory approval to launch a new drug in the market. Thus, many developed markets compensate for the period or marketing time lost during drug development and regulatory approval. Singapore's current PTE legislation, while on par in terms of the period of extension, does not consider development time of a new drug. Due to the lack of drug development time consideration as well as a few other technical differences with the PTE provisions of other jurisdictions[11], companies in Singapore are unable to exercise PTE today. A summary of the PTE periods and conditions of various markets are shown in Table 1 below.

[10] A*STAR's Experimental Therapeutics Centre (ETC) and Drug Discovery and Development Unit (D3) play a major role in the local drug development landscape. ETC, which focuses on translating early-stage drug discoveries into clinical applications, provides research facilities and services that can be utilised by local companies to test and develop new drugs. The compounds making up Singapore's first publicly-funded anti-cancer drug, ETC-159, were identified through screens conducted at the Singapore Screening Centre. Building upon the success of ETC-159, ETC and D3 (together with collaborators Duke-NUS and the Singapore Clinical Research Institute), Singapore announced its second publicly-funded cancer drug, ETC-206, which advanced into clinical trials in December 2016. The drug inhibits a specific growth enzyme in cancer cells, making it a potential treatment candidate for blood cancers such as leukaemia and lymphoma. https://www.a-star.edu.sg/News-and-Events/A-STAR-INNOVATE/Index05/Getting-the-formula-right-to-boost-Singapores-health-and-biomedical-sector

[11] Some technical differences include: (i) patents covering a process of manufacture claim (e.g. new indications), a Swiss-style claim and/or a medical device claim are not eligible for PTE in Singapore, (ii) patents which claim a drug for humans or animals, a medical device, a human or veterinary biological product, a food additive or a colour additive that requires regulatory approval are not eligible for PTE in Singapore, (iii) In the US, patent term adjustments due to the delay in granting the application are awarded by the USPTO automatically and includes the 3-month period for responding to Office Actions in the calculation of granting delay, whereas in Singapore, the applicant has to submit a request.

Table 1: Summary of PTE periods and conditions for various markets[12]

European Union	• Up to 5-year under Supplementary protection certificates (SPC) • Combined with patent conveys a maximum of 15 years of effective protection i.e. the time between granting of marketing authorisation and expiry of the patent • Compensates for the duration of the R&D and testing processes
United States	• Up to 5 years • Combined with patent conveys a maximum of 14 years of effective protection i.e. the time between granting of marketing authorisation and expiry of the patent • Compensates for marketing time lost during development and government approval
Japan	• Up to 5 years • The possible restoration period is calculated from the start date of clinical trials or patent, whichever is the latest, and ends on the day before the authorities send the final authorisation to the company
Australia	• Up to 5 years
Singapore	• Up to 5 years • Condition on unreasonable curtailment of the opportunity to exploit the patent caused by the process of obtaining marketing approval, and excludes development time

[12] Report on "Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe"

SECTION 3: MARKET APPROVAL PROCESS FOR DRUGS IN SINGAPORE

3.1 Overall process of obtaining marketing approval for a pharmaceutical product

In Singapore, pharmaceutical companies go through three routes when obtaining their marketing approval for any new drug applications[13]:

a. Full evaluation: applies to any first in the world new drug product that has not been approved in any other country. Full evaluation requires an independent and in-depth scientific assessment by HSA to ensure the quality, safety and efficacy of the drug. This route takes 270 working days, excluding screening periods and stop-clocks.

b. Abridged evaluation: applies to any new or generic product that has been evaluated and approved by at least one other WHO-designated regulatory agency. This route takes 180 working days, excluding screening periods and stop-clocks

c. Verification evaluation: applies to any new or generic product that has been evaluated and approved by two of the five Health Sciences Authority (HSA) reference agencies [the US FDA, the EMA, Health Canada, the UK Medicines and Healthcare Products Regulatory Agency (MHRA), and Australia's Therapeutic Goods Administration (TGA)], provided that the product and indications are the same as in the reference countries. It is based on the principle of leveraging the scientific assessment that has been performed by reference agencies, so as to minimise duplication of effort, thereby allowing expedited marketing approvals in a compressed timeline. This route takes 60 working days, excluding screening periods and stop-clocks.

3.2 Typical timeline for marketing approval applications (from filing to approval)

The typical timeline for marketing approval applications (from filing to approval, including stop-clocks) ranges from between 12 to 22 months, according to IQVIA's survey of selected major pharmaceutical players in Singapore.

Among the three submission routes, most pharmaceutical companies in Singapore file under the abridged route (estimated at 80 to 95%), followed by full and verification route respectively[14]. The abridged evaluation route is preferred by industry as it allows industry the flexibility to seek approval for clinical indications or quality specifications which may not be the same as those approved by reference agencies.

For the full evaluation route, it is widely cited by the industry that products that have not been registered in the US or Europe are unlikely to gain first in the world approval in Singapore. The

[13] IQVIA Market prognosis 2018; Health Sciences Authority.
[14] Consolidated feedback from IQVIA's internal survey of pharma companies.

industry interviewees for this survey are not aware of any first in the world NCE approval in Singapore.

Separately, most companies opt out of the verification route due to HSA's approach to product verification criteria. Currently, HSA requires for the proposed indication(s), dosing regimen(s), patient group(s) and/or direction(s) for use to be the most stringent among those approved by the reference drug regulatory agencies. In addition, most companies highlighted that the difficulty to obtain unredacted assessment reports from the US FDA has prevented them from using the verification route.

3.3 Singapore as next wave/jurisdiction where application for marketing approval for pharma products is filed and reasons

Feedback from pharmaceutical companies[15] suggest that Singapore is usually the second wave in the application for marketing approval of pharmaceutical products globally (i.e. most companies go for the abridged or verification route for new drug applications), after first wave countries such as the US, EU, Australia, Canada and Switzerland. The following reasons were cited on why Singapore usually falls under the next wave:

- Small and limited market size
- Regulatory process: The length of time required for approval (when filing under the first wave or full evaluation) is sometimes slower in comparison to other markets
- Perception that HSA prefers one of the major reference agencies to approve a new product first
- Cost of filing: Cost is cited to be higher when companies file under the first wave (i.e. full evaluation route) due to more resource commitments (compared to the abridged route)
- Priority review process is only available for abridged route in Singapore[16] (and does not apply under full evaluation route, unlike for most wave 1 countries)

In addition, most companies may also consider the following factors in deciding where to file marketing approval for a new drug:

- Protection of intellectual property
- Potential commercialisation
- Transparency of guidelines from the regulatory agency
- Strategic influence
- Other country-specific requirements

For companies that have successfully filed products for marketing approval using Singapore as a first wave country, considerations are often strategic. These considerations include the

[15] IQVIA's internal survey of pharma companies, September 2018.
[16] This usually only applies for a life-saving drug if there are unmet medical needs.

ability to provide first-in-class treatment for a specific epidemiology that is relevant to this region[17] and to position Singapore as a thought leader and pilot destination for launch of a new product.

