**Pharmaceuticals Industry Strategy Group**

# Directions Paper

**September 2008**

Senator the Hon Kim Carr
Minister for Innovation, Industry, Science and Research
Parliament House
CANBERRA ACT 2600

Dear Minister

On behalf of the Pharmaceuticals Industry Strategy Group (the Group), we have pleasure in presenting the Group's directions paper to you for your consideration.

The Group considers that the Australian pharmaceuticals industry faces significant changes in the global operating environment. These have been triggered by the increasing cost of drug development, falling R&D productivity, rapid technological change, increasing regulatory pressures and evolving health procurement practices. Collectively, they will challenge the sustainability of the global and Australian pharmaceuticals industry and, consequently, the companies and individuals of which it is composed. These changes, while challenging, also provide growth opportunities that have the potential to create annuities for Australia, delivering broader social and economic benefits to the whole community.

The future of the Australian pharmaceuticals industry will be determined principally by how it responds to these global challenges, none of which are easily ameliorated by national governments. Nevertheless, the Australian Government has a role to play in supporting the Australian industry's transition to a more technologically sophisticated, knowledge intensive, value adding industry that is more resilient to external shocks and better able to thrive in the face of these external pressures.

A viable and sustainable pharmaceuticals industry requires:

- predictable, timely and transparent regulatory and reimbursement systems that provide companies with a clear and streamlined path to market;
- an appropriate and balanced intellectual property regime;
- strong and effective capital markets that will fund high risk projects that are of high quality and have potential commercial returns;
- competitive taxation arrangements that provide incentives for companies to invest in relatively high risk activities like R&D or complex, value adding pharmaceutical manufacturing;
- an appropriately resourced tertiary education sector capable of producing high quality, job ready, science and medical research graduates; and
- strong and effective collaboration between industry and academic research.

While some of these outcomes are outside the scope of the review, the Group notes that they remain important to the Australian industry's long term viability.

The Group has developed a package of measures that it believes will increase investment in the Australian pharmaceuticals industry and leverage its world class medical research base to bolster Australia's ability to compete globally as a centre for high quality R&D, clinical trials and value added niche manufacturing (such as injectables, biologics, vaccines and blow fill seal based products).

These measures include strategies to:

1. encourage strategic investment in pharmaceuticals R&D, manufacturing and infrastructure;
2. increase Australia's attractiveness as a location for clinical trial activity; and
3. improve pharmaceuticals skills and education.

The Group does not view these three measures as alternatives, but rather as part of an integrated package. Measures 2 and 3 are not costly and should be pursued. The first measure is likely to be the most costly. Hence, while it can also be expected to deliver the largest net economic and social benefit, it will require more scrutiny in the context of broader Government priorities. The Group is aware that the broader innovation framework is being examined in another forum. Pharmaceuticals is an innovation-intensive industry, likely to be affected by changes in Australia's National Innovation System. The Group has steered away from measures that are better addressed at a broader cross-industry level, and has focused on measures that could complement changes at the national level.

The Group is mindful of its responsibility to develop proposals that will deliver a net social and economic benefit to the Australian community by 2020. Given the long lead times for most pharmaceutical projects and their innovative nature, it is possible that benefits may not be fully achieved within this time frame. Consequently, the Group has focused its recommendations on those that it considers have a significant likelihood of delivering at least initial net economic and social benefit in the short to medium term.

In developing these draft recommendations, the Group also noted that many aspects are not only relevant to the pharmaceuticals industry, but would also be relevant to the broader medical science sector.

Subject to your views, the Group intends to consult more broadly on the recommendations developed in this draft directions paper with stakeholders in the academic and medical research sectors. The Group will incorporate these views and refine its recommendations accordingly. The final report will then be presented to you by the end of the year.

On a final note, we would like to thank our colleagues and fellow Group members for generously devoting so much of their time and energy. While individually we have different perspectives, we all agree on the importance of a sustainable, viable, and value adding Australian pharmaceuticals industry. We are all committed to working constructively with Government to create an operating environment that enables the industry to flourish – to the benefit of all Australians – in an increasingly complex and globally competitive world.

Yours sincerely

*Original Signed By*

Brian McNamee
Co-Chair
Pharmaceuticals Industry Strategy Group

*Original Signed By*

Craig Pennifold
Co-Chair
Pharmaceuticals Industry Strategy Group

30 September 2008

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## Executive Summary

The pharmaceuticals industry is global in scope, with a value chain that is similarly global: promising research is sourced from wherever it emanates; pre-clinical research is generally conducted in suitably scaled units located close to head offices or large commercial business units; clinical trials are conducted by appropriately qualified investigators based at suitable hospitals and research centres around the world, placing a premium on speed, cost and quality; medicines are developed for global markets and manufactured from global networks of large scale production sites for international markets. There is intense competition for capital, for skilled resources, and for research prospects that have the potential to become useful medicines.

For most of the last three decades, the pharmaceutical business model has been based on vertically integrated multinational corporations (MNCs) developing 'blockbuster' medicines from in-house resources. Over the last decade, this model has become more fragmented under the increasing pressure of costs and duration of drug development, falling R&D productivity, the rise of new technologies, the increasing ability of smaller companies to monetise their intellectual property without first having to commercialise a product, and increasing competition from generic medicines when patents expire.

Many originator pharmaceutical companies are increasingly looking to reduce the risk and cost of drug development by in-licensing or acquiring potential drug targets from smaller, highly specialised biotechnology companies. These smaller biotechnology companies not only offer prospective biological agents that might be useful human therapies, but also offer expertise in a range of technologies valuable to larger pharmaceutical companies, such as identification of new drug targets and biomarkers.

Biotechnology will play an increasingly important role in the drug development process and the companies and research institutions that possess these technologies will represent a growing proportion of the industry's innovation effort. Australia is well placed to exploit this accelerating trend, with around 470 specialist biotechnology companies that can act as providers of new product opportunities and technological expertise to pharmaceuticals companies in their quest to develop new drugs.

The global industry's inability to develop sufficient new drugs to replace existing blockbusters - US$100 billion of which will move off-patent by 2012 – has led to a marked reduction in the value of the sector, and is particularly marked for the traditional large MNCs. The rapid rate of patent expiry has been matched by vigorous competition from and significant growth in the generics sector, which specialises in the manufacture and sale of off-patent small molecule medicines. At the same time, there has been major global consolidation of the industry over a relatively short time frame. An obvious rationale behind such consolidation is the opportunity to reduce costs through eliminating duplication of functions from R&D through to manufacturing and marketing.

The shift to out-sourcing of innovation and early stage R&D has resulted in continued expansion of the biotechnology sector, but this has been off-set by cost cutting resulting in global job losses in the originator sector. These pressures are particularly prominent in manufacturing (where they are associated with initiatives to centralise and upscale facilities in tax advantageous and low cost jurisdictions) and in commercial costs. A number of MNCs have announced plans to significantly reduce their numbers of global manufacturing plants, moves which are affecting Australian subsidiaries of multinational companies. These pressures will remain and Australian operations will continue to be affected by the global

industry's adjustment to lower R&D productivity and the need to reduce costs. Significantly, the value add of Australia's pharmaceuticals manufacturing has declined over the last decade from around 80 per cent formulation to just 45 per cent, with the balance replaced by packaging activities.

The changing global environment presents a number of challenges and opportunities for the Australian industry. If it responds effectively, the Australian industry will look significantly different in ten years time to what it does today. Currently, the industry employs 40,000 people, spends over $750 million a year on R&D, has a turnover in excess of $18 billion and is Australia's second largest manufactured export provider To place this in context, in 2007 the global pharmaceutical market was estimated to be worth US$712 billion with a total R&D spend of around US$67 billion. The comparatively low ratio of R&D to expenditure in Australia, and is an indication that there is scope to significantly raise the value added component of the domestic pharmaceutical sector.

The industry generates a relatively small amount of manufacturing value add (one symptom of which is the low and falling level of capital investment), has a weak track record of taking Australian products into later stage development and has few companies, probably just one, that could be considered scaled centres of excellence in a global sense. The Group does not consider that this is a solid profile for a sustainable industry. The future will depend on moving away from activities which are vulnerable to increasing competition from low cost competitors and from out-licensing discoveries at an early stage of development.

The Group therefore considers that the thrust of pharmaceuticals policy should be to:

- provide the knowledge, research skills base that underpins the sector and wider innovation system;
- support the industry to develop Australian technology and innovation to a later stage of development before out-licensing and to shift its profile to develop areas that deliver a specialised and sustainable competitive advantage; and
- for industry to seek to compete internationally on quality and capability rather than on the basis of lowest cost.

Key drivers of investment in the Australian industry are:

- The changing nature of medicines;
- *R&D* – quality of the scientific and medical research base and infrastructure, and the strength of the intellectual property (IP) regime;
- *Clinical Trials* – ability to add value to the global drug development program, investigator initiated clinical research proposals, and world-leading Australian clinicians (and centres of excellence) being sought for global advisory boards;

  - *Early Stage* – quality of scientific and medical research base and infrastructure, availability of clinical trial sites (suitable for early phase studies) and patients, speed in gaining regulatory approval to conduct the clinical trial;

  - *Late Stage* – quality of scientific and medical research base and infrastructure, availability of clinical trials sites and clinicians, speed in gaining regulatory approval to conduct the clinical trial, ability to recruit larger patient numbers per site, cost, growth/value of the market in the country and previous conduct of early phase trials with the compound in the country; and
- *Manufacturing* – scale, cost, skills and IP protection, quality, high level skills and specialised capability for niche production.

Key barriers to investment in the Australian industry are:

- *Tax* - Australia's corporate tax rate is higher than the OECD average and is a barrier to increased investment;
- *R&D* – lack of critical mass, infrastructure gaps and few globally significant companies from which to develop global centres of discovery R&D;
- *Clinical Trials* – small population, increasing difficulty in identifying and recruiting patients, declining cost competitiveness, declining competitiveness in speed of study start-up; and
- *Manufacturing* – not cost competitive against many of Australia's competitors and Australia does not offer the same levels of incentives as other jurisdictions.

The Group considers that the key to a sustainable pharmaceuticals industry that adds value to the economy is in leveraging the industry's knowledge base, to deliver a sustainable and valuable annuity. Australia has a world class medical research base which produces three per cent of the world's medical research – it punches 'above its weight. Scientific excellence is supported by extensive infrastructure in universities, medical research sectors and hospitals. Australian science has also been responsible for the development of a number of important new medicines such as Gardasil, Relenza and Naglazyme as well as improved formulations and delivery systems such as Kadian/Kapanol and Doryx that have generated global sales in excess of $100 million.[1]

Excellence in scientific and clinical research retaining the highest possible safety standards has made Australia a competitive location not only for R&D, but also for clinical trials, particular in the earlier phases. Australia has a competitive advantage as a location for Phase I and Phase IIa clinical research. Australia maintained rapid study start-up timelines when European timelines fell behind following the introduction of the European Union Clinical Trials Directive. More Phase I and II activity is likely to migrate to Australia over time, provided we continue to improve the Australian environment for clinical trials in the face of improving clinical trial capabilities in other countries.

Australia also has pockets of expertise around niche manufacturing that are largely responsible for the industry's strong export performance to date. The Group considers that Australia has the potential to build on these strengths to create a sustainable future around high quality R&D, clinical trials and value added niche manufacturing.

Industry's ability to make this transition will be dependent largely on the efforts of the companies and workers of which it is composed. However, Government will have a role to play in assisting industry to make this transition. The Group considers that the recommendations of the Review of the National Innovation System, in so far as they impact on the industry, will provide some support, but not effect this transition. Accordingly, further industry specific action is required. The Group is cognisant that there are many competing claims for government funding. It is important to ensure that any specific additional funding directed to the Australian pharmaceuticals industry is supported by a clear evidence based expectation of net economic and social returns to the Australian Community.
There are some aspects of the pharmaceuticals environment, for example in the regulations surrounding clinical trials, the importance given to the research as a part of the public health system and in the size and design of university and academic research funding, where

[1] Gardasil (cervical cancer vaccine), Relenza (influenza vaccine) and Naglazyme (treatment for rare genetic disease Mucopolysaccharidosis type 6), Kadian/Kapanol (pain relief), and Doryx (anti-infective).

Government is the key agent. Improvement and increased funding in these areas falls directly to Government.

In other areas, Government is important in creating the right operating environment for companies to invest. This includes appropriate levels of policy co-ordination between the Australian Government Health and Innovation portfolios and a strong and balanced IP regime.

Finally, where it can be demonstrated that spillovers are significant and there is a barrier to private investment for a project in Australia, there is a case for Government action beyond the level provided through the broad National Innovation System.

Accordingly, the Group believe that there is a role for Government in:

- maintaining Australia's strong medical research base;
- ensuring that graduates have the appropriate skills base;
- ensuring the regulatory environment appropriately supports high quality R&D and does not unduly obstruct clinical trial activity; and
- assisting companies to invest in new, qualitatively different R&D, manufacturing and infrastructure that results in a sustainable competitive advantage, which will then generate a significant net economic and social benefit and a sustainable annuity to the Australian economy.

In the process of considering its recommendations, the Group has considered the recommendations of the Review of the National Innovation System. The Group has concluded that, while there are some proposals that will encourage some individual companies, these proposals may not be sufficient to encourage the necessary development of the industry. Specifically:

- the combination of the Competitive Innovation Grants Program, the Pre Seed Funds and a fourth round of the Innovation Investment Fund may still leave a gap (>$10 million) in funding for the smaller biopharmaceuticals firms in Australia if alternative sources of capital (such as venture capital) are inadequate — this is particularly problematic in biopharmaceuticals because of the long development times;

- the Review did not offer specific mechanisms that would attract significantly more R&D investment from large pharmaceuticals companies;

- recommendations to build on the National Collaborative Infrastructure Strategy to fund R&D infrastructure would not provide a strong incentive for companies to undertake significant investment in qualitatively different infrastructure that would make the industry more competitive in the long term; and

- none of the Review's recommendations specifically addressed the skills gap in the pharmaceuticals industry, and more needs to be done to meet the skills gap by ensuring that graduates have the necessary knowledge, skills and experience to make them ready for a job in the pharmaceuticals industry – changes are also needed to improve the mobility of personnel between the public and private sectors.

The Group concluded that Government action, beyond that proposed in the Review of the National Innovation System, is necessary if the pharmaceuticals industry is to have a sustainable future in Australia. The Group has developed the following three recommendations to achieve this objective.

1. Government co-funding of strategic investment in pharmaceuticals R&D, manufacturing and infrastructure that will deliver a net ongoing social and economic benefit and will deliver future value to Australia. Some different means to achieve this are put forward.

2. Increasing Australia's attractiveness as a location for clinical trials activity, by:
    a. accelerating implementation of a national streamlined system of ethics approval processes for multi-centre clinical trials;
    b. implementing improvements to the regulation of clinical trials identified as part of the moves towards the establishment of the Australia New Zealand Therapeutic Products Agency;
    c. establishing a National Clinical Research Agency;
    d. implementing a national approach to clinical research training and accreditation; and
    e. accelerating use of e-health initiatives to improve the efficiency of conducting clinical trials in Australia.

3. Improving Pharmaceuticals Skills and Education by:
    a. establishing a program to gauge the feasibility and commitment of industry, education and government stakeholders in creating a national strategic framework for the future development of a biopharmaceutical industry training system and an Australian Government funded co-ordinating body to develop and oversee the implementation of the national strategic framework;
    b. allow the costs of hiring students and academics to be covered by any Government funded R&D grant program;
    c. encouraging universities to provide equal credit to engagement with industry as an alternative to publications as evidence of researcher productivity; and
    d. encouraging research funding organisations (such as the National Health and Medical Research Council and the Australian Research Council) to take account of research undertaken in commercial environments when assessing skills and capabilities of grant applicants.

The Group does not view these three measures as alternatives, but rather as part of a concerted package for improving the industry environment. The Group considers that measures 2 and 3 are not costly and should be pursued as soon as possible. They also contain quite specific actions, such as establishing a National Clinical Research Agency, the specific merits of which will be further reviewed in the final report. The first measure is likely to be the most costly. Hence, while it can also be expected to deliver the largest net economic and social benefit, it will require more scrutiny in the context of broader Government priorities. The Group will consider the amount of funding for its final report.

The Group also believes that there are several enhancements to be made to the business environment for pharmaceuticals, and these will be detailed in its final report.

# 1 Introduction

The Minister for Innovation, Industry, Science and Research, Senator the Hon Kim Carr, established a high level industry-union taskforce to secure the future of the Australian pharmaceuticals industry. The taskforce, known as the Pharmaceuticals Industry Strategy Group (the Group), was commissioned to develop a plan to increase investment in pharmaceuticals R&D, clinical trials and manufacturing in Australia over the next decade.

The global pharmaceuticals business model is changing because of industry consolidation in association with the increasing costs of drug development, the emergence of biologics, and outsourcing of early stage R&D. Also, increasing patent expiries and global cost cutting strategies to offset falling revenues in the face of increasing competition from generic drugs are creating challenges and forcing industry change. This shift presents both opportunities and challenges for the Australian industry.

## 1.1 Terms of Reference

Minister Carr announced the Terms of Reference for the Group on 26 May 2008[2], which are shown in Box 1.1. The Terms of Reference require the Group to:

- examine the barriers and drivers to increasing productive pharmaceuticals investment in Australia;
- identify strategies to overcome the impediments and capitalise on opportunities to attract pharmaceuticals investment in Australia;
- explain how these strategies will make a net economic and/or social contribution to Australia by 2010; and
- present a draft directions paper to the Minister by 30 September 2008 and a final report by the end of December 2008.

[2] Kim Carr (Minister for Innovation, Industry, Science and Research), *The Roadmap to Pharmaceuticals Research and Manufacturing*, media release, Parliament House, Canberra, 26 May 2008.

## Box 1.1 Terms of Reference for the Pharmaceuticals Industry Strategy Group

The Minister for Innovation, Industry, Science and Research has commissioned the Pharmaceuticals Industry Strategy Group (PISG) to develop a strategic plan to increase investment in pharmaceuticals research and development (R&D) and manufacturing in Australia over the next decade.

The Australian pharmaceuticals industry is defined as all those who contribute to the discovery, creation and supply of pharmaceutical products and services, including prescription medicines and vaccines. It covers from research through clinical trials, to manufacturing of pharmaceuticals. It includes the originator medicine sector, the generic medicine sector and the medical biotechnology sector.

The pharmaceuticals industry is highly globalised and is undergoing a period of global rationalisation that will impact on the sustainability of the Australian industry.

The Pharmaceuticals Industry Strategy Group (PISG) will:

1. Examine the drivers and barriers to increasing productive investment in R&D, clinical trials and manufacturing activity in Australia. In doing so, the PISG can take into account the impact of, but is not required to report on, regulatory and reimbursement systems such as the Therapeutic Goods Administration and the Pharmaceutical Benefits Scheme.

2. Identify strategies to overcome the impediments and capitalise on the opportunities to attract investment in R&D, clinical trials and manufacturing activity in Australia that:
    a) Builds on Australia's competitive strengths;
    b) Identifies the actions that industry and Government should take to:
        i) increase manufacturing activity and investment in manufacturing infrastructure; and
        ii) increase R&D activity and investment in R&D infrastructure;
    c) Provides a well reasoned business case (consistent with principles of appropriateness, effectiveness, efficiency, integration, performance assessment and strategic policy alignment) for how any proposed actions will attract new, internationally competitive and sustainable R&D, clinical trials and manufacturing investment to Australia together with an implementation timetable and key performance indicators; and
    d) Explains how the actions would make a net economic and/or social contribution to Australia by 2020.

3. Report to the Minister for Innovation, Industry, Science and Research with a draft directions paper by 30 September 2008 and a final report by the end of December 2008.

## 1.2 Membership

The Group has 24 members that span the pharmaceuticals industry value chain. The Group is co-chaired by Dr Brian McNamee, CEO and Managing Director of CSL Limited and Mr Craig Pennifold, Head of Innovation Division, Department of Innovation, Industry, Science and Research. The Group's other members are:

- Mr Nixon Apple, Industry and Economic Adviser, Australian Manufacturers Workers Union;
- Dr Graeme Blackman, Managing Director, Institute of Drug Technology Australia Limited;
- Mr Dan Brown, Managing Director, Genzyme Australasia Pty Ltd;
- Mr Ian Chalmers, Chief Executive Officer, Medicines Australia;
- Dr Greg Collier, CEO and Managing Director, ChemGenex Pharmaceuticals Limited;
- Mr Peter Cook, CEO and Managing Director, Biota Holdings Limited;
- Mr Richard Davies, Managing Director, Amgen Australia Pty Ltd;
- Mr Joe de Bruyn, National Secretary and Treasurer, Shop, Distributive and Allied Employees Union;
- Mr Will Delaat, Chair, Pharmaceuticals Industry Council;
- Mr Charlie Donnelly, National Secretary, National Union of Workers;
- Ms Alison Finger, Managing Director, Bristol-Myers Squibb Australia Pty Ltd;
- Ms Di Ford, Executive Director, Generic Medicines Industry Association;
- Mr Mitch Kirkman, Manager – Process, Training and Quality, Novartis Pharmaceuticals Australia Pty Ltd;
- Mr John Latham, Regional Director, Pfizer Global Pharmaceuticals, Pfizer Australia/Pfizer New Zealand;
- Dr Anna Lavelle, Chief Executive Officer, AusBiotech Ltd;
- Professor Graham Macdonald, Chair, Pharmaceuticals Education Council;
- Mr John Montgomery, Chief Executive Officer, Alphapharm Pty Ltd and President, Mylan Asia Pacific;
- Ms Cait O'Connor, National Policy and Research Officer, Australian Workers' Union;
- Dr Tim Oldham, President, Asia-Pacific, Hospira Inc;
- Dr Alan Robertson, Chief Executive Officer, Pharmaxis Ltd;
- Dr Merilyn Sleigh, Chief Executive Officer, In Avanti; and
- Mr Ken Windle, Chairman & CEO, Advent Pharmaceuticals

Previous members were:

- Mr Simon Efron, former National Policy and Research Officer, Australian Workers' Union – Mr Efron was replaced by Ms O'Connor; and
- Mr Dave Oliver, National Secretary, Australian Manufacturing Workers Union – Mr Oliver was replaced by Mr Apple.

## 1.3 Relationship with other Government Reviews

The Group is conducting its work at the same time as a number of other significant reviews commissioned by Government. These other reviews include:

- The Review of the National Innovation System;
- The Review of Australia's Export Policies and Programs;
- The Review of Australian Higher Education; and
- The Review of Australia's Tax System.

## The Review of the National Innovation System

On 22 January 2008, the Minister for Innovation, Industry, Science and Research, Senator the Hon Kim Carr, announced a review of the National Innovation System to be undertaken by an expert panel chaired by Dr Terry Cutler. Minister Carr asked the panel to:

- Identify a set of principles to underpin the role and participation of the public sector in innovation;
- Develop a set of national innovation priorities to complement the national research priorities, ensuring the objectives of research programs and other innovation initiatives are complementary;
- Identify regulatory and other barriers to innovation and recommend ways to minimise these;
- Examine the scope for simplifying and reducing program duplication and ensuring that any support provided is well-targeted and easy to access;
- Consider the appropriateness, effectiveness and efficiency of the Research and Development (R&D) Tax Concession Scheme in promoting innovation and make recommendations to improve innovation outcomes;
- Consider ways to improve the governance of the national innovation system to support higher expectations of government agencies and industry; and
- Assess the appropriateness, effectiveness and efficiency of the Cooperative Research Centres (CRC) Program and make recommendations to improve innovation outcomes.[3]

Minister Carr released the Review of the National Innovation System, V*enturous Australia*, on 9 September 2008.[4]

## The Review of Australia's Export Policies and Programs

On 21 February 2008, the Minister for Trade, the Hon Simon Crean MP, commissioned Mr David Mortimer AO and Dr John Edwards to review Australia's export policies and programs. The review will assess Australia's export and investment performance. It will make recommendations on future policies and programs to promote exports and investment flows, develop export capacity, and enhance Australia's competitiveness.[5] The review is scheduled to report to Minister Crean by the end of August 2008.

## The Review of Australian Higher Education

On 13 March 2008, the Deputy Prime Minister and the Minister for Education, Employment, Workplace Relations and Social Inclusion, the Hon Julia Gillard MP, announced a major review of Australia's higher education system which will examine and report on the future direction of the higher education sector, its fitness for purpose in meeting the needs of the Australian community and economy and the options for ongoing reform.[6] The review will be

[3] Kim Carr (Minister for Innovation, Industry, Science and Research), *Government Announces Review of the National Innovation System*, media release, Parliament House, Canberra, 22 Jan 2008.
[4] Kim Carr (Minister for Innovation, Industry, Science and Research), *Government Releases Innovation Review Paper*, media release, Parliament House, Canberra, 9 Sep 2008.
[5] Simon Crean (Minister for Trade), *Government Review of Export Policies and Programs*, media release, Parliament House, Canberra, 21 Feb 2008.
[6] Julia Gillard (Deputy Prime Minister, Minister for Education, Employment Workplace Relations and Minister for Social Inclusion), *A Higher Education Revolution*, media release, Parliament House, Canberra, 13 Mar 2008.

conducted by Emeritus Professor Denise Bradley AC and will present a draft report to Minister Gillard by October 2008 and a final report by the end of the year.

### The Review of Australia's Tax System

On 13 May 2008, the Treasurer, the Hon Wayne Swan MP, announced the review of Australia's tax system. The review will look at the current tax system and make recommendations to position Australia to deal with the demographic, social, economic and environmental challenges of the 21st century.[7] This review will be undertaken by Dr Ken Henry, Secretary of the Department of the Treasury and will report to Government by the end of 2009.

The Group considers that each of these reviews is important to the future competitiveness of the Australian pharmaceuticals industry. However, the Group will not be making recommendations which it considers likely to encroach on any of these reviews' terms of reference; rather it will note the importance of these matters to the industry. This will allow the views of the Group to inform the Government's response to the other reviews.

## 1.4 Why Have a Pharmaceuticals Industry Review Now?

The Australian pharmaceuticals industry is significant; it employs over 40,000 people, has a turnover in excess of $18 billion, produces exports valued at $3.9 billion and invests $752 million in R&D a year.[8] It is a significant component of the National Innovation System, and Australia's second largest source of elaborately transformed manufactured goods.

However, the environment in which the pharmaceuticals industry operates has changed dramatically over the last decade and a full and frank assessment of the current and future challenges and opportunities facing the industry is needed. This assessment is particularly timely considering that the current industry development program, the $150 million Pharmaceuticals Partnerships Program ($P^3$) will conclude on 30 June 2009.

This review will examine the challenges and opportunities facing the industry and also propose actions that both Government and industry can take to maximise investment in the industry over the next decade, including whether or not there should be a successor program to $P^3$, and if so, what it should look like.

## 1.5 Methodology Used to Address the Terms of Reference

The Group met on 7 July, 11 August and 19 September 2008 to address the terms of reference. To do this, the Group:

- articulated its vision for where the industry will be in 2020;
- conducted a SWOT – strengths, weaknesses, opportunities and threats – analysis of the industry;
- considered the impact of previous industry development programs;
- considered the implications of Australia's World Trade Organization obligations on future industry development program options;
- analysed submissions to the Review of the National Innovation System from relevant stakeholders;

[7] Wayne Swan (Treasurer), *Australia's Future Tax System*, media release, Parliament House, Canberra, 13 May 2008.
[8] Australian Bureau of Statistics, unpublished data; IBISWorld, *Medicinal and Pharmaceutical Product Manufacturing in Australia: C2543*, 2008; and IBISWorld, *Pharmaceuticals Wholesaling in Australia: F4797*, 2008.

