A Medical Research Institute Perspective
on
Public Support for Science and Innovation

Submitted by
Association of Australian Medical Research Institutes

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The Association of Australian Medical Research Institutes (AAMRI) represents 37 medical research institutes (MRIs) across Australia. The MRIs are independent, not-for-profit organisations, closely affiliated to hospitals and universities. The MRIs employ more than 6000 researchers and support staff, and train more than 1500 post-graduate students each year. They have a combined research income of more than $350 million dollars per annum, winning most of that in competitive grant funding. About half of this is derived from the NHMRC, and a significant amount is awarded by international funding agencies.

The AAMRI Institutes carry out much of Australia's most distinguished and world-renowned health and medical research, in almost every aspect of human health and disease and are major partners in commercialisation of Australian biomedical discoveries.

1. The economic, social and environmental impacts of public support

The role of public funding in the health and medical research (HMR) sector in Australia must be to fund basic research, from which the discoveries that will drive future innovation arise. It is important that public funding of HMR

- is adequate and sufficient to maintain a critical mass of scientific and medical experts with expertise in a range of different areas, in order to have the capability to respond to future and emerging health issues;
- has a strong investigator-driven component, because serendipitous discoveries made from basic research create the opportunities for translation;
- provides adequate funding for "proof-of-concept" studies; and
- encourages the careers of young investigators, who will become the next generation of leaders

Public Funding of Health and Medical Research Delivers Returns

Public funding for science and innovation in the HMR sector in Australia is absolutely critical for the health and welfare of the Australian population. The HMR sector has successfully produced many examples of basic, publicly supported research that have been translated into applications of great value to the community, either through improved health outcomes or direct commercial value. We believe that the NHMRC is the appropriate vehicle for administering public funding of HMR, since it is able to perform the function of priority setting and resource allocation within the sector.

Money spent on HMR is money invested in Australia's health and economic future and it generates returns by:

- keeping the Australian population healthy, increasing quality of life and longevity;
- keeping the Australian workforce productive by reducing time away from work due to, for example, illness and accidents; and
- reducing the cost of health care, e.g. usage of PBS medicines and/or hospital bed days, with improved techniques and technology, which contribute savings to the health budget.

The expense of medical research is very much less than the cost of health care delivery, which is now consuming such a high proportion of national budgets in every advanced country and will increase with our ageing and increasingly sedentary population. Additional examples of return on investment in HMR are provided at Appendices 1 and 2.

Public Support for funding HMR

The Australian community supports public funding of HMR and recognises the economic and social benefits resulting from that investment. (Research Australia Public Opinion Polls)

The Australian Government has recognised the importance of increased funding to HMR – after the Wills Review in 1999 and again, after the Grant review, in 2006 with the federal Budget announcement of additional $905 million for Australian Health and Medical Research over the next five years as a 'major investment in our future health'.

Such increases in Government investment are vital, because of the long lead times for economic outcomes from Health and Medical Research. .

It is also crucial that such investment be administered efficiently to deliver innovation that translates to health and commercial outcomes for Australia. We believe that the NHMRC is the appropriate vehicle for administering public funding of HMR, since it is able to perform the function of priority setting and resource allocation within the sector.

Public funding of HMR does not crowd out private funding

There is no evidence that public funding 'crowds out' private funding in health and medical research and innovation. On the contrary, while public funding in health and medical research increased 9% between 1993 and 2001 in Australia, private funding for basic research increased 13% in the same period.

The role of public sector funding of research is specifically to fund research that forms the framework of knowledge, which often cannot be captured directly as commercial benefit by the private sector. Paradoxically, this framework of concepts, methodologies and basic principles is the base on which all commercial discoveries also depend, but the inability of the private sector to gain direct and exclusive commercial benefit from this framework of knowledge means they will never fund it. Therefore, one role of publicly funded research is to create the environment in which the private sector can generally succeed through subsequent investments.

Public investment in health and medical research is also essential to ensure a public sector that is able to interpret research and apply it to the public good, as opposed to the private sector that has its own goals and responsibilities to shareholders. Public good goals may sometimes conflict with commercial aspirations and therefore cannot be left solely to the private sector. It also follows that it is the responsibility of the public sector to fund basic and applied research which has the potential for public good but would not be funded by the private sector for purely commercial reasons (e.g. by not being patentable, orphan or small market segments, product cannibalisation, etc). Important examples of critical public good areas in medical research include developing and communicating preventative health strategies, population and public health studies, health economics, biodefense and improved diagnostics

In 2005, AAMRI prepared a paper on this issue –Public versus Private Funding for Health and Medical Research- attached at Appendix 3.

Measurement parameters guide behaviours

In the area of HMR, measurement of inputs has little correlation with the impact of publicly supported research. Certainly the level of expenditure and the number of institutions and scientists is a reliable measure of the level of activity that will be produced, but the true impact of HMR can really only be measured by examining effects on the health and well-being of the Australian population.

It is absolutely clear that, to the extent that future funding is determined by past performance, the value assigned to different measures of performance will drive behaviours accordingly. Given this, it is essential that the altered behaviours are ones that will lead to the desired outcomes (greater positive impacts on knowledge, more competitive businesses, greater quality employment and national wealth, healthier society in body and mind etc). As a simple example, measurement of impact on knowledge by publication counts alone will encourage more publications but provide no incentive to publish high impact, long-term studies since the increased time and expense of these studies will only reduce the total publication count for an applicant. A better measure would be to determine the impact of published work on the overall body of knowledge by delineating the recognition and influence that the work has had. Similarly, in the commercial translation of research, simple counts of patents lodged, start-up companies created, consultancies etc will certainly see an increase in these activities. But real value is created when a patent is licensed and commercially developed, when a start-up achieves external capital investment and creates employment or creates an income stream etc. These latter activities represent a very small proportion of the starting pool but the greater investment of time and money required to achieve them and the much greater benefit that accrues to society must be recognized in the measures of performance. The same generic thinking can obviously be extended to measure impacts of research on health gains, cost savings and community well-being.