[17] This can include pandemic or major vector conditions e.g. dengue, avian flu.

SECTION 4: UNDERSTANDING OF THE PHARMA MARKET SIZE

4.1 Global Pharma Market Trends[18,19]

The overall global pharma market size is rapidly growing and is estimated to reach USD 1.4 trillion by 2022.

During the five-year period between 2013-2017, the US saw a major CAGR growth at about 8%. Amongst the emerging markets, India demonstrated a double-digit growth of about 12% closely followed by China at 8%. Singapore's pharma market sales only witnessed modest growth at a CAGR of 3% between 2013-2017, with sales at USD 820 Mn in 2017 (refer to Tables 2 and 3 below).

During the 5-year period from 2017-2022, the major contribution in terms of pharma market share will come from Northern American countries at 44%. European & South East Asian countries (including Japan) are forecasted to contribute 19% and 20% to global market share respectively. Among the major developed and emerging markets, USA, China and India will continue to largely dominate growth in their respective regions.

Table 2: Sales Value and Growth Rate for Ten Major Pharma Markets

Geography	Sales 2013 (LCUSD) in Bn*	Sales 2017 (LCUSD) in Bn*	CAGR (13-17)	CAGR (17-22)
USA	335.03	452.53	7.81%	5.04%
EU	180.94	214.96	4.40%[20]	3.07%
CANADA	17.30	21.24	5.26%	4.31%
JAPAN	75.39	78.11	0.89%	-1.43%
SOUTH KOREA	11.61	14.60	5.90%	4.67%
AUSTRALIA	10.12	12.66	5.75%	0.90%
NEW ZEALAND	0.84	1.14	8.13%	3.15%
CHINA	65.65	89.96	8.19%	5.52%
INDIA	10.47	16.24	11.59%	9.67%
SINGAPORE	**0.73**	**0.82**	**3.02%**	**4.80%**

*LCUSD = local currency sales converted to US dollars using a constant exchange rate (Q4 2017)

[18] Global Pharma Market Prognosis Report (2018-2022)
[19] MIDAS Sales (Yearly, Currency: LCUSUSD , 2013-2017)
[20] EU 24 – MIDAS Sales numbers not available for Cyprus, Malta, Netherlands and Denmark.

Table 3: Sales Volume and Growth Rate by Volume Sales for Ten Major Pharma Markets

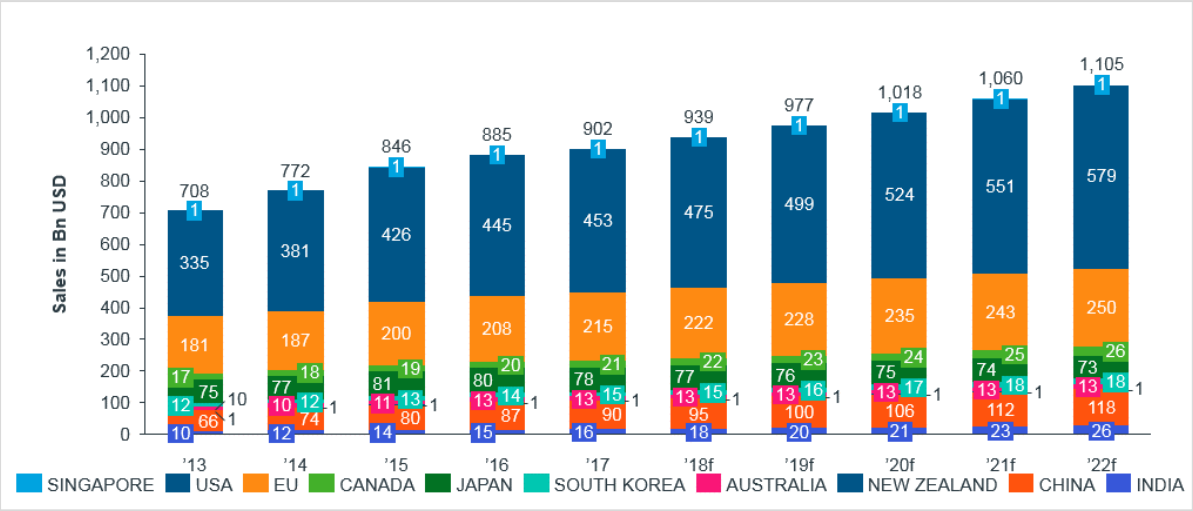
Geography	SU 2013 (Bn)**	SU 2017 (Bn)**	CAGR (13-17)	CAGR (17-22)
USA	367.40	345.99	-1.49%	-1.32%
EU	594.31	610.45	0.67%[21]	Not Available
CANADA	49.14	54.64	2.69%	-0.39%
JAPAN	229.20	235.69	0.70%	0.54%
SOUTH KOREA	65.00	68.96	1.49%	2.92%
AUSTRALIA	40.21	49.25	5.20%	0.91%
NEW ZEALAND	6.14	8.27	7.71%	Not Available
CHINA	268.08	317.02	4.28%	3.02%
INDIA	291.21	355.76	5.13%	6.44%
SINGAPORE	**4.38**	**4.11**	**-1.57%**	**3.25%**

**Standard Units equate the number of milliliters of liquid preparations to the standard solid dosage of one tablet, therefore making solid and liquid preparations comparable

The breakdown of each countries' market sales by value and volume, between 2013 and 2022 (forecasted), are showcased in Figures 2 and 3 respectively below.

