RESPONSE TO THE CRITICAL TECHNOLOGIES DISCUSSION PAPER: HEALTH

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RESEARCH AUSTRALIA

CONNECTING · ENGAGING · INFLUENCING

ABOUT RESEARCH AUSTRALIA

We are the national peak body representing the whole of the health and medical research pipeline.

Our vision: Research Australia envisions a world where Australia unlocks the full potential of its world-leading health and medical research sector to deliver the best possible healthcare and global leadership in health innovation.

Our mission: To use our unique convening power to position health and medical research as a significant driver of a healthy population and contributor to a healthy economy.

Our goals:

Engage

Australia in a conversation about the health benefits and economic value of its investment in health and medical research.

Connect

researchers, funders and consumers to increase investment in health and medical research from all sources.

Influence

government policies that support effective health and medical research and its routine translation into evidence-based practices and better health outcomes.

Nadia Levin
CEO & Managing Director
02 9295 8547
Nadia.levin@researchaustralia.org

www.researchaustralia.org
384 Victoria Street Darlinghurst NSW 2010

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Introduction

Research Australia is the national peak body for health and medical research and health innovation. We envision a world where Australia unlocks the full potential of its world-leading health and medical research sector to deliver the best possible healthcare and global leadership in health innovation. Our membership spans the entire health and medical research and innovation pipeline, including universities, not for profit research organisations, charities and corporations.

Research Australia's has provided a response to questions 1, 2, 3 and 9 below.

1. What are the priority critical technologies, current and emerging, in this sector over the next 10 years? Are these reflected in the list provided in the discussion paper?

Research Australia suggests amending the reference to “Molecular Robotics” so that it reads “Medical Robotics”. “Molecular Robotics” is too narrowly defined to be a relevant critical technology for the next decade, broader terminology would allow for the other forms of robotics already transforming healthcare (e.g. orthopaedic surgery). These are expected to increase in importance in the future.

Research Australia suggests amending the text to on Gene Therapies as follows: (edits in *italics*)

Gene technology **a. Genomic and genetic engineering/ analysis/ sequencing/editing**	Introducing foreign genetic material, reorganising existing genetic material, or constructing the entire genome of an organism from fragments of synthetic DNA or RNA. Includes technology related to stem cells, *mRNA, CRISPR and ~~various~~ other small RNA products (e.g. siRNA, miRNA).*	Development of novel vaccines, *cancer therapies, treatment of neurodegenerative, hereditary disorders, making crop and animal agriculture more sustainable*

Research Australia suggests adding the following category:

Active pharmaceutical ingredients (API) and other specialised raw materials for medicinal products	*Production of API’s for critical medicine to safeguard Australia if supply is interrupted. Produce high-value APIs and materials that underpin gene technology and biomaterial production and those required for fill and finish processes (e.g. borosilicate glass vials)*	*Raw materials for novel formulation in personalised medicine, advanced DNA and RNA based materials, novel delivery systems for gene technology and precision medicines*

2. Have you identified or experienced any supply chain issues associated with critical technologies?

There is currently a critical supply chain issue in Australia in respect of the later stage development of medical products as a precursor to full scale development and domestic manufacture of products

The development of medical products, including pharmaceuticals, therapeutics, diagnostics and medical devices is a long and expensive process, typically taking more than a decade. However, the rewards for successful products, and the companies and countries that manufacture them, can be substantial.

Australia already has many processes and programs to support the development and commercialisation of medical products, and many of these components are now working well. The Research and Development Tax Incentive is one such example.

Australia has existing advanced manufacturing capability in key areas, including medical devices.

ROMAR Engineering

'We provide advanced manufacturing and processing solutions for a wide range of highly regulated industries including aerospace, aeronautical, medical, defence and automotive applications.

At the heart of our advanced manufacturing capability is our DMG Mori Lasertec 65 3D 5-axis synchronous laser deposition, welding and milling machine.

It's a 3D printer with unique metal-on and metal-off capability … and it's the only one of its type in Australia. With the Lasertec 65, our additive manufacturing capability includes metal-on and metal-off manufacturing of even the most complex components.

So, we can engineer creative new designs – or repair, renew and replace existing parts, quickly and cost-effectively.

We are also particularly proud of our contract manufacture of medical devices within the healthcare sector, which we accomplish with leading expertise and superior facilities, including a Class 8 Clean Room.