The NHMRC has had a Working Party investigating this issue for the last 18 months, and have made a very careful analysis of the way in which HMR outcomes can be quantified. This group have been developing a tool that aims to provide a (mostly) quantitative measure of the impact of research in the knowledge, economic benefit and health gain domains. In each domain significantly higher scores are achieved by research that can demonstrate real impacts. In the knowledge domain, impact is primarily measured by citation ranking that is international and field-specific. In the economic domain, the primary measures are levels of investment, commercial income and employment creation. In the health domain, the primary measures are improvements in health practice and/or cost savings. A significant difficulty using such a framework for grants and fellowships is the 10-15 year time-frame required for significant impact versus the typically 5 year time frames for assessment for renewal. This should not, however, be a problem in developing a national policy for R&D development, which should have a 20-30 year timeframe.

We suggest the Commission consult the NHMRC Working Party for further insight on this matter

2. Impediments to the effective functioning of Australia's innovation system

The biggest impediment to most of the elements of the innovation system in the HMR sector (knowledge transfer; technology acquisition and transfer; skills development; commercialisation; collaboration between research organisations and industry; and the creation and use of intellectual property) is the funding gap between the completion of an academic research project and the development of a commercially attractive proposal.

This is a world-wide problem but is especially acute in Australia. The problem begins at the patenting stage where the funds required for entering the national phase (international patent) are prohibitive for most academic organizations and cannot be legitimately sourced from research funds. This results in most academic groups seeking commercial licensing far too early (to pay for patents) and at a time where it is either too hard to gain commercial interest or the value of the intellectual property is heavily discounted because it is so early. This results in heavy commercial losses to Australia. A telling statistic is that while Australia has a 2.5% share of world scientific literature it has only a 0.7% share of world patents.

While the NHMRC has attempted to develop a mechanism for funding "proof of principle" research via the Development Grant program, this scheme is very limited. The ARC funds the Linkage Grants program, but unfortunately funding via this scheme is only available to university researchers and MRIs are ineligible for funding. This funding should be available on a competitive basis to all Australian researchers, and should not be limited to a particular research sector. This argument is further expanded in Appendix 1, Part 2.

In some cases it is attempted to build value by creating a start-up company with a minimal seed capital investment. However, the time needed to create value in the company usually sees the company run out of cash before it becomes attractive even to venture capitalists and even to the venture capitalists that have received Government funding to provide seed or pre-seed capital.

These problems could be more effectively addressed if the Government could fund commercialisation of research from academic organizations more effectively by providing pro-rata commercialisation infrastructure funding similarly to the way it currently block-funds scientific infrastructure funding (though this should be extended to medical research institutes to capture biotechnology investments). These funds should be auditable and dedicated to patent protection, maintenance of a business development office and pre-seed funding for start-ups. The funded organization is best placed to make its own choices from its research portfolio of commercialisation opportunities and recurrent funding could be based on the effectiveness of its commercialisation choices (using the outcome measures described above).

The current approach of funding venture capital consortia (seed and pre-seed funds) to identify commercial opportunities in academia has not worked well because;

(1) such consortia necessarily take a very short term approach to liquidity and therefore identify only late stage projects (hence the funding gap)

(2) there is no incentive in this funding model for academic organizations to improve their commercialization performance

3. Evaluation of decision making principles and program design.

The reason for Australia's low GERD is the very small component of BERD. This strongly exacerbates the funding gap described above and emphasizes the potential value of additional Government expenditure on commercialization infrastructure grants. By allowing institutions to develop their intellectual property to a more mature commercial stage, the pool of real commercial opportunities available to Australian business will increase and therefore encourage a greater investment by business in those opportunities. We are currently in a vicious cycle that can be broken by commercialization infrastructure grants leading to an increase in BERD and GERD.

The reasons why many other OECD countries have relatively higher levels of GERD and BERD than Australia, even though public support in those countries appears relatively less are probably many and varied. In some countries there is a much more accepted culture of interaction between academics and businesses. In some, the nature of business enterprises is more research intensive (high tech) than in Australia and therefore investment in R&D is considered a core activity. In others there is a bigger pool of investment funds willing to invest in higher risk ventures than in Australia and the unit invested in each business is more likely to lead to success of the business.

In considering what criteria are most appropriate in guiding the allocation of available public funding (past performance, national priorities, new ideas) the answer is that each of these criteria has its place. For established researchers past performance is a pretty good guide to future performance although one might want to track the timeline of their performance to ensure that one does not fund past performers who have become out of touch in recent years. Younger researchers or researchers who have had career interruptions should be tested primarily against the quality of their ideas. Similarly this scheme might be used to address specific calls for proposals in identified problem areas although in this case it would be applicable to all researchers. Within both of these categories some funding can be quarantined for applicants working in strategically important or priority areas. The major difficulty will be in allocating funding percentages to each scheme but this will constitute the major strategic decisions made by policy makers. In the HMR sector it is critically important that the overall level of funding is sufficient to allow for a high percentage of investigator-driven research, as we believe this category provides the basis for serendipitous discoveries that provide the underpinning of out innovation in HMR. We believe it is vital that funding for HMR remains largely administered by the NHMRC, given the need to assess and

Contestability in the allocation of public support for science and innovation — that is, competition for funding is of course necessary to ensure that the limited funds available are delivered to the projects most likely to produce the desired outcomes. The only disadvantages are that this increases the time delay between the idea and its initiation and it requires considerable effort on the part of policy makers to get the judging criteria right and on the reviewers to do their job diligently. These are opportunity costs but the alternative of not formally assessing and ranking proposals would make it difficult to justify that the expended funds were used in the best interests of taxpayers.

