Protecting the health and wellbeing of all Australians

Building Australia's sovereign capability

An economic recovery blueprint

The Australian Medicines & Vaccines Manufacturing & Development Initiative

A proposal by

arrotex PHARMACEUTICALS

An Australian-owned pharmaceutical company

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Foreword

As the only Australian-owned pharmaceutical company; we believe Arrotex Pharmaceuticals (Arrotex) is ideally placed to work with the Australian Government to change the national conversation about our sovereign capability. In particular, our capacity to produce more of our own medicines, vital to the health of our most vulnerable patients.

We need to work quickly to mitigate Australia's current exposure to unstable and easily disrupted global supply chains in particular during times of a world-wide health crisis, such as COVID-19.

As a proud Australian healthcare company, we are a living case study of why we need to rethink our capacity to develop our own discoveries and manufacture affordable, safe and vital medicines, especially those where patients simply can't afford any delay or disruption to life-saving medication.

Arrotex is uniquely placed to help the Government build a cost effective, high tech, low emissions Australian Medicines and Vaccine Manufacturing and Development industry that puts the interests of Australian patients first whilst creating a new export opportunity, creating thousands of jobs in the process.

Unlike many of our foreign-owned counterparts operating in Australia; Arrotex is not beholden to the control and direction of other regimes during times of national and international economic and health shocks. Our revenue stays in Australia. Right now, like many other Australian companies, we manufacture overseas but we want to bring those jobs home.

This proposal creates that **investment, growth and export opportunity** for all Australian owned pharmaceutical companies and for all medical research institutions and universities who want to hold onto the patent of their own discoveries and commercialise their innovations.

This self-funding Australian Medicines Manufacturing and Development initiative will deliver financial autonomy to our medical researchers, relieving the pressure on a deeply overwhelmed Australian budget.

We believe this initiative will be nation building.

It is my philanthropic intention to help the Australian Government solve a very deep economic and national security problem with a solution that could protect of our most vulnerable Australians against future shocks to the global supply chain of medicines, mitigates the need for the Federal Government and State Governments to each host an expensive stockpile of medicines; and create an advanced technology export industry for generations of Australians to work in.

Almost 300 million prescriptions were dispensed on the Pharmaceutical Benefits Scheme (PBS) in the twelve months to December 2019 and one in four of those prescriptions (70 million) was filled with an Arrotex manufactured medicine. Importantly the Arrotex range of TGA approved medicines can fill 85% of all PBS prescriptions should supplies from all other manufacturers cease. We have the stability and skillset needed to keep delivering affordable medicines to Australians despite the mass disruption to global supply chains. We also have the ability to scale up our medicine exports, creating a greater value add economic opportunity for Australia.

Our low dollar and increase freight costs also underscores the urgent need to turn around our current approach to domestic pharmaceutical manufacturing.

Importing more than 90% of our vital medicines is no longer the economically sage approach it was pre-COVID-19. Nor is it in our national security interest.

Along with a shocking global path of death, illness, economic collapse and social and familial dislocation, the novel coronavirus has pulled the curtain back on the risks of Australia being so completely dependent on major trading partners of China, India and United States to deliver to us those vital medicines Australians need.

A cursory glance at the Therapeutic Goods Administration (TGA) critical medicine shortages list[1] in April showed that due to the global surge in demand, there loomed alarming shortages of vital medicines in Australia.

The medicines at risk were intended to help Australians with diabetes and high blood pressure, patients with Lupus and other serious auto-immune diseases, those at risk of a potential heart attack and Australians with severe mental illness. All of these key medicines are currently fully imported from off-shore manufacturers.

As a wealthy first-world nation, we can do better. Australian patients and their families need us to ensure uninterrupted access in all circumstances.

We believe we can help deliver the Government's important medium-longer term agenda of not just recovering from the novel coronavirus but creating a new advanced, low emissions, pharmaceutical manufacturing sector for Australia and importantly build our sovereign capability, protect patients and create jobs. We can better support our medical research community by allowing them an independent export income derived from their own discoveries.

Australia can offset the need to host expensive medical stockpiles (at a Federal and State level) often with medicines that have a short shelf life.

The time to act is now.

[1] https://apps.tga.gov.au/Prod/msi/Search/

We have all of the elements needed to create a sustainable, independent pharmaceutical manufacturing centre and a regional export market hub.

We can now draw on Australia's entrepreneurial spirit, advanced new technologies, such as automation and digitalisation, and a world-class medical research community that continues to demonstrate its collective ability to collaborate and translate new discoveries that the world will want. We also have strong political and regulatory leadership to work hand-in-glove with the sector.

I commit this proposal for Australia's very own **Medicines Manufacturing & Development Public Private Partnership** to the Australian Government to adopt now as part of our economic recovery.

Arrotex stands ready to deliver what we know will be a positive and exciting new export industry, creating jobs and building a prosperous export market whilst protecting the patients of today and tomorrow.

Dennis Bastas
Chairman and CEO
Arrotex Pharmaceuticals

Executive Summary

Australia, during the time of this horrendous pandemic, has been well served by our Prime Minister, the Minister for Health, the Chief Medical Officer, the Treasurer and our National Cabinet.

Strong and decisive action from our political and regulatory leaders has largely protected Australia from the worst of the health and economic impacts of COVID-19.

Whilst the immediate future is as unsettling as it is unpredictable; we do believe now is the time to create a revitalised world class, self-sufficient pharmaceutical development and manufacturing hub – one that works in the national interest of all Australians.

The Coronavirus brutally underscored just how exposed Australian patients are to the mass disruption of the global supply of medicines. The rapid virus spread caused factory and border closes across our key source countries of China, the United States and India. With the international aviation sector all but grounded, guaranteeing Australians can access the top 120 vital medicines is becoming more fraught with each day.