Our customers range from large multinational companies to start-ups, but what unites them is a desire for high quality, solutions-driven, strenuously tested and precision-built products that meet the highest standards.[1]

The transition from product development to the manufacture of medical products provides both a particular challenge and an opportunity for Australia. Clinical trials are an essential part of the process of bringing a medical product to market. The conduct of clinical trials requires having thousands (or tens of thousands) of the product being tested available for use with patients. The manufacture of the product for clinical trials requires facilities that are flexible enough to produce batches of products to the required standard for use in clinical trials but at a scale that is beyond research facilities.

Having more of this manufacturing capacity in Australia would:

- help support Australia as a destination for clinical trials,
- build Australian expertise in manufacturing for the latest types of devices, diagnostics, medicines and drugs; and
- support Australian research which is reliant on access to clinical trial materials to be able to continue research into promising new therapies.

This manufacturing capacity would provide direct economic benefits. It is also a good starting point from which to scale up to the manufacture of a range of new medical products on a fully commercial scale for products that prove to be viable.

If the initial manufacturing for clinical trials has been undertaken in Australia, it provides Australia with a natural advantage. It can be easier and quicker to expand the manufacturing capability here, drawing on the skills and expertise developed in the clinical trial production phase, rather than start the whole process from the beginning in another country. This natural advantage in scaling up can help avoid future supply chain issues; this advantage is lost where the manufacturing for the clinical trials has been undertaken overseas.

There are currently very few facilities in Australia with the capacity to produce the volumes of materials required for later stage clinical trials. In part this is because, as noted above, there has been a tendency in the past for Australian entrepreneurs to license promising products at an early stage of development to a foreign multinational company, which results in the further product development and manufacturing occurring overseas.

With an increasing trend towards developing products locally to a later stage, there is a need for greater local manufacturing capability. Australian medical product start-ups are typically still 'pre-revenue' at this stage of

[1] https://www.romareng.com.au/manufacturing-expertise/

their development and are not in a position to invest the capital needed to establish a new manufacturing facility. We need alternative solutions.

VAXXAS- Home grown technology, to be manufactured here [23]

Vaxxas is a privately held biotechnology company focused on enhancing the performance of existing and next-generation vaccines with its proprietary HD-MAP technology platform. The HD-MAP enables vaccines to be administered by a small patch applied to the skin, replacing a needle/syringe. The core technology was developed at the University of Queensland and the company was founded with initial investments from OneVentures Innovation Fund 1, Brandon Capital, the Medical Research Commercialisation Fund (MRCF), and US-based HealthCare Ventures. OneVentures Innovation Fund I and the MRCF are supported by the Australian Government's Innovation Investment Fund (IIF) program.

The HD-MAP is made of biocompatible polymer. It is smaller than a postage stamp and comprises thousands of micro-projections that are invisible to the naked eye. These micro-projections are coated with vaccine and can penetrate the outer layer of the skin to deliver the vaccine directly to dense populations of immune cells. The device is applied to the skin for just 10 seconds by using a disposable applicator.

To date, VAXXAS has developed and manufactured its product within the Translational Research Institute in Brisbane, but there is not sufficient manufacturing capability at TRI for the upcoming trials and early stage production.

In late 2020, the Queensland Government announced that it will partner with Vaxxas to establish a facility at Brisbane's Northshore Hamilton for the manufacture of products for late stage (Phase II and III) clinical studies.

This announcement followed Vaxxas securing US$22 million, through the U.S. Government's Biomedical Advanced Research and Development Authority (BARDA), to support pandemic deployment of their HD-MAP. The initial focus of the BARDA program will be on a pandemic influenza vaccine, but Vaxxas will also investigate opportunities to improve the performance of other pandemic vaccines, including against COVID-19.

The agreement with BARDA also provides access to manufacturing capability in the USA.

Readier access to manufacturing facilities to produce medical products for clinical trials could be key to keeping the further development of new medical products in Australia; and it could provide a base for establishing the full-scale manufacturing capability for medical products in Australia when the product is in the market and generating revenue.

While Vaxxas has succeeded in this first stage with support from the Queensland Government, there is scope for the development of several manufacturing facilities in Australia able to support the manufacture of devices, pharmaceuticals and other therapeutics for clinical trials.

The provision of manufacturing facilities for clinical trials would contribute to the development of new home-grown medical product companies undertaking full scale manufacturing in Australia, helping avoid further supply chain issues associated with overseas manufacture.

[2] https://www.mrcf.com.au/2020/10/05/vaxxas-announces-us22-million-a30-6-million-award-from-u-s-government-to-advance-vaxxas-needle-free-hd-map-vaccine-patch-technology-for-pandemic-response/

[3] https://statements.qld.gov.au/statements/90979#:~:text=State%20partners%20with%20world%2Dclass%20med%20tech%20company%20to%20create%20Qld%20jobs,-Published%20Sunday%2C%2004&text=A%20Queensland%20medical%20technology%20company,thanks%20to%20the%20Palaszczuk%20Government.