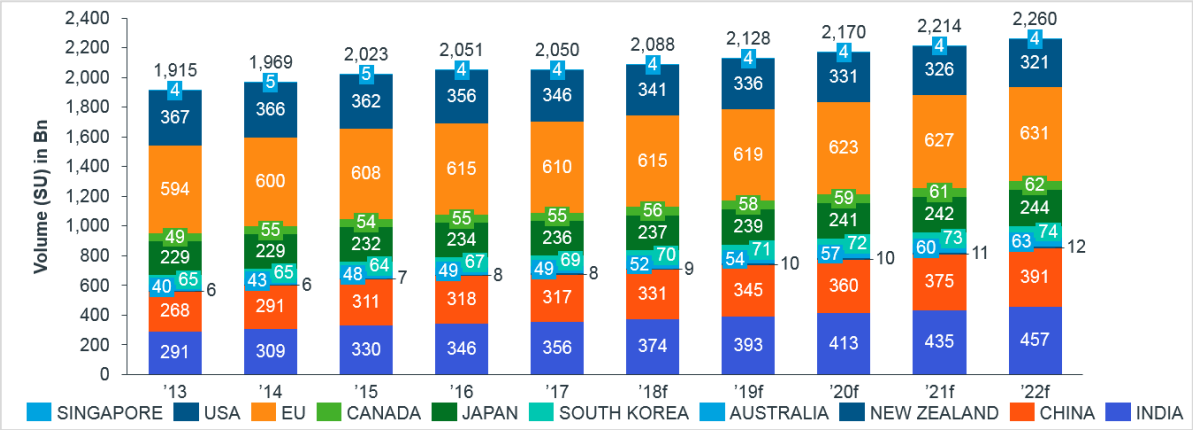
[21] EU 24 – MIDAS Sales numbers not available for Cyprus, Malta, Netherlands and Denmark.

Figure 2: Current and forecasted global market sales by Value (LCUSD*)



*LCUSD = local currency sales converted to US dollars using a constant exchange rate (Q4 2017)

Figure 3: Current and forecasted global market sales by Volume (SU**)



**Standard Units equate the number of milliliters of liquid preparations to the standard solid dosage of one tablet, therefore making solid and liquid preparations comparable

4.2 Market Drivers in Singapore[22,23]

The Singapore market has grown steadily at a CAGR of 3.0% between 2013-2017 and will reach 4.8% between 2017-2022. Sales is forecasted to cross USD 1 Bn in 2022 (see Figure 4 and 5 below). The current growth is in part owing to government initiatives, such as enhanced medication subsidies for low-to-middle-income groups and Pioneer Generation[24] members at polyclinics and strengthened capacity of public healthcare facilities in the primary

[22] https://www.globaldata.com/singapores-pharmaceutical-markext-set-break-1-billion-mark-2019/
[23] Global Pharma Market Prognosis Report (2018-2022)
[24] The 'Pioneer Generation' is defined as living Singaporeans who meet 2 criteria: (i.) Aged 16 and above in 1965 (born on or before 31 Dec 1949, which also means they are aged 65 and above in 2014); and (ii.) Obtained citizenship on or before 31 Dec 1986.

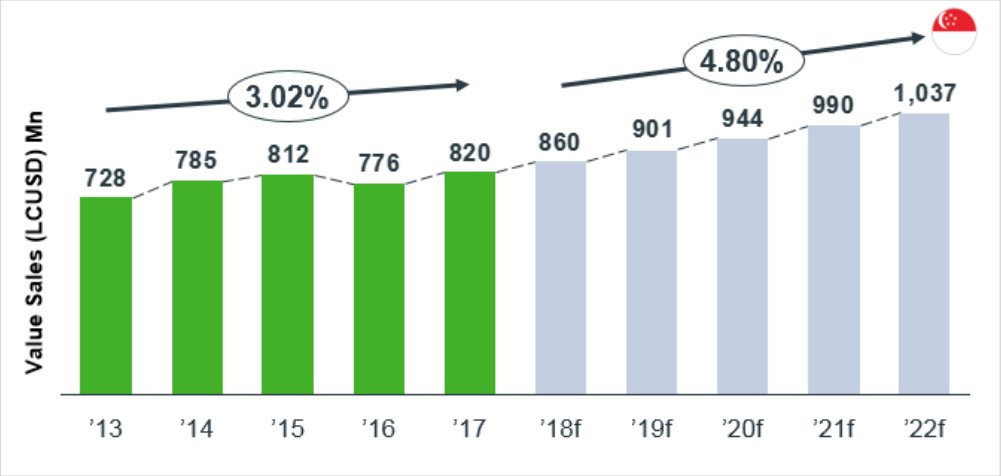
care setting. In terms of future growth, volume growth will be the primary driver. MoH's initiatives to strengthen and expand primary healthcare provision in the public and private sector, the increase in Medisave withdrawal limit to SGD 500 (from SGD 400) from June 2018 onwards, and the increasing prevalence of chronic diseases will continue to drive steady increases in demand.

With a low to modest projected real GDP growth of between 2-3% annually from 2018 to 2022, there is a limited scope for Singapore's pharma market to grow exponentially in the coming years.

Nonetheless, Singapore is a regional hub for biopharmaceutical companies and has world-class infrastructure for manufacturing and R&D facilities of several multinational companies. The biopharma sector is the second highest contributor to the total manufacturing output in Singapore and accounts for 3% of its GDP[25]. The opening of new sites like AbbVie's biologics manufacturing facility and ramp-up of other pharma companies such as Amgen and Novartis will continue to drive market growth in Singapore. Singapore will also likely benefit from planned drug approvals as it also currently hosts facilities of eight of the world's top ten pharma companies globally such as Roche, GlaxoSmithKline, Pfizer and Sanofi.

Over time, a corruption-free pro-business environment alongside strong government support, efficient infrastructure and low corporate tax have created a favorable environment for pharmaceutical companies[26].

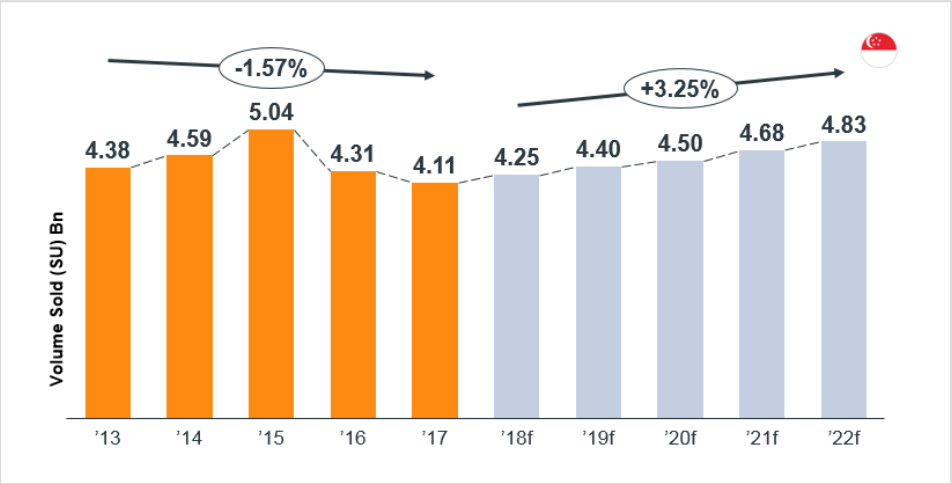
***Figure 4:* Current and forecasted Singapore market sales by Value (LCUSD*)**