- considered the relevant recommendations of the Review of the National Innovation System;
- developed proposals to stimulate growth of the industry; and
- commenced building the business case to justify these proposals.

The Group also held two teleconferences on 5 September and 9 September 2008 to help refine the proposals to stimulate the growth of the industry.

## 1.6 Structure of the Directions Paper

This Directions Paper will provide:

- an overview of the global and Australian pharmaceuticals industries (see Chapter 2 and Appendices A and B);
- an overview of previous Government programs and initiatives (see Chapter 3 and Appendix C);
- a discussion of the barriers and drivers to global and Australian industry activity (see Chapter 4);
- a strategic framework for how the industry will achieve a sustainable future (see Chapter 5); and
- the recommendations to achieve a sustainable future (see Chapter 6).

# 2 Overview of the Global and Australian Pharmaceuticals Industry

## 2.1 The Pharmaceuticals Industry Value Chain

The pharmaceuticals industry is defined as all those who contribute to the discovery, creation and supply of pharmaceutical products and services, including prescription medicines and vaccines. The stages of the value chain include discovery research, basic R&D, through to clinical trials, and then the manufacturing of pharmaceuticals. It includes the originator medicine sector, the generic medicine sector and the medical biotechnology sector.

## 2.2 Pharmaceuticals Industry Sectors

Companies in the pharmaceuticals industry are diverse and multifaceted, using a variety of technologies to develop medicines for global markets. Nevertheless most companies involved in or aspiring to sell medicines arguably fit within four different business models:

- developers and/or manufacturers of originator small molecule medicines;
- developers and/or manufacturers of originator biological medicines;
- research based biotechnology companies; and
- developers and manufacturers of generic (or off-patent) medicines.

A number of companies are also involved in service the development and manufacturing needs of these companies by offering contract manufacturing and contract clinical trial, and R&D services.

Many of the challenges and characteristics of the pharmaceutical industry – those companies that fit into these three broad categories – also apply to a broader set of businesses involved in medical science. These include, for example, companies involved in medical devices, diagnostic products, biomarkers and other therapeutic products.

### Originator Small Molecule

These companies earn most of their revenue from developing and selling new medicines based on small molecules (or chemically based drugs). Both globally and in Australia this is the largest sector of the industry by revenue and profitability. Because of the cost and time to market for new products and the low cost and relative ease and consistency of manufacture, a strong and effective intellectual property protection regime is critical to this sector.

Globally this sector is the largest employer in the industry and the biggest investor in R&D. Its manufacturing activities are characterised by a diverse network of global manufacturing facilities that supply all regions.[9] R&D facilities for each company generally consist of a handful of global centres of excellence for discovery generally located in Western Europe, North America and Japan that are supported by a large number of clinical trial sites located around the world. It has the most extensive sales and marketing network of the industry and is able to sell to all major markets. The cost of developing a new medicine increases dramatically as the molecule moves from research into preclinical development, and then through the phases of clinical development. Most notably, spend on the global clinical program is often the major component of the total development spend. These funds will flow into countries that can deliver clinical trial data in a timely and cost competitive manner with appropriate quality.

[9] Noting that there has been considerable centralisation, consolidation and increased scale in manufacturing in the sector, driven by the need to reduce costs and increase margins.

While this sector remains large and profitable, it is under considerable pressure with the impending patent expiration on major blockbuster drugs (such as Pfizer's atorvastatin), falling R&D productivity – raising the cost and difficulty of replenishing pipelines – increasing regulatory pressure, growing generic competition, and increasing pressure on reimbursement. This is translating into global rationalisation and globally significant job losses. In response, originator small molecule companies are exploring new structural models of R&D to improve productivity and to accommodate the increasing requirement for demonstration of cost effectiveness of expensive new medicines.

The Australian operations of these companies are not immune from these pressures. Part of the focus of the Group's work is on developing strategies to identify how Australian firms and divisions of MNCs can capitalise on the effects if these changes, or at a minimum survive. Other key challenges for this sector include a predictable and timely regulatory and reimbursement system that promotes effective market access and competition from low cost centres for clinical trials and manufacturing. These firms have been very successful in attracting global clinical trials, and the associated global spend, into Australia over the last twenty years. However the ability of Australia to retain this level of global spend is under intense threat, especially from fast growing markets, with lower costs and ever increasing quality – such as India and China.

### Originator Biologics

Originator biologics companies focus on developing new biologic medicines. Many biotechnology companies are found within this sector, although this group of companies has additional challenges as discussed below. The percentage of medicines made from biologics is set to increase, with some estimates indicating a rise from 18 per cent in 2006 to 27 per cent in 2012.[10] Like the originator small molecule sector, a strong system of intellectual property protection is critical for this sector, particularly as the knowledge and skills needed to manufacture biologics become more widespread. However, unlike the originator small molecule companies, most of these companies have been in business for less than 30 years and have developed in conjunction with the rise of biotechnology. Many of these companies have spun out of knowledge intensive precincts and remain in close proximity to these locations.

The majority of these companies are highly R&D intensive, have no more than a handful of products and specialise in a small number of therapeutic areas. Globally these companies tend to be characterised by strong drug development pipelines (relative to their marketed products), and unlike the originator small molecule sector face less generic competition[11], less pressure to rationalise and are still exhibiting strong and sustained growth. A key opportunity and challenge for this sector is having a regulatory and reimbursement framework that recognises the complexity of biologic medicines. Also, a framework that ensures these medicines can access markets in a timely fashion (market access is also a key issue for originator small molecule companies) with reimbursement that reflects the costs of development.

One of the challenges of the Group is to identify ways in which Government can most effectively progress this issue in a way that sees Australia take full advantage of this as an opportunity for the Australian community to access innovative therapies and also to position the nation as a pro-innovation destination for industry investment.

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[10] "Report finds poor management scuppers almost half of all licensing deals", *Scrip* no. 3330, 25 Jan 2008, p. 11.

[11] Although, competition is emerging with 'biosimilar' versions of products like human growth hormone, which are already available.

## Research Based Biotechnology Companies

Research based biotechnology companies operate across the full range of the pharmaceutical sector, with technologies and products in both the small molecule and biologics spaces. Many companies in this sector have promising if limited development pipelines but most have not yet developed a finished product, and indeed may not intend to do so. In these cases, the companies are generally not profitable and may not have a predictable and consistent revenue stream from product sales to sustain their activity. They rely on a combination of government grants, licensing deals with other companies and capital markets to finance their operations.

Those companies that have developed products have often outsourced (or out-licensed) the marketing and manufacturing of these products to concentrate on their core business of researching and developing new medicines. These companies are highly innovative, invest a large portion of their cash reserves on R&D, tend to specialise in discrete areas of technological sophistication and pursue unique technological platforms. An appropriate intellectual property regime is of vital concern to this group, as is a stream-lined environment for clinical research.

Australia has approximately 470 companies that operate in this sector. They account for a significant portion of total industry investment in Australia and generally have strong links to the medical research community. A key challenge for this sector is accessing the skills and capital required to advance its drug development portfolio and to manage the transition into later stage development towards product launch and sales. One of the challenges for the Group is to explore ways in which this sector can overcome its resourcing constraints. Biotechnology companies also require sophisticated assistance with business development, product development, and related skills.

## Generic Medicine Companies

Generic medicine companies specialise in the production of medicines that have come off patent (which are predominantly small molecules, although there is also growing interest in biosimilars), and are focused primarily on manufacturing, marketing activities, regulatory compliance and managing the legal and IP issues necessary to secure earliest possible market access. The R&D done by this sector has lower levels of technical risk than the R&D undertaken by the originator sector, however, it does conduct some R&D including proving bio-equivalence (the ability of a new version of a medicine to have equivalent strength and activity of the originator medicine) and the development of new drug formulations and delivery mechanisms. In Australia, companies such as Hospira and Alphapharm make significant investments in this type of R&D. An increasing amount of generic company R&D is spent on development of new formulations and processes.

Generic medicines companies are in the middle of an unprecedented growth opportunity arising from the large number of patent expirations of high revenue medicines. This is giving the sector access to larger and more lucrative markets. While manufacturing generic medicines requires the same skills as manufacturing originator medicines, it does not require the same levels of IP protection. Therefore, competition for generic manufacturing is more intense and may take place in a larger number of locations. One consequence of the intense competition between generic companies is increasing consolidation and adoption of large scale, low cost manufacturing operations in low cost jurisdictions, necessary to preserve margins.

The key challenges for this sector are a predictable and timely regulatory and pricing system, being able to gain access to markets as soon as patents expire and remaining competitive against lower cost manufacturing centres. The challenge of examining strategies to make

Australian manufacturing more competitive against lower cost competitors is a key focus for the Group, for example by finding niches which are difficult for others to replicate.

More information on each sector of the industry and a comprehensive description of the industry value chain is at **Appendix A**.

## 2.3 The Global Pharmaceuticals Industry

The pharmaceuticals industry is global in scope, with a value chain that is similarly global: promising research is sourced from wherever it emanates; pre-clinical research is generally conducted in suitably scaled units located close to head offices or large commercial business units; clinical trials are conducted at appropriately qualified hospitals and research centres around the world, placing a premium on speed, cost and quality; medicines are developed for global markets and manufactured from global networks of large scale production sites for international markets. There is intense competition for capital, for skilled resources and for research prospects that have the potential to become useful medicines.

### Global Industry Trends

For most of the last three decades, the pharmaceutical business model has been based on vertically integrated multinational companies ('MNCs') developing 'blockbuster' medicines from in house resources. Over the last decade, this model has become more fragmented under the increasing pressure of costs and duration of drug development, falling R&D productivity, the rise of new technologies, the increasing ability of smaller companies to monetise their intellectual property without first having to commercialise a product, and increasing competition from generic medicines when patents expire.

Many originator pharmaceutical companies lack sufficient new medicines to replace those coming off patent and are increasingly looking to reduce the risk and cost of drug development by in-licensing or acquiring potential drug targets from smaller, highly specialised biotechnology companies. The percentage of sales accounted for by drugs developed through licensing agreements is projected to double from 17 per cent in 2002 to 34 per cent in 2012.[12] These smaller biotechnology companies not only offer prospective agents (biologics or small molecules) that might be useful human therapies, but also offer expertise in a range of areas valuable to larger pharmaceutical companies such as identification of drug targets, drug screening technologies, product optimisation technologies and identification of biomarkers used to evaluate potential patient populations.

However, these strategies have not led to an increase in R&D productivity by the MNCs. The number of new products approved in 2006 was lower than in 1995, despite the industry spending three times as much on R&D in 2006 as in 1995.[13] Credit Suisse Research estimates that in 1980 the industry developed almost 17 new medicines for every billion dollars of R&D spent. By 2000 every billion dollars of R&D spent produced a little more than one marketed new medicine. While this estimate may be somewhat inflated by a focus on MNCs developing "blockbuster" drugs, the situation has led to an expectation of sharply reduced growth in future revenues for the sector of the industry and a substantial reduction in the value of pharmaceuticals companies to their shareholders.[14]

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[12] *Scrip*, op. cit. p. 11.

[13] United States Government Accountability Office, *New Drug Development: Science, Business, Regulatory and Intellectual Property Issues Cited as Hampering Drug Development Efforts*, 2006; and statistics on R&D spend from Pharmaceutical Researchers and Manufacturers of America (PhRMA), *Pharmaceutical Industry Profile 2008*, 2008.

[14] A Lewcock, "Pharmas to lose $100bn to generics", *DrugResearcher.com*, news article, 22 Feb 2007, <http:www.drugresearcher.com>.

Revenue pressures and consolidation in the MNC sector are leading to global job losses across the value chain, but are particularly prominent in manufacturing (where they are associated with initiatives to centralise and upscale facilities in tax advantageous jurisdictions) and in sales forces. A number of companies have announced plans to significantly reduce their numbers of global manufacturing plants. Australian subsidiaries of MNCs are affected by these pressures, with a number of companies announcing manufacturing job cuts of over 300 employees in the last twelve months. These pressures will remain while Australian operations continue to be affected by the global industry's adjustment to lower R&D productivity and the need to reduce costs.

These changes are fundamentally redefining the industry business model from one hitherto based on vertical integration, to one based increasingly on virtual integration, characterised by partnering at multiple points within the development chain with service providers, research based biotechnology companies, universities and medical research institutes, and diversification by several large originator pharmaceuticals companies into generics.

Australia is particularly well placed to exploit this trend. Australia has the world's sixth largest biotechnology industry with 470 biotechnology companies who can act as drug discovery and development partners for larger pharmaceutical companies. Many Australian companies have been successful in establishing lucrative relationships with MNCs: recent examples include Cytopia's $274 million drug development deal with Novartis and Bionomics' $50 million deal with Merck Serono.

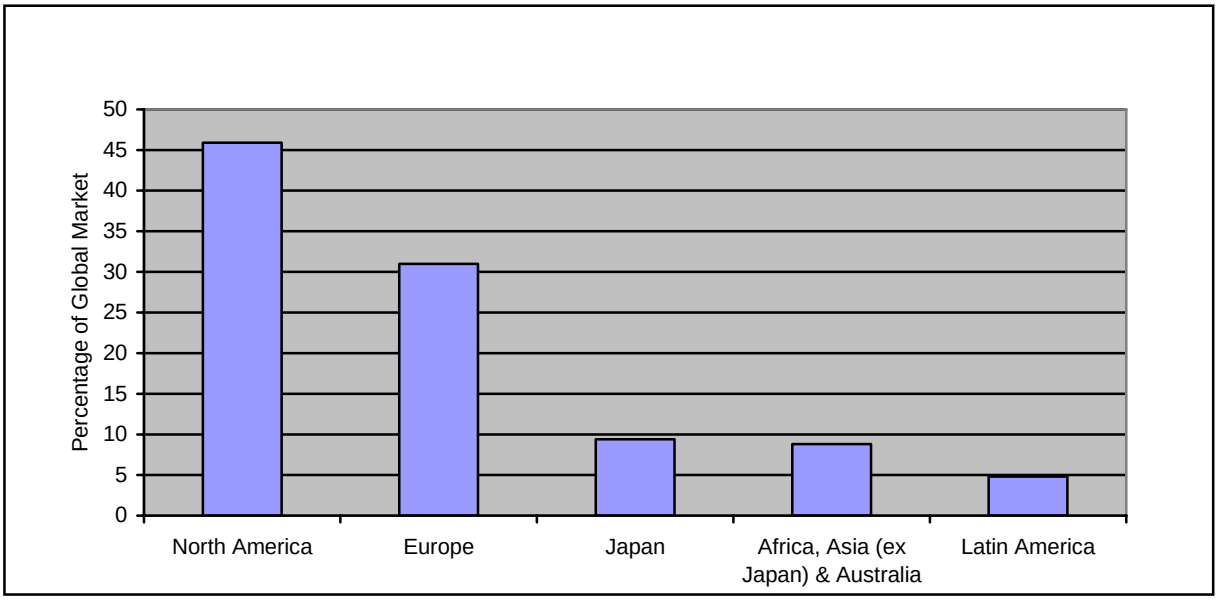
The trend towards outsourcing means, in particular, that the research-based sector will play an increasingly important role as a source of innovation. This implies that Governments aiming to create an environment conducive to industry innovation will need to focus increasingly on enhancing the research sector.

The progressive patent expiry for current block buster drugs has been matched by significant growth in the generics sector. Typically, a large number of generic versions of blockbuster drugs come to the market in a very short period of time resulting in intense price competition and large and rapid price reductions. The large number of impending patent expiries will present generic medicine companies with unprecedented opportunities for growth. High growth rates and relatively low barriers to entry will encourage new entrants to the generic market, both from those new to the pharmaceuticals industry and from originator companies wishing to develop generic brands to help ameliorate the loss of revenue from patent expirations on their key products.

## The Global Market

In 2007, the global pharmaceuticals market was estimated to be worth US$712 billion. Based on IMS Health estimates, North America accounts for nearly half of the global market (see **Figure 2.1**).[15]

**Figure 2.1 Global Industry Sales by Region**




The global market is projected to grow strongly because of an ageing population, rising global affluence and an increasingly health conscious market place. Espicom Business Intelligence projects that the global market will grow by 40 per cent over the next five years.[16]

The growth in the global market will present significant opportunities for manufacturing companies who will need to service the increasing global demand. This may also present an opportunity for Australian manufacturing operations, which are geographically well placed to exploit the growth in the Asia-Pacific region, which is estimated to be an average of 5.5 per cent a year for the next five years.[17] However, it should be noted that there are several locations within Asia-Pacific which are desirable manufacturing hubs, not least because of their favourable tax regimes, and successful manufacture in Australia is likely to be based on some unique local capability or skill that is difficult for others to replicate and is less subject to competition based only on cost.

The dominance of the US and Europe in the global pharmaceuticals market is also seen in global industry revenues. Figure 2.1 shows that over 75 per cent of sales revenues derive from these markets. A recent IMS Health report found that 65 per cent of revenue from new medicines launched since 2002 has come from the US.[18] The portion of global revenue generated in the US is higher for newer medicines than for all medicines. This reflects the fact that companies often seek to market medicines in the US before attempting to access other markets, a reflection of market size, sophistication, openness to new modes of treatment and prices paid. This dominance of the US market is a key factor for Australian

[15] "Global pharma market grew to $712 billion last year", *Scrip*, no. 3357, 30 Apr 2008, p. 30.
[16] Espicom Business Intelligence, *The World Pharmaceutical Markets Fact Book 2008*, 2008, p. 71.
[17] ibid., p. 162.
[18] IMS Health quoted in European Federation of Pharmaceutical Industries and Associations (EFPIA), *The Pharmaceutical Industry in Figures 2008*, 2008, p. 5.

companies involved in new product generation, and ready access to drug development and regulatory regimes in the US is a vital consideration for their success.

## Global Industry Activity

In line with the global pharmaceuticals market, industry activity is dominated by MNCs, headquartered in the United States, Western Europe and Japan. This trend has occurred predominantly because companies have traditionally located major manufacturing and R&D discovery centres close to company headquarters. The extent to which this is true is illustrated by a recent survey of US-owned multinational pharmaceuticals companies which found that these companies conducted nearly 80 per cent of their global R&D in their home market.[19] These markets are also the largest in terms of revenues and number of patients: and there are obviously advantages in developing products close to the final market. In pharmaceuticals, successful commercialisation often requires that late stage clinical research take place in that market involving its key opinion leaders.

Other locations around the world with strong scientific skills base, world class medical research infrastructure or populations who value late stage clinical trials as a means of securing advanced medicines have been successful in securing portions of R&D and clinical trial activity. Initially, this trend was linked to lower costs and large patient populations available for clinical testing. As the skills base in many emerging Asian and Eastern European economies has improved in recent years, significant R&D centres have been established and this region's share of R&D activity has increased. Both these regions' share of industry activity has increased in recent years, mainly at the expense of Western Europe.[20] The movement of R&D to countries such as India and China has allowed these countries to capitalise on the increasing ability of their scientists and to increasingly create their own intellectual property.[21]

## Global Industry Manufacturing

Estimates of global manufacturing are difficult to calculate, but the most reliable estimates indicate that nearly three quarters of all pharmaceuticals manufacturing takes place in either the US or in Europe.[22] While these estimates do not break down the proportion of pharmaceutical manufacturing activity performed in Australia, the Department of Innovation, Industry, Science and Research estimates that Australia's share of global production is around 0.9 per cent.[23]

## Global Industry R&D

The Pharmaceuticals industry is highly R&D intensive and according to some estimates is the largest source of private sector R&D in the global economy. Nearly one out of every five dollars spent by the world's largest 1,400 companies on R&D was on pharmaceuticals-related R&D, giving large pharmaceuticals companies an R&D intensity (i.e. R&D as a portion to sales) of 15.9 per cent.[24] Estimates of global industry R&D vary widely and there is no definitive source of how much is spent by the entire industry. However, the German Association of Research based Pharmaceutical Companies estimated that in 2005 the

[19] Pharmaceutical Researchers and Manufacturers of America (PhRMA), *Pharmaceutical Industry Profile 2008*, 2008, p. 54.
[20] EFPIA, 2008 notes that between 2001 and 2006, 14 new research sites were opened in Asia while 18 were closed in Europe. Over the same period the net number of research sites in the US remained close to neutral.
[21] Kauffman - The Foundation of Entrepreneurship, *The Globalization of Innovation: Pharmaceuticals*, 2008.
[22] EFPIA, op. cit., p. 15.
[23] This estimate is based on: estimates of global production, EFPIA, 2008; estimates of the value of Australian production from IBISWorld, *Medicinal and Pharmaceutical Product Manufacturing in Australia: C2543*, 2008; and converting the A$ to the Euro at the rate of $1 to €0.6.
[24] EFPIA, loc. cit.

industry's R&D spend in the US, Europe and Japan was US$67 billon.[25] Whilst this is an underestimate, since it excludes much of the Asia Pacific, using it as a proxy suggests that Australia accounts for little more than one per cent of global R&D.

## 2.4 The Australian Pharmaceuticals Industry

Australia is the 15th largest pharmaceuticals market in world, with sales worth approximately US$8.5 billion in 2007.[26] In 2006-07, the industry employed over 40,000, including around 15,000 in manufacturing, had a turnover in excess of $18 billion, and invested $752 million in R&D.[27]

The Australian industry comprises over 40 originator pharmaceuticals companies (most of which are subsidiaries of MNCs), around ten generic medicine companies, 470 core biotechnology companies (almost all of which are small scale by global standards) and over 20 world class medical research institutes. Australia has only one locally based MNC, which is CSL. The primary focus of most MNCs' activities in Australia is sales and marketing, although an increasing number are devoting more resources to R&D and clinical trials.[28] Less than ten of all these companies manufacture pharmaceuticals from Australia.

### Turnover and Market Size

The turnover of the Australian pharmaceuticals industry has grown strongly over the last decade, almost doubling since 1999-2000 (see Appendix B, **Figure B.1**). This growth has been driven by strong increases in domestic demand and exports, and the value of work undertaken by pharmaceuticals wholesalers.[29] A breakdown of industry turnover shows that domestic demand is the largest component, followed by exports, and the value of work conducted by pharmaceuticals wholesalers (see Appendix B, **Figure B.2**). The industry's turnover is likely to continue to increase rapidly in coming years on the back of strong and rising consumer demand for new medicines.

### Future Turnover and Market Size

Under a business as usual scenario, the Australian market is projected to continue to grow strongly, with Espicom Business Intelligence estimating that the market will record an average annual growth rate of 5.8 per cent from 2008 to 2013.[30]

The Group considers there is little role for Government in influencing domestic demand for medicines, but is of the view that Government can play a useful role in facilitating increased exports by providing incentives for companies to invest in new infrastructure that generates new capabilities for the Australian industry.

### Employment

Industry employment has been similarly growing in recent years to its current figure of 40,000 (see Appendix B, **Figure B.3**).[31] The strong growth in turnover and employment suggests that fundamentally the Australian industry has been in good health in recent years.

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[25] Statistics from German Association of Research Based Pharmaceutical Companies, 2007, <http://www.vfa.de>.
[26] Epsicom, loc. cit.
[27] Department of Innovation, Industry, Science and Research estimates based on Australian Bureau of Statistics (ABS) unpublished data and data from IBISWorld, *Pharmaceuticals Wholesaling in Australia: F4797*, 2008; IBISWorld C2543.
[28] A survey of Medicines Australia members revealed that 44 per cent of the members' workforce was in sales and marketing: Medicines Australia, *Australian Pharmaceutical Industry at a Crossroads: Report of the 2007 Medicines Australia Member Economic Survey*, 2008, p. 23.
[29] ABS unpublished data and IBISWorld, C2534 and F4797, 2008.
[30] Espicom, op. cit., p. 73.
[31] ABS unpublished data; IBISWorld C2543 and F4797, 2008; and Department of Innovation estimates.

Employment in the biotechnology sector in particular has grown significantly since 2004-05 (see Appendix B, **Figure B.4**).

The current skills profile of the industry suggests that the work force is, by Australian standards highly skilled, and more mobile than other sectors of the economy. Almost 95 per cent of the work force has either a university or TAFE or equivalent qualification.[32] While the Group remains concerned about a disconnect between the current level of training offered by the tertiary and vocational education sectors and industry's future training needs, the broad educational background of the current work force provides it with a degree of flexibility that is lacking in the industry workforces of some other industries.

Employees in the pharmaceuticals industry on average receive significantly higher wages than workers in other sections of the Australian economy. They are a well educated workforce which will remain a defining characteristic of the industry, ensuring that wages also remain high.

In the short term, manufacturing is likely to be displaced by employment in R&D as the industry's largest source of employment. Australian manufacturing operations are under intense pressure to maintain, let alone increase their employment, because of global rationalisation trends. However, employment in R&D is likely to increase on the back of continued strong growth in industry R&D spend and increases in public sector investment in the Australian medical research base. Employment in the biotechnology sector is also likely to rise as the sector continues to mature.

By 2020, it is likely that employment in both R&D and biotechnology will be larger than for manufacturing. This would mirror the trend in many other parts of the Australian economy, where the pharmaceuticals industry will be transformed from a predominantly manufacturing based industry, to an industry characterised increasingly by those providing high value services complemented by a smaller and specialised manufacturing sector.

### Manufacturing

Manufacturing remains the largest component of the industry by employment. While growth in pharmaceutical manufacturing employment has been relatively subdued in recent years, it has outperformed the rest of the manufacturing sector (see Appendix B, **Figure B.4**).[33] Pharmaceuticals manufacturing accounts for about one per cent of Australia's total manufacturing workforce, but produces almost 10 per cent of Australia's manufactured exports (by value). Pharmaceuticals are Australia's second largest export after automotive products and accounted for $3.9 billion in 2007.[34] Pharmaceuticals manufactured exports have grown at almost double the pace of all industry exports and more than double the pace of other manufacturing industries (see Appendix B, **Figure B.5**).

### Manufacturing Exports

The industry's export performance has been impressive and demonstrates the fundamental transformation that has occurred within the pharmaceuticals manufacturing industry, from one focussed principally on supply to the domestic market, to one focused predominantly on servicing global markets. IBIS World estimated that more than half of all pharmaceutical manufacturers' revenue is now derived from exports, up from a quarter a decade ago.[35] This strong export performance is likely to have impacted on manufacturing employment and is

[32] Medicines Australia, op. cit., p. 24.
[33] ABS unpublished data and *Manufacturing Industry, Australia, 2006-07*, (cat. no. 8221.0).
[34] ABS (cat. no. 8221.0).
[35] IBISWorld, C2543, 2008.

likely to be one of the reasons why employment in the pharmaceuticals manufacturing sector has outpaced the broader manufacturing sector.

Despite these impressive performances, the industry's net export performance is much less than $3.9 billion because of the significant cost of the imported ingredients used in the formulation and manufacturing of pharmaceuticals in Australia. Also, there has been a shift to lower value manufacturing activities (see below).

The Group considers there is a role for Government in assisting the industry to make the large capital investment required to substantially develop the nation's manufacturing capability where there are broader public benefits that extend beyond the firm making the investment. The Group does not anticipate that a large number of proposals would meet such a test. However the Group considers that targeted Government support is necessary to induce large scale significant investment that will deliver a sustainable annuity to the economy and broader social and economic benefits.

### Future Exports

Under a business as usual approach, the Department of Innovation, Industry, Science and Research estimates that pharmaceutical exports will fall by around 28 per cent to around $2.8 billion a year by 2010. These short term effects are largely as a result of industry consolidation and consequent rationalisation. In the longer term, if companies are unable to succeed in securing the investment necessary to develop economies of scale or niche production capabilities, industry exports will continue to decline. Australia will only remain competitive as a destination for manufacturing exports if we are able to leverage our knowledge base to undertake the high value added activity that other locations find difficult to replicate. Competing on cost is not a viable or desirable option.

See **Appendix B** for more information.

