HERBERT SMITH FREEHILLS

MANUFACTURING MEDICINES IN AUSTRALIA

EXAMINING THE NEED FOR INCREASED DOMESTIC CAPABILITY

MAY 2020

There has been much discussion about the need for Australia to increase "sovereign capability" in domestic pharmaceutical manufacturing. Against an international backdrop this article discusses the identified supply chain risks and considers whether such an initiative is commercially feasible in the absence of significant government investment and intervention. It also looks at two key initiatives already in place designed to help mitigate the risk of medicine supply chain shortages.

Shaun McVicar is a partner of Herbert Smith Freehills and Global Co-lead of its Pharmaceutical Sector.

Emma Iles is a Senior Associate at Herbert Smith Freehills focused on pharmaceuticals and life sciences.

With thanks to Mona Zhang, a graduate at Herbert Smith Freehills, for her research support.

The views expressed are the personal views of the authors.

Shaun McVicar
Partner
shaun.mcvicar@hsf.com

Emma Iles
Senior Associate
emma.iles@hsf.com

"Well before the pandemic emerged it had been recognised that Australia was 'dangerously dependent' on imported medicines and was vulnerable because of a lack of domestic capability."

Public discourse highlights vulnerability

"Never let a good crisis go to waste". Such is the battle-cry of vocal industry, market and political commentators as they watch the global Covid-19 pandemic, and the various national responses, unfold. Many of these commentators are propounding fundamental changes to the way the post Covid-19 world should be organised. One widely advocated view is that the Covid-19 pandemic has highlighted the need for individual countries to retool domestic industry and to "on-board" recently abandoned manufacturing industries. Doing so, it is said, will decrease dependence on unreliable international supply chains for strategically important or essential products, such as medicines.

Well before the pandemic emerged it had been recognised that Australia was "dangerously dependent" on imported medicines and was vulnerable because of a lack of domestic capability. It was recently revealed in The Age newspaper that the Department of Defence's Science and Technology agency had commissioned a report three years ago that analysed Australia's ability to develop "medical countermeasures" – vaccines and drugs – for threats including pandemics, radiation and chemical and bioweapons. The report had observed that Australia had "limited" manufacturing facilities and an insufficient number of experts who could take a drug from discovery through to a finished product, and had concluded that Australia lacked national, co-ordinated leadership to turn good science into products.

More recently, and in the public health context, in its February 2019 consultation paper on reforms to the generic medicines market authorisation process, the Therapeutic Goods Administration noted that Australia was "particularly vulnerable" to medicine shortages. The TGA highlighted two prevalent market scenarios which heightened the supply risk – the manufacturing of medicines at only one "location", even though they might be supplied by many companies, and the supply of medicines by only one manufacturer, even if the medicine might be manufactured in multiple locations. In each instance there is a single critical and inherently vulnerable link in the supply chain.

The risk of pharmaceutical supply shortages in Australia were again recently highlighted and identified as a strategic defence concern in the February 2020 report from the Institute for Integrated Economic Research Australia, which is chaired by retired air Vice-Marshall John Blackburn. Its report, "Australia's Medicine Supply", identified that Australia's medicines are "largely sourced through vulnerable and opaque supply chains which have single points of failure. Any supply chain that relies on only one point of manufacture for critical products is vulnerable regardless of where that single source of supply is located". Focussing particularly on the vulnerability of Australia's defence forces to medical supply bottlenecks and constraints it noted, for example, that the US imported between 40 and 45% of its penicillin supplies – a critical battlefield medicine - from a single supply source, China. While the IIER report ultimately concludes that full self-reliance in pharmaceuticals was "not practical" it recommended that national resilience could be improved by increasing "sovereign capability" – not only in the manufacture of medicines but in R&D and developing an increasingly skilled workforce.

This is just a snapshot of the discourse. In the midst of the current pandemic, politicians and

"largely sourced through vulnerable and opaque supply chains which have single points of failure. Any supply chain that relies on only one point of manufacture for critical products is vulnerable regardless of where that single source of supply is located".