*LCUSD = local currency sales converted to US dollars using a constant exchange rate (Q4 2017)

[25] https://www.straitstimes.com/business/economy/spore-pharma-on-recovery-path-after-dismal-2017
[26] https://www.pharmaceutical-technology.com/research-reports/report-singapores-pharmaceutical-market-witness-5-cagr-2021/

Figure 5: Current and forecasted Singapore market sales by Volume (SU**)



**Standard Units equate the number of milliliters of liquid preparations to the standard solid dosage of one tablet, therefore making solid and liquid preparations comparable

4.3 Health Expenditure Trends in Singapore[27]

With the aging population in Singapore, government spending on healthcare has increased over recent years. In comparison to other mature markets, Singapore has an almost equal mix of health expenditure[28] that is proportionally funded from public and private sector (52% vs. 48% respectively) as seen in Figure 6. Unlike Singapore, health expenditure for OECD countries like USA[29] and Japan are heavily dependent on government funding (between 80-85%).

The Singapore government is working on strategies to mitigate the challenges posed by rising healthcare costs through providing transitional premium subsidies to those who face an increase in their net premiums for MediShield Life[30] regardless of their income levels as well as providing means-tested drug subsidies for low to mid-income patients to help them reduce out-of-pocket costs on essential treatment medicines and some more expensive drugs. The government also recognises the need for Singapore's ageing population to have wider access to healthcare. Thus, the Pioneer Generation Package was introduced in 2014 to provide older generation of Singaporeans with additional subsidies to medical services and insurance premiums under the Medisave Life. Today, low-to-middle income patients are now entitled to 75% off their subsidised drugs bills, while Pioneer Generation members receive an additional 50% discount on top of such benefits.

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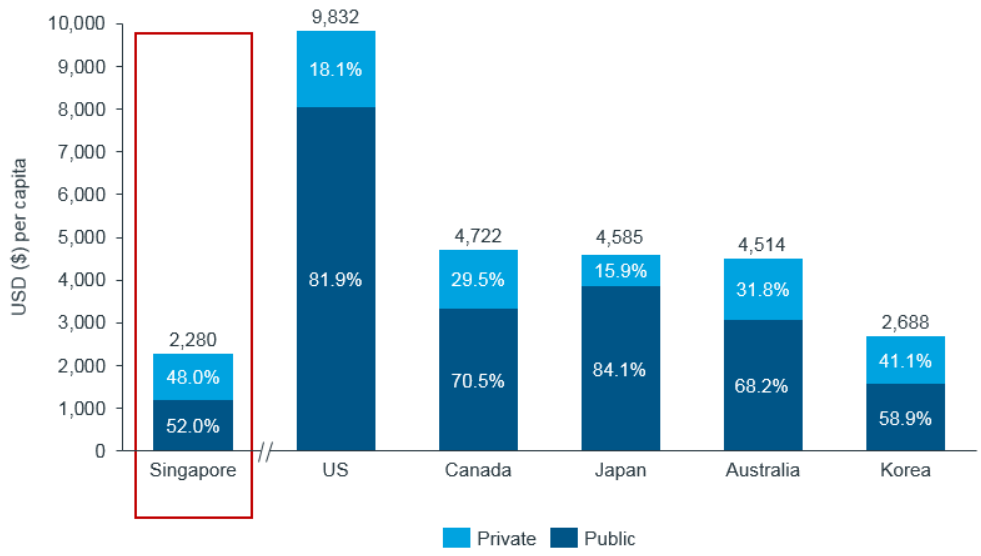
[27] Singapore Market Prognosis Report (2018)
[28] Public health expenditure refers to government spending and compulsory health insurance. Private health expenditure refers to voluntary health insurance and private funds such as households' out-of-pocket payments, NGOs and private corporations. OECD (2018). https://data.oecd.org/healthres/health-spending.htm
[29] In the US, public expenditure includes compulsory medical insurance.
[30] Medishield Life is a national health insurance that provides lifetime universal health coverage for Singaporeans to help with large bills and expensive outpatient treatments.

In addition, to ensure healthcare affordability as well as to tap into existing primary care capacity in the private sector, the Community Health Assist Scheme (CHAS) was introduced in 2012 to provide means-tested patients subsidized care for common illnesses, selected chronic conditions and selected dental services at about 1,690 participating private GP and dental clinics. Since its introduction, a total of around 1.3 Mn members (including 450,000 Pioneer Generation members) were enrolled, with more than SGD 170 Mn in subsidies disbursed annually[31].

When we examine government's expenditure on pharmaceuticals[32] per capita (see Figure 7), we note that most OECD governments spend on average **USD 314**. For Singapore, such number is not publicly available. As such, IQVIA's MIDAS pharma sales data was used as a proxy to estimate Singapore's total expenditure on pharmaceuticals per capita. This number turns out to be low at **USD 146**, when compared against OECD levels.

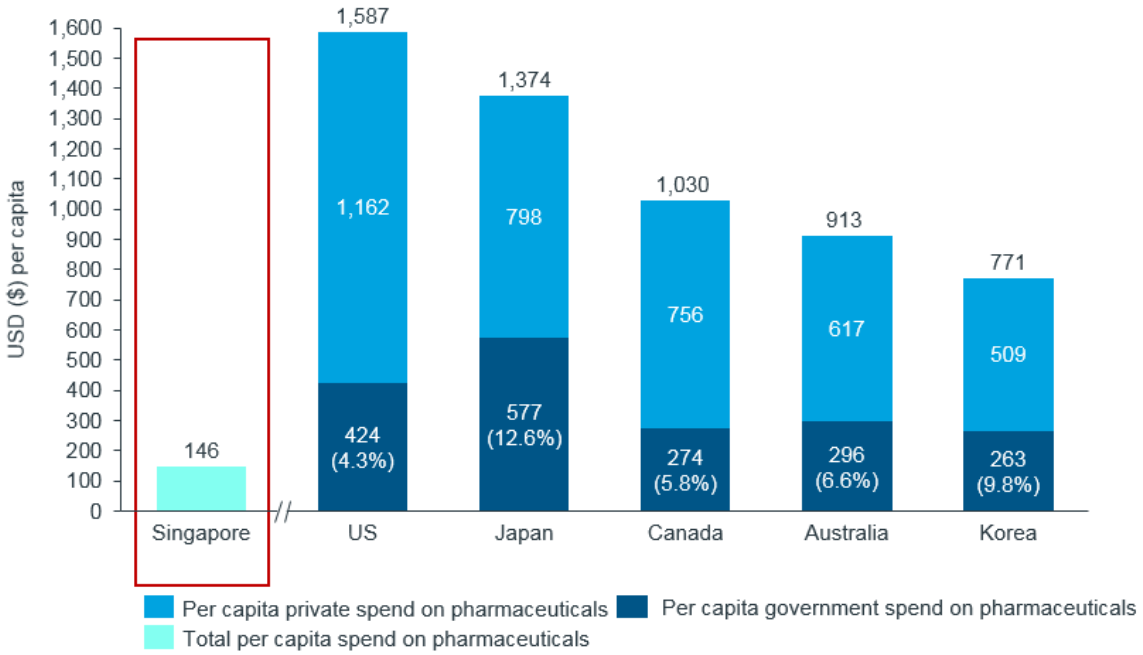
The current review of the PTE for pharmaceutical products can impact how the Singapore government allocates its drugs expenditures in future, while ensuring that cost impact on citizens is kept low.