Arrotex is one of only two generic pharmaceutical companies with a range of TGA approved medicines that can cover over 85% of all PBS prescriptions in Australia and we are the only one that is proudly Australian-owned.

Unlike our foreign-owned competitors, our loyalty belongs to Australia and it is Australian patients, for whom we have worked around the clock, to ensure they can access their vital medicines, regardless of where they live or their socioeconomic background.

But we know we need build our sovereign capability and we can do that quickly by leveraging our entrepreneurial determination, advanced low-emission technologies, flexible policy levers and a demonstrably strong international interest in buying medicines from Australia because we are safe and reliable.

This proposal outlines the case for an: Australian Medicines Manufacturing & Development Public Private Partnership that would serve three critical purposes:

1. provide secure emergency sourcing for Australians of essential medicines and vaccines;
2. create an advanced research and technology hub that would give Australia's medical R&D sector a crucial new weapon in its ability to keep greater value from its intellectual property creations within Australia, rather than outsourcing to the rest of the world; and
3. contribute to the economic recovery of Australia by building our own sovereign medicine and vaccine development and manufacturing capability whilst creating jobs and new value add export opportunities.

We are working with Australia's leading medical researchers, to determine how best they can leverage this initiative which, ultimately, will give them more autonomy, ownership and control over their own discoveries and, in turn, allow Australia to mitigate the national security risk we are currently exposed to.

The key elements of the proposed manufacturing capability should include;

- Active Pharmaceutical Ingredient (API) manufacturing
- Oral-Solid dose manufacturing of tablets and capsules
- Sterile injectable manufacturing of vials and pre-filled syringes
- Vaccines manufacturing
- Monoclonal antibody (mAb) biological manufacturing

*(NB: greater detail on these capabilities are available at **Appendix A**. Arrotex has provide confidential costings on all of these to the Government and COVID Commission. It demonstrates a strong return on investment to taxpayers.)*

This sovereign public-private investment vehicle will be initially supported by the Australian Government, superannuation funds, the pharmaceutical industry and other foreign investors. It will be cost neutral in that the Government's investment will offset the need for an expensive stockpile of medicines, many of which have a short shelf life.

This can also apply to all state governments and territories who can also access the facility when they need to, rather than waste taxpayers' money on stockpiling medicines they may never need or use.

Our proposal is to use those mix of private and public funds to build a new state of the art manufacturing and technology park and to support deeper collaboration between the industry, medical researchers and regulators such as the Therapeutic Goods Administration (TGA).

If implemented as intended we envisage that by the end of 2022, Australia will be capable of locally producing the most vital 120 medicines and vaccines for Australian patients, in the first instance, and then for export, in the second.

Australian researchers can use the facilities to test batch manufacture their own discoveries (which they can't do in Australia currently) and hold onto their patents through to commercialisation, rather than be forced to sell their patents to foreign big pharma or venture capitalists.

This world-class facility can be accessed by the Government, in times of any future pandemic, to produce – as demanded – the additional medicines and vaccines we need.

We believe this initiative will create jobs, provide sovereign strength against any future global shocks, boost our export complexity, protect our national interests and is well

aligned to the Government's agenda of developing an economy-boosting advanced technology sector.

As a company that knows both the domestic and international markets; Arrotex is well placed to help deliver a blueprint for the Australian Government with consultation with both international and national stakeholders, prescribers, pharmacists and patient groups.

Strategic observations

Even before the novel coronavirus exploded out of China and threw the world into an unprecedented crisis; the conversation had already begun about the need for Australia to demonstrate more sovereign smarts in developing our own new and advanced technologies, especially when it comes to pharmaceutical manufacturing.

As a high-income country, we were ranked as the 8th richest economy per capita out of 133 studied in 2017. In the same year, our 24.6 million inhabitants had a GDP per capita of $54,093.

However, despite our collective wealth as a nation, Australia's economic complexity[2] (the barometer preferred by Harvard University to determine our export potential) shows our country is suffering by a lack of diversification of exports.

Australia ranks as the 93rd most complex country in the Harvard University's Economic Complexity Index (ECI) ranking. Compared to a decade prior, Australia's economy has become less complex, worsening 22 positions in the ECI ranking. Australia's worsening complexity has been driven by a lack of diversification of exports.

Australia is less complex than expected for its income level. As a result, even before the coronavirus pandemic, our economy is projected to grow slowly. The Growth Lab's 2027 Growth Projections foresee growth in Australia of 2.2% annually over the coming decade, ranking in the bottom half of countries globally.

We can, and we must do better

The novel coronavirus global health crisis, and the sudden and ferocious impact on the global supply chains for critically important medicines, has shocked Australians deeply.

This is not because we didn't realise, we were vulnerable but because we always thought our major trading partners, such as India and China, would continue to be the world's ever churning, low-cost factories.

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2 https://atlas.cid.harvard.edu/explore?country=14&product=129&year=2017&tradeDirection=import&productClass=HS&target=Product&partner=undefined&startYear=undefined

Australia's overwhelming dependence on importing medicines and vaccines, from these countries, has been a concern for our Australian health regulators for some time.

The Therapeutic Goods Administration must be applauded for forcing all pharmaceutical companies to forewarn them and publicly list any medicines at risk of shortage.

Until now, when one company had manufacturing issues from their China-based plant, another could step in.

2020 and the coronavirus pandemic has smashed that comfortable assumption. The list of critical medicines at risk of being in shortage grew exponentially from February.

In the first week of April 2020 alone, life-saving medications for women giving birth, Australians having a heart attack, those with a severe thyroid condition have seen their vital medications listed as experiencing an 'unexpected high demand'.

The panic buying of toilet paper also triggered unjustified spikes in consumer demand for medication. This includes over-the-counter ones, such as Panadol and Ibuprofen (due to social media linking their so-called curative powers against the Coronavirus virus) but also more importantly, the ones many Australians need to manage life-threatening conditions.