### Type of Manufacturing Activity

Australian manufacturing activities are almost entirely in secondary manufacturing and packaging. Active ingredient manufacturing, such as alkaloid production from Tasmania's legal opium poppy crops, influenza vaccine and plasma products from CSL and niche manufactures such as the Institute of Drug Technology Australia, contribute less than 10 per cent of total pharmaceuticals production, according to a recent estimate.[36] Australia has only limited infrastructure to produce biologic drugs on a commercial scale.

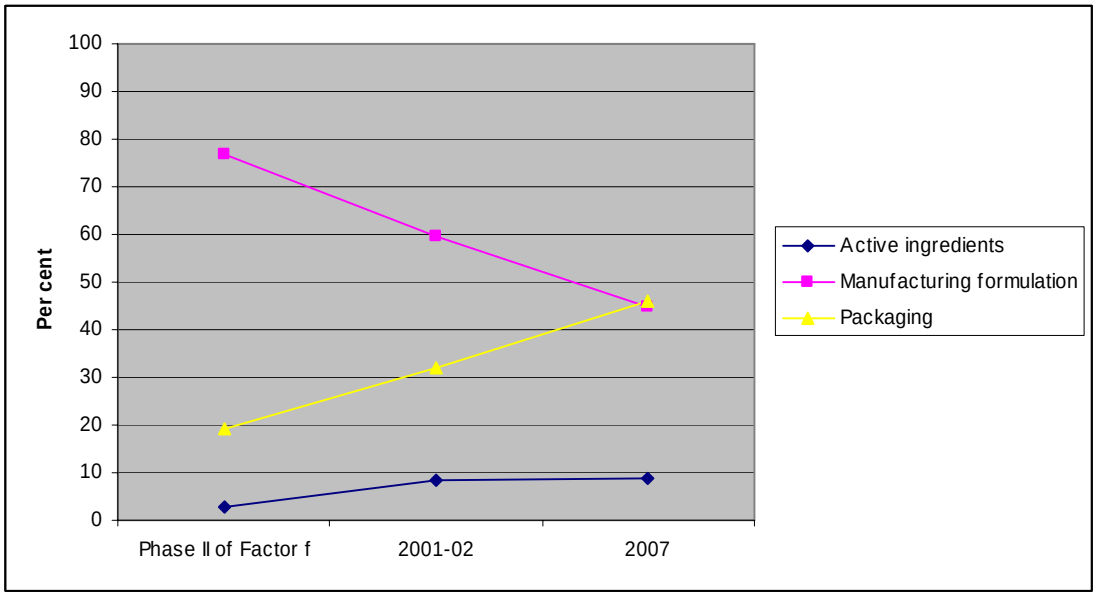
Previous Government programs, Factor f and the Pharmaceutical Industry Investment Program (PIIP), had little impact on value added, as measured by the Australian Bureau of Statistics (ABS) because they did not specifically require companies to do qualitatively different activity that would generate significantly higher levels of value add (as measured by the ABS) as opposed to simply more activity. The industry has become increasingly characterised by lower value packaging activities at the expense of more highly valued manufacturing formulation activities (see **Figure 2.2**).[37]

[36] Medicines Australia, *Australia's Pharmaceuticals Industry at the Crossroads*, 2008.

[37] Estimates of the type of manufacturing activity are based mainly on irregular surveys of incomplete industry coverage that provide limited data that do not coincide with the timeframe of Phase II of Factor f and PIIP. The most accurate proxies have been used here. Source: Industry Commission, *The Pharmaceutical Industry*, 2006; Productivity Commission, *Evaluation of the Pharmaceutical Industry Investment Program*, 2003; and Medicines Australia, loc. cit.

The Australian pharmaceuticals manufacturing industry's value added was over $1.8 billion in 2006-07,[38] and growth in pharmaceuticals value add has not kept pace with the rest of the manufacturing economy since 1999-2000, (see Appendix B, **Figure B.6**). This trend is consistent with falling levels of capital investment in the sector.

**Figure 2.2 Types of Pharmaceuticals Manufacturing**




## Future of Manufacturing Value Added

Under a business as usual scenario, the level of value added generated by the industry is likely to remain relatively low. If Australia is to maintain a viable pharmaceuticals manufacturing sector, companies will need to make the transition to a high value added future. Government assistance can play a role in facilitating this transition by providing incentives for companies to undertake the significant capital investment required to move into qualitatively different higher value added activity. The Group does not believe that either it or Government should attempt to codify what these activities may look like, since individual companies are best placed to determine the sort of investments that have the best chances of commercial success and long term sustainability.

In seeking Government assistance under the measures proposed by the Group or under other schemes, the onus should be on applicants to demonstrate that the supported project will achieve these ends. Assistance should only be offered to companies and projects that will deliver a net social and economic benefit and will create a sustainable annuity to the broader economy. The Group does not consider that many proposals will pass the test, but those that do are likely to significantly transform the capabilities and sustainability of not only individual companies, but the broader Australian pharmaceuticals industry. Consequently, the Group considers that Government investment in these circumstances is warranted and justified.

## R&D

Business Expenditure on R&D (BERD) for the pharmaceuticals industry grew significantly between 1998-99 and 2005-06, such that by 2005-06, the industry invested $752 million a year in R&D (see Appendix B, **Figure B.7**). The pharmaceuticals industry is a significant source of BERD in Australia accounting for 7.5 per cent of the total BERD across all industries. Pharmaceuticals BERD has increased faster than total BERD from 1998-99 to 2005-06 (see Appendix B, **Figure B.8**).

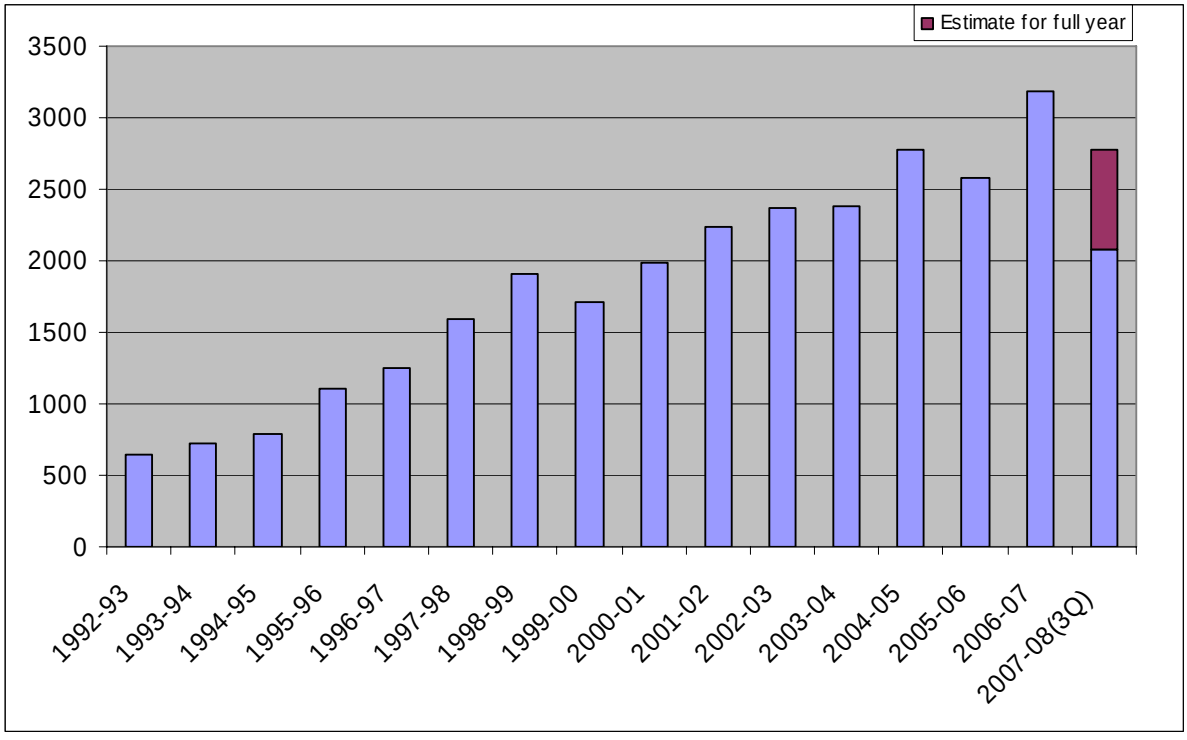
[38] ABS (cat. no. 8221.0).

## R&D and Clinical Trials

Early-stage medical research is strongly supported by Australian Government expenditure. Australia was ranked fourth in the Organisation for Economic Co-operation and Development (OECD) for government expenditure on health-related R&D as a percentage of GDP in 2006, and the rate of growth in this support from 2000 to 2006 was second only to Switzerland.[39] This support is continuing with research funding administered by the National Health and Medical Research Council planned to rise to around $750 million in 2011-12. Australia has a strong track record in medical research with a high publication rate for its population, six Nobel Laureates in medicine, and discoveries that led to the development of drugs like Gardasil (cervical cancer vaccine), Relenza (influenza vaccine) and Naglazyme (treatment for rare genetic disease Mucopolysaccharidosis type 6).

The Australian biotechnology sector, which is heavily based on early stage R&D and clinical trials, is strong and growing. The Australian drug development pipeline currently looks strong, with a total of 154 compounds known to be in human clinical trials, of which around 90 (or 58 per cent) are in Phase II/III clinical trials. The total number of clinical trials announced by the top listed companies and significant public sector and private organisations in 2007 was significantly greater than in 2006, increasing by over 200 per cent (see **Figure 2.3**).[40]

**Figure 2.3 Clinical Trial Notifications**




While Australian biotechnology companies are doing more clinical trials, Australia is also a significant location for clinical trials for international companies. According to data from the Therapeutic Goods Administration, 739 clinical trials were conducted in Australia in 2004-05: 536 of these were Phase II or III trials and 87 were Phase I.[41] More recent data from the evaluation of the Pharmaceuticals Partnerships Program ($P^3$) indicate that industry is increasingly doing more earlier phase research in Australia. This data shows that

[39] Organisation for Economic Co-operation and Development, *OECD Science, Technology and Industry Scoreboard 2007*, 2007, p. 37.
[40] K Hopper and L Thorburn, *2008 BioIndustry Review Australia and New Zealand*, 2008, p. 27.
[41] J Rankin, J Mason, N Kottege and N Y Andersson., "Clinical trials of unapproved medicines in Australia", *The Medical Journal of Australia*, vol. 18, 2006, p. 342.

61.2 per cent of all R&D expenditure in $P^3$ (recipients of which included both biotechnology companies and MNCs) was on discovery research or in very early stage Phase I clinical research.[42]

There are several reasons for this shift towards more early phase trials being conducted in Australia. Firstly, Australia now has a very strong track record over 20 years of delivering high quality data on clinical trials and global companies tend to be very conservative when placing early phase research outside of their usual research centres. Secondly, Australia has at present a global competitive advantage in the reputation of its medical researchers and a number of facilities that can meet the higher requirements for early phase research.

Thirdly, the Clinical Trials Notification Scheme has ensured Australia has a very competitive start-up time for very early phase research, especially first in human studies. Lastly, early Phase I and II clinical trials are more expensive to conduct and the relatively high costs for clinical trials in Australia are less pronounced when compared to other countries in these more complex studies. As such, global companies based in Australia are tending to preferentially bid for early phase trials from their global headquarters.

### Clinical Trials by Stage

A recent survey of Medicines Australia member companies, most of which are MNCs, suggested that most of the clinical trial R&D undertaken by these companies was in late stage clinical trials (i.e. Phase III clinical trials and beyond).[43] The survey also found that 29 per cent of all R&D was in unspecified clinical trials. For the purposes of trying to estimate how much R&D is done in each stage of the value chain, the Department of Innovation, Industry, Science and Research, has reallocated the 'ungrouped' 29 per cent to other parts of the clinical trials value chain based on the proportion of total clinical trials spent in each of these areas.

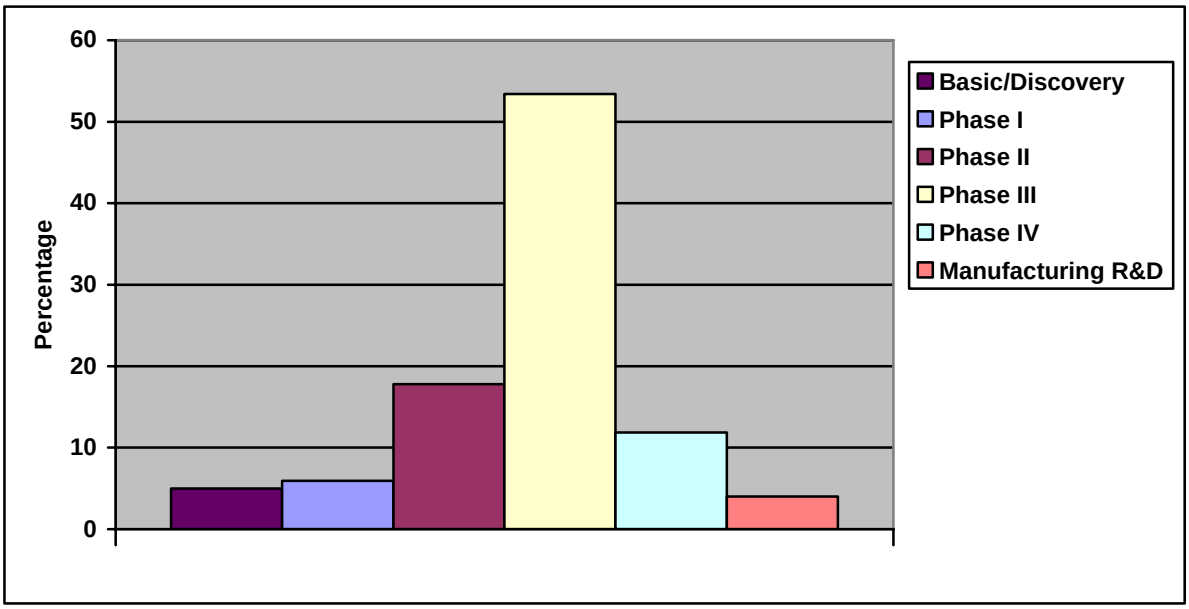
The Medicines Australia survey does not cover the results of R&D undertaken by other sectors of the industry, such as the biotechnology industry, and is therefore likely to overestimate the amount of R&D done in later stage clinical trials and underestimate the amount of Phase I clinical trials and basic R&D done by industry in Australia. Notwithstanding the bias of the Medicines Australia survey to MNC companies, it is the best available proxy to determine how much R&D is spent at each stage of the clinical trials value chain.

From this information it would appear that the vast majority of MNC industry R&D is spent in Phase II, Phase III clinical research (see **Figure 2.4**). Phase II and III trials are designed to provide pivotal or supporting data for the global regulatory dossier. Australia does not attract the proportion of investment in basic/discovery R&D compared to the US (see **Figure 2.5**).

In the future, the design of clinical studies will change. Adaptive trial designs will speed up drug development (as reducing down time between phases) and require somewhat fewer patients. These trials will start out like current Phase II trials but become more like a Phase III trial as they meet certain predefined inflexion points. If Australia wishes to target Phase I and II clinical trials, it will be important that it remains relatively globally competitive in Phase III type trials or risk exclusion from the new type of adaptive trial design.

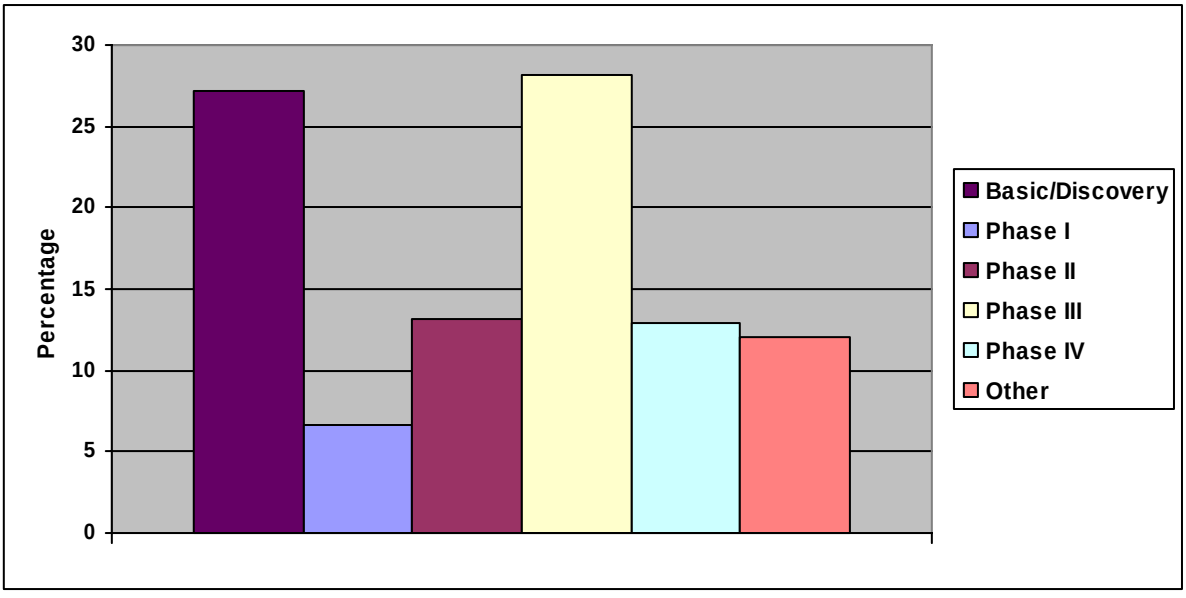
[42] Deloitte Insight Economics, *Evaluation of the Pharmaceuticals Partnerships Program*, 2008.
[43] Medicines Australia, op. cit., p. 28.

**Figure 2.4 Type of Industry R&D**




This profile is quite different from the MNC R&D spend in the US, where almost as much money is spent on basic/discovery research (which generally generates much higher levels of spillovers) as on Phase III clinical trials (see **Figure 2.5**).[44] This distribution reflects the absence of MNCs located in Australia, apart from CSL.

**Figure 2.5 Type of Industry R&D in the US**




## Spillovers from Pharmaceuticals R&D

The Productivity Commission (PC), the Centre for International Economics (CIE) and Deloitte Insight Economics (DIE) have all estimated the monetary value of spillovers associated with pharmaceuticals R&D that were induced by the Pharmaceutical Industry Investment Program and the Pharmaceuticals Partnerships Program.[45] These estimations are shown in **Table 2.1**.

[44] PhRMA, op. cit., p. 55.
[45] Productivity Commission, op. cit.; Centre for International Economics, *Pharmaceuticals Partnerships Program - First Year Evaluation*, 2006; Deloitte Insight Economics, loc. cit.

**Table 2.1 Estimation of Spillovers Associated with Pharmaceuticals R&D**

| | PC | CIE[46] | DIE[47] |
|---|---|---|---|
| **Basic/Pre-clinical R&D** | 57.5% | 65% | 57.5% to 80.5% |
| **Clinical R&D[48]** | 25% | 65% | 25% to 35% |

Table 2.1 demonstrates that there is a range of estimates of the value of spillovers associated with pharmaceuticals R&D. One can conclude that for each additional dollar spent by the industry on R&D, there will be a spillover benefit ranging from 25 to 80.5 cents depending on the type of R&D performed. This suggests that any scheme designed to promote additional pharmaceuticals R&D is well placed to deliver a net economic benefit, providing that the cost of the incentive is less than the benefits gained by the additional levels of R&D induced by the subsidy.

Table 2.1 also suggests that Australia is deriving only a small portion of the broader economic and social benefits potentially available from pharmaceuticals R&D, because of the relatively low proportion of early stage R&D done here by MNCs. It suggests that encouraging such companies to do earlier stage R&D either directly, or through association with research providers and biotechnology companies, or encouraging them to do more of the value adding later stage clinical activity in Australia — even extending into manufacture of clinical trial material where there is a sensible investment case — will have a significant impact not just on the capabilities of individual firms and the industry, but on the annuities delivered to the broader economy. Further information about spillovers from pharmaceuticals R&D is in **Appendix B**.

## Future of R&D and Clinical Trials

Because a disproportionately large share of industry R&D in Australia is spent by MNCs on Phase II and III clinical research, Australia is more vulnerable to the impacts of competition in this part of the value chain. The usually larger number of patients involved and the relative portability across countries (due to less reliance on close links to early stage researchers and growing quality in emerging markets) of Phase II and III clinical trials, means that it is the most cost sensitive part of the R&D value chain. Anecdotal evidence is emerging from the R&D Taskforce of the Pharmaceuticals Industry Council that Australia is under pressure to just retain, let alone increase its share of Phase II and III clinical trials. This is because of competition from countries able to use their lower cost base and larger patient populations to present a more compelling business case for Phase II and III clinical trials.

These pressures will only intensify as more countries around the world increase the extent and quality of their medical practice and research base and invest in the medical research infrastructure needed to conduct Phase II and III clinical trials. Australia is unlikely to have a sustainable long term future simply as a destination for Phase II and III clinical trials and under a business as usual scenario, Australia's activity in this space is likely to decline in relative terms, if not in absolute terms.

The Government can support a range of measures that seek to play to Australia’s competitive strengths that will help sustain Phase II and III trials activities in Australia against locations with larger populations of treatment-naïve patients and lower costs. While the Group does

[46] The Centre for International Economics combined spillovers arising from both additional and novel R&D activity to arrive at this figure.
[47] The Deloitte Insight Economics estimates have a broad range because it covered the two different payment rates offered under the Pharmaceuticals Partnerships Program.
[48] Note that Deloitte Insight Economics treated Phase I clinical trials as the same as basic and pre-clinical R&D in terms of the spillovers it generated.

not consider that it is possible or desirable for the Government to subsidise clinical trials in Australia to narrow the cost differential with lower cost countries, the Group believes that there is a role for Government to make Australia a more attractive location for clinical trials.

There are two aspects to costs of clinical trials that are evaluated by global decision makers – one is the direct cost of the trial (related to the hospital staff costs and procedures) and the other is the cost efficiency of maintaining a clinical research department in a local company (cost of headcount and the number of trials and patients that can be handled per headcount). Government policy can affect the direct costs of a trial in Australia through reviewing the costs in the health system to ensure they are reasonable. Industry understands that the government should not be subsidising clinical trials, but is concerned that trials are bearing a growing and inefficiently large share of institutional overheads. In effect, increasing institutional costs allocated to clinical trials that have the effect of reducing the volume of trials undertaken is counterproductive. Secondly, increasing the efficiency of the conduct of clinical trials in Australia will result in more patients and sites that can be being handled with fewer industry staff and bring the costs down for global decision makers.

A range of local costs measures are discussed which could achieve both these objectives, such as streamlined national ethics approval and innovative use of e-medical records. While there is a growing business case for doing Phase I clinical research in Australia, and most biotechnology companies would expect to follow this route, many multinational companies continue to use Australia principally as a location for Phase II and III clinical trials, because historically Phase I trials are conducted geographically close to the global headquarters or major R&D centres. As discussed above, there is a role for Government to play in directly encouraging such companies to undertake qualitatively different value added activities that deliver higher public benefits and greater levels of annuity to the Australian economy (such as more Phase I and early stage R&D, or a greater share of the high value components of later stage clinical trials).

However, as with manufacturing and infrastructure activities, the Group would not expect that there would be many R&D proposals that would pass this test. The Group would expect expenditure on early stage R&D to continue to increase provided the Australian biotechnology sector continues to grow, and the university and not for profit medical research sectors become increasingly active.

## Capital Expenditure

Many industry participants have claimed that the industry is undergoing a period of disinvestment that has the potential to reduce industry activity in the short term and capability in the longer term. While there is limited industry-wide data from which to prove or disprove this claim, evidence from a recent survey of Medicines Australia member companies suggests that companies' level of investment in long term assets (e.g. plant and equipment, R&D facilities) is less than half of what it was during the mid 1990s.[49] The Medicines Australia member survey probably underestimates the level of capital investment occurring in the industry because it does not pick up the capital investment undertaken by the biotechnology industry over the last decade, which has included the establishment of new laboratories and drug development facilities.

Nevertheless, the Group believes that the trend identified by Medicines Australia is broadly correct. It suggests that the business case for investing by MNCs in Australia has diminished over the last decade and that the reinvestments currently being made by the industry are insufficient to replace the value of past investments which have reached or are close to

[49] Medicines Australia, op. cit., p. 25.

reaching the end of their useful life. Some companies have decided not to renew their capital investments and have closed part or all of their manufacturing and R&D facilities in Australia. Current global rationalisation pressures will increase the prospect of increased disinvestment occurring in the short term.

Under a business as usual scenario it is likely that the MNCs will continue to reduce their level of capital investment. As discussed for both R&D and manufacturing, there is a role for Government to play in providing the companies with the incentive to undertake these investments, but only in a very limited set of circumstances when the broader benefits justify a public subsidy. At the same time, capital investment by maturing biotechnology companies can be encouraged.

## 2.5 Australian Industry's Strengths and Weaknesses

The Group assessed the state of play in both the global and Australian industry and conducted a SWOT – Strengths, Weaknesses, Opportunities and Threats – analysis of the industry that is shown in Box 2.1. The results of this SWOT analysis are explored in greater depth in Chapter 4, where the key barriers and drivers of industry activity are discussed.

## Box 2.1 Results of SWOT Analysis for the Australian Pharmaceuticals Industry

| Strengths | Weaknesses |
|---|---|
| **R&D**<br>• Quality medical research<br>• Cost competitive compared to North America, Europe and Japan<br>• 470 biotechnology companies<br>• Extensive and unique biological diversity<br>• Legal certainty for investment in biodiscovery through a national approach to access and benefit sharing<br>• Strong and effective IP Laws<br><br>**Clinical trials**<br>• Quality infrastructure<br>• Ethnically diverse population<br>• High volunteer rate for Phase I trials<br>• Well established track record and high number of ongoing trials for population size<br>• Globally recognised clinicians (and translational medicines capabilities)<br>• Fast-track approval system for Phase I trials.<br>• Strong and effective IP laws<br>• Southern hemisphere location<br><br>**Manufacturing**<br>• Strong and effective IP Laws and enforcement<br>• Springboarding provisions in place (generics)<br>• Short run manufacturing<br>• Niche production capabilities (including injectables, blow fill seal based products and vaccines)<br>• Strong and growing export base<br>• Existing manufacturing sites operating under GMP | **R&D**<br>• Limited pool of experienced management that can attract investment and guide commercialisation<br>• Some biotechnology companies having difficulty attracting funding<br>• Intellectual property capture and storage<br>• Infrastructure gaps<br>• Lack of critical mass<br>• Shortage of locally trained bench research staff<br><br>**Clinical trials**<br>• Small, geographically disperse population: results in higher numbers of sites and less patients per site compared to emerging markets, can also prolong recruitment period<br>• Australia's capacity to supply patients in some therapeutic areas is already stretched due to the number of trials ongoing in Australia – improved referral patterns and volunteer rates would increase capacity further<br>• Significantly more expense for Phase II and III trials than emerging markets<br>Appear less efficient - Multi-centre clinical trials require approvals from each institution- creates time and cost delays<br><br>**Manufacturing**<br>• Cost competitiveness compared to Asia and Latin America<br>• Distance from export markets adds to demands on cold chain management<br>• Manufacturing base has limited capacity to manufacture biologics<br>• Large trade deficit and terms of trade<br>• Corporate Tax rate not as low as some competitors<br>• Lack of global harmonisation of patent expiries |

| Opportunities | Threats |
|---|---|
| • Ageing global population: increasing demand for therapies<br>• Increasing wealth and health-consciousness of global population<br>• Global pharmaceuticals companies moving to outsource early stage R&D to fill product pipelines:<br>- partnering and out-licensing arrangements for biotechnology companies<br>- utilise biodiversity for drug discovery.<br>• Venture capital funds that are looking globally for investees<br>• Growing interest in personalised medicine as a means to improve health outcomes and cost-effectiveness<br>• Better and cheaper "omics" technologies: opportunities for R&D and personalised medicine<br>• Patent expiries: opportunity for generics manufacturing<br>• Development of new therapies, particularly biologics<br>• Different distribution and delivery models for new therapies<br>• Growing markets in Asia<br>• Rising demand for products with a reputation for quality | • Small market, with low growth compared to emerging markets<br>• Industry consolidation<br>• Distance from Global Headquarters – low visibility to key global investment decision makers<br>• Ageing population: governments seeking to reduce the cost of healthcare<br>• Rising costs of drug discovery<br>• Global rationalisation of pharmaceutical activities<br>• Global oversupply of manufacturing capacity<br>• Increasing competition from low cost manufacturing and clinical trial centres<br>• Patent expiries: threat for originator manufacturing<br>• Increasing scientific capability and reputation in lower cost countries such as China and India: competition for investment<br>• Global credit crisis affecting investment in biotechnology; intensifying competition from sectors that are seen as giving better return on risk capital, such as mining<br>• Climate change, emissions trading, increasing crude oil prices leading to increases in the cost of inputs and transport<br>• Workforce inadequate in number and skills, increasing global and regional competition for competent specialised biopharmaceutical staff at all stages of the value chain |

# 3 Overview of Previous Government Programs

## 3.1 Introduction

Since 1988, three sector specific programs have been implemented by Australian Governments to facilitate the growth of the Australian pharmaceuticals industry.