Different programs could be better coordinated to improve outcomes while minimising administrative and compliance costs through a huge range of measures. As mentioned below current academic funding schemes are considered grants-in-aid (partial funding) and the funding agencies hope that the additional funding required to fully fund a project will somehow be found from other sources. Paradoxically, if another grant is found to fund the project, the spectre of ‘double-dipping’ is raised. From the medical research institute’s perspective this is how we try and fully fund a research project. The senior researchers apply for NHMRC fellowships to fund their salary. They apply for an NHMRC research grant to fund the direct research costs and technical salaries associated with a project. The conventions and rules at NHMRC prevent them asking for all the direct research costs so additional funds are sought from the Institution. The Federal Government now provides 20c in the dollar of the NHMRC grants to fund indirect costs via the IRIIS scheme for independent medical research institutes. The various State Governments apply complex formulae to provide additional indirect costs. The real indirect costs required in MRIs are at least 60 cents in the dollar of the NHMRC grants but these are not met by any of these schemes and the shortfall is made up from the Institutional endowment funds.

It would obviously be much more efficient and transparent if all these funding mechanisms were directly linked to the research proposal. If the anticipated outcomes of the project are considered worthy of funding then all the components of funding should be delivered to the project team to ensure that the project can be delivered. As in the NIH funding system in the US the grant should be delivered in two components – the costs required to support all salaries and consumables and the indirect costs determined by auditing the individual institution.

Several funding schemes emphasize recent productivity (usually last five years) as one of the assessment criteria. This may seem natural because the funding scheme is usually for research to be carried out in the next few years and the funding agency needs to be convinced that the applicant is currently an active researcher. For many types of research however real societal outcomes from the research may take a decade or more to become evident (this is especially so in medical research where the time from discovery to clinical usage is often 15 years as a result of regulatory requirements). This problem should be able to be addressed by giving separate weightings to whole of career performance (perhaps divided by research active years) and recent performance depending on the aims of the funding scheme.

Almost all academic research programs are funded from multiple sources. Even when the primary funding is from Government there is a lack of integration of the funding for the research program. For example the direct costs of research are (inadequately) funded by research grants but the funding of researchers’ salaries (eg through fellowships) and the indirect costs of the research program (eg through research infrastructure block grants) are funded by completely different schemes so that consistent and full funding of the research is difficult to achieve. A business would not run its R&D program this way!

The concern about double dipping is misplaced as the result of the assumption that a research grant provides full funding for a research project. The concern ought to be that all research funding is applied to the purposes of the grant and there is no financial fraud or misdealing. This can be detected by random financial audits of administering institutions where expenditure against each grant can be acquitted.

Consequently most academic research programs have multiple funding and funders. One unfortunate consequence of this is that each funder may feel that they have IP rights as a result of their (partial) funding and many government (especially State) and philanthropic funders now include statements in their research contracts asserting ownership or a share in the commercial returns of the outcomes of the research program. The issue of multiple ownership of IP of course creates great impediments to commercialization and the issue of commercial returns to non-commercial funders may remove much of the institutional incentive to commercialise. The net result of these requirements by governments and philanthropic agencies is the exact opposite of what they desire – they prevent the development of products that may benefit society and they stifle the growth of new or existing commercial entities.

Appendix 1

Impact of Publicly Supported Australian Medical Research

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1. Examples of positive economic and social impacts of public support for preventive health research

"An ounce of prevention is worth more than a pound of cure."

Knowledge generated by public support for health and medical research relevant to disease prevention brings some of the greatest economic and social returns on investment in Australia. Yet these returns are often undervalued or worse, unrealised.

The immeasurable benefits of preventing infectious disease can be apprehended by simply comparing the economic and social circumstances of Western populations today with those two centuries ago. While the same infectious diseases remain major barriers to economic and social progress in the Third World (and are justly a focus of high-profile philanthropic support in the 21st century), Australia's main health barrier to productivity today is chronic disease. (Indigenous Australians, among whom both chronic illnesses and infectious diseases exact a heavy toll, are the exception.)

Next to cardiovascular disease, the foremost chronic disease process responsible for economic and social burden in Australia is cancer. Traditionally, seeking the "cure for cancer" has garnered most of the public's attention: treatment 'breakthroughs' have been hailed as signs that we are winning some battles (eg prolonged survival from breast cancer, childhood leukaemia, etc) if not the war against cancer. Increasingly however there is recognition that primary prevention ***upstream*** rather than treatment ***downstream*** will give the long-term victory over chronic diseases like cancer in the 21st century.

It comes as a surprise to many Australians that the cancer that costs our country by far the most is non-fatal skin cancer (1) –because treatment of skin cancer here is so common. Paradoxically skin cancer is also one of the most preventable cancers. Australia has the world's highest incidence of skin cancer; Australia leads the world in preventive research into skin cancer and sets the benchmark internationally for skin-cancer preventive community behaviour. Thus the socioeconomic value of public support for research into prevention of even the humble skin cancer is vast.

Another area of immensely valuable public support for research in Australia is Indigenous health research. The Cooperative Research Centre for Aboriginal Health (CRCAH) for instance is a notably low-technology Australian Cooperative Research Centre that symbolises the gains increasingly within our reach by dent of public suppport. CRCAH is a 'virtual' collaborative organization that aims to promote research partnerships involving key stakeholders, through increased Aboriginal participation and control and through better-defined ethical practices; to investigate health service delivery systems and the social determinants of health and health conditions; and to transfer research findings into policy and practice to improve primary health care practice. It also aims to reduce the burden of disease on Aboriginal communities and individuals and increase formal research training opportunities for Aboriginal people (2).

There are innumerable such examples of the potential for economic and social impact in the preventive knowledge being generated by public health researchers and others in Australia's medical research institutes and universities though this impact is too often ineffable. Transforming such health research into policy and practice is extremely difficult and is a high priority neither among governments nor among practitioners and communities at large, in Australia (3) and elsewhere (4). Indeed transforming our knowledge of preventive health into preventive behaviours is an everyday challenge that most can appreciate.