Institute for Integrated Economic Research Australia, February 2020.

bureaucrats, security hawks and economic nationalists increasingly espouse a focus on domestic national interest, moving further away from the paradigm of globalisation and comparative economic advantage which has been such a feature of the post-WWII international trading environment. This is a global narrative and Australia has been no exception. In a media interview reported in the Australian Financial Review on 13 April 2020 the Australian Industry Minister, Karen Andrews, confirmed that Australia would need to boost its capacity to make pharmaceuticals, even if it meant paying more for medicines over the counter. "What the coronavirus has proven to us is that it's wrong for us to be totally reliant, or even reliant to a whole large extent, on supply chains that bring in products from overseas. … We need to work with our pharmaceutical sector to see how they can pivot and how they can start producing different medicines, different pharmaceuticals if need be."

In a separate interview with the AFR reported by Political Editor Philip Coorey on 15 April 2020, Karen Andrews continued the theme and further identified that the pandemic had exposed specific areas of domestic manufacturing need which required special attention. She identified medical technology and pharmaceuticals as a government priority for domestic manufacturing. She confirmed that the Commonwealth Government would explore procurement policies, within WTO guidelines, to ensure the ongoing viability of such industries.

As recently as 7 May 2020 former Industry Minister Senator Kim Carr has been quoted as saying, in the context of domestic manufacturing of pharmaceuticals, that the Covid-19 pandemic has disclosed "dangerous weaknesses" in the Australian economy including in the form of " the decline in manufacturing, the attrition of our science and research resources, and the loss of jobs, skills and economic complexity resulting from both". These sorts of views have also been publicly echoed by pharmaceutical industry figures, including Dennis Bastas, the CEO of Australia's largest generic pharmaceutical company by value, who has proposed the establishment of an Australian Medicines Manufacturing and Development Future Fund to help improve "sovereign manufacturing capability".

But just how realistic is a return to large scale Australian domestic pharmaceutical manufacturing?

Do the historical facts and dynamics of the Australian pharmaceutical market support these calls? Does the performance of supply chains during this once in a lifetime event, considered with existing mitigation measures, suggest that the massive investment in establishing the mooted manufacturing capability is warranted and commercially viable? Frankly, without an innovative approach which ameliorates the challenging local market fundamentals it is hard to see.

While obtaining reliable statistics about the Australian pharmaceutical market can be difficult, it is clear that the Australian market accounts for less than 2% of the world's pharmaceutical market – a not surprisingly small number given the entire Australian population is less than some of the world's "mega-cities". Add to that unattractive commercial feature the additional facts that the Australian market is mature, operates within a high wage environment, that its small population is geographically dispersed and it has very high transport costs between distant coastal population hubs. Moreover, the market is dominated by a single central buyer – the

We need to work with our pharmaceutical sector to see how they can pivot and how they can start producing different medicines, different pharmaceuticals if need be.

Karen Andrews, Australian Industry Minister, 13 April 2020

Commonwealth government – which, through the PBS, is a price maker and whose objective is to balance "optimal health outcomes" with "acceptable economic objectives". Many industry participants would argue this latter consideration is code for "at the lowest possible cost". In those circumstances it is perhaps not surprising that margins are thin, local growth opportunities limited, and domestic capability retreating.

Given these domestic limitations, imports from more efficient markets and producers dominate. Indeed more than 90% of Australia's medicines are imported and this percentage has increased markedly over the last decade or more as local pharmaceutical operations of global companies such as Pfizer, Johnson & Johnson, GSK, Roche and Merck have been scaled back or mothballed in favour of producers in locations with a comparative advantage. Another significant plant closure planned by GSK to take place in 2020 has earned a recent reprieve as the Covid 19 crisis in Australia has led to unprecedented demand for the paracetamol products it produces, but the current crisis has only delayed the planned closure and inevitable loss of local capability.

To the extent that there still is a domestic Australian pharmaceutical manufacturing industry, it is largely accounted for by "national champion" CSL with its local vaccine manufacturing, a few manufacturers of niche products and several manufacturers which are largely focussed on export markets for specialist products, OTC products and/or complementary medicines which can be placed into retail markets in Asia outside the constraints of prescription medicine pricing regimes. Examples of domestic manufacturing for export include AstraZeneca that makes inhaler medicines in Sydney that are exported around the world and Sanofi that manufactures vitamin, mineral and supplement products in Brisbane.

While the top line percentage figures for imports are alarming from a self-reliance perspective, perhaps surprisingly to many, the figures also show that the medicines which Australia imports are largely sourced from open, democratic, developed and (generally) reliable trading partners and allies.