- *The Factor f scheme* provided almost $1 billion for companies to increase their R&D, manufacturing and export activity. The Factor f scheme was designed to compensate companies for the effects of low prices of pharmaceuticals under the Pharmaceutical Benefits Scheme (PBS). The factor f scheme was restricted to companies that supplied products to the PBS. It ran from 1988 to 1999 and 17 companies participated in the program. Detailed program information is in **Appendix C**.

- *The Pharmaceutical Industry Investment Program (the PIIP)* had a budget of $300 million to encourage companies to increase their R&D and production activities. The PIIP was designed to compensate companies for the effects of low prices of pharmaceuticals under the PBS. The PIIP was restricted to companies that supplied to the PBS. It ran from 1999 to 2004 and nine companies participated in the program. Detailed program information is in **Appendix C**.

- *The Pharmaceuticals Partnerships Program ($P^3$)* had a budget of $150 million to encourage companies to increase their R&D activities. $P^3$ was designed to provide an incentive for companies who could not access the R&D Tax Concession to undertake high quality, additional R&D in Australia and to provide incentives for companies to partner with Australian researchers. Entry to $P^3$ was restricted to firms doing pharmaceuticals R&D in Australia. $P^3$ will run from 2004 to 2009 and 23 companies have participated in the program. Detailed program information is in **Appendix C**.

As well as the three Government programs, the Pharmaceuticals Industry Action Agenda (PIAA) was begun by Government and Industry in 2001 to develop a ten year to double the Australian industry's share of the global market. Further details about the PIAA and its outcomes are in **Appendix C**.

## 3.2 Program Outcomes and Evaluation Results

All three industry development programs have been monitored for payment and activity levels, and evaluated to gauge their effectiveness and impacts on the industry.

Factor f saw a cumulative increase in exports and domestic production value added (PVA) to $5.135 billion (Phase I was $1.067 billion and Phase II was $4.068 billion). The cumulative increase in R&D expenditure was $765.4 million (Phase I was $205.4 million and Phase II was $560 million). Five new manufacturing facilities were created by Phase II participants. The extent to which this activity would have occurred but for the incentive provided by Factor f is unclear.

Factor f was evaluated by the Industry Commission in 1996.[50] The report's findings were mixed. The report found that the Factor f scheme may have positively influenced the heads of multi-national companies about the attractiveness of Australia as an investment location, and that important intra-industry links with the research sector and the equipment supply sector were formed. It also found that companies were overcompensated for the levels of activity

[50] Industry Commission, loc. cit.

due to a too-high payment rate, and that the benefits generated did not outweigh the costs of the program or enhance the welfare of the community.

The PIIP paid out $246 million of the possible $300 million funding to nine companies. This investment generated an additional $1.74 billion in pharmaceuticals activity, including an additional $359 million of R&D and an additional $1.38 billion in PVA activity. While no new facilities were established during the life of PIIP, program participants spent $245.1 million ($289.2 million in today's dollars) on manufacturing infrastructures and capital investments.

The PIIP was evaluated by the Productivity Commission in 2003.[51] The report found that:

> *"The estimates of additional R&D generated by the program per dollar of subsidy – the 'bang for a buck' – are much higher than have been found for other R&D incentives in Australia and internationally."*

The report concluded that the rationale for supporting manufacturing activity in light of the suggested low prices paid for PBS medicines had diminished since the establishment of the program. The costs to the economy of supporting manufacturing exceeded the benefits by $47 million, whereas the benefits to the economy of supporting R&D exceeded the costs by over $17 million. The main recommendation was that any future industry development program should only subsidise R&D.

In its first three years, $P^3$, a program funding R&D only, has supported over $130 million of additional R&D activity by paying companies over $38 million. Deloitte Insight Economics (Deloitte) evaluated the program in May 2008[52] and found that the program is likely to have only a low to moderate impact on half of its key performance indicators, and that $P^3$ will generate an overall public/economic impact in the range of -$23.8 million to +$9.8 million, but that is very likely to be close to neutral.

Deloitte concluded that the rationale for specifically supporting pharmaceuticals R&D has been reduced since the introduction of the 175 per cent Premium R&D Tax Concession, and there would need to be justification for the special treatment of the pharmaceuticals and biotechnology sectors through Government funding.

## 3.3 Summary of Activity

Companies that participated in the PIIP and Factor f programs increased their levels of manufacturing (production value added) over the course of their participation. However, the level of pharmaceuticals manufacturing value added undertaken in Australia as measured by the Australian Bureau of Statistics (ABS), increased from $1.414 billion in 1992-93 to $1.681 billion at the conclusion of Factor f in 1998-99. Conversely, the level of pharmaceuticals manufacturing value added fell from $1.625 billion to $1.526 billion over the life of the PIIP.[53] Since Factor f finished, manufacturers have increasingly moved away from higher value formulation work to lower value packaging activities.

Factor f and PIIP coincided with significant increases in employment and exports, but the extent to which these programs caused these increases is unclear, as they coincided with a period of sustained global industry expansion. Of the companies that received subsidies

[51] Productivity Commission, loc. cit.
[52] Deloitte Insight Economics, loc. cit.
[53] See ABS *Manufacturing Industry, Australia,* various editions (cat no 8221.0).

under Factor f and PIIP to increase their manufacturing activity, almost one third no longer operate the plants for which they received a subsidy.

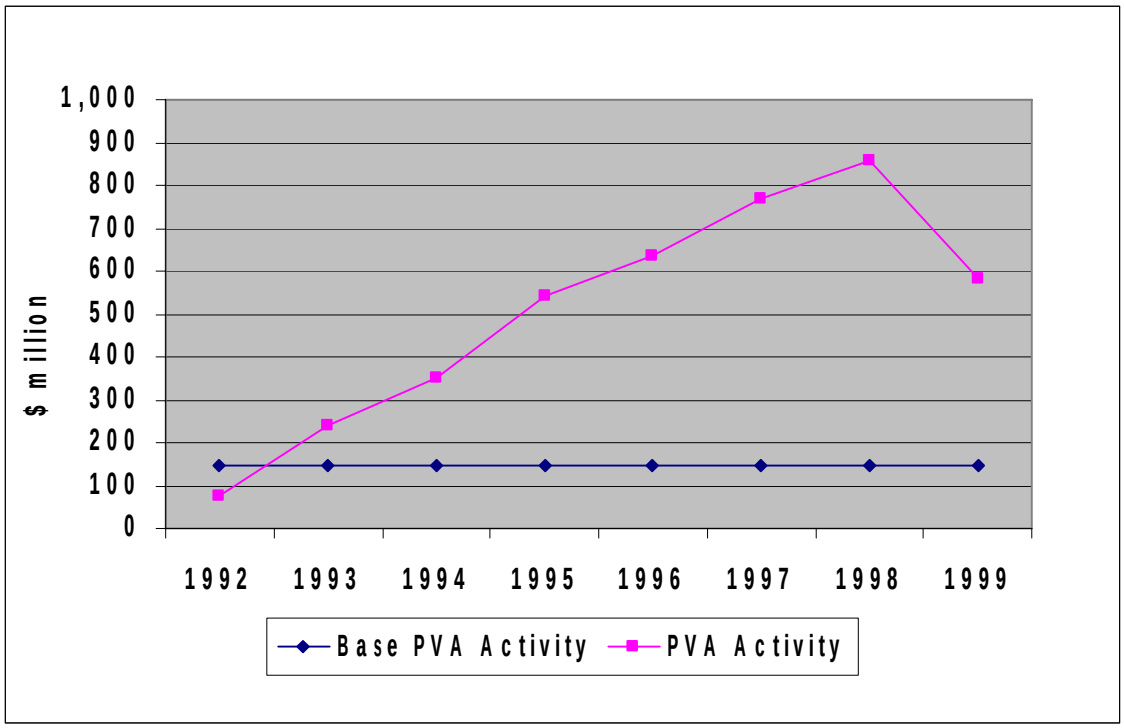
The Industry Commission estimated that anywhere between 10 and 40 per cent of additional activity would have occurred without Factor f funding. Similarly, the Productivity Commission estimated that anywhere between 20 and 90 per cent of additional manufacturing activity, but most probably 55 per cent would have occurred without PIIP funding. Because of the relatively low levels of spillovers associated with manufacturing activity, there was not a net benefit to the Australian economy from subsidising these activities under either Factor f or PIIP. This suggests that it would be very difficult to design a new manufacturing subsidy in a way that delivered a net economic benefit.

Deloitte's evaluation of $P^3$ estimated that 72 per cent of additional activity in Rounds 1 and 2, 53 per cent of additional activity in Round 3, would have occurred without $P^3$ funding. These figures support the Deloitte finding that higher levels of funding carry a higher inducement rate to encourage companies to invest in the Australian pharmaceuticals industry.

The more positive result from R&D incentive programs suggests that from an economic benefit perspective, there is more logic for the Australian Government to support additional R&D than additional manufacturing activity.

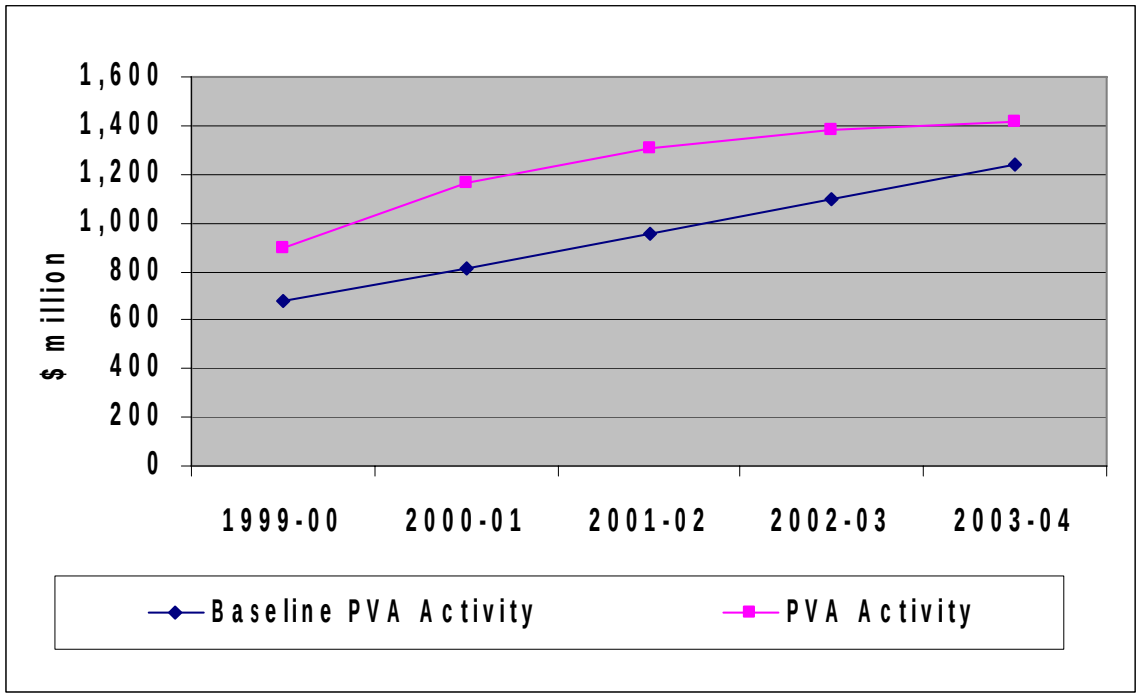
Production Value Added activity undertaken by participants during the life of Phase II of Factor f increased from $74.7 million in 1992 to almost $582 million in 1999 (see **Figure 3.1**). During PIIP, participants increased their Production Value Added activity from $893.5 million in 1999-00 to $1.42 billion per annum in 2003-04 (see **Figure 3.2**).[54] These graphs illustrate that both factor f and PIIP had an impact on the levels of value added undertaken by individual companies participating in the program.

**Figure 3.1 Factor f Participants: Production Value Added Activity**



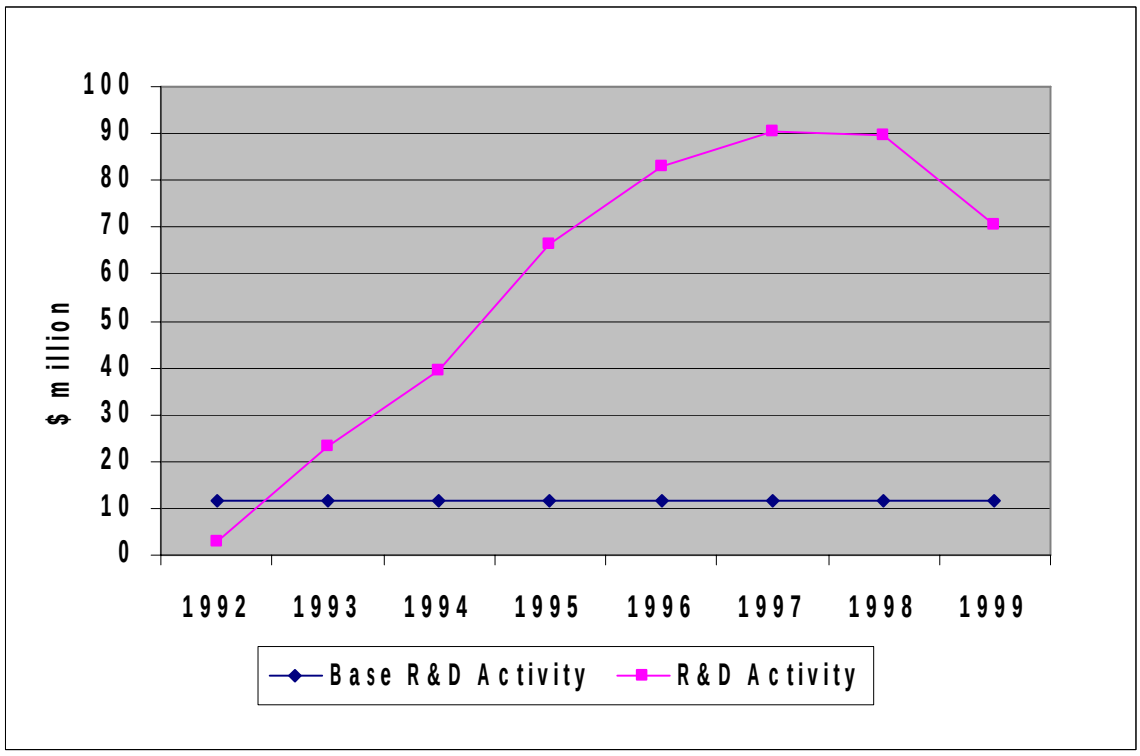

[54] Figures used for Factor f activity are gathered from company reports that vary in style and accuracy. These graphs should be used as a guide only. Base PVA refers to the base level of production value added that was used for the purposes of the program.

**Figure 3.2 Pharmaceutical Industry Investment Program (PIIP) Participants: Production Value Added Activity**



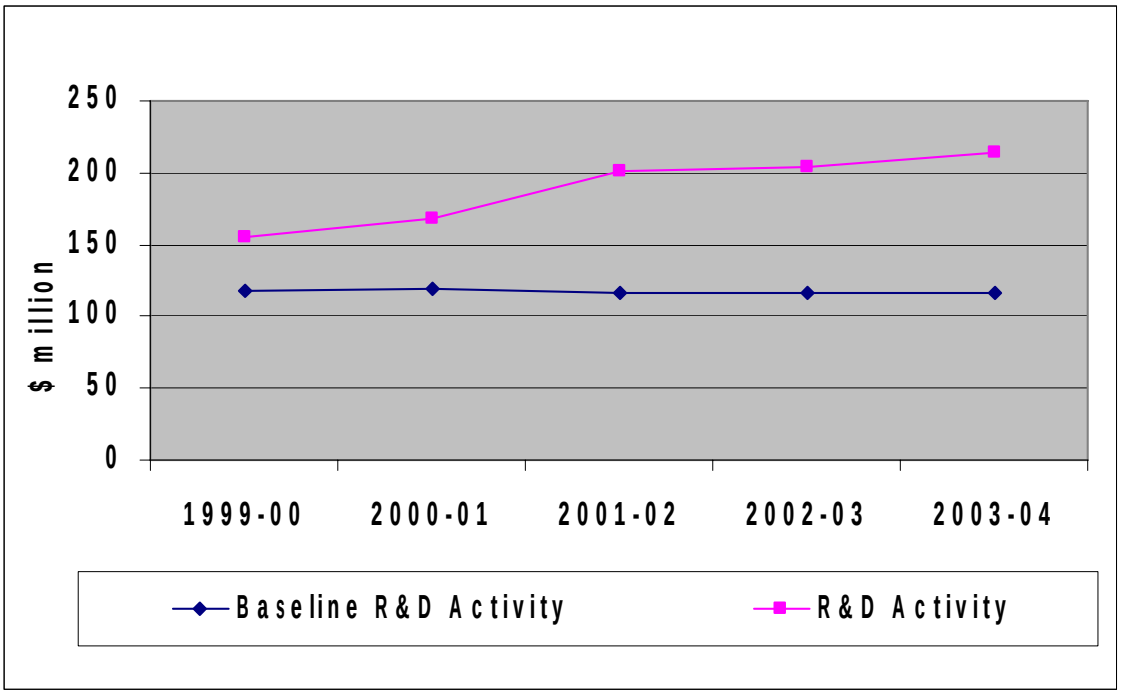

R&D carried out by participants throughout the history of sectoral specific support for the pharmaceuticals industry increased from $3 million to $210.5 million per annum (see **Figures 3.3, 3.4 and 3.5**). [55]

**Figure 3.3 Factor f Participants: Research and Development Activity**



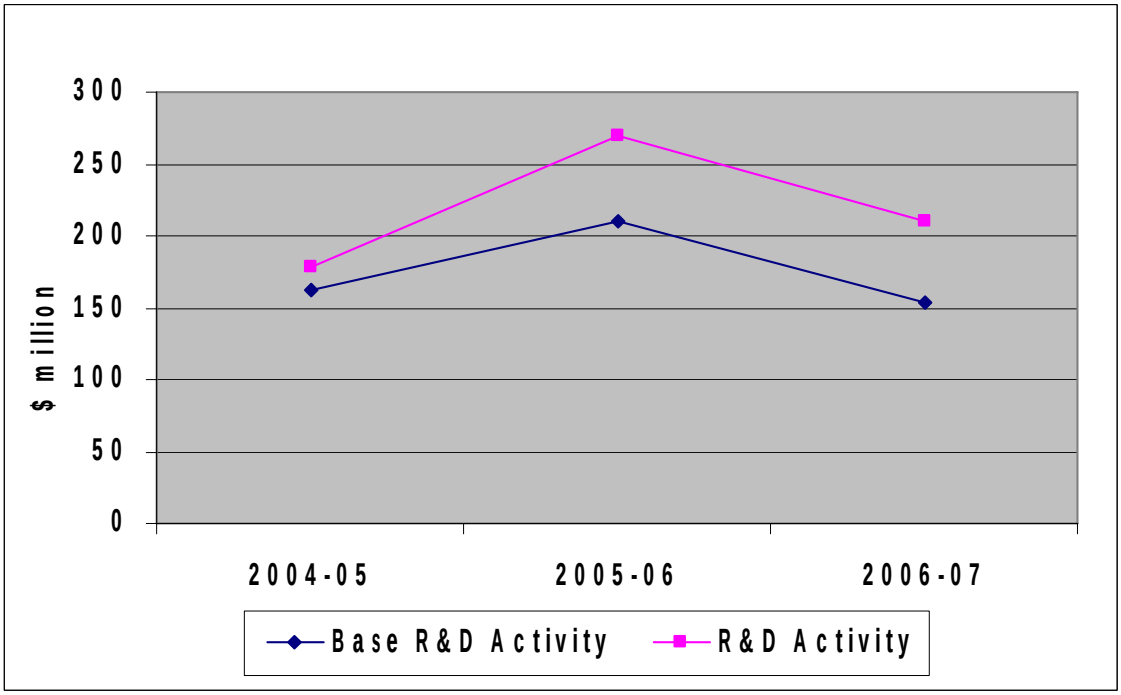

[55] Base R&D refers to the base level of R&D that was used for the purposes of each program. Graphs are based on program data from Factor f, PIIP and the first three years of $P^3$.

**Figure 3.4 Pharmaceutical Industry Investment Program (PIIP) Participants: Research and Development Activity**




In its evaluation of the PIIP, the Productivity Commission found that the "the estimates of additional R&D generated by the program per dollar of subsidy – the 'bang for a buck' – are much higher than have been found for other R&D incentives in Australia and internationally."[56]

**Figure 3.5 Pharmaceuticals Partnerships Program ($P^3$) Participants: Research and Development Activity**




[56] Productivity Commission, *Evaluation of the Pharmaceutical Industry Investment Program*, 2003, p.xxi.

## 3.4 Views of the Group

The Group broadly accepts the analysis of these reviewers, but is concerned that benefits are under-estimated because of the very long lead times before pharmaceuticals R&D yields benefits. For example, Gardasil, the development of which was supported by Factor f, did not deliver a royalty stream to CSL or the University of Queensland until 2006. As the formal reviews into previous programs were conducted before these programs had concluded, these reviews were not able to capture the long term net economic gains that may arise from supporting pharmaceuticals R&D and manufacturing. Consequently, these reviews are likely to underestimate the benefits from these programs and supporting pharmaceuticals R&D and manufacturing more generally.

Given that the analysis generally shows limited net economic gains from these government support schemes, the Group believes that projects seeking support in any future scheme will need to demonstrate that net economic gains will arise.

The Group also agrees that the most effective programs will be those that offer access to larger amounts of funding over a longer period of time to a select number of projects that are able to demonstrate the potential for significant net economic gains, rather than programs that offer more limited funding over shorter periods of time. The time-frame over which the effectiveness of these programs should be measured also needs to increase, particularly for R&D funding, recognising the long development cycle in pharmaceuticals.

# 4 Drivers and Barriers to Pharmaceuticals Investment in Australia

## 4.1 Introduction

The Australian pharmaceuticals industry is part of the global industry, as described in Chapter 2. In developing strategies to increase pharmaceuticals investment in Australia, the Group considered the factors that drive global investment decisions. The Group also looked critically at the Australian industry and its operating environment to determine the barriers that exist to attracting this investment to Australia. This work addresses Term of Reference 1.

## 4.2 Early stage R&D

For early stage R&D, the ultimate aim is to identify new targets and candidates for new medicines. As such, the quality of research outputs and the protection of IP is paramount. Early stage costs are generally small (in comparison with total costs) so are of lesser importance in determining the location of early stage R&D.[57] Australia is a competitive location for investment in early stage R&D because of its world class medical research base and infrastructure and large, maturing biotechnology sector. Australia also has extensive biological diversity that could be the source of new drug candidates. Its IP regime is globally recognised as being one of the strongest in the world.[58] With recent Budgets announcing increased Government funding to maintain the quality of Australia's medical research base (see **Figure 4.1**), Australia is well positioned to take advantage of the global trend to outsource early stage R&D.[59]

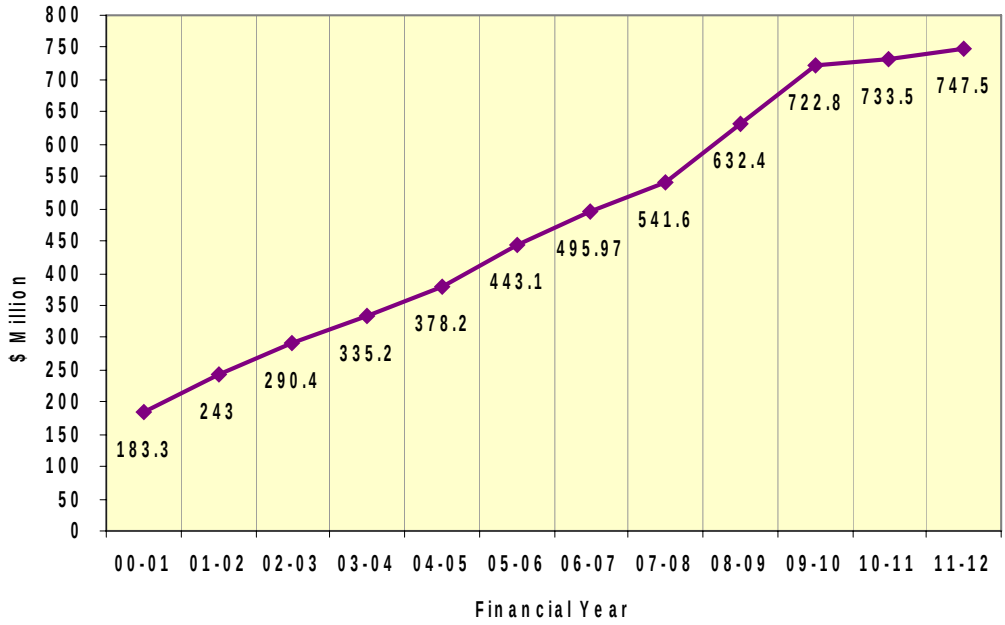
Nevertheless, there are some barriers preventing Australia from fully exploiting this strength. Group members feel that Australia lacks critical mass in some areas of early stage research and does not have the necessary infrastructure to do key parts of pre-clinical research, such as large animal testing. Critical mass and networks are important for R&D productivity and also attractiveness as an investment location. With large R&D centres or well-coordinated networks, including virtual networks, R&D productivity is boosted by the benefits of multidisciplinary teams, the ability to try different approaches simultaneously and by reducing duplication, in addition to economy of scale benefits on the costs of inputs, services and infrastructure.

Australia is beginning to achieve critical mass in some areas of medical research and this can attract investment, a recent example being the establishment of the Translation Oncology Research Collaborative Hub at the Peter MacCallum Cancer Centre, with funding from Pfizer. However, the Group notes that such success stories are exceptions rather than the rule. Also, the absence of many multinational companies headquartered in Australia means that Australia has only one global centre of discovery R&D for new medicines (CSL) and one global centre of R&D

[57] A survey of the headquarters of ten multinational pharmaceuticals companies in 2005 identified human resources and infrastructure for R&D as the most important factors in investment decisions. Source: The Allen Consulting Group, *Drivers of Pharmaceutical Investment: Understanding Australia's Competitive Position*, report to Medicines Australia and Research Australia, 2006.
[58] In 2007, Australia was ranked 12th in the world for enforcement of IP rights. Source: Institute for Management Development, *IMD World Competitiveness Yearbook 2007*, 2008.
[59] See National Health and Medical Research Council Agency Budget Statement for 2008-09 for further funding details.

developing generic brands of existing medicines and new formulations (Hospira). This has resulted in Australia doing a disproportionately large share of activity in late stage clinical trials which, particularly when they are satellites of larger international trials, or are not designed, controlled or supplied with products invented and manufactured in Australia, generate lower but nonetheless significant spillovers and annuity to the Australian economy (see chapter 2 for more information).