Research Australia submits the Commonwealth Government should investigate how it can support the development of domestic manufacturing capability of medical products for clinical trials. This includes funding a feasibility study into establishing one or more manufacturing facilities for clinical trial materials to capitalise on Australia's global competitive advantage in clinical trials. It should investigate the provision of facilities in partnership with the health and medical research and innovation sector and funding models involving consortia of government and private investors.

Commonwealth Procurement

Part of the solution to this problem in respect of medical products rests in the Commonwealth's key role as a purchaser of many of these products and technologies, both directly and through programs such as the Pharmaceutical Benefits Scheme and the Medicare Benefits Schedule.

In 2016, Innovation and Science Australia undertook a review of the performance of Australia's innovation performance. One of the ways it identified the Australia Government could better support Australian innovation was through its procurement processes.

> '***Relative to other countries, government procurement could do more to foster innovation.***
>
> *The majority of OECD countries use procurement approaches 'not only to foster value for money but also to pursue other policy objectives'.137 Australia ranks 63rd out of 138 countries for the extent to which government purchasing decisions foster innovation.138*
>
> *Australia's relatively poor performance on this measure may be related to the emphasis government procurement guidelines place on value for money. This could discourage domestic innovation and investment in innovation.*
>
> *Conversely, overseas examples highlight the potential for governments to use procurement as a direct mechanism to increase the incentives for innovation. For example, the government-wide US Small Business Innovation Research programme was established in 1982 to encourage small businesses to participate in US Government R&D and potentially commercialise their outputs. The programme requires government departments spending more than $100 million on extramural R&D to set aside a portion of this spend for small businesses. Similarly, the UK Small Business Research Initiative was established in 2001 to improve the number of small R&D-based businesses winning contracts from government'.* [4]

Medical products provide an ideal opportunity for the Australian Government to use its role as customer to support Australian R&D and manufacturing. This is because the Australian Government is a major purchaser of healthcare products and services on behalf of the Australian population.

The VAXXAS case study above refers to the funding the company received from the U.S. Government's Biomedical Advanced Research and Development Authority (BARDA). While similar to the US Small Business innovation Research Program referred to in the ISA report, it has a more specific and strategic focus.

Research Australia submits the Government should develop an Australian equivalent of the US Government's Biomedical Advanced Research and Development Authority (BARDA) and Centers for Innovation in Advanced Development and Manufacturing (CIADM), with the objective of supporting the development and domestic manufacture of new medical products needed to protect the health of the Australian population.

[4] Innovation and Science Australia (2016) Performance Review of the Australian Innovation, Science and Research System 2016. Commonwealth of Australia. Canberra. Page 29

BARDA

Biomedical Advanced Research and Development Authority (BARDA), part of the HHS Office of the Assistant Secretary for Preparedness and Response, was established to aid in securing our nation from chemical, biological, radiological, and nuclear (CBRN) threats, as well as from pandemic influenza (PI) and emerging infectious diseases (EID). BARDA supports the transition of medical countermeasures such as vaccines, drugs, and diagnostics from research through advanced development towards consideration for approval by the FDA and inclusion into the Strategic National Stockpile. BARDA's support includes funding, technical assistance and core services, ranging from a clinical research organization network to Centers for Innovation in Advanced Development and Manufacturing, and a fill-finish manufacturing network. BARDA supports a diverse portfolio of medical countermeasures and these products have received a total of 55 FDA approvals, licensures, or clearances.

Our mission is accomplished through successful public-private partnerships with industry to share risk, improve efficiency and accelerate development all while sustaining a marketplace that guarantees continued access to countermeasures vital to our national security.[5]

The focus is on products the US Government needs to protect its population and BARDA provides financial and other support from later stage research through to manufacture of the product and then acts as a cornerstone purchaser. The manufacturing capability is delivered through three BARDA sponsored Centers for Innovation in Advanced Development and Manufacturing (CIADM).

Centers for Innovation in Advanced Development and Manufacturing

BARDA has established three Centers to develop and manufacture medical countermeasures, such as vaccines and therapeutics used to protect health in emergencies, which can transition quickly and cost effectively between products. Created as public-private partnerships, the Department of Health and Human Services' (HSS) Centers for Innovation in Advanced Development and Manufacturing (HHS CIADM) will provide a significant domestic infrastructure in the United States capable of producing medical countermeasures to protect Americans from the health impacts of bioterrorism as well as pandemic influenza and other disease in response to public health emergencies.