Quantifying the positive impact i.e. quantifying the lack of negative impact wrought by "successful avoidance of/ the absence of chronic disease" is also a formidable challenge. Notably some have tried. The Australian Chronic Disease Prevention Alliance, with financial support from the Australian Government, Department of Health and Ageing, has published a seminal report "Chronic Illness: Australia's Health Challenge. The Economic Case for Physical Activity and Nutrition in the Prevention of Chronic Disease"(5), for instance.

Most recently, the UK Evaluation Forum, an initiative supported by the Academy of Medical Sciences, the Medical Research Council and the Wellcome Trust, called for the development of improved methods to capture and evaluate the impact of medical research on national health and prosperity in the UK. Professor Martin Roland who chaired the published report's (6) working group, was quoted thus: "Government data testify to the excellence and efficiency of UK medical research, but despite significant activity in quantifying research outputs in terms of papers, citations and patents etc., there are few examples where the broader impact of medical research on health and wealth generation have been assessed. [….] Studies from the United States suggest that the investment in, for example, cardiovascular and stroke research is worth more than $1.5 trillion per year to the US economy: 20 times greater than the annual spend on such research. It is now time to consider how such an economic analysis might be applied to the UK. ….[However]… There is seduction in numbers and the UK should avoid becoming too wedded to quantitative indicators. It is extremely difficult to identify the impacts of medical research in what is usually a complex, slow and incremental process to eventual health benefits. Ultimately, there is no one 'best' method for evaluating research. Rather, a range of both quantitative and qualitative approaches should be used." There are lessons here for Australia.

2. An impediment to the effective functioning of Australia's innovation: lack of translational funding in biomedical research.

Australia produces some 2.9% of the world's scientific literature. It is quoted about 1.14 times more than average. Half of it is in the biomedical field. Australia also produces only about 0.7 % of the world's triadic patents (filed in the major jurisdictions of USA, Europe and Japan). We are thus more than 4 fold worse than the world average at translating our research.

A substantial percentage of public support for biomedical science and innovation is through medical research institutes, who produce some of the best biomedical research in Australia. Inexplicably, medical research institutes are not eligible for Australian Research Council (ARC) linkage grants, despite the fact that about 70% of Australian biotechnology is in the human therapeutic and diagnostic sector. The ARC Linkage Scheme has been highly successful in channeling intellectual property from Australian science into commercial entities. In any given year about 1500 linkage grants receive about $100k per annum from this scheme. The scheme requires a company to contribute money into the project, thus much of the due diligence regarding commercial potential is already undertaken by the company concerned.

An argument that is sometimes levelled against the ARC linkage scheme is that it can be exploited by some business enterprises who may simply invent 20 odd companies and invite investment bodies or some other university donors to "invest" in these companies. They can then invite staff to submit linkage grants with those companies. This is a spurious argument however: the ARC have very sophisticated systems that allow identification and culling of such applications from bona fide applicants to the ARC Linkage Scheme.

The NHMRC currently do not have a similar scheme. Indeed they invest a very small proportion of their research budget in the 'route to commercial market' for translational research. The NHMRC's Development Grant scheme does not have the critical elements for a good translational funding policy ie there is neither a real commercial partner nor any kind of monetary contribution from the commercial entity, and due diligence on the commercial potential is not assured.

That medical research institutes are ineligible for ARC Linkage Grants is a stark example of a missed opportunity for knowledge that is generated by public support of medical research institutes to be fully and profitably translated.

Beyond this specific measure, there is a range of other measures that might be profitably address to overcome the present lack of translational funding in biomedical research. These include:

- ARC Linkage Grant expenditure should be doubled.
- Patents and commercial activity should become KPIs for biomedical scientists in academic institutions and scrutinised as closely as their scientific publication output.
- Commercial activity & patents in academic institutions should be viewed as vital for the national interest and be appropriately supported.
- The large government investment in basic biomedical research should be exploited for contract R&D to support local biotechnology industries.

- Institutions should be encouraged to be major centres for local biotechnology R&D.
- More focus is needed on sponsored IP.
- Better assurances are needed for **inventor** returns for in-house IP.
- Adherence to Research Quality Frameworks should be mandated.

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Appendix 2

FURTHER EXAMPLES OF RETURN ON INVESTMENT IN HEALTH AND MEDICAL RESEARCH

Cardiovascular Disease

Source: Prof Garry Jennings, Baker Heart Research Institute

Publicly funded research into cardiovascular disease showed returns nearly 8 times the annual investment in terms of the positive effect on the health of Australians. (Access Economics Exceptional Returns The Value of Investing in Health R&D in Australia 2003 p 72)

Heart failure is both a common cause of death and of disability, particularly in the older population. 30,000 new cases are diagnosed each year (AIHW: Field 2003) and over 40,000 hospital admissions each year.

Case studies:

1. Mark Cooper (Baker MRI) and his research on ACE inhibitors preventing kidney disease in diabetics has resulted in the rate of renal failure and use of dialysis being reduced by 30% in diabetic patients.

2. David Kaye, Murray Esler and Garry Jennings (Baker MRI) demonstrated that use of beta blockers reduced mortality in those with heart failure by 50%. Another observation that moderate exercise in heart failure patients reduced the sympathetic drive to the heart in a similar way to beta blockers and also improved physical capabilities and quality of life this has led to the introduction of physical rehabilitation programs for heart failure patients (rather than bed rest as in the past).

The use of beta blockers and exercise programs have shown a flow-on effect, improving quality of life after heart failure and reducing hospital readmissions. This research has now been incorporated into the Heart Foundation guidelines for patient treatment.

Infectious Disease- Rotavirus Vaccine Development

Source: Dr Moira Clay, Murdoch Children's Research Institute

Rotavirus was discovered by Ruth Bishop and Graeme Barnes at the Royal Children's Hospital in 1973. Work in this area is continuing today as part of the Enteric Virus Research Group at Murdoch Children's Research Institute.