**Figure 4.1 National Health and Medical Research Council Grant Funding: Expenditure and Forward Estimates**




## 4.3 Clinical trials

Clinical trials need to produce results on efficacy and safety that meet the regulatory requirements of each market. This requires quality clinicians and world class teaching hospitals with the infrastructure available to conduct clinical trials. Speed of regulatory approval for trials is important because it impacts on the already long timelines for drug development and the drug's effective patent life. Similarly the capacity to rapidly identify and recruit patients for clinical trials is important in this regard.

As later stage clinical trials (i.e. Phase III clinical trials) are less dependent on close collaboration between clinicians and pre-clinical researchers but more expensive to conduct and more mobile, they are more sensitive to cost. This is also true for bioequivalence studies for generic drugs which are becoming increasingly cost sensitive. The ability to recruit large numbers of patients per trial site can help to keep costs down.[60] Companies are more likely to conduct later stage trials in a country if early stage trials for that compound have already been conducted there. This is partly because the knowledge to administer the trial is already established, but also because of the move to adaptive trial design strategies where a trial will start like a current

[60] A Hajos and S Kamble, "The road to site selection in India", *Good Clinical Practice Journal*, vol. 15, no. 6, 2008, pp. 30-33.

Phase II trial and transform into a current Phase III type trial. Also, companies prefer to conduct later stage clinical trials in the key markets for potential commercial applications, as it helps in obtaining the right information for approval in that country and helps to build relationships with clinicians and key opinion leaders.

Australia is competitive as a location for Phase I clinical trials due to a generally fast approvals process, high quality clinical practice, an English speaking population, and a high volunteer rate. Australia's regulatory framework results in faster approval times for first in human studies than in other jurisdictions. Under the Clinical Trial Notification Scheme, the approval of the Therapeutic Goods Administration is not required where clinical trials have received appropriate scientific and ethical approval from an appropriate Human Research Ethics Committee.[61]

As a result of these factors, Australia has a growing Phase I clinical trial sector that employs over 300 people and earns over $50 million a year in revenue, most of which comes from overseas companies. According to a 2007 survey of the Phase I clinical trial sector, industry considered that Australia's most competitive advantage in early phase trials was the current regulatory system, followed by a quality of work conducted equal to anywhere else in the world. Cost was not seen as a major factor for early phase clinical trials. The survey also shows that the industry strongly believes Australia has a sustainable future as a destination for Phase 1 clinical trials for global clients and could easily become one of the world's top centres for early phase drug development.[62]

Quality clinical infrastructure and an ethnically diverse population, also make Australia a good location for all stages of clinical trials. However, there is evidence that the approval process for later stage clinical trials, as opposed to first in human studies, is slower in Australia than in other comparable countries.[63] In particular, the need to obtain separate scientific and ethical approvals for each site of a multi-site trial (typically Phase II and Phase III clinical trials) increases the cost and time burden disproportionately for these trials. Australia faces difficulties in recruitment for late stage clinical trials, including inefficient access to potential volunteers, often due to a lack of strong referral networks.[64] These delays in gaining approval and in recruiting patients are contributing to a decline in competitiveness for study start-up.

This is not the only barrier impacting on Australia's ability to attract later stage clinical trials. Australia is facing increasing competition from developing countries with larger patient populations, more treatment-naïve patients and the ability to perform later stage clinical trials for lower costs, and larger potential commercial markets. Group members reported that increasing charges for ethics approval and institutional overheads in Australia were affecting cost competitiveness. More clinical

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[61] Therpaeutic Goods Administration, *Clinical Trials at a Glance*, viewed 24 Sep 2008, <http://www.tga.gov.au/ct/ctglance.htm>.

[62] Department of Industry, Tourism and Resources, *Report on a Survey of Australia's Phase I Clinical Trials Units*, 2007, p. 4.

[63] In 2005, Australia was ranked equal last out of seven countries for the time taken for ethics approval of clinical trials. Source: Economist Intelligence Unit, *Benchmarking Study of the Characteristics of the Australian and International Pharmaceuticals Industries*, 2005.

[64] Pharmaceuticals Industry Council, *Clinical R&D in Australia: Innovation and Global Competitiveness*, report on the 3rd Pharmaceuticals Industry Council R&D Taskforce Forum, Sydney, 2-3 April 2008.

trials are being conducted in those lower cost locations that can provide the required quality of clinical infrastructure and trial delivery.[65]

Australia's competitive advantage lies in being a highly skilled, cost effective and timely place to conduct high value drug development activities, not in being the lowest cost location. This suggests that our long term competitive advantage in clinical studies lies more in Phase I clinical trials, and to the extent that we conduct Phase II and III trials, we should do so with a high value element retained in Australia. Additional clinical research investment from multinational companies can be attracted through Australian-based investigators initiating proposals for clinical trials and making use of R&D capabilities to value add to global drug development programs.

Australia's strong medical and clinical research base means we are well-placed to take advantage of these opportunities and these activities can create more value add for Australia. Having world-leading Australian clinicians on global advisory boards can also increase the profile of Australia as a clinical trials location. However, if the quantum of global Phase II and III studies conducted in Australia diminishes significantly, then the opportunities for Australian-based investigators to propose these projects and attract global funding will be greatly diminished.

## 4.4 Manufacturing

Key investment drivers for manufacturing are scale, cost, skills and IP protection. Low taxation rates are also important determinants of the location of large scale active pharmaceutical manufacturing plants, particularly for manufacturing sites that are distant from the largest markets.

Australia performs well in respect of IP protection and some skills, but less so against cost and taxation arrangements.[66] Australia is not cost competitive compared to many locations around the world such as India, China, Eastern Europe and South America. Similarly Australia does not match the significant taxation incentives offered by other countries such as Singapore and Ireland to encourage manufacturing activity.[67] As the quality of production in these ‘cheaper’ locations improves, the Australia's manufacturing sector will come under greater pressure. This pressure is likely to intensify in the face of broader global rationalisation trends.

Under a "business as usual" scenario, pharmaceuticals manufacturing in Australia may decline in future years – indeed the significant shift from full formulation to packaging only manufacturing in the past decade, and the closure of several facilities in the past 12 months is evidence that this is happening at a rapid pace already. However, trade figures suggest a more complex situation. Australia has an overall trade deficit in pharmaceuticals, but it is not low cost countries that are supplying

[65] On 7 April 2008, The Times of India reported that India was the most popular destination in Asia to conduct clinical trials and the value of trials - expecting skills shortage of 50 000 by 2010.

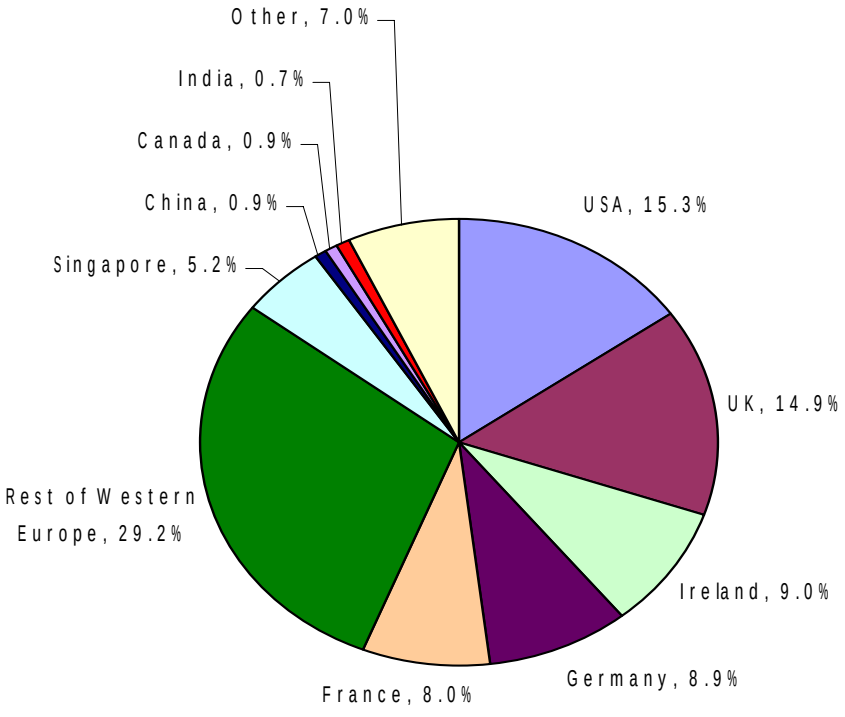
[66] According to a survey of the headquarters of ten multinational pharmaceuticals companies in 2005, The Allen Consulting Group, op. cit.; and a ranking of the Australian pharmaceuticals industry and operating environment against those of six other countries in 2005, Economist Intelligence Unit, *Benchmarking Study of the Characteristics of the Australian and International Pharmaceuticals Industries*, 2005.

[67] Submissions to the Review of the National Innovation System, 2008, by Hospira, Medicines Australia, Pfizer and the Pharmaceuticals Industry Council.

most of our imports: 85 per cent of 2006 imports were from the US, UK and Western Europe[68] (see **Figure 4.2**). Australian export destinations include low cost manufacturing locations like South Africa, South Korea, Taiwan, Thailand and China. In fact, Australia had a pharmaceuticals trade surplus with China of A$80 million in 2006. Australian pharmaceuticals exports have actually grown faster than those of India and China: export growth rates at 2005 were Australia 29.3 per cent, India 26.4 per cent and China 18.7 per cent.[69]

The industry's impressive export performance suggest that subsidiaries of international companies and locally owned companies have been successful in securing domestic and regional manufacturing rights and developing and maintaining niche production capabilities to offset competition from low cost centres. One example of this is a capability to produce small production runs with a multiplicity of labelling and packaging requirements for diverse Asian markets. Australian manufacturers will have a sustainable future if they focus on high quality, knowledge intensive, value added activity that is driven by quality and which low cost production centres find hard to replicate. The capacity of Australian manufacturers to do so will depend on their success at securing additional capital investment to maintain and develop these capabilities. However, major greenfield and brownfield investments will be unlikely while other countries are offering the sort of tax concessions available in Singapore, India, or Ireland.

**Figure 4.2 Origin of Pharmaceuticals Imports to Australia 2006**




[68] ABS unpublished data.
[69] Epsicom, op. cit..

.There may be the opportunity to expand Australia's alkaloid manufacture as the global demand for pain management increases with the ageing of the population. Australia is well placed to help meet this increased demand. The climate in the opium growing regions and the industry's advanced yield techniques make production attractive. Also the strict regulatory oversight in Australia would be seen favourably by the United Nations, which regulates the location of legal alkaloid production.

There may also be an opportunity for niche manufacturers to incorporate service aspects to their manufacturing and supply activities, particularly as distribution and delivery models change. For example, a possible future area of activity is product support for steps in personalised medicine: diagnostic testing, result interpretation and choice of therapy. This type of service could be delivered via Information and Communication Technology to healthcare professionals around the world, like other types of knowledge intensive business services which currently contribute to Australian exports.[70]

The timing of patent expirations is also a driver of the production of generic drugs. A report by the Intellectual Property Research Institute of Australia found that in around 66 per cent of cases, pharmaceuticals patents which have been extended expire later in Australia than they do in comparable countries.[71] As patent laws prevent generic companies from using Australia as a base to export generic medicines while patents are still in force in Australia, for many products, companies can only export generics from Australia much later than their competitors. There is compelling evidence that the majority of the returns to generic manufacturers accrue to first or second entrants, so this constraint places Australian generic manufacturers at a disadvantage, even to generic manufacturers located in USA, Canada or Western Europe.

## 4.5 Whole value chain

The changing nature of medicines is also an important factor that is influencing investment decisions across the value chain. The research driven industry is likely to shift from blockbuster drugs that are developed and marketed to treat large numbers of patients, to more drugs developed to treat patient subgroups.[72] Increases in novel delivery methods, biologic drugs, as well as associated testing (use of biomarkers) to identify suitable patients for treatment, gene therapy and cell-based therapies are forecast as part of this change. An increasing emphasis on preventative healthcare is also predicted, again linked to an increase in novel diagnostic procedures As pharmaceuticals business models shift over the next decade, it is expected that these emerging areas can offer greater opportunities to attract investment.

Australia has capabilities in a number of areas that can help it to take advantage of these emerging opportunities. The shift to more targeted therapies will be underpinned by genetics, genomics and other "omics" platform technologies, which are important for characterising the molecular basis of disease, identifying drug targets and developing biomarkers to identify the patient subgroups that will benefit most from particular therapies. Australia has world-class facilities for the use of these technologies, including those supported by the Australian Government through the

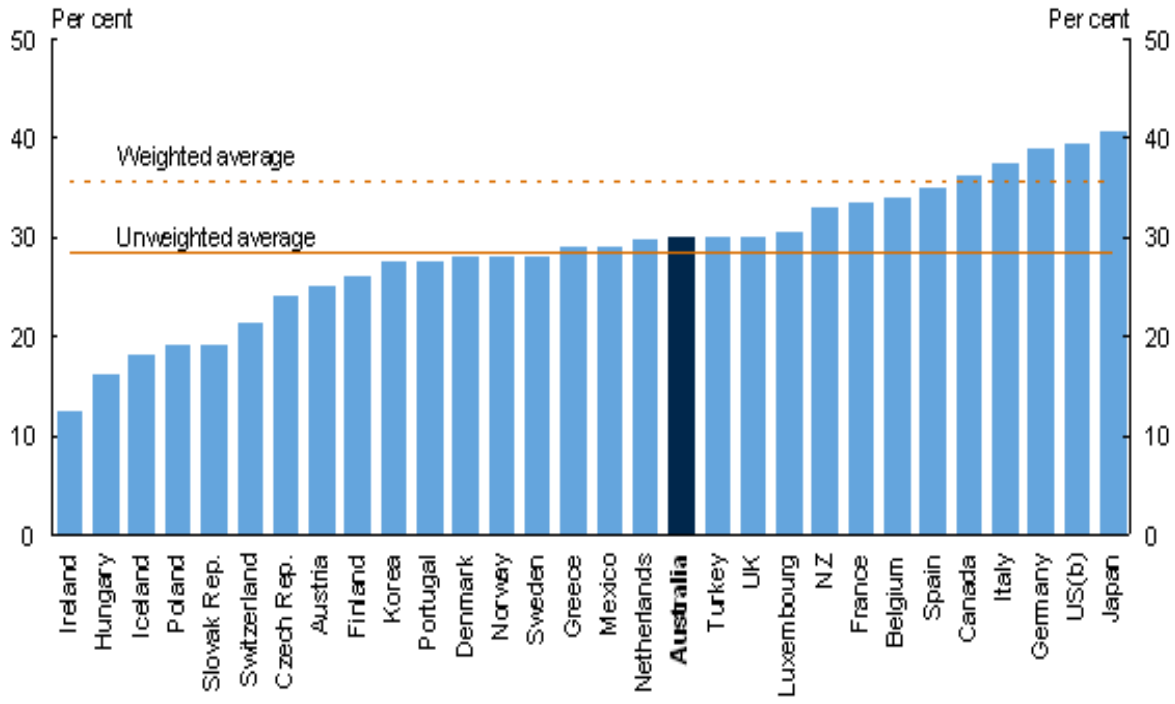
[70] Department of Industry, Tourism and Resources, *Australian Services Sector Trends*, Canberra, 2007.
[71] Intellectual Property Research Institute of Australia, *Review of Pharmaceutical Patent Extension and Springboarding Provisions in Various Jurisdictions*, 2002.
[72] PriceWaterHouseCoopers, *Pharma 2020: The vision. Which path will you take?*, 2007.

National Collaborative Research Infrastructure Strategy.[73] Australia also has a diverse population in respect of inherited diseases, which can benefit from targeted therapies. This can be seen as a driver for investment in developing targeted therapies for its own population, and it also makes Australia a suitable location for clinical trials for targeted therapies.

Australia's public and private sectors possess expertise in the new types of therapies: including companies developing and commercialising novel drug delivery methods, biologic drugs, therapies based on changing gene function and therapies that use human stem cells. Australia also has expertise in the development of vaccines, which are a key element of preventative healthcare. Australia's location places it across several infectious regions, making it a good location for conducting clinical trials for certain types of vaccines and for vaccine manufacture to supply the Asia Pacific region. Australia has global scale vaccine manufacture in CSL's facilities in Melbourne.

In terms of overarching barriers, the Group members noted that Australia's corporate tax rate was higher than many competitors and that this can be a disincentive for investing in Australian operations. **Figure 4.3** shows that Australia's corporate tax rate ranks equal 18th amongst the Organisation for Economic Co-operation and Development (OECD) economies.[74]

**Figure 4.3 Corporate Tax Rates in OECD Economies**




[73] Department of Innovation, Industry, Science and Research, *Evolving Bio-Molecular Platforms and Informatics*, viewed 29 Sep 2008, http://ncris.innovation.gov.au/capabilities/evolving_biomolecular_platforms_informatics.htm>.

[74] R Warburton and P Hendy, *International Comparison of Australia's Taxes*, 2006, p. 143.

## 4.6 Key drivers and barriers

The drivers for global pharmaceuticals investment, present opportunities to increase pharmaceuticals investment in Australia. In order to be able to take full advantage these opportunities, the barriers impeding this investment also need to be addressed.

Having considered the range of drivers and barriers, the Group chose those drivers and barriers that were priority issues to be addressed in the strategic plan for the industry. The agreed key drivers and barriers are shown in **Box 4.1**.

### Box 4.1 Key Drivers and Barriers to Investment in Pharmaceuticals R&D, Clinical Trials and Manufacturing in Australia

**DRIVERS**

- The changing nature of medicines.
- ***R&D*** **-** quality of the scientific and medical research base and infrastructure and the strength of the intellectual property (IP) protection regime.
- ***Clinical Trials*** **-** ability to value add to the global drug development program; investigator initiated clinical research proposals; and world-leading Australian clinicians (and centres of excellence) being sought for global advisory boards.
  - ***Early Stage*** **-** quality of scientific and medical research base and infrastructure, availability of clinical trials sites (suitable for early phase studies) and patients, speed in gaining regulatory approval to conduct the clinical trial.
  - ***Late Stage*** **-** quality of scientific and medical research base and infrastructure, availability of clinical trials sites and clinicians, speed in gaining regulatory approval to conduct the clinical trial, ability to recruit larger patient numbers per site, cost, growth/value of market in the country and previous conduct of early phase trials with the compound in the country.
- ***Manufacturing*** **-** scale**,** cost, skills and IP protection; quality, high level skills and specialised capability for niche production.

**BARRIERS**

- ***Tax*** **-** Australia's corporate tax rate is a barrier to increased investment.
- ***R&D*** **-** lack of critical mass, infrastructure gaps and few globally significant companies from which to develop global centres of discovery R&D.
- ***Clinical Trials*** **-** small population, increasing difficulty in identifying and recruiting patients, declining cost competitiveness and declining competitiveness in speed of study start-up.
- ***Manufacturing*** **-** not cost competitive against many of Australia's competitors and Australia does not offer the same levels of incentives as other competitors.

# 5 The Strategic Framework for Achieving a Sustainable Pharmaceuticals Industry

The changing global environment in which the industry will operate requires the development of a new strategic framework to facilitate industry growth. The Group evaluated the barriers and drivers to R&D, clinical trials and manufacturing and considered a number of options for how Australia could best position itself to attract higher levels of these activities.

## 5.1 Creating Local Strengths in a Global Value Chain

The Australian pharmaceuticals industry's future depends on its ability to enmesh itself within and add value in the global industry value chain. Manufacturers must seek to supply global markets and researchers developing medicines must continue to do so for global consumption. The industry's long term sustainability will depend on how successful local firms are in accessing global supply chains.

Our future rests with manufacturers who are able to win the rights to supply key products to global markets; researchers and biotechnology companies that are able to develop and commercialise new compounds; and companies who can commit to doing more early, globally-significant clinical trials here.

These are ambitious but realistic objectives for the industry to pursue. The industry does not need critical mass in every area of the value chain to be competitive. It is unlikely that Australia will ever have significant large scale active manufacturing ingredient capacity as these investments are mainly driven by tax incentives and are more sensitive to low operating and labour cost drivers as well as having lower quality/compliance requirements. Gaps in the industry's manufacturing and research infrastructure are likely to remain. The issue for Australia is how to leverage its significant strengths within the constraints of its relatively small population and significant distance from key global industry decision makers.

Australia has a world class medical research base, a highly skilled industry workforce and globally significant medical research infrastructure. These skills have the potential to provide Australia with a significant competitive advantage that can underpin early stage R&D, early clinical trials, later stage clinical trials with a high Australian value added component and value added niche manufacturing. The Group has not prescribed the niche areas that individual companies may choose to pursue, but notes that existing areas of niche specialisation exist around injectable products, products requiring blow fill seal based technology to produce and pockets of biologics manufacturing such as vaccine. Utilising its skilled workforce will be the industry's most effective mechanism to overcome increasing competition from low cost suppliers.

As chapter 4 outlined, the key drivers for R&D are the quality of the science base, medical research infrastructure and effective intellectual property protection. Because of the substantial and regular investments required to develop a world class medical research infrastructure and skills base, these attributes are harder for developing, low cost countries to create. However this is not a reason for complacency. Many countries that were not previously active in pharmaceuticals R&D have targeted the

industry as a priority and have begun to make significant investments in their science and research base. Australia has an advantage in this area that it is likely to maintain by continuing its recent heavy investment in medical research and research infrastructure.

At the same time, encouragement of continued investment of capital to support the maturing biotechnology industry will ensure that promising discoveries from the research sector can be picked up and developed locally, while close collaborations between industry and academic researchers will feed back into a deeper commercial awareness in the research sector.

Similarly, these strengths also mean that Australia is well placed to increase its share of early stage clinical research. Because later stage clinical trials are largely driven by factors unrelated to quality (such as cost and number of available patients), Australia is likely to face increasing competition for Phase III clinical trials, akin to the pressure it faces in respect of pharmaceutical manufacturing and meriting a similar response. Australia is unable to win a 'race to the bottom' on costs, nor will Australia ever have the same patient populations as emerging economies such as Russia, China, Brazil and India. Accordingly, Australia needs to increase its efforts to win more early stage clinical trial activity, which delivers higher spillovers, and to support later stage trials that include a high Australian value added component, which are therefore also likely to deliver high spillovers. Having the right regulatory framework, and research and skills base for this activity will be critical to ensuring that this objective is met.

Australia's skills and knowledge will also support a viable and sustainable manufacturing sector. While secondary manufacturing – primarily fill and finish rather than novel active material infrastructure – is one of the more cost sensitive parts of the value chain, skills remain a critical component of high value added manufacturing. Industry feedback is that whilst emerging economies like China have significantly cheaper labour costs, China is not as cost-effective as Australia on an operational costs basis. This is because lower labour costs are offset by the costs of quality assurance, compliance with strict international safety standards, managing staff turnover and efficiency of production.

Industry feedback is that, as a result, for more complicated manufacturing operations that involve greater levels of value added, Australia remains as cost-effective as 'cheaper' locations like China. The Department of Innovation, Industry, Science and Research is aware of one company that has been short-listed to become a regional supplier to Asia for complex products based on niche manufacturing technologies because it was rated to be more cost effective than competitor locations in China, India and Japan. The Australian operation was deemed to be more cost effective, not because it paid workers lower wages but because it was able to draw upon a more highly skilled and highly trained workforce that was more readily able to meet strict quality control standards and had greater production capabilities.

This is not an isolated example and is a model that should be used to sustain Australia's manufacturing sector. This model will lead to increased exports, employment and value added activity. The Group is confident that Australia has great potential to expand its value added niche manufacturing sector, but is less confident that this will result in a net increase in the pharmaceuticals manufacturing sector. This is because not all areas of pharmaceuticals manufacturing have the same complexity.

Packaging operations, which are the least technologically sophisticated aspect of the manufacturing value chain, are much more sensitive to cost. Australia's skilled, efficient and adaptive workforce will not provide the same buffer to low cost competition for this phase of the value chain. Australia does not have a competitive advantage in this space and is likely to lose activity to competition.

Therefore the future of the manufacturing sector relies upon the ability of the industry to invest in the skills and infrastructure required to expand its value added, niche production capabilities. Opportunities in this area are expected to increase as more biotechnology companies develop products through to clinical testing stage, with a workforce already skilled though MNC manufacturing activities available to take up these new opportunities as they arise.

The Group notes that existing lower cost economies, which may be highly competitive in the lower value added manufacturing but less so in more complex areas, are investing heavily in infrastructure and skills to improve their competitiveness. The Australian industry – with well targeted government support - needs to improve and leverage it existing sources of comparative advantage. Hence, any package of measures to increase investment in the industry will need to leverage Australia's skills and knowledge base, not simply seek to offset the cost advantages of some other economies in lower value added manufacturing. Any strategy that does not seek to exploit this strength and react to incentives or cheaper costs offered elsewhere is unlikely to succeed in the long run.

## 5.2 Vision for a Sustainable Pharmaceuticals Industry

Following on from the consideration of the local strengths in the value chain, the Group developed a vision for what an industry with these attributes would look like in 2020. This vision is shown in **Box 5.1**.

### Box 5.1- Vision Statement

*By 2020 Australia will have globally competitive and sustainable R&D, clinical trials and manufacturing sectors that make a positive and increasing economic and social contribution to Australia. These sectors will:*

- *draw on and support the best of Australia's medical and related R&D;*
- *foster the formation and progression of commercial enterprises from discovery through clinical development, manufacturing and product sales, supported by an associated service sector;*
- *optimise the interactions between large and smaller enterprises across the industry; and*
- *compete successfully in the global environment.*

*By 2020 the Australian industry will be characterised by:*

- *sustainable growth;*
- *an environment conducive to attracting investment in R&D, clinical trials and manufacturing;*
- *world class early stage R&D;*
- *strong links between industry and the academic research community;*
- *a capability to deliver effective, timely and high quality clinical trials;*
- *effective partnerships that provide global reach for local Australian companies;*
- *a growing and increasingly mature biotechnology sector developing therapeutic products for global markets;*
- *a complementary, growing and value adding manufacturing sector supporting high skilled, high wage jobs; and*
- *a world leading regulatory and reimbursement system that has adapted innovatively and effectively to the opportunities presented by biological and other targeted therapies.*

## 5.3 Alignment with Government Policy

Any strategy for the pharmaceuticals industry must be consistent with existing Government policy, particularly relevant health and regulatory policy, and obligations under our trade agreements. The Group acknowledges that the complexity of the full range of industry activities requires a whole of Government approach.

The Group considers that this is an opportunity to build on the framework set out in the National Medicines Policy (NMP) to co-ordinate health and industry policy objectives. The four principles of the NMP are:

- timely access to the medicines that Australians need, at a cost individuals and the community can afford;
- medicines meeting appropriate standards of quality, safety and efficacy;
- quality use of medicines; and
- maintaining a responsible and viable medicines industry.[75]

[75] Department of Health and Ageing, *National Medicines Policy 2000*, Canberra, 1999.

Whilst the fourth arm of the policy is the only one that explicitly refers to the industry, the others have significant industry policy implications. Timely access to medicines for consumers cannot be achieved without providing industry with predictable paths to market, the ability to access markets quickly, and an engaged and leading clinical community at the forefront of medical practice – an outcome in part sustained by ongoing excellence in clinical research in Australia. Similarly, medicines of appropriate safety and quality can only be delivered by a world class regulatory system that is internationally recognised for its quality.