Figure 6: Total Health Expenditure (Public vs. Private) in USD per capita across select countries, 2015[33, 34]



[31] Latest MoH Singapore Statistics as of March 2018
[32] Pharmaceutical expenditure covers spending on prescription medicines and self-medication, often referred to as over-the-counter products. OECD (2018).
[33] OECD, 2015 Statistics considered for OECD countries
[34] WHO Global Health Expenditure Database, 2015 statistics considered for Singapore

Figure 7: Total Expenditure on pharmaceuticals per capita (including government share), 2015 (or nearest year)[35,36,37,38]



[35] WHO Global Health Expenditure Database, 2015 statistics
[36] Department of Statistics, Singapore (https://www.singstat.gov.sg/modules/infographics/population; Accessed on 27th September 2018
[37] OECD, Pharma Spending, 2017 (https://data.oecd.org/healthres/pharmaceutical-spending.htm; Accessed on 27th September 2018
[38] For Singapore sales data is taken from MIDAS Total Sales Audit (LCUSD)

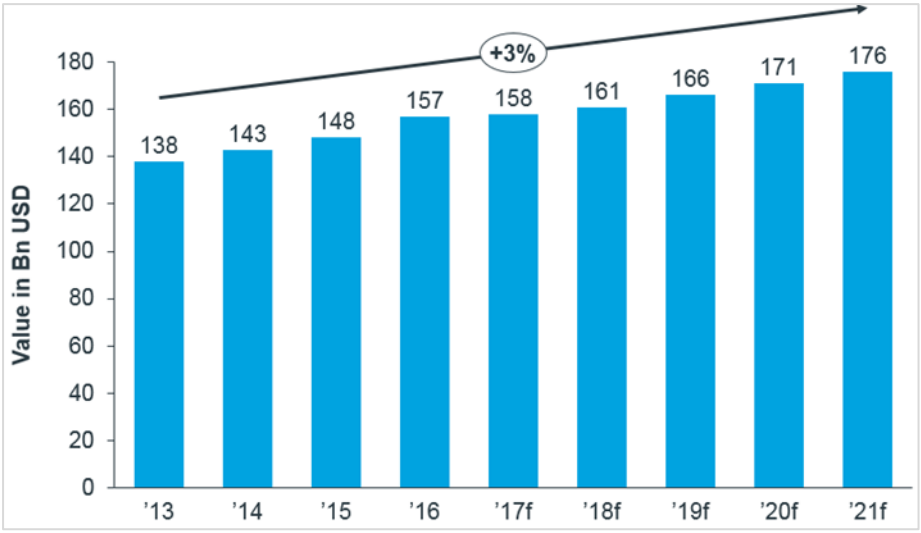
SECTION 5: SINGAPORE'S AND OTHER COUNTRIES' PHARMACEUTICAL INVESTMENTS

5.1 Global Pharma R&D Investments

The research-based pharmaceutical industry plays a unique role in developing new medicines and vaccines to prevent and treat diseases and improve the lives of patients worldwide. Its key contribution to global health turns fundamental research into innovative treatments.[39]

Today, the cost of developing a successful medicine can exceed, according to some studies, USD 2 Bn compared to USD 179 Mn in 1970s. The worldwide pharmaceutical R&D spend totalled USD 157 Bn in 2016, representing an increase of 5.9% on the previous year.[11]

Figure 8: Total pharma R&D spend globally (USD Bn) in 2013-2021[40,41]



Over the past year, the top 10 pharma companies have spent USD 75 Bn on R&D (see Table 4 below).

Table 4: Top 10 pharma company spend on R&D globally in 2017(USD Bn)[42]

Company	2017
Roche	11.40
Merck & Co	10.10
Novartis	9.60
Johnson & Johnson	9.10

[39] https://www.ifpma.org/wp-content/uploads/2017/02/IFPMA-Facts-And-Figures-2017.pdf
[40] https://www.statista.com/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/
[41] http://info.evaluategroup.com/rs/607-YGS-364/images/WP17.pdf
[42] https://www.strategyand.pwc.com/innovation1000#VisualTabs1

Pfizer	7.90
AstraZeneca	5.90
Sanofi	5.50
Eli Lilly	5.20
Gilead	5.10
Bristol-Myers Squibb	4.90
TOTAL **(Top 10 Pharma)**	**74.70**

5.2 Regional Pharma R&D Spend

5.2.1 R&D spend across select countries

In the US, the R&D investment has expanded from USD 52 Bn in 2013 to USD 66 Bn in 2016 but saw fluctuations in growth during this period[43]. This trend reflects the various technical, regulatory and economic challenges facing R&D pipelines. Companies often experience loss in R&D investments. This is accredited to increase in failure during later phases of clinical trials. A phase III failure is significantly costlier than a preclinical failure because each phase is associated with a certain amount of required investment.[44]

In Canada, the pharmaceutical sector is one of the most innovative industries. The country captures 4% of global clinical trials and is recognised for the quality and expertise of its research clinicians.[45]

For EU countries, the research-based pharmaceutical industry plays a critical role in restoring Europe to growth and ensuring future competitiveness. In 2016, companies invested about USD 40 Bn in R&D in Europe.[46]

Japan is the second-largest pharmaceutical market in the world, with over 40 Japanese pharma and biotech companies are engaged in original drug discovery research. In 2016, the pharma industry invested around USD 13 Bn in R&D. [47]

While the global pharmaceutical markets have typically been dominated by US, Europe and Japan, emerging markets have been steadily increasing their presence in the global space. China has stepped up investment in drug innovation in recent years, both in basic research

[43] https://read.oecd-ilibrary.org/science-and-technology/main-science-and-technology-indicators/volume-2018/issue-1_msti-v2018-1-en#page1
[44] https://www.ifpma.org/wp-content/uploads/2017/02/IFPMA-Facts-And-Figures-2017.pdf
[45] https://www.ic.gc.ca/eic/site/lsg-pdsv.nsf/eng/h_hn01774.html
[46] https://www.efpia.eu/media/361960/efpia-pharmafigures2018_v07-hq.pdf
[47] https://eolas-bio.com/market/

and in industry research and development. As a result, pharma R&D spend has increased from USD 0.98 Bn in 2013 to USD 14 Bn in 2016. See Table 5 for the R&D spend breakdown.