The main impediment to being able to translate this work to a commercial vaccine at the time was the failure to secure industry support of several million dollars in the early 80's, despite around 30 companies being approached. Failure to take up this discovery was multifactorial:

- the main focus of the work was paediatrics, and thus not viewed as being broadly applicable,
- community perceptions were that rotavirus infection was basically gastroenteritis and not life threatening,
- there was a low risk /low return approach to investment, and
- geography.

This year, 2006, both GSK and CSL/Merck have released commercial vaccines. The World Health Organisation has recommended that every child in the world be vaccinated for rotavirus, which highlights the potential health and economic benefits.

The current priority is to obtain a vaccine that can be used in neonates, thus maximising opportunity for administration, especially in the third world, ahead of the high risk period for intussusception. Murdoch Children's Research Institute has a competitive advantage in this regard, given that the vaccine has been raised to virus isolated from newborn babies at the Royal Children's Hospital.

Public health programs

Source: Dr Moira Clay, Murdoch Children's Research Institute

Public health programs such as the evidence-based school physical activity program in South Australia, developed by Terry Dwyer at Murdoch Children's Research Institute, which recognised the need for children to have a period of physical activity every day have now been withdrawn due to lack of funding. The major impediment has been the failure to recognise how health outcomes intersect with other sectors such as education.

PUBLIC VERSUS PRIVATE FUNDING FOR HEALTH AND MEDICAL RESEARCH

This paper has been prepared for AAMRI by Dr Julian Clark, Head, WEHI Business Development Office, to support the *Accelerating Discovery and Capturing the Returns* document prepared by AAMRI, ASMR and Research Australia, which argues the case for increasing the funding base of the NHMRC over the next five years, 2006-2011, as recommended in *Sustaining the Virtuous Cycle for a Healthy, Competitive Australia,* the report of the Investment Review of Health and Medical Research Committee, chaired by Mr. John Grant.

SUMMARY

Increased public funding of medical research is highly unlikely to "crowd out" private investment in Australia. Experiences from developed economies and particularly the US show that government funding of research leads to enhanced outcomes through subsequent public good outcomes and commercialisation. The purpose of government funds from a commercialisation perspective is to establish proof-of-principle and "de-risk" a private investment.

Enhanced public sector funding in Australia is critical due to several key issues and these include:

- The positive impact of public funds on broad capability development, public good and contribution to commercialisation initiatives
- The need to address areas of low attraction to private investors (e.g. infectious disease, vaccines, orphan/small market indications)
- Increasing global academic involvement in drug development to attract private sector partners
- A relatively weak philanthropic and endowment culture
- Loss of top scientists and limited attraction due to restricted career opportunities
- Low level of engagement of Australian private sector player in early stage research and development
- The need to address prevention and public health issues that remain less attractive to private sources of funds
- Enabling access to essential "big science" capabilities
- Attracting the best possible postgraduate students

The argument for increased public sector funding of Australian biomedical research is supported by the following:

- The "valley of lost opportunity" – the major funding gap between public sector basic and directed research and private sector investment that prevents value creation and translation
- In spite of presenting some of the most compelling development opportunities, medical research institutes are not eligible for pre-seed funds
- The poor relative performance of Australia in R&D investment relative to other OECD economies
- -both public and private investment
- The characteristics of the weak but growing business base in Australia
- Increasing engagement of Australian investors with sources of funds that establish proof-of-principle, Comet and Commercial Ready funds.

Background

The role of public sector funding of research is specifically to fund research that forms the framework of knowledge, which often cannot be captured directly as commercial benefit by the private sector. Paradoxically, this framework of concepts, methodologies and basic principles is the base on which all commercial discoveries also depend, but the inability of the private sector to gain direct and exclusive commercial benefit from this framework of knowledge means they will never fund it. Therefore, one role of publicly funded research is to create the environment in which the private sector can generally succeed through subsequent investments.

Public investment in health and medical research is also essential to ensure a public sector that is able to interpret research and apply it to the public good, as opposed to the private sector that has its own goals and responsibilities to shareholders. Public good goals may sometimes conflict with commercial aspirations and therefore cannot be left solely to the private sector. It also follows that it is the responsibility of the public sector to fund basic and applied research which has the potential for public good but would not be funded by the private sector for purely commercial reasons (e.g. by not being patentable, orphan or small market segments, product cannibalisation, etc). Important examples of critical public good areas in medical research include developing and communicating preventative health strategies, population and public health studies, health economics, biodefense and improved diagnostics.

Public versus private sector funds

The proposition that government funding crowds out private sector investment in research has been debated since the 1960s[1]. The argument is that private sector sources of funds become less engaged in research when governments provide funds, and the private sector therefore begins to rely on such funds to provide a pipeline of later stage development opportunities[2]. Furthermore, this proposition is usually debated on the basis of major economies such as the US and Japan, and is considered to be supported by examples of private sector investments in research which in reality are overwhelmingly dominated by ICT, engineering and defense. Indeed, even in these economies, the majority of the basic research is publicly funded, then licensed to corporate ventures.

Specific examples from the US illustrate the importance of high levels of government funding if there is to be a nexus between investment in science, translation to deliver outcomes and commercialisation. The Massachusetts Institute of Technology (MIT) is a world leader in translating basic research into commercial and public good outcomes and provides indicators with respect to best practice[3]. In 2003 MIT created 17 new spin out companies, negotiated 90 commercial licenses and filed 238 US patents. This result was achieved from a research budget of US$994 million, 87% of which was from government sources, 5% from non-profit sources and 8% from the profit/corporate sector. Royalties from commercialisation amounted to 2.7% of

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[2] Cotter, Ashiya & West (2001) Commercialisation Models at US Research Institutions, Harvard Business School Note N9-602-119
[3] http://web.mit.edu/tlo

the annual research budget.