As an Australian owned pharmaceutical company (the only one in Australia), we are on the frontline of this battle to ensure supplies are monitored and managed, every single day.

We are working closely with the TGA to help manufacture (for the Government's stockpile) some of those medications now at risk, and especially some of those medications that some GPs are repurposing for patients with COVID-19. This redirection of medication comes at the expense of those patients for whom it is intended. The ones with the ongoing chronic conditions.

And for Australian patients, especially those whose lives depend on the timely and affordable access to medicines when they need it; we are still only now appreciating that Australia is far too vulnerable to disruptive shocks dealt by our international trading partners.

Why we need to strengthen our sovereign capability in medicine production

In a globally integrated world, a drive towards efficiency has caused an increasing consolidation of production of medicines in lower cost geographies — primarily based in China, India, Poland or other low-cost economies.

China, India and USA produce over 80% of the world's raw Active Pharmaceutical Ingredients (API). India and USA import a significant proportion of other component pharmaceutical manufacturing ingredients from China.

Australia, in turn, imports very few API's as we import the majority of pharmaceuticals as finished medications from India, North America and the European Union.

The Indian government moved in February to selectively restrict API exports and then followed with some hard closures of its internal borders. While China's factories are now re-opening, there still remains extraordinary challenges to get much needed medicines into Australia and into the hands of our hospitals, prescribers, pharmacists and their patients.

With the pandemic starting in China and hitting countries across the globe, and the resultant fallout and shortages, the need for mitigating risk has become more evident than ever. And it is not just the pandemic that puts Australians at risk of not accessing vital medicines when they need it. Escalating border disputes between source countries, India and China are adding to that angst.
https://www.bloombergquint.com/business/india-china-standoff-threatens-to-disrupt-worlds-biggest-exporter-of-generic-drugs

Even the US regulator, the FDA, expressed concerns before a Congressional inquiry in December 2019[3] about the US's over-reliance on China for importing medicines and hence losing its own domestic capacity to manufacture pharmaceuticals.

With our own dollar low, our aviation industry virtually grounded and subsequent freight costs escalating to now cost more than the value of the medicines being shipped in, it is more than timely to develop a blueprint for the future of a robust advanced Australian pharmaceutical manufacturing hub.

Economically, the novel coronavirus, might have caught the global pharmaceutical industry by surprise but it certainly has opened our eyes to the potential of what Australia can and must do to boost our export might, create a strong sovereign capability and rebuild a prosperous pharmaceutical high technology industry.

[3] https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019

Empowering Our Medical Researchers

Australian medical researchers want to manufacture their own test batches of both new treatments and vaccines in Australia. This important step in clinical trials can't currently be achieved due to cost and a lack of technology and infrastructure.

They absolutely want to hold onto the intellectual rights to their own discoveries past the notoriously difficult 'valley of death' stage II and III in clinical trials; rather than lose the patent of their life-time work to deep-pocketed foreign pharmaceutical companies or venture capitalists.

This frustration is compounded by the reality that despite our medical researchers being at the forefront of finding a safe vaccine for COVID-19; Australia is not guaranteed that it will have access to that vaccine, if bought by a foreign entity.

It is in our national security interests to urgently empower Australia's medical researchers with the financial and technical capacity to produce their own test batches of vital medicines and vaccines.

This much longed for opportunity, will unshackle our research institutions (supported by this public-private investment vehicle) to make their own choices about whether they can scale up to export to the markets of their choice or partner with an Australian pharmaceutical company to support their export endeavours.

Either way, it is a critical offering that will ensure that Australian patients, and our economy, reap the value-add benefits of our world-class research community.

This initiative will also offset the need for universities and medical research institutes to rely on foreign students and government funding. It will allow them an exciting and sustainable income stream.

International Investment Interest

We know creating an advanced research, development and manufacturing hub for vital medicines and vaccines will strengthen Australia's attraction as an investment destination.

Across Australia, clinical trials currently generates $1.1billion each year and supports 7,000 tertiary-qualified jobs. But investment in the sector is declining rapidly and its Australians who are paying the price. This initiative will help reverse this decline, again at a critical time when funding for, and access to, clinical trials has been undermined by the impact of the virus.

Whilst this proposal is proudly Australian, aimed at protecting Australians by Australians and building a wholly new medicine and vaccine development and manufacturing sector; it also lays the foundation of new and unique trade agreements.

Arrotex has already had high level discussions with countries such as the United Arab Emirates (UAE), Canada and India. Like Australia; the UAE does not have their own robust sovereign medicine manufacturing capability and, like Australia, is highly vulnerable to major supply chain shocks leading to shortages of critical medicines. Its Government is investing $3 billion in developing its own medicine development and manufacturing capability.

There is an opportunity to enter into a medicine manufacturing share arrangement; where Australia could produce some of the vital medicines required and the UAE could produce others and both commit to ensuring our respective countries had dual equity of access, especially in times of a global health crisis.

In other discussions with manufacturers around the world, including those from India, Arrotex notes there is significant interest in investing in an Australian Medicines & Vaccines Manufacturing & Development public-private partnership with a view of then of those investors manufacturing medicines and vaccines in our high-tech facilities destined for export.

Australia has long held a reputation of reliably producing agrifood products and consumables that are clean, safe and premium. While the global community is still reeling from massive supply chain disruptions, dealt by COVID-19; we have the opportunity to turn a shattering global health crisis into a long-term economic opportunity.

Leveraging new low emission technologies, utilising automation and AI, will allow Australia to counter our high labor and energy costs and compete effectively with the traditional source countries of China, India and the US.

Our ability to discover and produce high quality premium and safe medicines and vaccines that the world wants makes this proposition a very financially attractive one for Australia.

Add that to our own low dollar, an aviation industry virtually grounded and subsequent freight costs escalating, it is more than timely to deliver this blueprint for the future of a robust advanced Australian pharmaceutical development and manufacturing hub.