A strong and effective regulatory environment is especially important in providing the industry with the confidence to conduct R&D into products based on converging technologies (drugs, devices, therapies and diagnostics) and those based on enabling technologies such as nanotechnology. Increasing technological convergence is providing companies with a wider array of choices to develop new therapies. Future industry R&D is likely to be increasingly targeted towards the development of medicines that, based on the current regulatory framework, need to be considered by multiple agencies and multiple divisions within agencies.

Australia's challenge is twofold: to extend the Therapeutic Goods Administration's (TGA) reputation for global excellence into these fields; and to streamline and simplify the regulatory environment for dealing with these new-style medicines and therapies. This would help Australia develop a 'first regulatory mover' advantage that would help to position Australia as a global centre for R&D into these activities.

The Group would also encourage the Australian Government to explore greater harmonisation of international regulatory systems for pharmaceuticals to reduce the time and cost of seeking regulatory approval in other markets around the world.

The Group takes the position that Australia's regulatory framework is already world class but that relatively small refinements could lead to a significant improvement in Australia's attractiveness for pharmaceuticals R&D. This is especially true for the regulatory environment for multi-centre clinical trials, which, compared to other jurisdictions around the world, is relatively cumbersome and is an impediment to investing in Phase II and III clinical trials in Australia.

The Pharmaceutical Benefits Scheme (PBS) is a critical determinant of market access and from industry's perspective needs to offer a transparent, timely and predictable system of reimbursement. The Group resolved that the PBS issues and opportunities are best addressed through established mechanisms such as the Access to Medicines Working Group, the Pharmaceutical Industry Working Group and the Department of Health and Ageing and Generic Medicines Industry Association Working Group. Accordingly, the Group has developed its recommendations in the context of the PBS as it currently stands. The Group does not believe that this is an appropriate forum for suggesting changes or improvements to the PBS, nor to recommend industry support mechanisms that are contingent upon firms supplying products to the PBS.

Nevertheless, the Group believes that pharmaceutical market developments present the PBS with significant opportunities and challenges. For example, the rapid emergence of targeted therapies, particularly biologics, presents Australia with a real opportunity to provide timely access for the Australian community and also position Australia with the international industry as a nation that understands key global

industry directions. Typically, the data required to clearly delineate the full range of economic benefits from targeted biologic therapies cannot be obtained until patients have broader access to the therapy. Collection and provision of evidence may therefore need to be seen as an ongoing process, in order to allow timely listing of these therapies, many of which are either truly life-saving or offer major quality of life benefits. Providing this flexibility could also encourage additional clinical trials into these therapies to be located in Australia. The Group would urge that these issues are examined in the foregoing forums.

The rate of corporate tax also has an impact on Australia's attractiveness as a location for industry activity. The Group supports the statements in the Review of the National Innovation System that: lower company tax raises economic growth by increasing investment, particularly foreign investment; and the case for lowering company base rates in Australia is strengthened by the fact that over the last 15 years, many OECD countries have cut their tax rates such that Australia is now clearly above the OECD average.[76] While there is some conjecture within the Group on the precise effect of this factor in attracting investment, it is likely to be material, particularly for the more cost sensitive activities. Nevertheless, the Group resolved that this issue is best addressed through the Review of Australia's Taxation System.

## 5.4 Role for Government

The Government has an important role to play, in partnership with industry, to help achieve the 2020 vision the Group has articulated. The Government can facilitate the growth of the industry through targeted grant programs to provide industry with the assistance and incentive to undertake value added activities that generate broader benefits.

While these interventions can be beneficial, the Group considers that the Government's role in creating the right operating environment for industry growth will have as much impact on the industry's long term sustainability as a granting scheme alone.

A viable and sustainable pharmaceuticals industry requires:

- predictable, timely and transparent regulatory and reimbursement systems that provide companies with a clear and streamlined path to market;
- an appropriate and balanced intellectual property regime;
- strong and effective capital markets that will fund high quality and high potential but risky projects;
- competitive taxation arrangements that provide incentives for companies to invest in relatively high risk activities like R&D and complex, value adding pharmaceutical manufacturing;
- an appropriately resourced tertiary education sector capable of producing high quality, job ready science and medical research graduates; and
- strong and effective collaboration between industry and research.

[76] The Review of the National Innovation System, *Venturous Australia*, 2008, pp. 99-100.

Many of these factors will not be addressed through Government grants to industry but through the regulation of medicines, clinical trial approval, higher education funding and maintaining an effective IP regime. To this end the Group considers that the Government needs to develop an innovative across-Government approach to dealing with the complex policy issues that impact on industry growth such as regulation, reimbursement, taxation and skills.

Policy responsibility for many of these issues lies outside the innovation and industry portfolio and developments in these areas should take account of their impact on industry growth and competitiveness.

The Group welcomes the Government's decision to reconvene and revitalise the Pharmaceutical Industry Working Group (PIWG).[77] The Group considers that PIWG is an important forum for ensuring that issues that affect the growth of the pharmaceuticals industry are considered in a whole of Government context. The Group would urge the Government to invite other senior Ministers to PIWG meetings on an as needs basis to allow it to discuss issues relating to tax and skills.

The Group is mindful of its responsibility to develop proposals that will deliver a net social and economic benefit by 2020, without disadvantaging other sectors of the Australian economy. Given the long lead times for most pharmaceutical projects and their innovative nature, it is difficult to define precise projects that will do this. Consequently, the Group has limited its recommendations to those that it considers have a significant likelihood of delivering a net economic and social benefit in the short to medium term. To the extent that the recommendations involve support for specific projects, the Group has suggested competitive criteria that are most likely to select projects that deliver superior economic and social gains. These proposals are detailed in Chapter 6.

## 5.5 Existing Proposals for Strategies

In considering options for future strategies, the Group considered proposals developed through other processes: submissions to the Review of National Innovation System and other submissions by relevant industry bodies. The Group also considered the lessons learned from previous Government programs and considered the findings of the evaluation of the Pharmaceuticals Partnerships Program ($P^3$).[78]

### Comments on Evaluation of $P^3$

The Group felt that the evaluation of $P^3$ did not adequately quantify the impacts of $P^3$. First, there is inherent difficulty in undertaking an impact analysis where the results depend on the methodology and assumptions that are used. Second, the three year timeframe for evaluation of the program does not allow the long-term benefits to be captured, particularly the benefits of partnerships and the development of new drugs, which have long lead times. It may be 10 to 15 years before R&D supported under $P^3$ results in significant economic return to Australia in the form of increased exports, employment and tax revenues. Third, it is particularly difficult to measure the broader economic and social benefits of pharmaceuticals activity, such as faster patient access

[77] Kim Carr and Nicola Roxon (Minster for Innovation, Industry, Science and Research, and Minister for Health and Ageing) *Govt Revitalises the Pharmaceutical Industry Working Group,* media release, Parliament House, Canberra, 8 Apr 2008.
[78] Deloitte Insight Economics, *Evaluation of the Pharmaceuticals Partnerships Program*, 2008.

to innovative medicines through clinical trials and better patient health outcomes through attracting and retaining clinicians with cutting-edge knowledge. These limitations, which are acknowledged in Deloitte's report, mean that the estimated neutral impact of $P^3$ is likely to be a significant underestimate of the benefits that will accrue to Australia.

Deloitte found that $P^3$ had only a moderate to low impact on half of its key performance indicators, including the number of multinational companies establishing new regional or global R&D operations in Australia, and the number and quality of linkages and new collaborations. Group members emphasised that a key failing of $P^3$ was the $10 million cap, which meant that grants were too small to influence the decision-making of multinational companies. To be effective, grants would need to be commensurate with the size, complexity and timelines of commercial R&D activities.

Given the difficulty in estimating a value for the impacts of $P^3$, members felt that the important issue was not the numerical value of the estimated impact, but to consider what features would be needed in any new program to ensure that greater benefits were captured. In this respect, members agreed with Deloitte's finding that $P^3$ should not be renewed in its current form. Approaches to maximise the net social and economic benefits have been central to the Group's development of proposals for Government and industry action for the pharmaceuticals industry into the future.

## Recommendations of the Review of the National Innovation System

Minister Carr released the report of the Review of the National Innovation System (the Review) on 9 September 2008. The Group considered the recommendations of the Review that are relevant to the work of the Group, specifically those recommendations that could help to address the key barriers to attracting investment in pharmaceuticals R&D, clinical trials and manufacturing to Australia.

### *Small biotechnology companies conducting R&D and clinical trials*

Lack of critical mass was identified as one of the key barriers to attracting significant R&D investment to Australia. One way to build critical mass is through the growth of the R&D-focused biotechnology sector, through growth of individual companies and mergers and acquisitions. The Group was supportive of the recommendation of the Review that would support small biotechnology companies that are pursuing quality projects – those founded on good science, with sound commercial prospects if they overcome the technical risks – in progressing their R&D programs to later stage development in Australia.

Members were supportive of the **Competitive Innovation Grants Program (recommendation 9.1)** as a way to provide capital to biotechnology companies conducting early stage R&D. The program is aimed at companies in the high-risk, proof-of-concept and development stages with limited access to capital. With the long development times and high costs of pharmaceuticals, some members were concerned that the program may not provide sufficient capital for biotechnology companies to move beyond this high risk stage to a position where they can attract investment from other sources. Linking eligibility to national innovation priorities also creates some uncertainty as to whether drug discovery and development would be recognised as eligible for funding, as this would depend on how the priorities were defined. Pharmaceuticals are central to meeting the current and future healthcare needs of Australia and should be explicitly included in the suggested population health priority.

Developing national innovation priorities that unambiguously capture pharmaceuticals R&D would ensure that the benefits of this high spillover R&D activity could be supported.

Some, but not all members supported the recommendation that the R&D Tax Concession be changed from a tax deduction to a tax credit (**recommendation 8.2**). Similarly, some but not all of the Group supported the **refundable 50 per cent tax credit for R&D (recommendations 8.3 to 8.6)** on the basis that it would provide an increased level of support to local biotechnology companies undertaking R&D. In particular, some members felt that this tax credit would provide more support to smaller companies than the current R&D Tax Offset because the increased turnover limit of $50 million is more appropriate for R&D intensive biotechnology companies. Biotechnology companies in tax loss typically have a high cash burn rate to support their R&D programs.

Members welcomed the Review's recommendations to strengthen early stage venture capital in Australia. Some members put forward the view that the capital market in Australia does not have an appetite for the risk profile associated with pharmaceuticals development, particularly in the face of competition from mining investment opportunities, and that the resulting undercapitalisation of Australian biotechnology companies was limiting Australia's ability to capture annuity from investment in medical research.

Members supported the recommendation to establish additional **Pre-Seed Funds (recommendation 9.9)**, to encourage commercial development of public sector research, and the recommendation to continue the **Innovation Investment Fund (IIF) program to a fourth round (recommendation 9.8)**.

Members agreed that the benefits of the IIF program lie not only in it acting as a direct incentive for investment in early stage, R&D intensive companies, but also in building the pool of experienced fund managers that then have sufficient investor confidence to be able to raise larger funds, independent of the program. This will be beneficial in the longer term, but some members felt that the Review's recommendations would still leave a gap in the availability of funding in amounts above $10 million, investment amounts which are needed at the mid stage of biotechnology company development, as capital requirements rise for early and mid stage clinical trials. It has been difficult to get data that gives a clear picture of the availability of venture capital for biotechnology, and members agreed that this issue should be explored further as the work of the Group continues.

### *R&D in large pharmaceuticals companies*

R&D critical mass can also be built through investment from large pharmaceuticals companies. Members agreed that the Review did not offer any incentives that would attract significantly more R&D investment from large pharmaceuticals companies. Members were disappointed that there was no incentive to increase R&D intensity and they also felt that, while the 40 per cent tax credit would provide a benefit to a range of R&D activities (e.g. R&D by multinational companies that had not previously been able to access the 125 per cent R&D Tax Concession), the level of benefit may not be enough to drive a significant increase in R&D investment in Australia.

### *Infrastructure*

Gaps and lack of scale in R&D and manufacturing infrastructure are limiting Australia from capturing more value from investment in medical research and the opportunities to be part of global pharmaceuticals supply chains. The Review included recommendations to build on the National Collaborative Research Infrastructure Strategy to fund R&D infrastructure **(recommendations 6.13 and 6.14).** Members agreed that recommendations could lead to some multi-user R&D infrastructure that was useful to the pharmaceuticals industry, but would not provide a strong incentive for companies to undertake significant investment in qualitatively different infrastructure that would make the industry more competitive in the long term. The Review offers no incentive for the development of infrastructure to support high value, sustainable pharmaceuticals manufacturing.

### *Skills and education*

Having identified the undersupply of job ready graduates as a significant issue facing the pharmaceuticals industry, the Group welcomed the Review's recommendations on human capital. A number of recommendations would add to science training opportunities and the attractiveness of R&D careers: reforms to build high quality human capital **(recommendation 5.1)**; an increase to the Australian Postgraduate Award Stipend **(recommendation 6.11)**; and an early career fellowship scheme **(recommendation 6.12).** The recommendations to align immigration policy and innovation policy **(recommendation 5.2)** and for accelerated pathways for professional transitions **(recommendation 5.3)** could assist in filling the skills gap.

However, members agreed that more needs to be done to meet the skills gap by ensuring that graduates have the necessary knowledge, skills and experience to make them ready for a job in the pharmaceuticals industry, whether this is in small biotechnology companies or larger pharmaceuticals operations. Changes are also needed to improve the mobility of personnel between the public and private sectors. This would help to provide highly skilled personnel for industry and would also facilitate greater transfer of skills and knowledge. For this reason members expressed in principle support for continuation of a modified Cooperative Research Centres (CRC) Program (**recommendation 9.4**) as one way to assist in industry-relevant research training, but acknowledged that none of the Review's recommendations specifically addressed the skills gap in the pharmaceuticals industry.

### *Issues that still need to be addressed*

Having considered the recommendations of the Review of the National Innovation System, the Group’s members agreed that even if all the recommendations were implemented, several key barriers to attracting pharmaceuticals investment would not be addressed.

1. The Review does not offer enough to address the undersupply of skilled workers for the pharmaceuticals industry.
2. The Review does not address changes that are required to the operating environment to make Australia a more attractive location for pharmaceuticals investment, including reform of the regulatory approval process for clinical trials.
3. The Review provides no incentives that would encourage the type of high value, strategic pharmaceuticals investment in R&D, clinical trials and manufacturing that would provide enduring benefit to Australia.

# 6 Recommendations to Achieve a Sustainable Pharmaceuticals Industry

The Group considered a number of options to increase R&D, clinical trials and manufacturing in the Australian pharmaceuticals industry. However, the Group discounted a number of options because they do not consider they would deliver a net economic or social benefit or that there was sufficiently strong rationale to justify Government action. The Group has so far agreed to put forward three recommendations which we hope would be further refined through stakeholder consultation. These recommendations include strategies to:

1. encourage strategic investment in pharmaceuticals R&D, manufacturing and infrastructure;
2. increase Australia's attractiveness as a location for clinical trial activity; and
3. improve pharmaceuticals skills and education.

The Group does not view these measures as alternative strategies. Measures 2 and 3 are not costly and should be pursued. They also contain quite specific actions, such as establishing a National Clinical Research Agency, the specific merits of which will be further reviewed in the final report. The first measure is likely to be the most costly. Hence, while it can be expected to deliver the largest net economic and social benefit, it will require more scrutiny in the context of broader Government priorities.

These strategies are proposed on the basis that the recommendations of the Review of the National Innovation System are implemented, as discussed in Chapter 5. Also, the Group believes that there are several other enhancements to the business environment for pharmaceuticals that are needed. These have been discussed earlier and will be considered further as the Group prepares its final report.

This chapter:

- describes the reforms the Group is seeking;
- articulates why these reforms should be undertaken;
- presents the preliminary business case for why the Government should enact these reforms; and
- identifies the performance metrics that should be used to determine the effectiveness of these reforms.

## 6.1 Proposal for a Pharmaceuticals Investment Fund (PIF)

PIF is a new program targeted to the biopharmaceutical industry to achieve lasting value from four principal drivers:

- facilitating the growth of the local industry;
- helping to sustain existing manufacturing and infrastructure;
- growing new infrastructure in strategic areas; and
- achieving sustainable employment and exports.

The PIF is an investment fund to act as an incentive for strategic investments in the pharmaceuticals industry that will result in a net benefit to Australia. It will:

- co-fund investments that will support sustainable, high value industry activity, with the level of co-funding dependent on the assessed future benefit to Australia (a maximum co-funding level recommendation will be made in the final report);
- be open to R&D, clinical trials (including Phase I, II and III clinical trials), manufacturing and infrastructure investments that build sustainable new capabilities in Australia;
- fund both infrastructure and activity that meet the merit criteria and are assessed as being of future benefit to Australia;
- attract footloose investment (not tied to a particular location) that might not otherwise not occur in Australia;
- be accessible by all Australian companies in the areas of pharmaceuticals, diagnostics, delivery mechanisms, medical devices and other therapeutic products and devices;
- include support for firms that are seeking registration for their products by the EMEA or FDA;
- award funds only after a rigorous, competitive assessment process undertaken by an independent, appropriately qualified panel, using merit criteria that will ensure selection of projects that will result in a net benefit to Australia;
- be of a size to support significant investments;
- not award monies unless applications of significant merit are received; and
- be subject to standard Australian Taxation Office clawback provisions.

### Possible Merit Criteria

Key criterion: investment will generate a net benefit to Australia.

- Economic and social benefits to be considered, such as:
  - workforce training and skills development that would be valuable more widely than to the project in question;
  - creation of sustainable, high-skilled jobs;
  - building international and domestic R&D networks;
  - partnering opportunities for Australian companies, research institutes and academic institutions;
  - identifiable diffusion of new knowledge;
  - improved industry productivity through reduced duplication and critical mass to reduce input costs.
- Evidence of enduring benefit, such as:
  - building a capability that will be difficult for competitors in other countries to replicate;
  - capturing increased value from Australia's investment in medical research;
  - anchoring high spillover activities in Australia;
  - delivering a sustained royalty and/or value added manufacturing to Australia.
- Claims against the merit criteria to be substantial and tangible.

## What are the Problems that this Strategy will Address?

The biopharmaceutical community in Australia has several components required for an economically important driver for the nation, utilising highly educated and skilled people and generating wealth, jobs, and international competitiveness in a consolidating market.

Market Failure exists as follows.
Innovation in terms of new medications can only be justified at the global level. Australia's ability to derive long term economic value from R&D is limited by the underdeveloped state of local capital, infrastructure and human resources to take discoveries to market. The local capital market, the limited range of skills and experience in the industry, and lack of internationally harmonised infrastructure are examples of the challenges Australian institutions must overcome to be successful internationally and to add Australia's long term value.

The areas to be addressed include:

- scarce areas of critical mass (higher risk of failure, difficulty of financing);
- appropriate skills and experience (across the R&D spectrum, mainly development R&D);
- translation of opportunities for the developer of the drug, device or diagnostic (e.g. taking an early stage product to commercialisation and manufacture) into long term gain for Australia;
- variable but often inadequate linkage of universities and research institutes to the established biopharmaceutical industry, over a range of areas (funds, leadership, skills, sponsorship);
- short-termism (premature commercialisation, agreements prior to creating enduring value for Australia);
- suboptimal capital resources and incentives to build manufacturing capability; and
- inefficient provision/interstate competition.

The trend to globalise supply chains makes it difficult for Australian subsidiaries of multinational companies to justify continuing investment in local plants.

The areas which need to be addressed include:

- harmonising international regulatory compliance with foreign regulators;
- developing skills and qualifications relevant to manufacture for export; and
- recognising the incremental costs involved in being able to acquire international approval and qualification.

## Business case – Outline

### *Briefly describe how the proposal is consistent with the principles of:*

### *- appropriateness*

A new Government co-funding scheme is needed to address these issues of critical mass and scale and these must be aligned with the development, regulatory, manufacture and commercialisation spectrum. It should be restricted to applications which optimise long term contributions to Australia. The program should thus encourage local development leading to local capture of value and, where appropriate, manufacture of end products, to maximise return in investment and benefit to Australia.

Companies could bid for co-contributions at any stage of the development-manufacturing-registration cycle, where the level of co-contribution from the complementing investment would be measured on the basis of ultimate long term net economic value.

PIF should also make co-payment for skill development as a necessary component of the registration process, for the plant which manufactures the product(s), and participants who exploit existing infrastructure, public and private.

In these ways the PIF scheme attempts to redress the market failure where Australian resources, (capital, skills, regulatory pathway, infrastructure) are inadequate to build an industry with global capabilities.

### *- effectiveness and efficiency*

This program will be effective at inducing new high quality pharmaceuticals activity in Australia. It will provide a commercially attractive incentive that will encourage companies to do qualitatively different activity in Australia that will boost the industry's capabilities.

Funds will only be awarded to activities that have been independently assessed as having a high likelihood of delivering a net economic and social benefit to Australia and an ongoing annuity to the economy. This will ensure that scarce public resources are focused on activities that will deliver spillovers. It will also develop industry capability that will position companies for a sustainable, value adding future in Australia to maximise the industry's ongoing contribution to the Australian economy.

This new scheme rewards applicants for optimum Australian activity and long term benefits to Australia. Only Australian-based activities would be funded, with approved exceptions where it is impractical to undertake activity in Australia (as agreed by an advisory committee, due to factors such as patient access, regulatory requirements, lack of infrastructure). The program should include a range of co-funding ratios which reflect the future value to Australia from the activity. Examples of activities that would qualify are:

- extended development of a biotechnology product from Australia prior to out-licensing, ensuring greater capture of value from Australian-derived research;

- enhancement of the skill base and specialised activity within the industry including training and re-skilling in Good Manufacturing Practice certification; and
- activities which expand local capability through the later stages of the development-manufacture-registration cycle.

The PIF would need to offer a significant level of support to achieve its objectives. The Group will consider levels of support for its final report.

### *- performance assessment used by Government to assess whether the program is meeting its objectives*

AusIndustry would deliver the program, advised by an expert committee recruited from the relevant and experienced industry/institutional communities.

The expert committee would need members with first hand experience, and to provide suitable expertise across the range of investments that would be eligible, Members might also be co-opted when there is a need for specialised advice, (e.g. a familiarity with FDA, commercialisation experience, manufacturing and quality expertise, etc.).

Program administration details including the milestone driven process, variation approval and governance, which characterise the current $P^3$, are appropriate to continue.

Consideration should be given to developing new rules and guidelines for issues such as change of control, and migration of Australian activity offshore.

### *- integration and strategic policy alignment*

- Aligns with general funding for health, NHMRC grants, existing institutional support, venture capital funding.
- Represents a continuing development of a series of programs which have invested in and supported the fledgling Australian biopharmaceutical industry to date, including the proposed Competitive Innovation Grants, which would act as a feeder system for this program.
- Seeks to grow high value adding industries.
- Expands manufacture for exports.
- Capitalises on Australia's world class discovery capability.
- Provides Commonwealth incentives to continue developing infrastructure for the nation's benefit.
- Gives leadership to the industry which in turn will encourage investment in innovation and commercialisation.
- Offers internationally-owned and Australian companies the same rights of access, and extends the previous schemes in terms of infrastructure support.

### Suggested implementation timetable

By July 2009 as $P^3$ expires on 30 June 2009.

## 6.2 Proposal for a Strategy to Increase Investment in Clinical Trials

### Reforms to Increase Australia's Attractiveness as a Location for Clinical Trials

A package of reforms to increase Australia's attractiveness as a location for clinical trials, including:

- acceleration of implementation of a national streamlined system of ethics approval processes for multi-centre clinical trials (including a National Patient Consent Form);
- implementation of improvements to the regulation of clinical trials identified as part of the moves towards the establishment of the Australia New Zealand Therapeutic Products Agency;
- establishing a National Clinical Research Agency to
    - undertake and expedite the development, implementation, and coordination of initiatives to improve global competitiveness through reforms of clinical research in Australia designed to improve Australia’s quality, timeliness, value and capacity for clinical trials
    - actively promote Australia as a destination for clinical research, and
    - regularly review global trends in clinical research to measure Australia's attractiveness as a competitive destination for clinical research;
- implementing a national approach to clinical research training and accreditation;
- acceleration and cutting edge use of e-health initiatives (consistent with privacy concerns) to create global competitive advantages and improve efficiency for clinical trials in Australia including
    - ensuring electronic medical records implemented in public hospitals meet industry needs, especially in regard to appropriate access for study monitors
    - requiring that new systems and health system policy allow remote access for study monitors to hospital records (with appropriate security measures in place) to allow remote monitoring (which will improve efficiency through reducing travel needs for onsite monitoring of trial data, thereby reducing greenhouse gas production)
    - instituting an exploratory project to propose innovative uses of Australian e-health initiatives to further support patient recruitment for clinical trials in Australia, including use of pathology results and taking into account appropriate considerations in regards to the relevant privacy acts (e.g. use of pathology results to identify trial patients in New Zealand)
    - ensuring that the national ethical approval system and/or the Clinical Trial Notification scheme will include an IT platform that creates an up-to-date and comprehensive record of clinical trials across Australia that can be used as an activity metric, as well as to monitor the effect of policy changes and observe trends in clinical trial activity over time; and

- implementation of coordinated, national patient referral networks in areas of high trial activity (supported by above e-health initiatives).

### What are the Problems that this Strategy will Address?

A number of features of the Australian environment for clinical trials provide disincentives for placing global trials in Australia or may result in Australia losing global competitiveness:

- the regulatory environment imposes cost and time delays on businesses and reduces Australia's international competitiveness as a destination for pharmaceuticals investment, particularly in the area of clinical trials;
- a relatively small and geographically dispersed patient population provides challenges for trial efficiency (smaller patient numbers per sites and larger site numbers compared to emerging markets such as India and China) and higher travel costs to monitor the study;
- significant increases in trial costs in Australia (especially related to ever growing institutional overheads and increases in ethics fees) in recent years have seriously compromised Australia's global competitiveness for trials on a cost basis;
- Australia's success in attracting trials in some therapeutic areas means that further growth will need to be supported by development of improved patient referral networks and other means to improve the capacity of Australia to supply more patients for clinical trials; and
- the lack of a clear and co-ordinated policy approach to clinical trials in Australia at both a Federal and State level and across the health system, especially needed in recognition of the systematic and determined approach being taken in competitor locations to attract clinical trials.

These features, many of which are unnecessarily cumbersome, make it more expensive to conduct clinical trials (and other activities) in Australia, and can in some cases tip the balance in favour of doing this activity elsewhere in the world.

### Business case – Outline

#### *Briefly describe how the proposal is consistent with the principles of:*

#### *- appropriateness*

The implementation of these regulatory reforms would increase the competitiveness of the Australian pharmaceuticals industry by strengthening Australia's attractiveness as a destination for clinical trials by removing unnecessary costs and time delays.

The inefficiencies of the current regulatory system prevents Australia from appropriating the economic and social benefits associated with clinical trials and prevents the industry from developing critical mass in this area.

The inefficiencies of the current regulatory system are making it harder for Australia to compete against a growing number of competitors who are now faster and more cost-effective at performing clinical trials than Australia. Government intervention is required to remove these inefficiencies to allow Australia to compete more effectively

with other locations. This will result in an increase in clinical trials in Australia, generating broader economic and social benefits.

Many of these initiatives have already been agreed to by Government. This proposal will ensure the implementation of these initiatives is accelerated and the regulatory 'bottlenecks' preventing more clinical trial activity are removed.