Details of the Langer Laboratory at MIT[4] give an insight into the importance of government funds in the development of commercial opportunities and the success in attracting private sector funds when government funds increase. The Langer Laboratory is a leader at MIT and specialises in biotechnology and related materials sciences. The laboratory has a track record of more than 500 patents files, more than 100 licensing deals and more than a dozen start-up companies. Over 5 years to 2003 the Langer Laboratory has had an annual increase of 25% government funds. During this period 79% of funds were from government sources, 7% from the non-profit sector and 10% from the profit/corporate sector. In these five years 4 companies were created, 199 patents submitted and 159 peer-reviewed articles were published from a total research investment base of US$24.7 million.

The success of the US in commercialising medical research is driven not just by a large corporate sector willing to invest in translation of basic and directed research, but by a strong philosophy of public investment in research. The investment by the US National Institutes of Health over the 10 years from 1991 to 2001 highlights this commitment to building a strong and competitive foundation for subsequent translation into outcomes[5]. Over these 10 years funding increased 2.3 fold, the number of research grants (RO1) increased from 14,000 to 19,000 per year, the value of each grant increased from US$200,000 to $330,000 and the number of postdoctoral fellows increased from 20,000 to 30,000

Some issues for Australia

The case for increased public investment in Australian medical research is strong and specifically related to Australia's unique circumstances. This investment is required to secure both public good outcomes and research and develop opportunities to a stage when the private sector is prepared to invest, irrespective of area. It is extremely dangerous for Australia to entertain the argument that public medical research funds crowd out private funds since:

a) there is no significant local business capacity or capability to make the levels of investment required to deliver significant health outcomes to Australians,

b) this is not the experience in other developed economies, and critically

c) there is a major funding gap preventing translation of basic research into commercial and public good outcomes

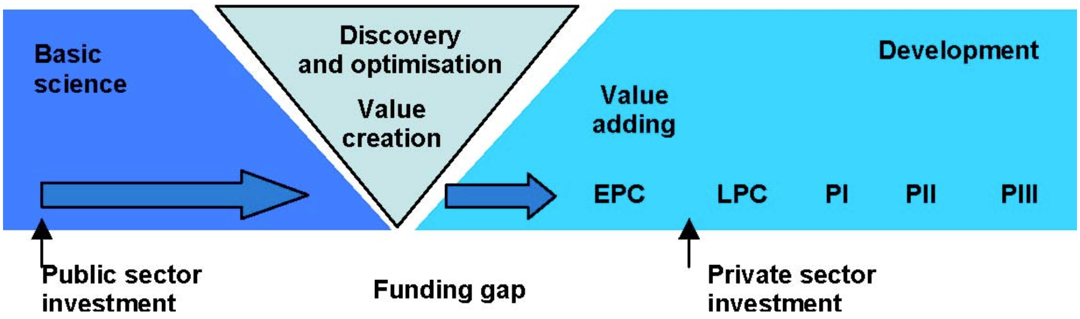
Critical issues to consider when entertaining the notion that public funding suppresses private investment are illustrated but not limited to the following examples:

Australia's "valley of lost opportunity" -The major gap between public investment in

[4] Bowen K (2004) The Langer Lab: commercialising science. Harvard Business School Case Study 9-605
[5] West, Sagar and Ashiya (2004) Judah Folkman and the war on cancer. Harvard Business School Case Study N9-604-091

basic research and private sector investment in downstream, "de-risked" opportunities must be addressed. Rather than there being competition and crowding out of private investment by public funds there is in fact a major gap in required funding that is currently not being filled by either sector. As a consequence this gap has created a serious market failure and the frequently experienced "valley of lost opportunity" (Figure 1). Such a gap is experienced in other economies however, Australia does not have the strong culture of alumni, angel capital and early risk ventures, strongly supportive tax environment or public entrepreneurial approaches that support medical and biotechnology opportunities in other developed economies. The need to address this gap has been recently emphasised in a report to the Prime Minister's Science Engineering and Innovation Council[6].

Figure 1: The "valley of lost opportunity" in Australia[7]



The real challenge for Australia is to find ways of bridging the funding gap required to achieve engagement with private capital. The importance of bridging this gap is further illustrated by the real value that is created during the discovery and optimization (proof-of-concept) stage of translation. Without this investment true outcomes from public investment in basic research will not occur. The experience of Rochester University in the US provides a clear precedent. COX-2 is a target for inflammatory conditions, was discovered by Rochester and sales of drugs targeting COX-2 are several billion. After a US court ruling Rochester University receives no commercial returns since Pfizer (the leading company) created the real value through composition of matter claims related to specific drugs[8]. This experience highlights the need for public funds to extend to early discovery and proof-of-concept if value is to be captured.

Access to pre-seed funds -The funding gap noted above is further exacerbated by the inability of medical research institutes in Australia to access pre-seed funds. These funds were specifically established to facilitate commercialisation of early stage development in order to attract later venture capital, and in spite of presenting some of the most

[6] PMSEIC (2005) Biodiscovery working group report

[7] EPC- early preclinical, LPC – late preclinical, PI – Phase 1 clinical trials, PII – Phase 2 clinical trials, PIII – Phase 3 clinical trials

[8] US court of Appeals for the Federal Circuit (2004) University of Rochester vs Searle, Monsanto, Pharmacia and Pfizer (03-1304, July 2 2004)

compelling investment opportunities medical research institutes are specifically excluded. Ironically, the pre-seed funds are having difficulty finding projects in which to invest and the limit of $1 m for investment does not permit adequate development to the stage of follow-on investment[9]. This absence of public pre-seed funding has not lead to increased investment from the private sector thus demonstrating that public funds are not crowding out private sector funds and that private sector funds do not fill the translation gap.

Infectious disease – For many years there has been a major under-investment in infectious disease in both the public and private sectors, and the private sector has had every opportunity to seriously address infectious disease and has certainly not been crowded-out by public sector funds. The threat of epidemics, pandemics and new adventitious organisms has been present for many years. The threat of antibiotic resistance has been well known with continuing global increases in severity across a wide range of diseases. The combined public and private sector investment in HIV for the developed nations is generally regarded as being successful but it required major public funds to initiate research activities – industry followed. The threat of Creutzfeld Jakob Disease has been funded from public sources and in spite of the possible ramifications there is surprisingly little global investment from industry. The recent interest in influenza is driven by a public fear of a pandemic with response from industry more related to stockpiling existing drugs and preventing government exercise of “march-in-rights” rather than significantly increasing investment in research. It should also be noted that the current anti-influenza agents are based on Australian science initially funded by the public sector (e.g. *Relenza*).