Table 5: R&D spend across select countries (USD Bn)[48]

Region	2013	2014	2015	2016
US	52.43	56.61	58.68	66.27
EU	N.A.	26.4	38.46	39.62
Canada	0.34	0.38	0.40	N.A.
Japan	14.19	14.51	14.19	13.48
South Korea	1.25	1.29	1.55	N.A.
Australia	0.37	N.A.	N.A.	N.A.
China	0.98	11.11	12.69	14.06

5.2.2 R&D spend in Singapore

Singapore's pharmaceutical sector is set for a promising growth. More R&D facilities are making its way here as Singapore offers an excellent talent pool and infrastructure for biopharmaceutical companies.[49]

As part of its five-year Research Innovation and Enterprise (RIE) 2020 plan, the Singapore government has committed SGD 3.2 Bn over 2016-2020 to advanced manufacturing and engineering, of which biologics and pharmaceutical manufacturing is one key component. RIE 2020 aims to focus on areas where Singapore has the potential to be internationally competitive, and to align R&D efforts with national healthcare priorities to deliver the best value health and economic outcomes.[50]

From 2013 to 2015, the business expenditure on R&D in the Biomedical Sciences field (comprising of pharmaceuticals and medical devices) grew by a CAGR of 19.64%, from SGD 0.51 Bn to 0.73 Bn as shown in Figure 9. From 2015 to 2016, the investment declined by 7.6% to USD 0.67 Bn.[51] This is consistent with the growth trends of clinical trials over the same period.

Given that pharmaceutical business spending on R&D and the number of trials in Singapore has been relatively flat or on the decline in recent years (Figure 10), it may be timely for the government to relook at Singapore's competitiveness and positioning as a biopharma R&D innovation hub. Greater inter-agency coordination and deeper industry consultation may be

[48] Source: IFPMA, OECD
[49] https://www.linkedin.com/pulse/overview-singapore-pharmaceutical-industry-2017-2018-scarlet-lee/
[50] https://www.edb.gov.sg/en/news-and-resources/insights/manufacturing/future-proofed-pharma.html
[51] https://www.a-star.edu.sg/News-and-Events/Publications/National-Survey-of-R-D

needed to determine the right policy levers to ensure that Singapore keeps up with other emerging countries, such as China.

Figure 9: Singapore's Business R&D spend (SGD Bn) in 2013-2016[52]

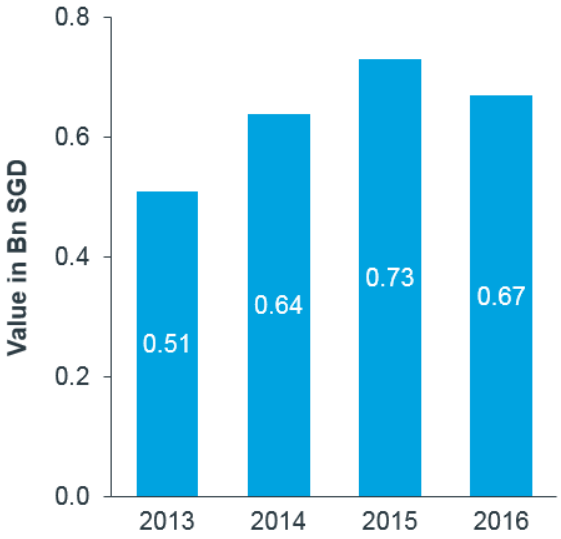
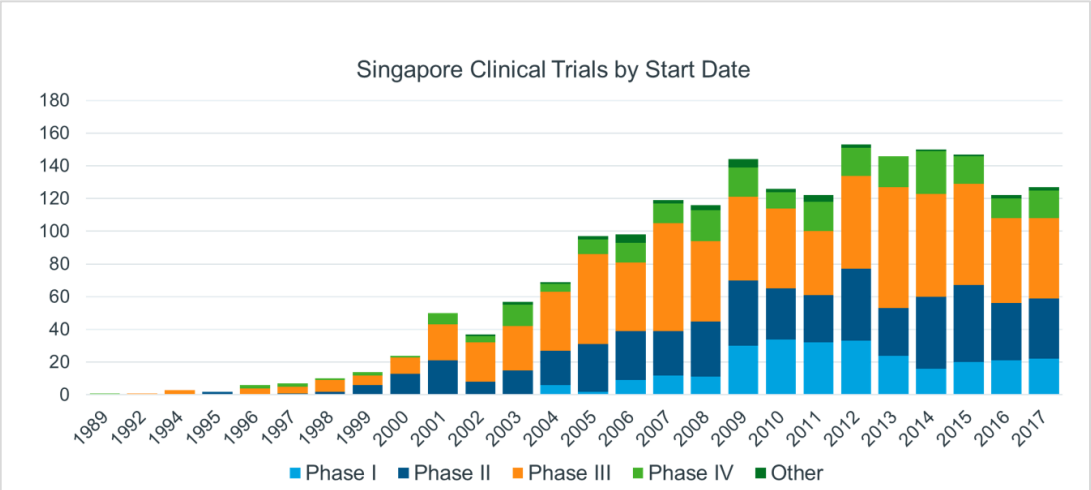


Figure 10: Singapore as a Clinical Trial Destination over time[53]



5.3 Pharma manufacturing and production trends

The pharmaceutical industry's activities have a strong and positive influence on the economy. This economic footprint is most visible in the form of investments in manufacturing and R&D, but it often has other positive socioeconomic impacts, such as spurring greater quality of

[52] Source: Economic Development Board
[53] Source: Informa Citeline Trialtrove

scientific research. The biopharma industry also drives the creation of ancillary companies that support parts of the research and development process, which ultimately contribute to GDP, as shown in Table 6 below.[54]