The Proposal

Key strategies are urgently needed to help Australia recover and prosper, to foster in a resilient future for Australia that secures:

1. support for medical researchers to hold onto the patent of their own innovative treatments, through phases 2 and 3 “valley of death” clinical trials;

2. the capacity for medical researchers to manufacture test batches here in Australia;

3. access to the most vital medicines and vaccines for all Australians, regardless of what economic shocks are occurring at the time and the response of other countries to create their own protective stockpiles;

4. the development of a high tech, advanced manufacturing hub for Australian pharmaceutical sector, creating thousands of high value jobs;

5. relief for Federal and State Governments to not be forced to stockpile expensive and expiring medicines and vaccines instead manufacture them on an as-needs basis; and

6. new value export chains that strategically position Australia as the global leader in quality sourcing and advancing technology for vital medicine and vaccine manufacturing.

We believe the now is the right time to focus on developing home-grown pharmaceutical self-sufficiency as a key plank in our recovery from this crippling economic and health crisis for 2020/21 and beyond.

We believe Australians will robustly support the development of a **public-private partnership** that both attracts financial investment from all governments, here and overseas, superannuation and financial institutions and the patient capital from a world now recognising the need to broaden the world’s secure supply chains of safe and vital medicines and vaccines.

We can use those funds to establish our capability to manufacture the 120 most important medicines that Australians need. Medical researchers can create their own next block buster (see case study Appendix B) treatment without losing their patent to foreign big pharma or venture capitalists.

The public-private partnership would initially support the construction of a world-class, state-of-the art factory that can be used to manufacture those vital medicines for domestic use in the first instance but also for export to other regional markets.

Rather than stockpiling expensive medicines that have a short shelf life, the Australians government can access the facility in times of national pandemics or critical shortages.

We recommend the Australian Government work with Arrotex and the medical research community to design and establish the **Australian Medicines & Vaccine Manufacturing & Development Public-Private initiative**

Phase one:

The first phase would be to develop a blueprint on how the public-private partnership would be leveraged and to prepare a feasibility study into the construction of an advanced manufacturing and technology park to manufacture both key API's and the finished medicinal product. It would also scope the elements for a research commercialisation 'funding bridge' to support medical researchers past phases 2 and 3 of clinical trials.

We estimate the cost to the Government would be $3 million. We believe this work can be undertaken intensely and delivered within six months.

Phase two:

Creation of the Australian Medicines and Vaccine Manufacturing & Development Public-Private Partnership.

The Government commit an initial $250m and Superannuation/PE funds asked to commit an additional $250m with the possibility of other international interests, including foreign governments, to also contribute $250m in return for a commitment on purchasing the medicines to create a further scaling of manufacturing capacity.

These initial funds for 2021 would go into the sovereign **public-private investment vehicle,** co-ordinated and managed by a Government-held trust, with Arrotex and other industry leaders as key board advisers.

The cost of the fund could be offset by charging a levy for non-Australian industry participants.

Phase three:

- Construction of a world-class pharmaceutical manufacturing and development technology park.

- This is estimated to cost $1 billion - $1.5 billion, depending on the number of APIs and vaccines that are deemed necessary for production. This can be scaled up or down, as required.

- This facility can be accessed by medical research institutes and universities to manufacture test batches of their own treatments to enable them to progress through to commercialisation.

- This facility could be accessed by the Federal and State Governments during times of health crisis (such as the current one) to manufacture medicines and vaccines as needed. This would offset the need for expensive medical stockpiles (including the need to replace the many medicines that expire within two years).

- There could be some policy lever adjustment of the PBAC to fast track applications for medicines manufactured in Australia and for PBS priority listing for domestically produced medications.

- The commercial translation of newly discovered pharmaceuticals by Australian scientists can be manufactured here for a global market – thus truly creating a full value add export opportunity.

- During normal times, the operation of the facility could be offset by the transfer of contracts for the large-scale production of high-volume products by Arrotex and other Australian companies such as CSL.

    - For example, a vital, high volume medicine that Arrotex manufactures is Metformin – critical to the management of Diabetes. It is currently produced in India with the raw ingredients (API) sourced from China.

      Other contracts could include two of the highest volume medicines sold in Australia; Rosuvastatin (cholesterol) and Esomeprazole (gastrointestinal). Arrotex would move the production of the API (China) and the finished product (India) to Australia.

- Creation of Emerging Technology Program (ETP).

- Development of new PBS pricing guidelines on on-shoring manufacturing and IP requirements for local manufacturing capability.

  Based on the model developed by the FDA and managed by the TGA, this program could help encourage the adoption of innovative technology to modernize pharmaceutical development and manufacturing through close collaboration with industry and other relevant stakeholders starting from early technology development.

The size of the prize

Never before has it been so important for the Australian and State governments and industry to promote collaboration and consultation in preparing for a transition to a new sovereign capability that focusses on our ability to manufacture and export the vital medicines Australians and our global neighbours need.

Whilst Australia is the 20th largest export economy in the world, our manufacturing industry is in a trade deficit.

In 2015, the total value of manufactured products imported was $246 billion, with the value of exports just under $100 billion.

The Harvard Atlas of Economic Complexity, judged our exports of pharmaceutical products to be valued at $2.3 Billion in 2017, compared to $7billion of imports.[4]
In a study of Australian business undertaken by PWC,[5] the transition to digitalisation and smart automation was poised to add 14% or $1.5T to global GDP gains by 2030.

We know that combining our smarts with the new technology and our reputation for producing the highest quality, break through medicines, we can convert the need to import our vital medicines to a vibrant local pharmaceutical manufacturing hub.

Advanced manufacturing technologies could enable Australia-based pharmaceutical manufacturing to regain its competitiveness with China and other foreign countries, and potentially ensure a stable supply of medicines critical to the health of Australian patients.