Vaccines -Related to the lack of investment in controlling infectious disease is the general market failure to invest in vaccines. This failure was clearly exposed by the US government’s attempts to find capacity for vaccines related to bioterrorism post “September 11”. Due to lack of profitability and liability concerns, the private sector vaccine players reduced to only three serious global companies in the last two decades. In fact most private sector interest in vaccines is related to veterinary applications and there is strong subsidisation from government funds. In this case it is clearly incorrect to argue that public funds have driven out private funds -public funds are essential to fill an important research and development gap largely ignored by the private sector. The recent success of the HPV vaccine invented and researched by Ian Frazer at the University of Queensland and subsequently developed by CSL and Merck illustrates the opportunity for continued major advances from publicly funded research. Neither CSL nor Merck alone had the specific capabilities and intellectual property provided by this public investment in research that should see a major impact on prevention of cervical cancer.

[9] Hopper K, Thorburn l (2005) Bioindustry review

Advancing the war on cancer -Over two decades ago the US government declared war on cancer and this focus on increasing public funding of cancer has been followed in all developed economies. Rather than drive out private investment in cancer this public investment has resulted in major breakthroughs that have attracted an unprecedented increase in the global private sector investment transforming oncology into a major strategic focus of many small and large companies[10].
Increasing academic involvement in drug development -The drug development landscape has changed radically in recent years. The opportunity for Australia is highlighted by a global trend for academia to become successfully involved in drug development and translation. This trend is a consequence of the increasing academic nexus between chemistry and biology, the migration of large pharma to late stages of clinical development and lack of angel or seed capital. Examples of very successful academic drug development centres include the Victorian Pharmacy College Centre for Drug Candidate Optimisation (Monash University, AU), Centre for Cancer Therapeutics (UK), Auckland Cancer Society Research Centre (NZ), University of Helsinki Viikki Drug Discovery Technology Centre (Finland), Vanderbilt Institute of Chemical Biology (US), Harvard Centre for Neurodegeneration and Repair (US), University of Kansas Centre for Drug Discovery (US), University of Dundee Centre for Interdisciplinary Research (UK), Northern Cancer Centre (UK) and PharmaStart (Stanford and University of California, US). Rather than discourage private sector funds these initiatives largely funded from government sources have provided a means of engagement with the private sector and resulted in the creation of many spin-out companies and commercialisation licenses.

Areas of low direct return -There is general private sector failure to engage in health areas that promise low financial returns. Private sector funds tend to be directed towards major indications where “blockbuster” products must result in >$1 billion in peak sales. Therefore, there is a major under-investment by the private sector in developing world health concerns (e.g. malaria, tuberculosis, leishmania) and diseases with relatively low incidence but high social and economic impact (e.g. coeliac disease). The business sector will invest in areas where an economic return to shareholders can be demonstrated within a reasonable period. The recent interest in some areas shown by “large pharma” such as cheaper drugs for Africa, support for malaria vaccines, or making *Tamiflu* available to governments, is driven by public relations and has no bearing on a strategic investment in science areas that show little direct economic return for the companies. The argument for increased public funding of medical research is further strengthened by Australia’s obligation to use its intellectual strengths for the benefit of the international community. Co-investment in public-private development initiatives is increasing but is dependent on public funders taking a lead role[11].

Philanthropic sources and drivers – The private sector also includes not-for-profit sources of funds such as philanthropy, endowments and trusts. Unlike the US or UK, Australia does not have a strong culture and depth of philanthropic support of medical

[10] Pharmaprojects (2005)
[11] Wellcome Trust (2005) The new landscape of neglected disease drug development. London School of Economics and Political Science

research. While the Walter and Eliza Hall Institute, the Garvan Institute and the Murdoch Institute are often cited as being good examples of Australian recipients of philanthropy and endowments, they are highly dependent on public funds for advancing medical research. Failure to capture increased funding from the NHMRC and offshore public funding bodies such as NIH will seriously curtail these and other Australian institutions' global competitiveness. Examples of two major sources of philanthropy illustrate that this source of private funds cannot substitute for an increased Australian public investment in medical research. The Bill and Melinda Gates Foundation provides competitive grants but these are entirely focused on global challenges for *developing* nations. Atlantic Philanthropies has made major infrastructure investments in Australian medical research but does not cover the all-important operating funds required to deliver research outcomes. Furthermore, philanthropists invest in science organizations with a proven track record of delivering outcomes from public funds.

Continued loss of scientists – Due to Australia's poor business investment in medical research, our scientists will continue to move to more favourable development environments off-shore if adequate public funds are not available. There is a disproportionate number of Australian scientists in overseas medical research and development environments – both public and private. This reflects the limited opportunities in Australia. Public investment in medical research and a commensurate encouragement of development at the academic/industry interface and private sector investment is essential for Australia's science base to remain internationally relevant. Public investment in research and careers is essential to growing the national capacity[12]. In fully integrated economies such as the US and UK there are opportunities for scientists in both the public and private sector that simply do not present in Australia. If Australia were to rely on the private sector for increased investment in medical research, a continued loss of skills off-shore would be certain and, importantly, attempts to attract expatriots and world leaders would be undermined.

Australian industry response -One can observe that the various schemes[13] used to compensate pharmaceutical companies for the lower prices of pharmaceuticals under the PBS have not resulted in major investment by these companies in early stage drug development in Australia. Such companies have not been crowded out by government funds, they have in fact been offered an incentive but elect to invest in later stage product development rather than significant early investment in research and discovery in Australia. *Kapanol* (Faulding/GSK) and *Relenza* (Biota/GSK) still remain the only drugs fully developed in Australia in recent times.