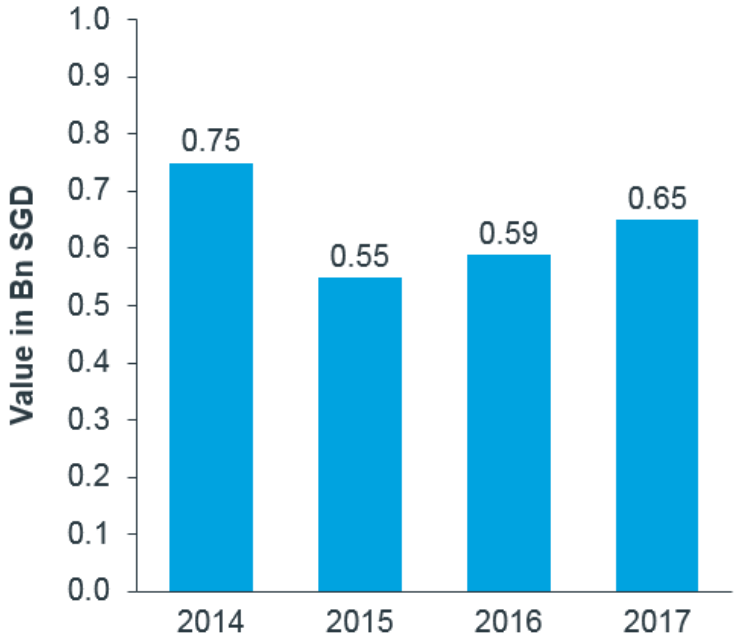
Table 6: Regional breakdown of gross value added in the pharma industry (USD Bn)

Region	2010	2011	2012	2013	2014
Asia	148.70	157.20	163.30	148.30	153.90
Europe	135.10	146.00	134.80	140.90	142.80
North America	104.90	102.60	105.30	108.30	111.80
Latin America	20.40	25.20	24.90	21.70	24.60
Africa	5.00	5.00	5.10	6.20	6.80
Oceania	3.50	3.20	3.30	3.60	2.70
Worldwide	**417.60**	**439.20**	**436.80**	**428.70**	**452.80**

Singapore's pharmaceutical manufacturing and production sub-sector plays an important role as it is the second largest contributor to the country's manufacturing output, accounting for 3% of its GDP. The industry's investment in the biomedical manufacturing decreased by 26% in 2015, from SGD 0.75 Bn in 2014 to SGD 0.55 Bn in 2015 but picked up in the last 3 years (see Figure 11). During this period, the investment has grown by a CAGR of 8.7%.[55,56]

[54] https://www.ifpma.org/wp-content/uploads/2017/02/IFPMA-Facts-And-Figures-2017.pdf
[55] https://www.straitstimes.com/business/economy/spore-pharma-on-recovery-path-after-dismal-2017
[56] https://www.edb.gov.sg/en/news-and-resources/insights/manufacturing/future-proofed-pharma.html

Figure 11: Singapore pharma manufacturing investment (SGD Bn) in 2014-2017[57]



[57] https://www.mti.gov.sg/ResearchRoom/Pages/Economic-Survey-of-Singapore-2017.aspx

SECTION 6: IMPACT ON PHARMA MARKET SIZE IF PTE IS IMPLEMENTED

6.1 Impact on the pharma landscape if PTE were to be implemented

Singapore prides itself for building a strong and reliable IP regime that is well plugged into international networks. The Intellectual Property Office of Singapore (IPOS) is recognised as a competent International Authority by IP offices around the world including US and Japan. In addition, IPOS is a key member of numerous patent acceleration initiatives, covering a network of more than 30 countries. With these recognitions, Singapore-based companies have good access to foreign markets through the many IP partnerships that Singapore has forged with our key export destinations. One of the key recommendations of the Singapore IP Hub 10-year Master Plan include allowing for innovative companies to protect their IP effectively to secure and maintain their competitive edge in the global market. Thus, IP should be viewed as part of any biopharma company's business strategies and having a more robust PTE regime aligned with international standards would spur more biopharma industry players to develop and register their new products in Singapore.

On the economic front, Singapore is a leading location for biopharmaceutical companies to site their best-in-class manufacturing plants, where innovative products are launched and produced. Industry leaders like Pfizer, Novartis, Sanofi, AbbVie and Amgen have global manufacturing hubs in Singapore for a wide range of products. Since 2014, the industry has also worked with Singapore government to develop new talent training programs. A world-class PTE regime will allow Singapore to reinforce its position as a regional biopharma hub.

In addition, Singapore's extensive and integrated research ecosystem continues to deliver impact and value to pharmaceutical companies. Pharma firms have forged strong partnerships with key opinion leaders, institutes, emerging biotechnology companies, as well as clinical and contract research organisations to rapidly advance pipeline assets for drug discovery and development. Thus, a potential outcome of a PTE review is a stronger ecosystem to support innovation.

6.2 Impact on the total Singapore pharma market size if existing patented products were compensated by the PTE of up to 5 years for their respective R&D investments

We have built the following linear model to evaluate the potential impact on pharma market sales using all patented products launched in 2012[58] as the baseline for illustration purpose. We took the year 2012 to illustrate because it is the earliest a launch could take place and lose exclusivity by 2017 as per the average timelines on Figure 1 i.e. 2012 launch products are assumed to have 6-year patent protection remaining (i.e. Current State). For the same set

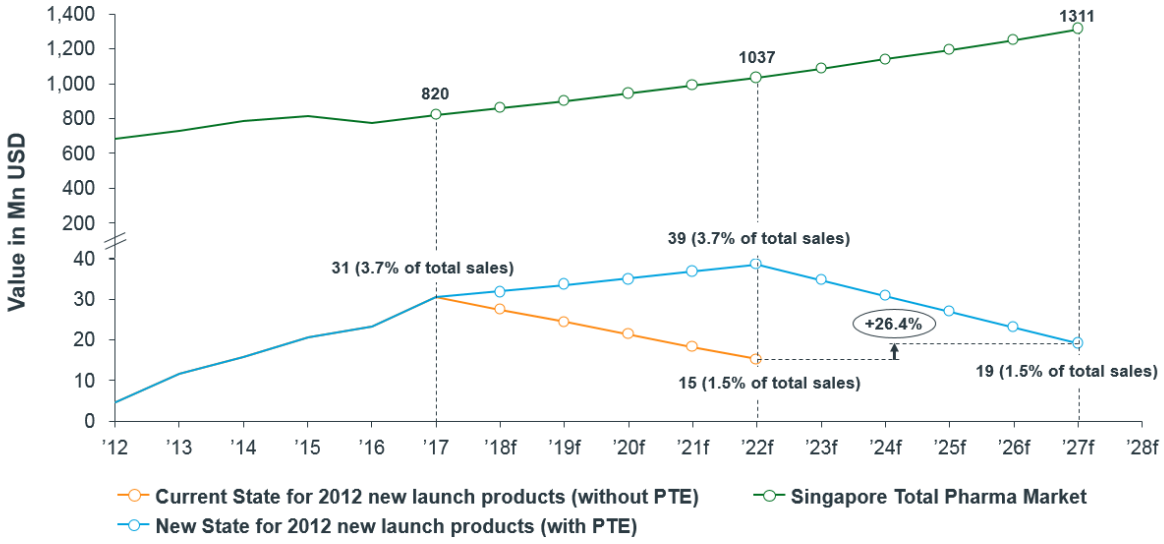
[58] New chemical entities launched in 2008 are considered.

of products, we also considered PTE for an additional 5-year period (i.e. New State). See Figure 12 below.