The HHS CIADMs were created through a public-private partnership model, bringing together the innovative ideas of small biotech firms, the training expertise of academic institutions, and the development and manufacturing experience of large pharmaceutical companies. This helps to ensure a sustainable domestic medical countermeasure infrastructure with unprecedented ability to accelerate development and manufacture medical countermeasures in time of need. These Centers will also be used to explore emerging and innovative technologies that could be applied to current or future medical countermeasure development efforts to reduce risk, increase yield, and ultimately to reduce total life-cycle costs through flexible manufacturing, consolidating other costly product development expenditures, or any other economy-of-scale opportunities.

To date BARDA has funded three Centers with contracts capable of renewal for up to 25 years, representing a long-term commitment to this partnership with industry and to national security. Under these contracts, the HHS CIADM performers will retrofit existing facilities, or build new facilities to incorporate flexible, innovative manufacturing platforms that can be used to manufacture multiple products. These facilities will be capable of using modern cell- and recombinant-based vaccine technologies that have the potential to produce vaccines for not only pandemic influenza but also other threats more quickly and economically.

Emergent Manufacturing Operations Baltimore LLC, with facilities in Baltimore and Gaithersburg, MD, will lead one Center, working with a network of partners; Michigan State University, Kettering University of Flint,

[5] https://www.phe.gov/about/barda/Pages/default.aspx

Michigan, and the University of Maryland, Baltimore. This contract is for approximately $163 million over the first eight years.

Novartis Vaccines Division will head a second Center, leveraging existing public-private investments by HHS in a state-of-the-art, multi-purpose facility in Holly Springs, NC, and working with North Carolina State University and Duke University. The Novartis contract is valued at approximately $60 million over the first four years.

Texas A&M University System will lead a third Center collaborating with GlaxoSmithKline Vaccines of Marietta, PA, Kalon Biotherapeutics of College Station, TX, and their extensive network of institutes. This contract is valued at approximately $176 million over the first five years.

Establishing the Centers achieves a core recommendation cited in the 2010 Public Health Emergency Medical Countermeasure Enterprise Review; a comprehensive, government-wide review called for by Secretary Sebelius to address challenges encountered in developing biodefense medical countermeasures. These Centers also address concerns raised by the President's Council of Advisors on Science and Technology in the August 2010 Report to the President on Reengineering the Influenza Vaccine Production Enterprise to Meet the Challenges of Pandemic Influenza, which called for flexible, nimble, and modern vaccine manufacturing technologies.[6]

BARDA and the CIADM have been critical components of the US Government's vaccine development response to the COVID-19 pandemic. [7][8][9]

Medical products provide an opportunity for the Australian Government to use its role as customer to support Australian R&D and manufacturing, while also protecting Australia's population and ensuring supply of essential medical products, including in emergencies.

The Government could support the development of products in areas where it thinks the product will be useful and it will be a potential purchaser- this includes pharmaceuticals, therapeutics and medical devices, as well as drug delivery mechanisms like Vaxxas.

The Australian Government already provides some of this support on an ad hoc basis. An example is the recent agreement reached with CSL in which the Government has supported the development of a new manufacturing facility here and has committed to buying vaccines.

> *'Global biotechnology leader CSL Limited (ASX:CSL; USOTC:CSLLY) today announced that Seqirus, a wholly owned subsidiary of CSL, plans to invest more than AUD$800 million in the construction of a new biotech manufacturing facility in Melbourne to supply influenza vaccines to Australia and the rest of the world.*
>
> *This investment decision follows the agreement with the Australian Government for the supply over 10 years of influenza pandemic protection for the Australian population, anti- venoms for Australian snakes, spiders and marine creatures and Q-Fever vaccine.' 16 November 2020*[10]

The USA's CIADM program provides a model for Australian Government involvement in a more systemic manner.

[6] https://medicalcountermeasures.gov/barda/core-services/ciadm.aspx
[7] https://www.hhs.gov/about/news/2020/07/27/hhs-reserves-and-rapidly-expands-manufacturing-capacity-for-covid-19-vaccines-at-texas-center.html
[8] https://www.tamus.edu/update-on-production-of-covid-19-vaccine-candidates-by-texas-am-system-subcontractor/
[9] https://www.medicalcountermeasures.gov/newsroom/2020/emergent-plasma/
[10] https://wcsecure.weblink.com.au/pdf/CSL/02309014.pdf

3. How fast are critical technologies taken up in this sector? What barriers to uptake?

As noted in our response to Question 2, the development of medical products, including pharmaceuticals, therapeutics, diagnostics and medical devices is a long and expensive process, typically taking more than a decade. However, the rewards for successful products, and the companies and countries that manufacture them, can be substantial.