Market investors in Australia focus primarily on resources and service business sectors and will cyclically invest in technologies driven by medical research. Although there is

12 Wood FQ ed (2004) Beyond brain drain: mobility, competitiveness and scientific excellence. Centre for Higher Education Management and Policy, UNE, Armidale.

13 Factor F, PIIP, P-3

no actual shortage of capital (e.g. superannuation funds) Australia does not have the consistent culture of investment in health and medical research evident in the US and UK. This lack of private sector investment is partly due to a) risk aversion, b) requirement for short-term returns, and c) fewer mature opportunities for a full health investment portfolio. It should be noted that the major relative decline in NHMRC funding in the late 90s did not result in a dramatic private investment to fill the "opportunity void".

Prevention and public health – In reality there is little incentive for the business sector to invest in prevention and public health research due to the low likelihood of intellectual property positions in these areas. With respect to prevention, the greatest opportunity for commercial investment lies in diagnostic and prognostic tests. Failure to increase public investment in prevention and public health will significantly increase future social and economic burdens. Importantly, there is an increasingly intimate link between knowledge of basic biology, clinical science and epidemiology and therefore a balanced public research investment is required and highly unlikely to come from business investment.

Collaboration and "big science" is increasing – Contrary to the view that medical research can rely on the serendipitous findings of small research groups is the need to access "big science" resources. Such resources are not provided by the private sector in Australia and both infrastructure and operating funds are essential to becoming competitive and achieving translation outcomes from our research investment. Currently, Australian medical researchers require collaborative investments in systems biology, informatics, imaging, synchrotron, NMR, animal facilities, robotics and high throughput capabilities among other investments. These are not the realm of the traditional small biomedical research group and the private sector has largely failed to make any significant contribution to such core capacities in Australia.

Impact on postgraduate students -Postgraduate students remain both the "engine room" and future of global biomedical research. A broad soundly based environment of scientific inquiry is essential to their training and development. This environment must include sufficient funds, committed supervision and importantly, strategic consistently throughout their candidature. It is important that Australia invests further public funds in postgraduate students in biomedical science in order to secure a competitive future. Private sector funding of students is thwart with challenges, not least of which include publication and confidentiality issues and changes in company priorities or fortunes.

Australian competitive position

Medical research and translation of its benefits remains tightly dependent on public sector funding and in fact it is well established that such funding presents as a wise social and economic investment with substantial returns to Australia[14]. In the medium term, and probably

[14] Access Economics (2003) Exceptional returns: the value of investing in health R&D in Australia. Australian Society fort Medical Research.

the long term, it is critical that public sector funding increases in this area due to the continued market failure with respect to adequate private sector investment in medical research in Australia. This is a strong argument in other developed economies but Australia finds itself in a vulnerable and under-performing strategic position. The current public investment in medical research in Australia has clearly not crowded out the private sector and the case for increased public investment in Australian medical research is based in part on two critical areas:

a) Poor relative investment performance

The potential for significant private sector investment in medical research in Australia must be considered in the light of the current poor relative performance. Total investment in research and development in Australia ranks poorly with respect to most other OECD countries, for both public and business investment. Total research and development investment as a proportion of GDP is 1.62% with business investment in research and development being 0.89% of GDP[15]. However, the ratios for investment in health research and development as a proportion of GDP are much weaker, with a total investment of 0.10% and a business investment of 0.06%.

Company researchers per 1000 total employed in Australia is less than half the OECD average and indicates a current low business ability to compete globally with insufficient private researchers to deliver research and development outcomes[16]. Since the majority of these business researchers are employed by companies in the resources, minerals, engineering and ICT sectors, the competitive situation for business medical health research is even weaker. Less than 10% of business investment in research and development is in the medical science sector and more than 80% is in the engineering/software sectors[17].

b) Weak business base

Business funds approximately 25% of all health research and development in Australia. However, on closer examination the fact that 87% of research and development in the public sector is financed publicly and 74% of private research and development is financed privately illustrates the lack of relationship between the two investment flows[18]. There is no evidence to suggest that public investment has crowded out business interest in Australian medical science. To the contrary, schemes such as Comet and Commercial Ready are genuine incentives to encourage earlier engagement from the private sector.

The most important aspect to comprehend from Australia's business investment in medical health research and development (approximately $280 m per year, of which approximately $200 m comes from the pharmaceutical industry) is the fact that the majority is related to

15 ABS (2005) Research and experimental development, business (8104.0)
16 IPRIA (2003) Assessing Australia's innovative capacity in the 21st century
17 IPRIA (2005) R&D and intellectual property scorecard (1444.2639)
18 Access Economics already cited

later stage clinical development and trials[19]. Business has elected to invest a very low, and in reality insignificant amount, in national basic and discovery medical research. The established business players in Australia such as CSL, Mayne, ResMed, and Cochlear invest primarily in product concepts and increasingly reflect the global trend for "de-risking" through encouraging earlier academic investment and only engaging in later stage financing once the product concept has been established. Venture capitalists invested $380 million over 5 years[20] in all biotechnology and healthcare initiatives in Australia against a cumulative NHMRC budget of >$1.5 billion. Most of this venture capital investment related to projects where products had been identified, i.e. very little or currently no funds are available for early stage discovery research.

In summary, it is strongly argued that a failure to further increase public investment in medical research in Australia presents a real threat to evidence-based healthcare and delivering competitive outcomes from an essential public investment in basic research. Public funds do not crowd out private funds in the context of Australian medical research and in fact provide the essential link to discovery activities, proof of principle and translation to the clinic through research-based clinicians. It is this proof of principle that is required before business investments are made and it is firmly believed that increased public investment in research is in fact required for both public good and improved commercial outcomes.

[19] Productivity Commission (2003) Evaluation of the pharmaceutical industry investment program

[20] Hopper K, Thorburn L (2003) Bioindustry review