A 50% sales erosion rate was factored and distributed it proportionately throughout a 5-year period, after loss of (patent) exclusivity for these new products. This rate was determined using benchmarks of sales erosion among a few developed markets[59]. Under the New State scenario, we also built in a 4.8%[60] sales growth for the assumed 5-year patent extension period. When comparing the market impact of PTE, we note that a 5-year PTE would result in a modest increase in launched-in-2012 patented product sales from USD 15 Mn to USD 19 Mn (or 26% increase).

In addition, we showcased the PTE impact of launched-in-2012 patented products against that of the total pharma sales. At its current state peak in 2017 and the new state (forecasted) peak in 2022, sales of launched-in-2012 patented products are 3.7% of total pharma sales. After the loss of (patent) exclusivity for these products in both states, their sales dropped to 1.5% of total market sales.

Figure 12: Forecasted sales based on 6-year remaining patent term and 5-year patent extension for patented products launched in 2012 (USD Mn)[61]



[59] Reference benchmarks for sales erosion were taken from US and Australia from IQVIA's Forecast Link data. Singapore's benchmark is unavailable.

[60] Singapore's CAGR 2017-2022.

[61] Source: MIDAS Sales, Global Market Prognosis Report (2018-2022).

***Figure 13:* Impact on the 2018-2022 total Singapore pharma market size if existing patented products launched between 2012 and 2016 were compensated by the PTE of up to 5 years for their respective R&D investments[62]**

Increase in market size in USD Mn	2018 impact	2019 impact	2020 impact	2021 impact	2022 impact	Total impact
Launched-in-2012	4.5	9.1	13.8	18.5	23.4	69.3
Launched-in-2013	-	1.6	3.2	4.9	6.6	16.3
Launched-in-2014	-	-	4.0	8.2	12.4	24.6
Launched-in-2015	-	-	-	5.1	10.4	15.5
Launched-in-2016	-	-	-	-	3.1	3.1
Total Impact						**128.8**

The cumulative impact on the total Singapore pharma market size across 5 years (2018-2022) would be $128.8Mn if existing patented products launched between 2012 and 2016 were compensated by the PTE of up to 5 years for their respective R&D investments.

[62] Source: MIDAS Sales, Global Market Prognosis Report (2018-2022).

SECTION 7: CONCLUSION

The considerations for reviewing existing conditions for PTE in Singapore are multi-dimensional, with benefits outweighing costs.

Firstly, a strong and robust PTE regime that is aligned with international standards such as that of the US and EU would allow Singapore to gain greater recognition as a global IP hub. This would allow Singapore to capture opportunities presented by increasing IP activities internationally to drive business and economic growth.

In addition, the biopharmaceutical industry forms the core pillar of Singapore's manufacturing sector, contributing to 3% of the country's GDP or SGD 26Bn of manufacturing output. The country hosts more than 50 manufacturing plants, over 50 R&D Centres and over 30 regional headquarters of biopharmaceutical companies. Thus, sustaining investments and growth in this industry is crucial to maintaining an innovative ecosystem in Singapore.

Secondly, a compelling PTE regime creates new incentives for research and development of new products that are subject to pre-market regulatory approval, thereby boosting Singapore's competitive position as a leading hub for biopharma R&D innovation.

Thirdly, as new medicines develop and launch in the Singapore market, Singapore will benefit from granting the same PTE treatments as the US and EU today. At the same time, this reinforces the spirit of reciprocity under the other related patents legislations of the two FTAs (i.e. USSFTA and EUSFTA).

Finally, Singapore's healthcare model has been consistently ranked as one that offers the best value and is the most efficient system globally[63]. The cost impact of a PTE will be low on the government front, with the right policy levers put in place. Based on our estimates, total cumulative impact for providing PTE up to 5 years to recognise the R&D investment would cost approximately $129 Mn across 5 years. When we examine government's expenditure on pharmaceuticals per capita, we note that most OECD governments spend on average USD 314. We estimate this figure to be USD 146 for Singapore, compared to USD 771 for Korea and USD 1,374 for Japan. Based on these figures, the Singapore government's expenditure on pharmaceuticals per capita is low when compared against OECD standards and the pharma market size impact will be minimal with a PTE granted for time spent for R&D investment. As such, the trade-off in terms of allowing more pharma companies to enjoy the benefits of their patented investments that drive medical innovations would be greater than the costs associated to the Singapore healthcare system.

[63] Bloomberg Healthcare Efficiency Index, 2017; Philips Future Health Index, 2018.

LIST OF ABBREVIATIONS

ABBREVIATIONS	FULL FORM
SAPI	The Singapore Association of Pharmaceutical Industries
PTE	Patent Term Extension
USSFTA	US-Singapore Free Trade Agreement
EUSFTA	European Union-Singapore Free Trade Agreement
US	United States
EU	European Union
IP	Intellectual Property
ETC	Experimental Therapeutics Centre
SPC	Supplementary Protection Certificates
R&D	Research and Development
FTA	Free Trade Agreement
MoH	Ministry of Health
WHO	World Health Organization
CPP	Certificate of Pharmaceutical Product
ITG	Innovative Therapeutics Group
A*STAR	Agency for Science, Technology and Research
FDA	Food Drug Administration
HSA	Health Sciences Authority
EMA	European Medicines Agency
MHRA	UK Medicines and Healthcare Products Regulatory Agency
TGA	Australia's Therapeutic Goods Administration
CAGR	Compound Annual Growth Rate
LCUSD	Local Currency US Dollars
SU	Standard Units
Bn; Mn; USD; SGD	Currency: Billion; Million; United State Dollar exchange; Singapore Dollar exchange
GDP	Gross Domestic Product
RIE	Research Innovation and Enterprise

OECD	Organization for Economic Cooperation and Development
IPOS	Intellectual Property Office of Singapore