The USA is Australia's largest source of pharmaceutical products. Other significant suppliers are UK, Germany, Ireland, Switzerland and France. China and India, who tend to be the subject of much of the discussion about potential supply chain bottlenecks accounted for just 5.5% of Australian pharmaceutical industry imports in 2018-2019.

Australian market accounts for less than **2%** of the world's **pharmaceutical** market

more than **90%** of **Australia's medicines** are **imported**

Significantly the **Commonwealth government** has **announced** that as part of its response to **COVID-19** it is investing an additional **$1.1 billion** to **increase** the supply of **PPE and pharmaceuticals** held in the Stockpile.

However, while Australia's imports are largely sourced from trading partners that most would consider commercially reliable and politically benign, this is not itself a cause for comfort. The supply chain risk becomes much more stark when the source of the active pharmaceutical ingredients found within those imported medicines is considered. APIs are the substances which provide pharmaceuticals with therapeutic efficacy. Australia's imports of medicines are mostly finished or partly finished products but the APIs already incorporated within those imported formulations are produced overwhelmingly in China or India. Indeed 80% of the APIs formulated in medicines sourced from the US are imported - mainly from India and China. Consequently the supply chain risk, and concerns about its vulnerability to supply chain shocks and bottlenecks in either of those two markets, is clear and well-founded.

So, despite the fears of the doomsayers, how have the supply chains held up so far?

The Covid 19 pandemic caused unprecedented disruption to manufacturing in China and, shortly thereafter, to Indian pharmaceutical exports. In China, lockdowns and travel restrictions were in place from January to March 2020. Pharmaceutical companies were exempt in some places (e.g. Shanghai). But Hubei facilities and many others were closed – particularly in and from early February, and travel restrictions made it difficult for workers to return to work after the extended New Year holiday, and for necessary supplies and raw materials to be delivered. However by early March the vast majority of Chinese SOEs had resumed production, with small and medium-sized manufacturers recovering more slowly. By all reports Chinese factories have now restarted operations.

In India the "lockdown" occurred later. And there has been a specific domestic regulatory response aimed at controlling pharmaceutical exports in the national interest. On 3 March, 2020, India restricted the export of 26 APIs - accounting for 10% of all Indian pharmaceutical exports – so as to prevent a shortage of essential drugs for domestic use due to the lockdown in China's Hubei province, which is itself a major source of APIs for Indian product. The restrictions were lifted on 6 April for 24 of the APIs, not including paracetamol. On 4 April, India specifically banned exports of hydroxychloroquine, an important medicine for malaria and other conditions but promoted by some as a potential treatment for Covid-19. India lifted the ban a few days later following backlash from other countries, the threat of retaliation from President Trump, and the recommendation of an expert panel. A major manufacturing hub in Baddi was closed in mid-April as a result of lockdown in the region. It alone is responsible for 35-40% of India's pharmaceutical production. 50 facilities partially or fully shut down, including those of Sun Pharmaceuticals and Abbott Laboratories. The hub has now re-opened. Rather topically, the Indian government recently announced it will invest US$1.3 billion in expanding domestic pharmaceutical manufacturing capability. The aim of this government intervention is to reduce reliance on Chinese API imports (which in themselves amount to 70% of India's overall imports of APIs) including paracetamol, metformin and ampicillin where 100% of India's requirements are sourced from China.

But, despite these upstream disruptions Australia's supply chains for pharmaceuticals have proved resilient. So far. Apart from initial panic buying of OTC products like ibuprofen and paracetamol at retail level and the early stockpiling of prescription medicines including asthma and diabetes medicines by patients the Australian supply chain has not seen major disruption. On 23 April 2020, Australia's Chief

"increased protectionism would only harm the world's recovery from COVID-19, slowing the necessary return of economic and employment growth. Putting in place more trade barriers would be the worst possible response to global economic uncertainty. More barriers would further erode business confidence and would slow the investment needed to restart many economies"

Australia's Trade Minister Senator Birmingham, UK International Trade Secretary Liz Truss, Singapore Trade Minister Chan Chun Sing and New Zealand's David Parker, 28 April 2020

Medical Officer, Professor Brendan Murphy provided testimony to a Senate Enquiry about aspects of the Department of Health's handling of the COVID-19 pandemic. Speaking on supply chain resilience Professor Murphy confirmed that the Commonwealth Government "absolutely had concerns" about the large number of APIs being made in China, and the consequences of the shutdown of the Chinese economy during the outbreak in Hubei on supply, but had not yet seen any critical drug shortages arising from the pandemic's impact on supply chains.