### *- effectiveness and efficiency*

Reforms to Government regulation are not costly to implement but require significant consultation across a number of jurisdictions. Much of the work on these initiatives has already commenced, but needs to be accelerated and implemented consistently and quickly across State and Territory jurisdictions.

The implementation of these measures will lead to an increase in the number of clinical trials in Australia and reduce the time patients need to wait for medicines, which will deliver significant sustainable economic and social benefits.

A simpler, more streamlined and cheaper approval process for conducting clinical trials will make it easier for Australian biotechnology companies to take their potential products further along the drug development chain rather than out-licensing them at an earlier stage. This will help to retain more of the value from doing R&D in Australia.

### *- performance assessment used by Government to assess whether the program is meeting its objectives*

Indicators that could be included in assessment:

- reduced time to approve clinical trials;
- reduced cost of achieving these approvals for both companies and regulators; and
- increase in the number and value of clinical trials conducted in Australia.

### *- integration and strategic policy alignment*

This package is consistent with the Government's broader deregulation agenda. It is also consistent with the national e-health implementation strategy. This proposal is not an alternative to the initiatives currently underway in relation to e-health; rather it is designed to complement existing Government policy in this area. Similarly, these initiatives would need to be undertaken in away that is consistent with Australian Government privacy principles.

### Suggested implementation timetable

- Identify regulatory reform priorities by July 2009 including mapping work already being undertaken in jurisdictions.
- Outstanding regulatory reforms in the Australian Government's responsibility concluded by 30 June 2011.
- State and Territory Governments encouraged to complete their actions.

## 6.3 Proposal for a Strategy to Improve Pharmaceuticals Skills and Education

### Initiatives to Improve the Quality of the Higher Education and Research Sector and its Responsiveness to Industry's Needs

These initiatives will increase the higher education and research sector's capacity to produce job ready scientists and clinicians and provide more incentives to researchers and clinicians to move more easily between academia and industry. This will increase the quality of Australia's medical research base and strengthen Australia's competitiveness as location for R&D and clinical trials. These initiatives include:

- the development of a network of industry, training institution and government stakeholders who will determine commitment to, and operating principles for, establishing
    - a national strategic framework for the future development of a biopharmaceutical industry training system
    - A Federal Government funded Coordinating Body (CB) which represents the industry, academic and government sectors to develop and oversee the implementation of the national strategic framework;
- provide Government funded incentives to companies that offer apprenticeships or internships for medical science students and students from relevant manufacturing disciplines.;
- allow the costs of hiring students and academics to be covered by any Government funded R&D grant program;
- encouraging universities to provide equal credit to engagement with industry as an alternative to publications as evidence of researcher productivity; and
- encourage research funding organisations (such as the NHMRC and the ARC) to take account of research undertaken in commercial environments when assessing skills and capabilities of grant applicants.

### What are the problems that this strategy will address?

The current higher education funding model acts as a disincentive for researchers and academics to freely transfer to and from the private sector. Commercial engagements are not currently rewarded by the university sector and are often see as being inferior to publishing activities. This inhibits collaboration between industry and researchers and inserts barriers to the effective commercialisation of Australia's world class medical research base.

The implications of this problem are particularly acute for companies in the Australian biotechnology sector, many of whom lack the financial resources to offer the incentives required to lure high quality researchers away from the university system and would benefit from broader funding and administrative arrangements that allow researchers and clinicians to more readily move back and forth between the research and commercial worlds.

A recent study by the Pharmaceuticals Education Council found that the biopharmaceutical industry's requirement for skilled workers will almost double over the next five years but that the higher education sector has produced an insufficient

number of job ready graduates for current needs. If no action is taken to change the way that the higher education sector trains students, particularly through offering appropriate postgraduate-level industry-specific training, and engages with industry in delivering this, Australia will be unable to produce the critical mass of skilled workers required to maintain its current strengths in R&D and clinical trials. This will jeopardise Australia's ability to attract R&D and clinical trials in a global environment in which other countries are actively increasing the quality of their skills and medical research base.

### Business case – Outline

#### *How the proposal is consistent with the principles of:*

#### *- appropriateness*

Skills shortages are inhibiting the development of the Australian pharmaceuticals industry and a lack of movement of scientists, clinicians and physicians into the biotechnology sector may result in many good ideas 'withering on the lab bench'. This is likely to result in Australia missing out on the significant social and economic benefits that would have accrued had these good ideas been further developed through R&D.

Intervention will encourage the free interchange of skilled clinicians and research scientists with the biotechnology sector, by breaking down many of the barriers that currently prevent this movement. There are mainly disincentives for academic researchers to facilitate commercial development of their findings. There is a perception that the requirements of industry for patenting rather than publication, secrecy rather than open discussion and commercial focus rather than curiosity driven breadth, pull in opposite directions from what is rewarded by academic promotion and recognition systems. The government provides a significant proportion of the money for research so can implement such a change in recognition and reward focus both through the universities, and through its own granting agencies.

Funding of a review of industry-relevant training programs will assist in identifying both current best practice, and any gaps, and ensure that higher education resources directed to developing new programs are used in the most needed areas.

#### *- effectiveness and efficiency*

These initiatives will remove many of the disincentives preventing closer collaboration between the academic and commercial sectors. They will also overcome many of the factors that have led to the skills gaps emerging in the industry and provide a foundation for future skills needs to be satisfactorily addressed.

The measures proposed are designed to improve Australia’s performance across the whole drug development value chain. While improved performance in pre-clinical research may not attract international investment immediately, it will facilitate skills formation in areas critical to it in the medium to long term. Ultimately, a skilled and able workforce will not only support the efficient development of the biotechnology industry, but also attract sustainable R&D to Australia and allow us to build on its internationally recognised expertise and quality in Phase I to IV clinical trials. Such a development is essential to Australian companies’ ability to bring new products to market and establish an onshore pharmaceutical industry.

### *- performance assessment used by Government to assess whether the program is meeting its objectives*

Indicators that could be included in assessment:

- increase in number of clinicians/researchers moving between academia and industry;
- increase in number of researchers hired by industry;
- increase in the number of apprenticeships/internships offered by the industry to medical science students and students in relevant manufacturing disciplines; and
- formation of skills development ecosystems.

### *- integration and strategic policy alignment*

These initiatives are consistent with the Government's broader innovation, science and research policy objectives.

The Group gave serious consideration to putting forward a competitive clinician/physician fellowship scheme to provide incentives for clinicians and physicians to conduct translational R&D for a period of up to 3 years.

- The scheme would subsidise companies for paying the salaries of clinicians/physicians to conduct translational research on the company's product pipeline.
- The scheme would provide different streams of incentives for hospital clinicians, and academic researchers in recognition of different circumstances in which clinicians and researchers work.
- At the conclusion of the placement, the clinician/physician's original employer would be obligated to offer the clinician/physician an ongoing position equivalent to the one they filled prior to undertaking the scheme.

However in recognition of the broad number of fellowships and industry linkage programs offered by the NHMRC, the ARC and the individual universities, the Group decided that a brand new fellowship was not required but that the existing fellowships schemes should be expanded and made more accessible, with an increased focus on encouraging recognition of achievements while undertaking these placements as part of career development.

### Suggested implementation timetable

- Funding for the Federal Government Coordinating Body to commence on 1 July 2009.
- Reforms to Higher Education and other university funding arrangements to be considered as part of the Government's response to the Bradley Review of the Australian Higher Education Sector.

# Appendix A

## A.1 The Pharmaceuticals Industry Value Chain

### Discovery Research

Discovery research involves very early stage research aimed at better understanding the cause of disease and how it affects the body. Before any new therapy can be created, researchers work to acquire a thorough understanding of the disease to be treated, and the underlying mechanisms causing the condition. This in depth knowledge of the disease requires an understanding of many different complex aspects of the human body. Much of this work is undertaken in universities, hospitals and medical research institutes, although industry also plays a contributory role. While this type of research is time intensive, it is more blue sky than research in other parts of the value chain and has the greatest potential for knowledge spillovers.

### Target Identification

Once researchers have a sound understanding of the underlying disease mechanisms, the next step is to select a "target" for a new therapy. This target is usually a single molecule involved in the disease pathway. It could be a part of the DNA or a protein. The most important aspect of target selection is to make sure that the target is "drugable," meaning that there is potential for a drug molecule to interact with it and possibly alter it in some way.

### Target Validation

Once a potential target is selected, it is important for researchers to prove that the particular molecule is involved in the disease pathway and that it can be affected by a drug. This work is complex and is conducted in different disease models such as living cells grown in the lab, and in animals. Validating the target molecules is a very important step and stops researchers from possibly pursuing research that may not provide any therapeutic outcomes.[79]

### Basic R&D

Once targets have been identified and validated researchers focus on isolating and developing potential drug compounds for future treatments.

The rate of failure at this stage is high – only one out of every 10,000 compounds tested is developed into a medicine. Because of the very high failure rate this process takes a number of years but, as it is not labour intensive, is relatively inexpensive per unit of activity compared to other aspects of the value chain. This activity is highly knowledge intensive and requires a highly skilled science base and a quality research infrastructure. Access to the necessary skills and infrastructure and strong and effective intellectual property protection are critical drivers of this activity. Cost is not a significant driver of this activity. Many multinational companies have centralised their discovery work into global discovery centres, which tend to be located close to their headquarters.

[79] For more information, see Pharmaceutical Research and Manufacturers of America (PhRMA), *Drug Discovery and Development: Understanding the R&D Process*, 2007, pp 2-3.

This basic research is largely carried out by industry (although universities and the public funded research organisations have an important role to play in this process) and it has the potential to generate large spillovers. This is because of the novelty of the compounds being tested, which means the research generates new knowledge that can provide insights into how to treat diseases more effectively and helps to build a critical mass of researchers to attract more basic and discovery R&D.
In Australia most multinational companies do little basic R&D. The vast majority of this work is done by local biotechnology companies who have close links with the universities and hospitals where much of this work takes place.[80]

### Pre-clinical R&D

Once this aspect of the basic research is completed, compounds will enter pre-clinical testing to determine if the drug is safe enough for human testing. Even though a large number of compounds are discarded during the earlier basic R&D process, the rate of failure at this stage remains high. Only one out of every 250 compounds that enter pre-clinical testing will become a medicine. Given the reliance on animal testing to complete this aspect of R&D, infrastructure, skills and government regulations in relation to animal testing are critical drivers of this activity. The Productivity Commission has found that pre-clinical trials:

> *"are likely to have an enabling role for discovery/basic research…[and] have an influence on the likelihood of phase I clinical trials going ahead in the same location."*[81]

The absence of a large scale non-rodent animal testing facility in Australia means that Australia does less of this activity than would otherwise be the case.

### Clinical Trials

After a compound has successfully passed pre-clinical testing and shown that it is safe to be tested on humans, it will enter clinical trials. Clinical trials test the safety and efficacy of a compound in treating a particular disease in humans. The clinical trial process is the most expensive part of developing a medicine and requires the testing of thousands of patients across the world to produce the data required to demonstrate a compound's safety and efficacy. This process can take up to seven years to complete.

#### *Phase I Clinical Trials*

Phase I clinical trials are designed to test the safety of a compound in humans. These studies are usually conducted on small populations of healthy volunteers to specifically determine a drug's toxicity, absorption, distribution and metabolism (typically 10-50 subjects, but can involve as many as 100 subjects).[82] The rate of failure for Phase I clinical trials is still high – recent estimates suggest that only one of every five compounds that enter Phase I clinical trials result in a medicine.

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[80] Latest data suggest that of the total R&D expenditure conducted by Medicines Australia members in Australia, which is used as a proxy for multinational activity, only 5 per cent is spent on basic medical research. See Medicines Australia, op. cit., p.28.
[81] Productivity Commission, op. cit., p. 4.8.
[82] Department of Industry, Tourism and Resources (DITR), *Survey of Australia's Phase I Clinical Trials Units*, 2007, p. 25.

The key drivers for Phase I clinical trial activity are the availability of skilled clinicians and world class teaching hospitals and speed of regulatory approval. Because of the relatively small number of patients involved, Phase I clinical trials are a relatively inexpensive component of the clinical trial process. Additionally, since Phase I trials are the first time that compounds are tested in humans they generate higher knowledge spillovers. Phase I trials provide clinicians with new insights into how to treat new diseases. In its evaluation of the Pharmaceuticals Partnerships Program, Deloitte Insight Economics found that

> *"In the context of the Australian pharmaceuticals industry, which undertakes relatively little discovery research and relatively more clinical trials, pre clinical and early stage clinical trials can play an important role in the diffusion and adoption of new technologies and innovations developed overseas".*[83]

### *Phase II Clinical Trials*

After the successful completion of Phase I trials, a drug is then tested for safety and efficacy in a slightly larger population of individuals who are afflicted with the disease or condition for which the drug was developed (typically 100-200 subjects, although it can be as large as 500).[84] The ability to identify and recruit suitable numbers of afflicted patients as well as quality of skills and infrastructure is an important factor in determining the location of Phase II clinical trials.

### *Phase III Clinical Trials*

The third and last pre-approval round of testing of a drug is conducted on large populations of patients. Phase III clinical trials test the compound in comparison with the standard therapy currently being used for the disease in question. The results of these trials usually provide the information that is included in the package insert and labelling (typically 1,000 to 5,000 subjects).[85]

Phase III is the most expensive part of the clinical trial process because of the large numbers of patients required to generate the necessary data. Accordingly, cost and ability to recruit sufficient numbers of patients quickly is an important driver of this activity. Because of the large numbers required to complete a Phase III clinical trial and regulators desire for potential medicines to be tested on peoples of various ethnicities, Phase III clinical trials need to be conducted in a number of locations around the world and cannot be conducted in just one market.

### *Registration*

Once a compound has successfully shown that it is safe and efficacious it is submitted to regulatory agencies around the world to be approved for sale as a medicine. Because of the sheer scale and complexity of clinical data that needs to be assessed, regulators can often take up to two years to approve a medicine to be sold.

[83] Deloitte Insight Economics, op. cit., p. 50.
[84] DITR, op. cit., p. 25.
[85] ibid.

### *Phase IV Clinical Trials*

After a compound had been registered as a medicine, Phase IV clinical trials are undertaken to compare the drug to a competitor, explore additional patient populations, or to further study any adverse events. There is little level of innovation or technical risks in Phase IV clinical studies, which are largely undertaken for commercial marketing reasons.

Longer development and approval times, larger and more complex clinical trials involving biologics medicines, increased expenditures on new technologies, and shifts in product portfolios towards riskier, more expensive therapeutic categories have contributed to a real increase in the development costs. Recent estimates of the costs of developing a medicine suggest that development costs area as high as US$1.3 billon.[86]

## Manufacturing

Historically, most medicines were extracted from plants (morphine, opiates) or animals (insulin). Although some important medicines still come from plants or animals, most medicines used in the developed world are manufactured through chemical or biotechnology processes.

Small molecule or chemically based medicines are developed via chemical synthesis, which are a series of chemical reactions and purification steps required to generate a product, or several products. This happens by physical and chemical manipulations usually involving one or more reactions. Whilst this activity is technologically intensive and requires a very high skills base to produce, once the process is mastered it is easily and reliably replicated in multiple locations and most chemically based medicines are made in more than one manufacturing facility. In 2006, 82.2 per cent of all medicines used worldwide were chemically based medicines.[87]

In the 1980s, biotechnology advances enabled the production of large molecule drugs, termed biologicals (biologic drugs or biologics) that are identical to, or derived from, proteins and other molecules present in nature. Biological drugs are much more complex, both in structure and function, than small molecule drugs. These drugs are so complex that living cells must be harnessed to manufacture them, rather than utilising synthetic chemical production techniques. Because of this complexity it is not possible to produce both chemically based medicines and biological medicines in the same facility.

Biological medicines such as vaccines, hormones, antibodies and blood factors are currently made in a range of genetically engineered host cell culture systems: microbial (bacteria and yeast), and mammalian cells (from mouse, hamster or human). Cells are grown in large quantities, in stainless steel tanks or giant disposable plastic bags, in laboratories. Although the development of a biological medicine is an

[86] J A DiMasi and H G Grabowski, "The Cost of Biopharmaceutcal R&D: Is Biotech Different?" *Managerial and Decision Economics 28*, 2007, pp. 469-479, quoted in Pharmaceutical Researchers and Manufacturers of America (PhRMA), *Pharmaceutical Industry Profile 2008*, 2008.
[87] "Report finds poor management scuppers almost half of all licensing deals", *Scrip*, no. 3330, 25 Jan 2008, p. 11.

established activity, it is not straightforward and requires the right combination of know-how and equipment.

The process is complex because it is based on living cells which are physically fragile, sensitive to slight changes in handling and temperature and are vulnerable to contamination and infection. The skills set to produce biological medicines are much more technically demanding than the skills set to produce a chemical based medicine. Unlike chemically based medicines, the production of biologically based medicines is not as easily transferable and the production of particular products is centralised in a smaller number of larger scale manufacturing facilities that undertake most aspects of the manufacturing process.

The pharmaceuticals industry has traditionally relied on chemically based medicines to treat diseases but new classes of biological medicines derived from human hormones and human antibodies (antibodies are produced naturally in the body to combat disease) are proving to be effective against otherwise intractable diseases such as cancer and arthritis. Biological medicines are also more effective at treating diseases at the genetic level and providing opportunities for the development of medicines that treat more personalised diseases. Consequently, market estimates have predicted that the share of medicines based on biologics will increase to 27 per cent by 2012.[88]

With the exception of CSL's blood and plasma products and vaccine manufacturing facilities, virtually all of Australia's commercial scale pharmaceutical manufacturing capacity is focused around the production of chemically based medicines.

Both chemical and biological based manufacturing are highly capitally intensive exercises in which significant investment in infrastructure and equipment is needed. Although they both require highly skilled workforces they are not as labour intensive as manufacturing in other industries such as the automotive and the textiles, clothing and footwear industries.

The components of the pharmaceuticals manufacturing value chain are described below.

### *Primary Manufacturing*

Primary manufacturing is the production of the active ingredient that triggers the therapeutic impact on the body. Developing the active ingredient makes up most of the manufacturing cost of a finished product. In 2002, the Pharmaceuticals Industry Action Agenda found that *"primary manufacturing plants are situated either in the home countries of the multinationals or in countries that have actively attracted these facilities through investment incentives*".[89] This finding remains valid in 2008, when the location of active manufacturing plants is arguably more sensitive to investment incentives and low corporate tax rates. Consequently, Australia has few primary manufacturing facilities.

[88] ibid.
[89] Department of Industry, Tourism and Resources, *Pharmaceuticals Industry Action Agenda: Local Priority-Global Partner*, 2002, p. 16.

### *Secondary Manufacturing (Formulation)*

Secondary manufacturing involves the formulation of the active ingredient with other substances to stabilise it and make it in a form that can be or injected by patients. While not as technologically intensive as the manufacture of the active ingredient, it is a still an activity that requires a highly skilled workforce to complete. The location of formulation plants is determined principally by the availability of a skilled workforce and the cost effectiveness of that skilled workforce in producing medicines to the necessary quality control standards.

### *Packaging*

Once the active ingredient has been stabilised and manufactured into a tablet, capsule or liquid for injection, it must be packaged for pharmacy or hospital use. Packaging activities are the least sophisticated aspect of pharmaceutical manufacturing and generate the least amount of value. Most of the Australian pharmaceuticals manufacturing industry is comprised of packaging activities.[90]

### Sales and Marketing

Once a medicine is approved as being safe and efficacious it can be sold to hospitals, pharmacists and consumers. The sales and distribution channels within the pharmaceuticals industry are more heavily regulated than in other sectors of the economy, with restrictions on advertising, distribution and selling medicines. Many pharmaceutical companies employ large sales and marketing workforces and a significant portion of the industry's employment in Australia is in this area of the value chain.

## A.2 Pharmaceuticals Industry Sectors

### Originator Small Molecule

Prominent examples of companies in this sector who operate in Australia are:

- Pfizer;
- GlaxoSmithKline;
- Sanofi-Aventis;
- Janssen-Cilag;
- AstraZeneca;
- Merck Sharp & Dohme;
- Bristol-Myers Squibb;
- Novartis;
- Wyeth; and
- Eli Lilly.

This is not an exhaustive list, as many other companies within this sector have some operations in the Australian market. However, the list illustrates that most of the companies in this sector of the industry are large, well established multinationals active at all stages of the industry value chain in a number of locations across the globe. This sector makes a significant contribution to industry manufacturing, R&D and employment in Australia and is represented by Medicines Australia and AusBiotech.

[90] Medicines Australia, loc. cit.

Many of the companies in this sector have undergone significant merger and acquisition activity throughout the last 20 years, substantially increasing their size and their revenue base. This has given rise to large vertical integrated companies that have focussed on developing blockbuster medicines (medicines that earn over a $1 billion a year treating diseases with large populations like cholesterol, blood pressure and ulcers).

Despite the increased resources that originator small molecule companies are using to develop new medicines, many of these companies lack new blockbuster drugs to replace those coming off patent. This and the rise of biologics have led many companies in this sector to develop new biologic medicines that are more effective at treating defined patient subgroups and have the potential to generate higher margins. Companies have developed this capability through either in-licensing, acquisitions or by growing new internal capabilities.

### Originator Biologics

Many biologics companies have signed alliances with larger originator small molecule companies where originator small molecule companies market biologic medicines in a number of global markets. Similarly, because of the complexity of manufacturing biological products, many originator biologics companies operate large manufacturing facilities that specialise in manufacturing key products for global markets.

Prominent examples of companies in this sector who operate in Australia in this sector are:

- Amgen;
- CSL;
- Genzyme;
- Shire;
- Merck Serono;
- Biogen Idec; and
- Gilead Sciences.

These companies do not manufacture in Australia and are progressively increasing their Australian operations including their R&D commitment. This sector is also represented by Medicines Australia and AusBiotech.

### Research Based Biotechnology Companies

Prominent examples of companies who operate in Australia in this sector are:

- Biota;
- ChemGenex;
- Pharmaxis;
- Arana;
- Acrux;
- Avexa; and
- Mesoblast.

### Generic Medicine Companies

The products of these companies are based mainly on small molecules. This is because many of the patents on originator biologic medicines have yet to expire. The complexity of manufacturing biological medicines has created questions as to how regulators can assess whether a product grown from different cell lines in different locations can be deemed to be an equivalent copy in some jurisdictions. However generic versions of biologic medicines (or 'biosimilars') have been approved in a number of jurisdictions around the world including Australia. The manufacture of biosimilars is an example of the high value, niche manufacturing activities upon which the future of the Australian industry may be based. Some companies involved in producing biosimilars are also members of AusBiotech.

Prominent examples of companies who operate in Australia in this sector are:

- Alphapharm (Mylan);
- Hospira;
- Sigma;
- Sandoz;
- Apotex;and
- Ranbaxy.

Only Alphapharm, Hospira and Sigma conduct R&D and manufacturing in Australia. Other generic companies use Australia primarily as a sales and marketing base.

### Contract Manufacturing and Clinical Trial Service Providers

A number of companies do not manufacture or develop their own products but conduct manufacturing and R&D services on behalf of other companies. The drivers and challenges for these companies are the same as those for companies doing these activities in-house.

Prominent examples of companies who operate in Australia are:

- Institute of Drug Technology Australia;
- QPharm;
- Clinical Trials Network; and
- Kendle.

# Appendix B

## The Australian Pharmaceuticals Industry

### Turnover and Market Size

**Figure B.1 Pharmaceuticals Industry Turnover[91]**

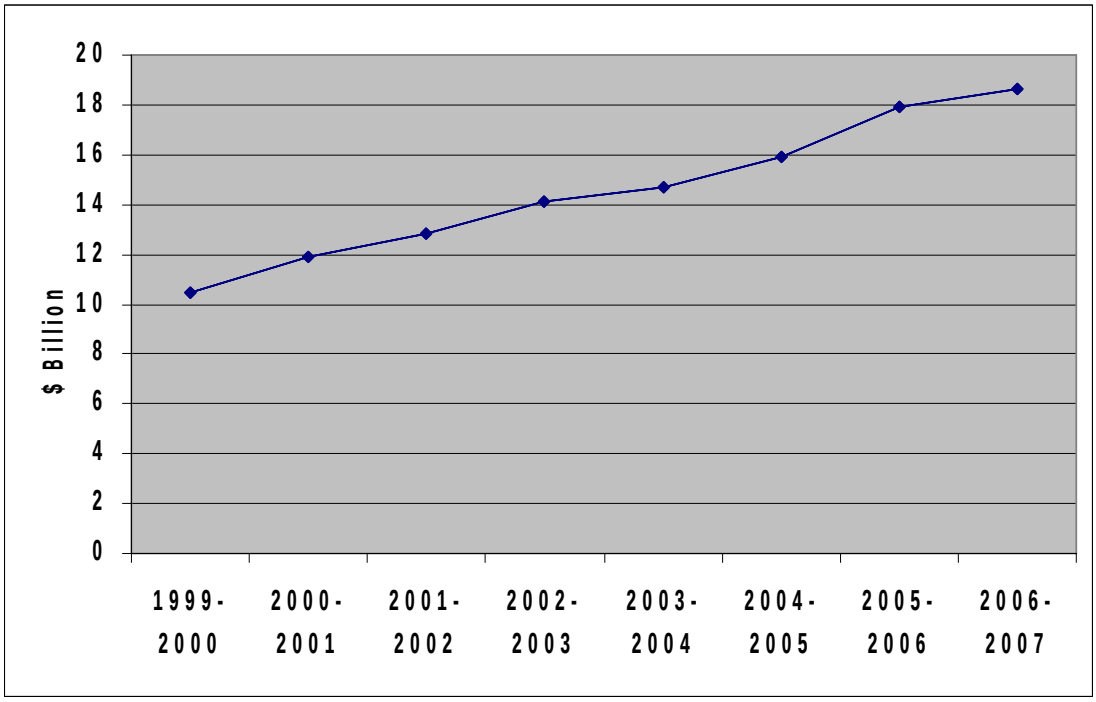
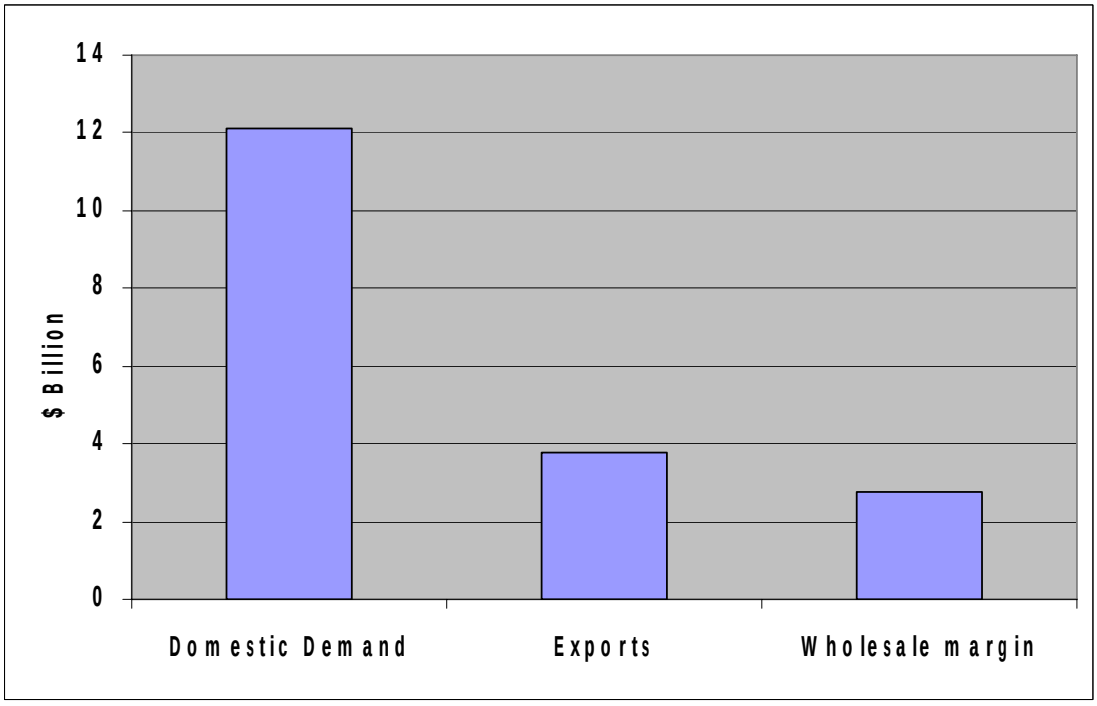



**Figure B.2 Breakdown of Industry Turnover [92]**




[91] ABS unpublished data and IBISWorld, C2534 and F4797, 2008.
[92] ABS unpublished data and IBISWorld, C2534 and F4797, 2008.