To be successful, we need to ensure we provide a clear and rapid process for identifying and progressing research with commercialisation potential.

In Australia, we currently have some government funded commercialisation programs, but these are fragmented, each supporting only one part of the research and development pathway. For example, an NHMRC Ideas Grant may progress research to a particular point, but not typically fund the Proof of Concept experiment. This experiment may be able to be funded through an NHMRC Development Grant but requires a fresh application through the NHMRC's annual funding calendar; any successful application will be funded some 18 months later.

We need to streamline this current collection of separate grants and create a single process, where the ultimate objective of developing a new product is identified at the outset, and where progress towards this objective is better planned for and evaluated at each stage, with progress to the next stage and funding assured if the appropriate requirements (scientific and commercial) have been met. Doing this requires a new mindset, changes to what is funded, and when.

Central to this approach is a clearly defined outcome being worked towards, with clear criteria for success against which progress can be measured at key stages. This idea of clear, outcome focused research needs to be further developed as does the question of how research is identified as suitable for such a commercialisation scheme. Research Australia has looked at the question of measurement closely in the context of the MRFF and is happy to advise the Department on both research impact and return on investment models to measure success.

A co-investment approach such as that adopted in the Biomedical Translation Fund, where management of the individual commercialisation projects is devolved to by professional investment managers, may help provide the necessary rigor and overcome some of the existing barriers The BTF is best characterised as late-stage venture capital investment, well beyond the Proof of Concept stage, but there is an opportunity to introduce similar models at earlier stages of the commercialisation and investment cycle.

9. Is there anything else you want to say about the approach to critical technologies in Australia?

The Government's Modern Manufacturing Initiative has identified Medical Products as a priority area. A broad category, this includes, for example, pharmaceutical products. Australia already has world class research to support the development of new medicines and pharmaceuticals. We also have expertise in the manufacturing and supply chain for pharmaceuticals. The same is true of many other categories within medical products, and we congratulate the Australian Government on playing to our strengths.

26 of the world's nations accounted for 95% of global pharmaceutical exports in 2018, valued at $570 billion. The world's Number One exporter of pharmaceutical products was Germany at $94.1 billion, with 16.5% of global pharmaceutical exports. Number 26 was Australia, with exports of $2.5 billion, or 0.44% of global exports.[11]

In the same year (2018), Australia imported pharmaceutical products valued at $7.17 billion, or 1.26% of global pharmaceutical imports.[12]

Pharmaceutical manufacturing, including vaccines and serums, is a sensible area for Australia to seek to expand its capability, particularly in critical products. It is an area where security of supply is paramount; it is also an area where we have existing expertise in manufacturing and world leading expertise in life sciences that we can leverage. It is a growing market, and one where capability is relatively well dispersed around the developed world.

Research Australia submits Australia needs to set some clear and ambitious goals if we are to position ourselves up for the economic success the Prime Minister has stated as his Government's objective. One such goal would be to become a net exporter of key critical pharmaceuticals by 2035.

Achieving such a target will involve a focus on the Australian manufacture of new, high value pharmaceutical products in Australia. It would significantly boost our terms of trade in a key world market and create high value jobs. It would also create an ecosystem which would further support new research and commercialisation of new products.

Pharmaceutical products is the case study used here, but similar opportunities exist with other types of critical medical products and technologies, including diagnostics and medical devices. There is increasing evidence we can develop new products in Australia, capitalising on our world class research.

The Medical Commercialisation Research Fund, started in 2007, has an increasing suite of products under development at advanced stages. While there was a tendency even five years ago to license promising new products to international pharmaceutical companies to complete their commercialisation, we have a growing capability to undertake the later stage commercialisation of these products in Australia. The Government's Biomedical Translation Fund is following a similar trajectory, investing in the commercialisation of promising Australian research.

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[11] Sourced 19 November 2020 from https://atlas.cid.harvard.edu/explore?country=undefined&product=129&year=2018&productClass=HS&target=Product&partner=undefined&startYear=undefined

[12] Sourced 19 November 2020 from https://atlas.cid.harvard.edu/explore?country=undefined&product=129&year=2018&tradeDirection=import&productClass=HS&target=Product&partner=undefined&startYear=undefined

RESEARCH AUSTRALIA LIMITED
384 Victoria Street, Darlinghurst NSW 2010
P +61 2 9295 8546 **ABN** 28 095 324 379
www.researchaustralia.org