Advanced manufacturing is a collective term for new medical product manufacturing technologies that can improve medicine quality, address shortages of medicines, and speed time-to-market.

Every field has a different set of production techniques that are considered advanced. Examples of some cross-cutting advanced manufacturing technologies include continuous manufacturing and 3D printing.

A new advanced manufacturing hub could be cost neutral as Arrotex brings manufacturing of its medicines back to Australia (contracts would go to Australia not to India or China).

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[4] https://atlas.cid.harvard.edu/explore?country=14&product=129&year=2017&tradeDirection=import&productClass=HS&target=Product&partner=undefined&startYear=undefined

[5] Transforming Australian Manufacturing: Preparing businesses and workplaces for Industry 4.0 https://www.pwc.com.au/education/industry-proposal-13may2019.pdf

Advanced manufacturing technology has a smaller facility footprint, lower environmental impact, and more efficient use of human resources and energy than traditional technology.

For medical research institutes and universities, this initiative will allow them a substantial income independent of taxpayers or foreign students.

Case studies

Anti blood clotting breakthrough - Heart Research Institute

As a live case study (attached separately); the researchers at the Heart Research Institute have developed a new treatment for treating blood clots that is needed now for COVID-19 patients (up to 70% of whom are dying from a storm of blood clots that attacks all of the major organs including the lungs, heart and brain).

Even beyond this pandemic, the treatment, that is proving safer than aspirin and prevents patients from bleeding out (a common side effect of the current anticoagulants); can then be used to treat the world's biggest killers – stroke and cardiovascular disease.

This treatment has been subject to almost 20 years of trials (phase 1) and has received numerous grants from the NHMRC but now, as the researchers enter the critical 'valley of death' phase 2; ongoing funding is not available via the traditional funding platforms.

The medical researchers at the HRI have the world exclusive rights but can only test batch manufacture overseas as there is no Australian facility of the standard required for the trials.

There is no funding from the MRFF for manufacturing nor for allowing trials to include overseas patients. If the medical researchers cannot access up to $15m, they (and this global blockbuster treatment) will be stuck in the 'Valley of Death', with the only funding option to sell their patent to foreign big pharma to fund the trials.

Based on cutting-edge science, HRI anticipates this new anti-clotting treatment will be a USD $1 billion per annum **export opportunity**. By way of comparison, the current thrombolytic medicine used in stroke made more than USD$1.2b in 2017 alone. HRI research demonstrates their breakthrough can build on the outcomes of this drug. Without seed funding now for a commercialisation 'funding bridge'; that export income will be lost to Australia.

Gardasil – Professor Ian Frazer and UQ

This is what the researchers behind the breakthrough the discovery of the first vaccine for a cancer (Gardasil) were forced to do to the detriment of their own financial future.

Former Australian of the Year, Professor Ian Fraser and colleagues were celebrated globally for developing the vaccine for certain strains of human papillomavirus (HPV).

However, he too was forced to sell the global patent to the American pharmaceutical company Merck in order to fund the ongoing trials.

In 2019, Gardasil sales for Merck rose 27 percent to USD$828 million[6].

If the US regulator is worried, should we be?

The US drug regulator, the Food and Drug Administration (FDA), maintains a list of medications that are used as medical countermeasures (MCMs) against threats in four categories: biological threats, chemical threats, influenza, and radiation threats.

In November last year, it told Congress that many of these medications were contained in strategic drug stockpiles, for use in a public health emergency severe enough to cause local supplies to run out.

For API's for 14 medicines in the biological threat category, China has 37 facilities, the United States has 19, and the rest of the world has 117. Australia has none.

The security of the US vital medicines supply is the same as ours.
It rests on three main factors:

1. freedom from dependence on foreign sources of API;
2. the resilience of our domestic manufacturing base; and
3. the reliability of the facilities that make products for the domestic market.

Australia, more so than the US, is even more precariously dependent on foreign regimes delivering safe and timely medicines to our people.

The FDA called this over-reliance on foreign countries for its medicines as a "national security risk".

Should Australia share that concern?

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6 https://www.reuters.com/article/us-merck-co-results/merck-raises-full-year-forecasts-as-vaccines-power-profit-beat-idUSKCN1S616K

Australia's medical countermeasures (MCM) capabilities

We know the Department of Defence, through its Defence Science and Technology (DST), is reviewing Australia's medical countermeasures (MCM) capabilities.

Medical countermeasures refer to medical interventions such as vaccines, and therapeutic and diagnostic technologies which can protect people against emerging infectious diseases, pandemics, as well as chemical, biological, and radiological threats.

In its 2012 and 2017 audits, the Department of Defence's key findings[7] underscore the need for great sovereign capability in the development and manufacturing of vital medicines and vaccines. Among the recommendations:

- Establish the initiative as a public-private partnership where industry leads the management and execution of product development activities.
- Develop incentives, including R&D tax incentives and innovation grants that would support and encourage industry engagement in product development.
- Align existing Australian state and federal research grants to encourage national and international cross- sector engagement in achieving a national medical countermeasures capability.
- Encourage engagement of state and local governments to support a national MCM product development initiative.
- Integrate the Australian MCM product-based initiative into the existing national emergency response network.
- Stimulate the creation of advanced manufacturing platforms of therapeutics and diagnostics through specialised funding mechanisms.

7 https://www.dst.defence.gov.au/sites/default/files/publications/documents/Medical%20Countermeasures%20Initiative%20Summary.pdf

Establishing an Australian Medicines & Vaccines Manufacturing & Development (public-private) initiative

The **Australian Medicines & Vaccines Manufacturing & Development initiative** will create the opportunity for Australia to establish a public-private partnership, that will, as its core focus, protect our most vulnerable Australians from global supply disruptions to vital medicines.