A strategic reserve

One of the topics for discussion before the same Senate Enquiry was the Department's approach to managing the National Medicines Stockpile. The Stockpile, of which few Australians would be aware, is a Commonwealth initiative which helps mitigate against supply chain disruption. Together with another recent initiative by the TGA, mandatory reporting of medicine shortages, the risks of serious disruption to essential medicines, at least over the short term, are reduced. Both these initiatives are critical aspects of the Australian regulatory environment which, on one view, counter-balance the calls for the need for a significant increase in domestic production capability.

The Stockpile is "a strategic reserve of drugs, vaccines, antidotes and protective equipment for use in the national response to a public health emergency which could arise from natural causes or terrorist activities". It is intended to increase Australia's level of self-sufficiency during a time of potential high global and domestic demand and service delivery pressures. It was established in 2002 as part of the government response to the threat of international terrorist attacks. Since 2002 the Stockpile has expanded from a relatively small reserve valued at approximately $11 million intended to deal with chemical, biological, radiological and nuclear threats, to a resource with a reported value of almost $196 million in 2012–13. In 2012-13 it was said to comprise 42 products and over 110 million items, dominated by products associated with human influenza pandemic preparedness. In the decade 2004-2014, $750 million in budget funds was allocated to the Stockpile.

The Commonwealth Department of Health is responsible for management of the Stockpile, while State and Territory governments are responsible for deploying Stockpile items within their jurisdictions in a national health emergency. Approval to access to the Stockpile is given by Australia's Chief Medical Officer, Professor Brendan Murphy. The Stockpile is kept in various strategic locations around Australia and specific details regarding the location and content of the Stockpile is not released publicly for security reasons. Some stock is pre-positioned in the States and Territories to ensure more rapid deployment in emergency situations.

Eighty percent of the Stockpile's value is tied up in pharmaceuticals, including antivirals such as Tamiflu and Relenza. It also holds a limited supply of "highly specialised drugs" which, in an emergency, may not be available elsewhere in the Australian pharmaceutical supply system. During the 2009 swine flu pandemic, more than 900,000 courses of antivirals were deployed from the Stockpile, with 2.1 million pieces of PPE also handed out.

The stockpile has been actively utilised during the Covid-19 pandemic - but primarily in relation to PPE it seems. On 8 March 2020 Minister for Health Greg Hunt announced that 54 million additional face masks had been secured for the Stockpile. On 18 April Greg Hunt announced that 58 million masks had actually been received with almost 22 million masks from the Stockpile already distributed to frontline healthcare workers. Significantly the Commonwealth government has announced that as part of its response to COVID-19 it is investing an additional $1.1 billion to increase the supply of PPE and pharmaceuticals held in the Stockpile.

"One possibility to avoid the blunt tools of protectionist barriers, might be to build into the "economic objectives" considered by the PBS when assessing applications for the funding of medicines, the express objective of encouraging domestic Australian manufacturing of medicines."

At the time of writing there are currently **581 shortages,** with **74 classified** as having **critical patient impact**

Mandatory shortage reporting

The second key mitigation measure, introduced by the TGA in 2019, is a mandatory reporting scheme for anticipated medicine shortages and discontinuations. The aim of the reporting scheme is to improve awareness of supply chain issues and enable early action by industry and the TGA to minimise the impact of shortages. The scheme permits the TGA to provide temporary approvals for supply of overseas-registered alternative products to mitigate the effects of shortages of medicines. An important aspect of the scheme is the maintenance of the Medicines Watch List which is a legislative instrument used to simplify and streamline decision-making when determining the impact of the shortage of a particular medicine. Any shortage of a medicine listed on the Medicines Watch List is automatically deemed to have a "critical patient impact" and consequently triggers various additional obligations on the drug's sponsor, including an obligation to report the anticipated shortage within 2 days of becoming aware of it.