It will allow us to quickly adopt advancing green technology and access the global asset funds now available.

There is already high-level interest in investing in this fund, by other jurisdictions, who have long respected Australia as a sound and safe producer of vital medicines; albeit not in the quantity that we could be achieving.

Arrotex stands ready to help deliver a blueprint for the Australian Government with consultation with both international and national stakeholders, medical researchers, prescribers, pharmacists and patient groups.

The **Australian Medicines & Vaccines Manufacturing & Development Fund** will complement the Government's recently announced $500m Australian Business Growth Fund for SMEs that is intended to be funded by co contributions of the major banks, superannuation companies and the government.[8]

This in turn follows the success of the United Kingdom's Business Growth Fund[9], which has now invested $2.7 billion in a range of sectors across the economy.

And it also a similar Canadian Fund that helps its businesses with the capital, talent, and expertise they need to drive growth and realize their potential.

Supported by Canada's leading banks and insurance companies, it has a national mandate to provide long-term, patient, minority capital to entrepreneurs pursuing growth and expansion strategies.

This Canadian fund also has initial capital commitments of $545 million and is projected to increase to $1 billion over time.

It will complement the existing Medical Research Future Fund that is restricted and does not cover manufacturing of drugs for trials and often does not fund 'valley of death' phases 2 and 3.

[8] https://treasury.gov.au/small-business/bgf

[9] UK Business Growth Fund

Why advanced manufacturing makes a domestic medicines manufacturing hub a cost-effective reality

Advanced manufacturing offers many advantages over traditional pharmaceutical manufacturing, and if Australia invests in this technology, it can be used to reduce the Nation's dependence on foreign sources of API's, increase the resilience of our domestic manufacturing base, and reduce quality issues that trigger medicine shortages or recalls.

For example; product quality can be precisely controlled with modern automation and control systems and can be closely monitored during production by using high-resolution analytics. High technology, computer-controlled production facilities are better able to rapidly respond to changes in demand because they typically do not have the equipment scale-up issues associated with traditional methods and can be capable of seamlessly producing a variety of dosages and even dosage forms.

Advanced manufacturing platforms also have a much smaller footprint than traditional manufacturing platforms, and the manufacturing is moved closer to markets, reducing the need for transcontinental shipping of components and further reducing costs.

Medicines can be produced at lower cost than by traditional methods, especially as the two biggest cost inputs of energy and labour in Australia can be dramatically reduced.

In turn, the environmental impact of manufacturing is significantly reduced.

By supporting the growth of advanced manufacturing in Australia, we can reduce our dependence on China and other overseas manufacturers for API's as well as improve the resilience and responsiveness of our manufacturing base and reduce medicine shortages.

Adopted as intended, this new domestic manufacturing hub will create hundreds of jobs and cement Australia's reputation as a safe and sustainable investment destination.

The role of our TGA will be pivotal in our success

As mentioned above, the FDA, has recognised the US growing reliance on China for vital medicines as a 'national security' risk.[10]

And in turn, it is fostering its own country's development of a pharmaceutical manufacturing industry in several ways.

We believe the TGA could also follow suit.

Emerging Technology Program (ETP)

The ETP, launched by the FDA in late 2014, encourages and supports the adoption of innovative technology to modernize pharmaceutical development and manufacturing through close collaboration with industry and other relevant stakeholders starting from early technology development.

To reduce barriers to entry for advanced manufacturing, the Emerging Technology Team (ETT) provides a gateway for the early (pre-submission) discussion of innovative technologies and approaches, even before a candidate drug is identified. The ETT supports the entry, assessment, and lifecycle management of advanced manufacturing at its Center for Drug Evaluation and Research (CDER).

It provides subject matter experts and fosters coordination within CDER and FDA's Office of Regulatory Affairs (ORA) for precedent-setting issues regarding quality and good manufacturing practices.

ETT serves as a hub for identification of application-driven regulatory and research needs and provides strategic input for supporting advanced manufacturing innovation.

Based on the ETT efforts in continuous manufacturing, CDER's Office of Pharmaceutical Quality (OPQ) published a draft guidance, "Quality Considerations for Continuous Manufacturing" of solid oral dosage forms in early 2019.[8]

Under this program, CDER has approved five drug applications utilizing continuous manufacturing for FDF manufacturing, and the first application utilizing 3-D printing technologies.

We believe the TGA could adopt a similar role, if properly funded.

[10] https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019

Regulatory and Policy Initiatives

The adoption of advanced manufacturing technologies may pose a challenge to the current regulatory framework, because most regulations were developed based on traditional batch manufacturing methods under a unified pharmaceutical quality system. As a result, the FDA has launched an effort to identify and implement needed changes in the regulatory structure.[11]

For example, new policy and regulatory topics, related to emerging technologies include the management of data-rich environments, the evolving concepts of process validation for advanced manufacturing systems, and the regulatory oversight of post-approval changes for such systems.

Furthermore, the CDER, in collaboration with the Biomedical Advanced Research and Development Authority (BARDA), is working on a strategy and new regulatory framework to develop and implement miniature, mobile manufacturing platforms ("Pharmacy on Demand") for manufacture of essential medicines near or at the point of care.
FDA actively engages with stakeholders in industry, academia, and other regulatory agencies to identify and address regulatory hurdles to the adoption of advanced manufacturing.

For example, CDER, in partnership with FDA's Centre for Biologics Evaluation and Research (CBER), is leading the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) effort to develop the Q13 guideline on continuous manufacturing of drug substances and drug products for both small-molecule and biological products, which will help to achieve global regulatory harmonization.

Again, we would recommend working with the TGA to identify what, if any potential there is for Australia to follow a similar path of collaboration.

[11] https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019

History of Pharmaceutical Manufacturing

Australia, through our investment in biomedical research, has become a world leader in the discovery and development of breakthrough treatments.

Right now, our medical researchers are leading the race for a vaccine for COVID-19.

This is recognised globally and our Government needs to be applauded for continuing to support the collaboration of translational research through the Medical Research Future Fund. However, the Government rarely funds clinical trials through the critical 'valley of death' phases two and three. It does not cover trials that need to be undertaken with patients overseas or any manufacturing of test batches of drugs and vaccines.

This is a keenly felt gap in the medical research commercialisation capability that this proposal seeks to rectify.

Australia has also long lost its once robust pharmaceutical manufacturing industry, despite various attempts over the decades to revive it, and therefore once the initial R&D phase has completed the truly valuable commercialisation phase is moved offshore, including the manufacturing development and implementation.

In the early to mid 1980's, Australia's place in the international pharmaceutical industry was seen to be under threat[12]. The Australian Productivity Commission in its review of the sector in 1996 declared that there was a widely held industry perception of the Australian operating environment as 'hostile'.

It was argued that this perception, combined with international business rationalisation, led to some disinvestment in the Australian industry, a general decline in activity, a running down of production facilities, an increasing deficit on the pharmaceutical balance of trade and the threat of more departures.

According to the Productivity Commission, Eli Lilly closed its manufacturing facilities in Australia and confined activities to sales and marketing, Ciba-Geigy and Upjohn ceased local production, and Roche and Riker closed their research and development (R&D) facilities. Furthermore, the Bureau of Industry Economics (BIE) noted declines in activity by Merck, Sharp & Dohme and Parke Davis through shifts of varying degrees from local manufacturing to imports.

In the 1980's, the main elements contributing to the industry's 'hostile environment perception' were low prices on the Pharmaceutical Benefits Scheme (PBS) and an idiosyncratic and slow regulatory system. Industry was also highly critical of the patent system at the time.

[12] https://www.pc.gov.au/inquiries/completed/pharmaceutical/51drugsv1.pdf

In a bid to change the perception of Australia as a hostile environment and encourage companies to stay in Australia and undertake further investment, the Commonwealth Government announced, in September 1987, the establishment of the Pharmaceutical Industry Development Program (PIDP).

Through a series of complex policy changes, it effectively worked to leverage the PBS to incentivise the pharmaceutical sector to continue to invest in Australia and maintain a manufacturing presence here.

In a review of the scheme in 1991, the Bureau of Industry Economics[13] concluded that, overall, around 85 per cent of increased manufacturing and export activity had probably been induced by the Government's policy changes.

That was more than three decades ago. And a lot has changed again in the pharmaceutical sector landscape in Australia.

Policy changes such as Price Disclosure and Accelerated Price Disclosure have delivered billions of dollars in savings to the taxpayer but left a generic pharmaceutical sector with so little margin that local manufacturing is all but impossible.

And how we look now

Right now, from the generic medicines industry, there are only two companies with manufacturing sites here in Australia. One is Mylan and the other is Aspen. Both are foreign owned.

But, in terms of the IP ownership for manufacturing, Arrotex Pharmaceuticals has the largest portfolio of PBS medicines that it can manufacture. Currently Arrotex manufactures over 95% of its volume in India, Europe and Canada in order to deliver the most cost effective high quality product for the PBS and Australian taxpayers.

Australian owned**, Arrotex Pharmaceuticals** was formed following the merger of Arrow Pharmaceuticals (Arrow) and Apotex Australia (Apotex) in July 2019 and is today the largest privately owned Australian pharmaceutical company operating in Australia.
Arrotex medicines are available in every Australian pharmacy and Arrotex manufactures over 250 of the most prescribed medicines on the PBS which account for almost 85% of all prescriptions written by Australian doctors.

An Arrotex product is dispensed for 25% of all prescriptions, patients bring to their local pharmacy. Also, many of Australia's most trusted over-the-counter private label medicines are supplied by Arrotex with almost 60% of every private label OTC medicine Australians choose in pharmacy being an Arrotex manufactured product.

[13] BIE 1991

Against this unique position; Arrotex is well placed to support the initiative to have an **Australian Medicines & Vaccines Manufacturing & Development Public-Private Partnership.**

Conclusion

What Australia, and the world, is experiencing with COVID-19 is deeply shocking. This rampant virus shatters lives, splinters families, destroys whole economies and is placing unbearable stress on our global supply chains.

But from this unprecedented devastation, Australia is well placed to build a new dynamic, stable and efficient pharmaceutical industry, delivered by smart Australians with access to advanced, low emission technologies and a state-of-the art manufacturing facility that can be accessed by Australian medical researchers and companies, and the Australian Government, to be sure we never again endure the threat of an internationally-triggered shortage of critical medicines.

It can collectively produce a multibillion-dollar export industry, securing jobs for thousands of Australian now, and for generations to come.

As the Minister for Industry recently questioned[14]: "What is manufacturing going to look like in Australia? What are the key industries where we have a unique contribution - particularly to the rest of the world - and how do we make sure that in a crisis we can support ourselves?"

Arrotex, utilising its breadth of pharmaceutical manufacturing IP and global commercial credentials, is committed to support the Government to build our sovereign capability, develop an exciting world-class pharmaceutical hub and become an investment destination the world will be drawn to.

But most importantly, Arrotex stands ready to protect and support all Australian patients and their families.

We recommend this proposal for your consideration and in particular, as part of the recovery efforts for our beleaguered economy.

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[14] https://www.smh.com.au/business/companies/coronavirus-leaves-local-manufacturers-exposed-20200410-p54iuu.html

About Arrotex Pharmaceuticals

Arrotex Pharmaceuticals is Australia's largest generic pharmaceutical and private label over the counter (OTC) medicines company. Arrotex Pharmaceuticals was formed following the merger of Arrow Pharmaceuticals (Arrow) and Apotex Australia (Apotex) in July 2019 and is today the largest privately owned Australian pharmaceutical company operating in Australia. The company is 50% owned and operationally controlled by Dennis Bastas (Australian) with the Sherman Family (Canadian) owning the other 50% as a passive investment.