The mere fact of the mandatory reporting scheme and the Medicines Watch List does not prevent shortages occurring. In fact as at the time of writing there are currently 581 shortages, with 74 classified as having critical patient impact. These include Epipen, panadol, and antibiotics such as gentamicin and vancomycin. Anticipated critical impact shortages include Airomir salbutamol inhaler. However, the notification to the TGA and publication of shortages provides notice (often advance notice) to industry and government and consequently early awareness of the need to source alternatives or, if need be, issue directives to pharmacies, for example imposing restrictions around how many dosages of a given medicine may be dispensed at one time. For example a serious shortage of 500g modified release metformin, a diabetes medicine, has just resulted in the TGA issuing a notice allowing that medicine to be substituted with a range of alternatives until supply improves. Also, importantly, to the extent that anticipated shortages arise or are likely to arise in a National Emergency situation, scarce product may be able to identified and efficiently pre-allocated for future deployment from the Stockpile.

Calls for a return to domestic pharmaceutical manufacturing

So, in light of all this, what of the calls for a return to domestic pharmaceutical manufacturing? It seems clear from the challenging characteristics of the limited domestic Australian pharmaceutical market that there is little commercial attraction to bring back pharmaceutical manufacturing without a significant change of market dynamics and most likely Government intervention and investment. But moves for the introduction of subsidies, or the erection of tariff walls, or introduction of nationalistic procurement policies would jeopardise Australia's world trade standing and put our own export industries – captured and exploited as a result of maintaining a strong, open market based economy - at risk of retaliation.

The USA is Australia's largest source of pharmaceutical products. Other significant suppliers are UK, Germany, Ireland, Switzerland and France. China and India.

Furthermore, doing so would run counter to Australia's long-held and recently re-stated position supporting free and open global trade. In a joint call-to-arms with several other Commonwealth nations, Australia has recently pledged to work to reform the WTO by "modernising its rules, improving its transparency and making more efficient its settlement of disputes". Writing in The Australian on 28 April 2020, Australia's Trade Minister Senator Birmingham, UK International Trade Secretary Liz Truss, Singapore Trade Minister Chan Chun Sing and New Zealand's David Parker expressed their resolve "to lead the world in restoring and deepening global trade". They wrote that "increased protectionism would only harm the world's recovery from COVID-19, slowing the necessary return of economic and employment growth. Putting in place more trade barriers would be the worst possible response to global economic uncertainty. More barriers would further erode business confidence and would slow the investment needed to restart many economies".

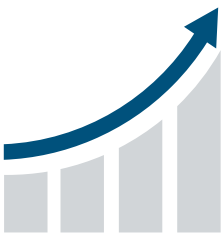
Moreover, quite apart from Australia's commitment to free and open trade, the supply chain risks that commentators have been warning about and which are said to warrant Commonwealth government intervention have not materialised. Admittedly the lag effect may see some additional shortages emerge over time, but industry figures do not seem to be flagging major and abnormal supply risks in coming months. And the risk mitigation measures in the form of the Stockpile and mandatory shortage reporting provide the Commonwealth with seemingly effective tools to help deal with the most significant impacts of any future shortages.

Consistent with Australia's position on global trade, to the extent that supply chain bottlenecks and risks are a genuine security concern, we contend that Australia would be likely get more "bang for buck" by encouraging those of our own trusted allies, with domestic and accessible export markets of a sufficient size and dynamic to make it commercially warranted, to build up their own domestic manufacturing capability. Doing so would increase the range of alternative reliable and transparent supply sources for Australian medicines and thereby expressly address the supply chain risk factors identified by the TGA in its discussion paper.

However, if, as a matter of domestic economic policy, Australia elects to take measures to encourage more domestic manufacturing, then a more innovative approach than simply the direct funding of domestic manufacture should be considered. One possibility to avoid the blunt tools of protectionist barriers, might be to build into the "economic objectives" considered by the PBS when assessing applications for the funding of medicines, the express objective of encouraging domestic Australian manufacturing of medicines. Doing so may encourage price negotiations between drug sponsors and the Commonwealth, as purchaser, that take a more nuanced and holistic approach than the current, one dimensional, search for the lowest possible price. In such a scenario there might just be enough "left on the table" for the supplier to reinvest and reinvigorate its domestic activities, including steps in the manufacturing chain.

What do you think the future holds for Australia's domestic pharmaceutical sector?

To discuss your strategy, contact our leading advisors here.



Since 2002 the Stockpile has expanded from a relatively small reserve valued at approximately **$11 million** to a resource with a reported value of almost **$196 million** in **2012–13.** In **2012-13** it was said to comprise **42 products** and over **110 million** items. In the decade **2004-2014**, **$750 million** in budget funds was allocated to the Stockpile.

For a full list of our global offices visit **HERBERTSMITHFREEHILLS.COM**