Dennis Bastas has extensive experience across pharmaceuticals and is currently the Chairman and CEO of Arrotex Pharmaceuticals and Chairman of Juno Pharmaceuticals.

Dennis is an entrepreneur, and passionate thought leader for generic medicines and the supply of medicines through the value chain, from manufacturer to patient. Dennis also sits as a Director of the Generic and Biosimilars Medicines Association (GBMA) and is a member of the Australian Institute of Company Directors (MAICD).

Dennis is also currently the major shareholder and Chairman of myDNA – a world leading pharmacogenomic and health genomic platform technology.

Appendix

Basic Manufacturing Capacity

API Manufacturing

Active Pharmaceutical Ingredients (API) are the basic component that provides the therapeutic benefit in a medicine.

API manufacture is a highly concentrated industry with China and India dominating world supply. The concentration of supply stems from the pharmaceutical market's desire to source the lowest cost API, as it is the largest cost element of any medicine.

To ensure supply of vital medicines in a time of crisis it will be essential that Australia has a facility capable of manufacturing the API for a number of medicines where the API is unable to be stockpiled effectively or is too costly to do so in order for the downstream finished formulation facilities to produce the required dosages of those drugs for consumption by patients.

The API manufacturing capability should include a separate antibiotics area. API production of antibiotics is likely to be important in any potential pandemic crisis.

The estimated production volume of the total number of API's that may be required is for a subset of the finished formulations that the other four manufacturing facilities will produce.

Finished Solid-Oral Dosage Manufacturing

The manufacturing of finished solid-oral dosage products involves the production of tablet and capsule medications which is the main format for medicines that Australians consume today.

Australians take approximately 10 billion prescription tablets and capsules each year. 500 drug types represent approximately 95% of the total volume of oral medicines.

It is estimated that only 100-150 drug types will be required to meet the vital needs of most Australians during a crisis. The key factor is that most vital medical conditions can be managed with several different drug types, but in consultation with the medical fraternity and the TGA, it will be decided which drug types can serve vital conditions best and they will be selected for manufacture in an emergency.

Advanced Manufacturing and Development Capacity

Vaccine Manufacturing

Vaccine manufacturing capacity will be a major requirement for managing the risk of a future global pandemics. The manufacturing capability will also allow us to quickly produce in quantities any novel vaccines that may be developed during a new viral outbreak in order to ensure Australians receive timely supply.

Vaccine manufacturing capability will also be a strong attraction to local research and development enterprises to commercialise new products using the local facilities to supply a global marketplace.

Many of Australia's medical researchers are on the frontline of discovering a vaccine for COVID-19 but there is no current capacity to manufacture the vaccines in this country.

If our researchers sell the IP of their discovery to an international pharmaceutical company or government, there is no guarantee that we will have access to the very vaccine we discovered.

This sovereign risk needs to be addressed as a matter of urgency.

Monoclonal Antibody Biological Manufacturing

Specialised and personalised drug manufacturing is moving toward small volume production of biological medicines in high tech flexible facilities.

The proposed facility will give Australia one of the largest most advanced manufacturing capabilities in the world with the ability to offer contract manufacturing capacity to global pharmaceutical and research companies.

Biological drugs are growing in use in Australia and to future proof our sovereign manufacturing capability it is proposed that a state-of-the-art advanced manufacturing facility will give us the necessary future proofing.

A manufacturing facility of this nature is also expected to attract local and global pharmaceutical companies to set up development operations in close proximity and would create the need for high tech offices and labs which would be built with outside investment.

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International Investment Interest

We know creating an advanced research, development and manufacturing hub for vital medicines and vaccines will strengthen Australia's attraction as an investment destination.

Across Australia, clinical trials currently generates $1.1billion each year and supports 7,000 tertiary-qualified jobs. But investment in the sector is declining rapidly and its Australians who are paying the price. This initiative will help reverse this decline, again at a critical time when funding for, and access to, clinical trials has been undermined by the impact of the virus.

Whilst this proposal is proudly Australian, aimed at protecting Australians by Australians and building a wholly new medicine and vaccine development and manufacturing sector; it also lays the foundation of new and unique trade agreements.

Arrotex has already had high level discussions with countries such as the United Arab Emirates (UAE), Canada and India. Like Australia; the UAE does not have their own robust sovereign medicine manufacturing capability and, like Australia, is highly vulnerable to major supply chain shocks leading to shortages of critical medicines. Its Government is investing $3 billion in developing its own medicine development and manufacturing capability.

There is an opportunity to enter into a medicine manufacturing share arrangement; where Australia could produce some of the vital medicines required and the UAE could produce others and both commit to ensuring our respective countries had dual equity of access, especially in times of a global health crisis.

In other discussions with manufacturers around the world, including those from India, Arrotex notes there is significant interest in investing in an Australian Medicines & Vaccines Manufacturing & Development Future Fund with a view of then of those investors manufacturing medicines and vaccines in our high-tech facilities destined for export.

Australia has long held a reputation of reliably producing agrifood products and consumables that are clean, safe and premium. While the global community is still reeling from massive supply chain disruptions, dealt by COVID-19; we have the opportunity to turn a shattering global health crisis into a long-term economic opportunity.

Leveraging new low emission technologies, utilising automation and AI, will allow Australia to counter our high labor and energy costs and compete effectively with the traditional source countries of China, India and the US.

Our ability to discover and produce high quality premium and safe medicines and vaccines that the world wants makes this proposition a very financially attractive one for Australia.

Add that to our own low dollar, an aviation industry virtually grounded and subsequent freight costs escalating, it is more than timely to deliver this blueprint for the future of a robust advanced Australian pharmaceutical development and manufacturing hub.

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