## Employment

**Figure B.3 Pharmaceuticals Industry Employment** [93]

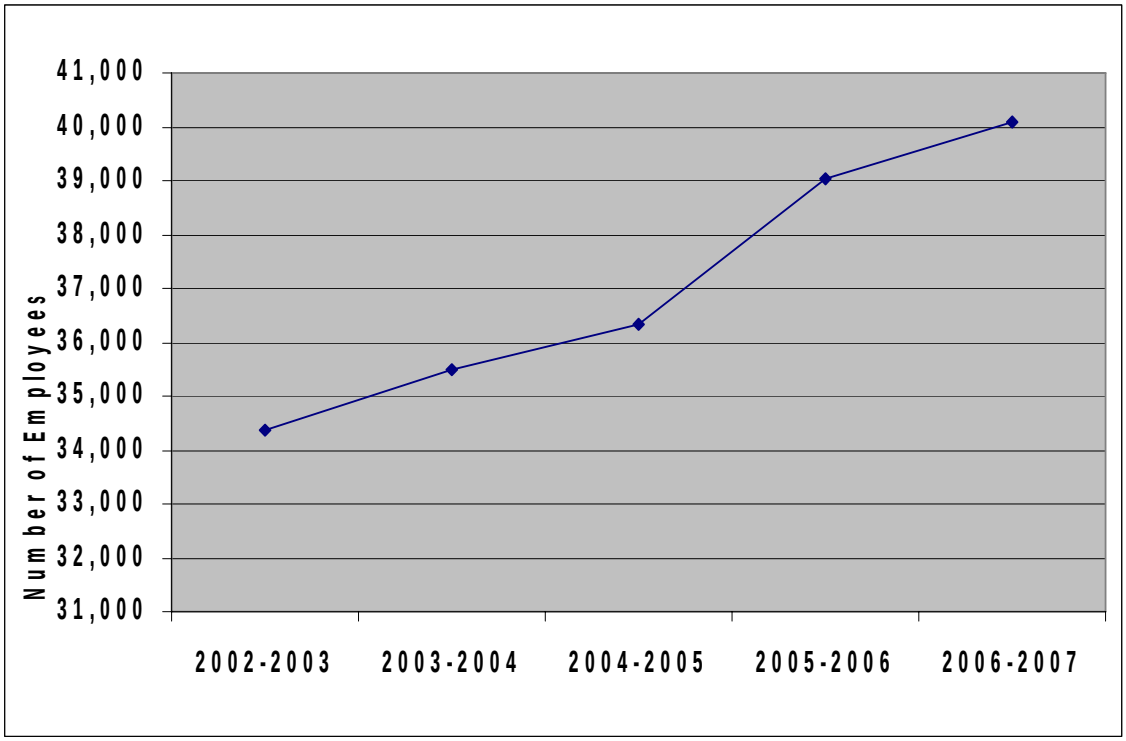
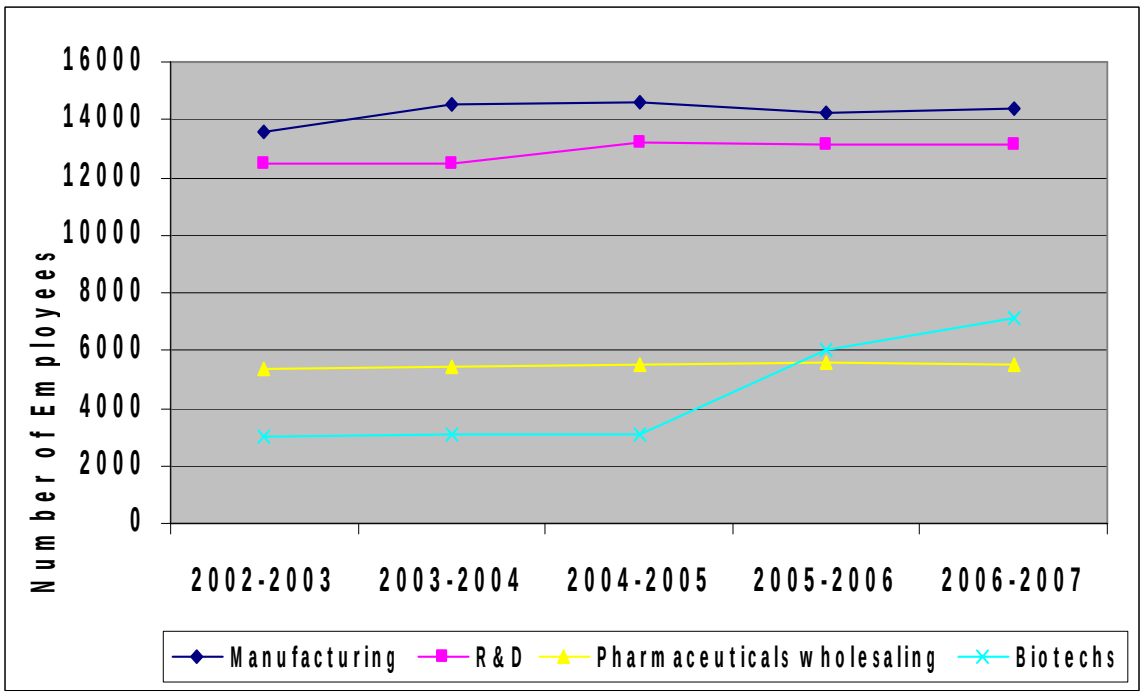



**Figure B.4 Breakdown of Industry Employment**




[93] ABS unpublished data; IBISWorld C2543 and F4797, 2008; and Department of Innovation estimates.

**Figure B.4** provides a more detailed breakdown of industry employment, illustrating that the majority of growth in industry employment in recent years has been from the biotechnology sector.[94] Figure B.4 also shows that manufacturing remains the largest component of industry employment, but that employment in manufacturing has been relatively static in recent years. Figure B.4 also shows that with the exception of the biotechnology sector, employment in the rest of the industry has been - at best - constant over the last five years. This suggests that the industry has not kept pace with the growth in employment in the broader economy, which has increased significantly in the last ten years.

**Figure B.5 Pharmaceuticals Exports v All Exports[95]**

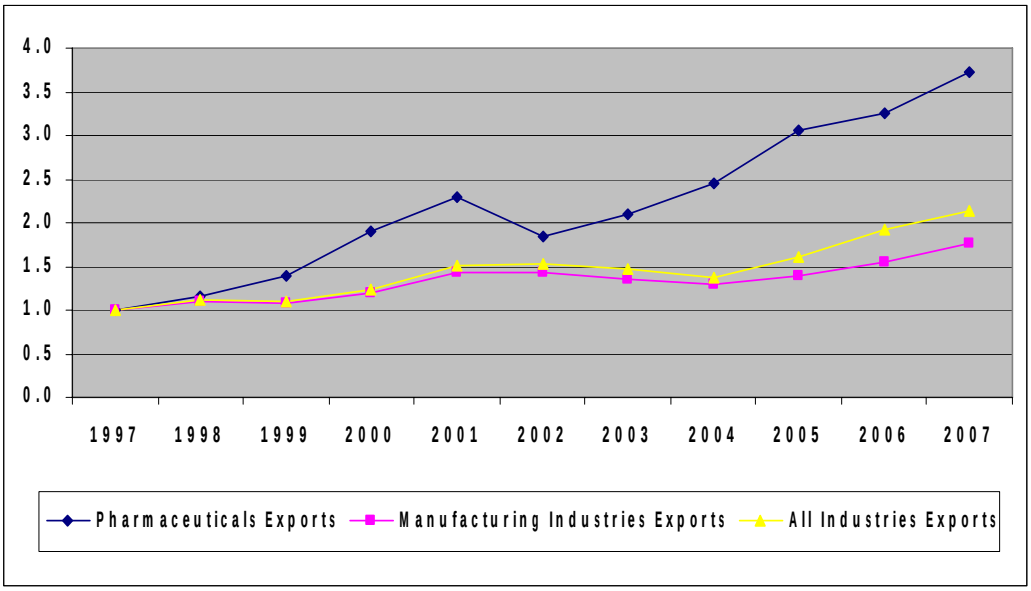
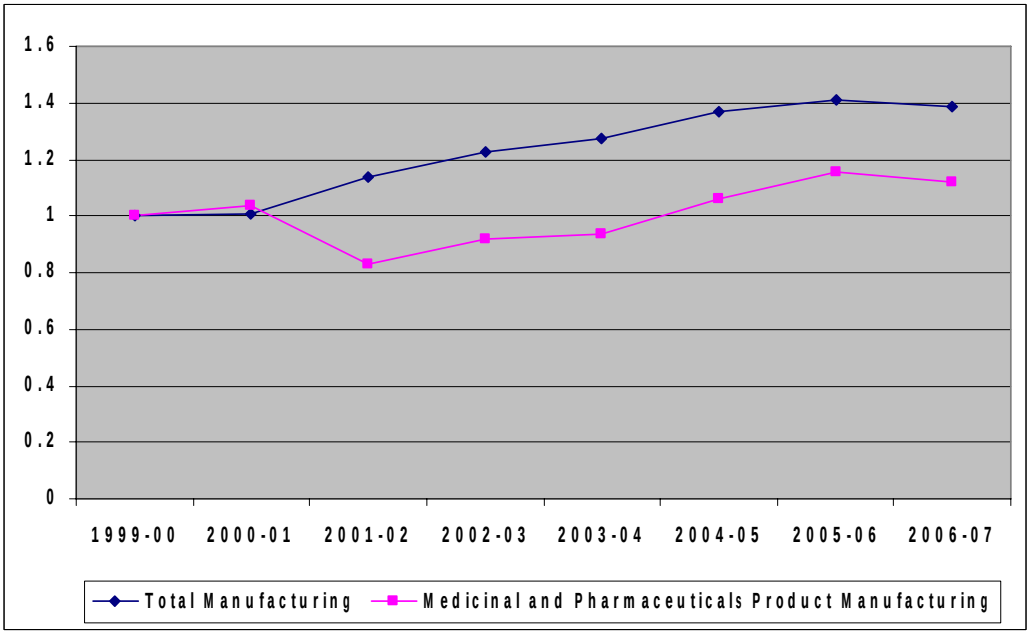



**Figure B.6 Change in Manufacturing Value Added [96]**




[94] ABS unpublished data; IBISWorld C2543 and F4797, 2008; and Department of Innovation estimates.
[95] ABS unpublished data.
[96] ABS (cat. no. 8221.0).

**Figure B.7 Pharmaceuticals Business Expenditure on R&D[97]**

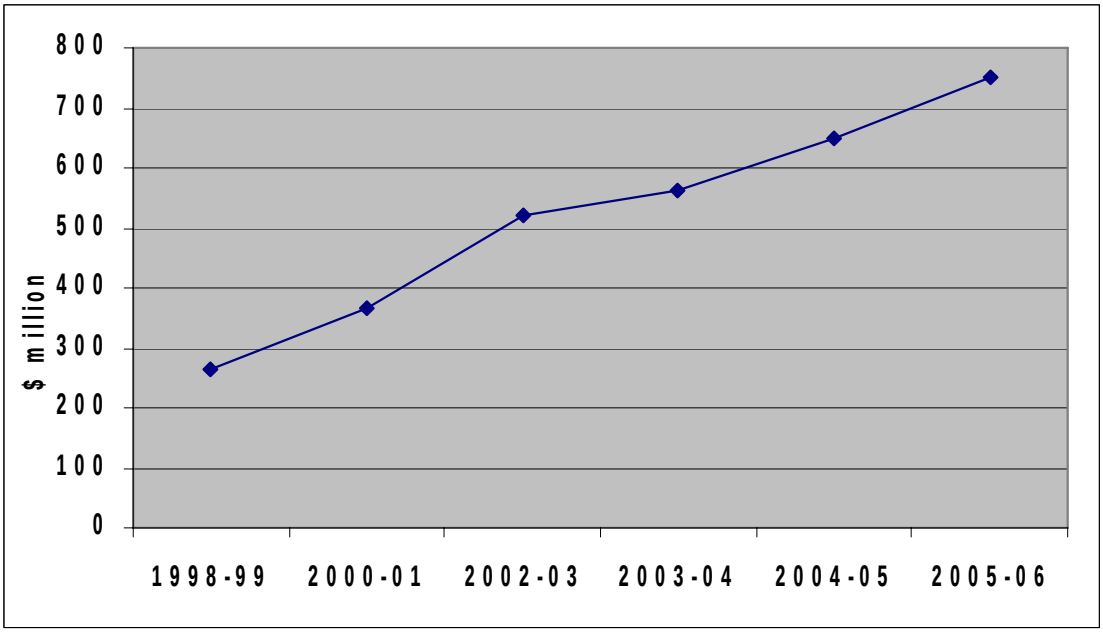
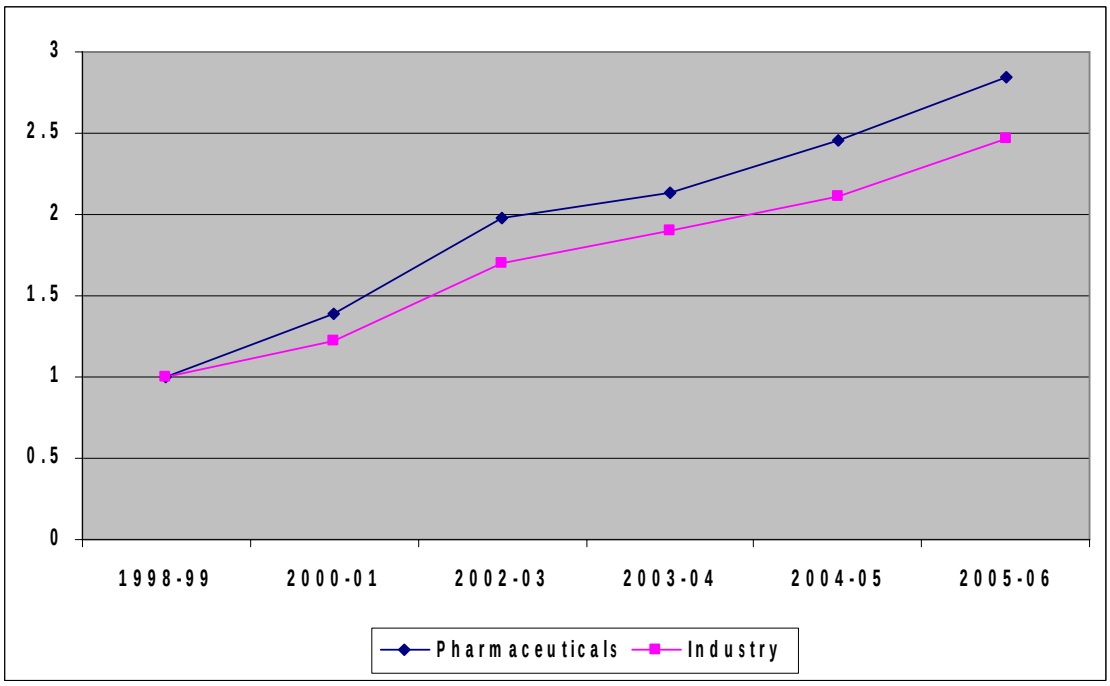



**Figure B.8 Growth in Pharmaceuticals BERD v Growth in BERD[98]**




## Spillovers from Pharmaceuticals R&D

When the activities of a firm have beneficial effects on third parties that are not paid for by third parties, economists call the gains externalities. Activities that give rise to positive externalities are referred to as spillovers.[99] From an economy wide perspective, spillovers are desirable because they create broader public benefits. The

[97] ABS unpublished data.
[98] ABS *Research and Experimental Development Businesses Australia*, (cat no.8104.0) and ABS unpublished data.
[99] Productivity Commission, op. cit., p. 4.2.

funding of R&D by companies is likely to generate positive externalities that can be enjoyed by the wider community

### Where do Spillovers Occur?

One of the most common forms of spillovers is knowledge. A large body of literature has concluded that R&D generates a significant stock of new knowledge that can be used and appropriated by those that do not pay for the generation of this knowledge. In its report into Public Support for Science and Innovation, the Productivity Commission (PC) suggested that as knowledge spills over cheaply to others, a market failure exists that result in the private sector undertaking "R&D at a societally sub-optimal level."

The PC also found that the strongest case for public support based on spillovers occurs in basic research and in private sector R&D that triggers cycles of innovation by rivals. The spillovers will be greatest when there are many potential domestic beneficiaries (i.e. generic technologies, or many potential users of the technology because of industry structures).[100]

### What are the Spillovers from Pharmaceuticals R&D?

Recent evaluations of pharmaceuticals R&D programs have identified spillovers in the industry. In its 2006 interim evaluation of the Pharmaceuticals Partnerships Program, the Centre for International Economics (CIE) identified the following factors as sources of spillovers in the industry:

- building the capacity and size of the specialised labour force;
- providing critical mass for the establishment of suppliers, including purchase of specialised equipment;
- building networks between researchers, domestic and internationally which speeds learning and knowledge generation, reduces duplication of effort, and can attract new entrants;
- development of platform technologies where these are shared and non-exclusive; and
- drug discovery, where this utilises and hence adds value to Australian biota.[101]

Deloitte Insight Economics (DIE) completed the formal evaluation of the Pharmaceuticals Partnerships Program in 2008. This evaluation found that spillovers were present in the industry through:

- development of new technologies;
- diffusion and absorption of new knowledge;
- reduced duplication;
- establishment of a specialised labour force; and
- establishment of a critical mass of suppliers.[102]

[100] Productivity Commission, *Public Support for Science and Innovation*, 2007, p. 73.
[101] Centre for International Economics, *Pharmaceuticals Partnerships Program: First Year Evaluation*, 2006, p. 30.
[102] Deloitte Insight Economics, op. cit., p. 48.

Neither of these evaluations identified the broader benefits of faster access to new medicines that can accrue through pharmaceuticals R&D. The PC has argued that as new medicines are developed through global R&D activities that will happen regardless of the level of local incentives offered, it is not relevant to try and calculate these benefits in determining issues of industry assistance.[103]

Notwithstanding this view, it is clear that there are broader public benefits from the R&D that leads to the development of new medicines. Similarly, clinical trials provide patients with faster access to medicines than would otherwise be the case. This is especially true for clinical trials involving terminal illnesses, since clinical trial participants may be receiving faster access to life prolonging medicines.

[103] Productivity Commission, op. cit., p. 4.13.

# Appendix C

## Overview of Previous Government Programs

### Factor f

The Factor f scheme was administered in two phases. Phase I commenced on 1 January 1988 and concluded on 30 June 1995. Phase II commenced on 1 July 1992 and concluded on 30 June 1999. Ten companies participated in Phase I and eleven companies in Phase II. However, because of the overlap between companies who participated in both phases of the scheme, only 17 individual companies participated.

In return for higher notional prices on some of their PBS products, companies were required to increase their R&D expenditure, as well as their domestic manufacturing and export activity in Australia. Companies received the 'benefit' of a notional price increase in the form of a grant.

Factor f was an entitlement scheme, which meant that companies that met the eligibility criteria were eligible for assistance. To gain entry to Phase II of the scheme companies had to increase value added on Australian pharmaceutical production by up to 50 per cent over a three year period and achieve an R&D intensity (i.e. R&D spend as a percentage of turnover) of 3 per cent. The eligibility requirements were similar but slightly different for Phase I. Under Factor f companies were also required to commit to Broad Activity Commitments including capital investments.

The Factor f scheme paid companies up to 25 cents for each dollar of additional domestic and export value added activity. Companies received the lesser of 50 per cent of the increase in after tax R&D expenditure or 25 per cent of the increase in total R&D expenditure. Payments were directly linked to performance targets in R&D and Production Value Added (PVA). Payments to participating companies were uncapped and one company (Glaxo Wellcome) earned $204 million under the scheme. The total cost of the Factor f scheme was $948 million.

### Factor f Participants

Ten companies participated in Phase I:

- Bristol-Myers Squibb Australia Pty Ltd;
- CSL Limited;
- Cyanamid Australia (now Wyeth Australia Pty Limited);
- F H Faulding (now Hospira Australia Pty Ltd);
- Glaxo Australia Limited (now GlaxoSmithKline Australia Pty Ltd);
- ICI Australia (now Astra Zeneca Pty Ltd);
- Merck, Sharp and Dohme (Australia) Pty Limited;
- Schering-Plough Pty Limited;
- Sigma Pharmaceuticals Limited (now Sigma Pharmaceuticals (Australia) Pty Ltd; and
- SmithKline Beecham (now GlaxoSmithKline Australia Pty Ltd).

Eleven companies participated in Phase II of the Factor f Scheme, seven of whom continued from Phase I. They were:

- 3M Pharmaceuticals (Australia) Pty Ltd (now iNova Pharmaceuticals Australia Pty Ltd);
- AMRAD Corporation Limited (now part of CSL Limited);
- Astra Pharmaceuticals Pty Limited (now Astra Zeneca Pty Ltd);
- CSL Limited;
- F H Faulding & Co Limited (now Hospira Australia Pty Ltd);
- Glaxo Australia Limited (now GlaxoSmithKline Australia Pty Ltd);
- Merck Sharp & Dohme (Australia) Pty Limited;
- Pfizer Pty Limited (now Pfizer Australia Pty Ltd);
- Rhône Poulenc Rorer Australia Pty Ltd (now Sanofi-Aventis Australia Pty Ltd);
- Upjohn Pty Ltd (now Pfizer Australia Pty Ltd ); and
- Wellcome Australia Limited (now GlaxoSmithKline Australia Pty Ltd).

### *Outcomes of Factor f*[104]

Phases I and II of the Factor f scheme drove the cumulative increase in exports and domestic production value added to $5.135 billion (Phase I was $1.067 billion and Phase II was $4.068 billion). The cumulative increase in R&D expenditure was $765.4 million (Phase I was $205.4 million and Phase II was $560 million). Total entitlements paid to participants were $948 million (Phase I was $157.6 million and Phase II was $790.4 million).

During Phase II of the scheme $4.068 billion ($5.451 billion in today's dollars) was invested in manufacturing activity and over $840 million ($1.126 billion in today's dollars) was invested in new plant and equipment, and upgrade of existing facilities. Phase II participants also established five new manufacturing facilities including:

- CSL's plasma fractionation facility in Broadmeadows (Victoria);
- CSL's vaccine facility in Parkville (Victoria) to manufacture novel vaccines for use in clinical trials;
- Astra Zeneca's sterile plastics product plant at North Ryde (New South Wales);
- Sanofi-Aventis' manufacturing facility at Baulkham Hills (New South Wales); and
- Pfizer's manufacturing facility at Rydalmere (New South Wales).

As part of companies' broad activity commitments, other companies committed to significant capital upgrades of existing facilities including:

- $6.3 million capital upgrade of iNova's (then 3M) manufacturing facility;
- $35 million invested in plant and equipment at Hospira's (then F H Faulding & Co) Adelaide and Melbourne manufacturing facilities;
- $56 million invested in plant and equipment at GlaxoSmithKline's (then Glaxo Wellcome) Melbourne manufacturing facility;
- $97 million capital investment by Merck, Sharp & Dohme in upgrading its Sydney manufacturing site; and

[104] This information is sourced from unpublished Department of Innovation reports on the performance of the Factor f scheme.

- $41 million capital investment by Pfizer (then Pharmacia & Upjohn) in upgrading its Perth manufacturing site.

Many of these upgrades continue to be used and have exerted an impact on the industry's productive capacity for many years after the subsidy that helped induced this investment ceased. On the other hand, many of the incentives that were offered as part of the program did not achieve sustainable results.

### *Evaluation of the Factor f Scheme*

The Factor f scheme was reviewed by the then Industry Commission as part of its 1996 inquiry into the pharmaceutical industry. The Industry Commission's findings were mixed. The Industry Commission found that:

> *The Factor f scheme "appears to have positively influenced the views of foreign head offices of Australian MNE subsidiaries about the attractiveness of Australia as an investment location …[and] may have also positively influenced the investment decisions of some non-participating companies".*
>
> *"many multinational companies now have a better understanding of the capabilities of Australian manufacturers and researchers and this may result in future activity not subsidised by the scheme. The benefits of increased investment can be expected to continue for some time."*
>
> *"Some important intra-industry linkages have been formed…the development of broader skills in the research community and the equipment supply sector will allow new opportunities to be taken."*

The Industry Commission also found that:

> "*a number of design features of the Factor f scheme have reduced its effectiveness through overcompensation of some participants…overcompensation came about mainly because the payment rate was too high"*
>
> *"The activity of…participants grew faster than that of non-participants [but] the overall difference in growth rates is not significant."*
>
> *"Some companies, which were likely to have increased their activity in a deregulated pricing environment, were excluded from the scheme."*
>
> *"The generous nature of the subsidy is likely to have induced more activity than would have occurred in the absence of price suppression."*
>
> "*The scheme is likely to have paid for at least some activity that would have been maintained anyway."*
>
> *"It is unlikely that the benefits generated by the current scheme are large enough to cover its costs…the scheme has not operated in a way that enhances the community's welfare."*

The Industry Commission concluded that *"should the Government decide that fundamental reform of PBS processes is not a current priority or likely to take considerable time to implement, it could choose to introduce a Factor f type scheme as an interim measure.*[105]

The full version of the report can be downloaded from the Productivity Commission's website at http://www.pc.gov.au/ic/inquiry/51drugs/inquiry_documents/finalreport.

## Pharmaceutical Industry Investment Program (the PIIP)

The PIIP was designed to compensate the pharmaceuticals industry, in part, for the impact on activity of lower prices, which are due to the Government exercising its monopsony purchasing power under the PBS. Companies received higher notional PBS prices in return for increasing their R&D and production value added activities. The PIIP was allocated up to $300 million from 1 July 1999 to 30 June 2004.

The PIIP was a competitive entry program. Companies that participated were selected on the relative merits of their broad programs of proposed activity. The companies that gained entry to PIIP demonstrated the capacity to contribute to further development of the industry and, through increased activity, to generate a high level of spillover benefits to the wider economy. Eligibility was limited to companies that could demonstrate they were experiencing price suppression by listing medicines on the PBS.

PIIP companies were eligible to receive 20 cents for every additional dollar of R&D and production value added performed in Australia, up to a cap of $60 million. However, no-one company performed sufficient levels of additional activity to earn this cap, and the most any company received under the PIIP was $38.955 million (this was Mayne Pharma, now Hospira). PIIP participants elected whether the higher prices for their nominated PBS products would be applied as actual or notional price increases.

The PIIP operated according to four guiding principles designed to encourage:

- additional R&D activity undertaken in Australia;
- additional high value added activity undertaken in Australia;
- activity that is different in scope from existing activity or is otherwise new to the company and of significance to its operations and/or its position in the global environment; and
- a sustainable pharmaceutical industry: internationally competitive and of benefit to Australia.

### *PIIP Participants*

The nine participating companies were:
- Amrad Corporation Limited (now part of CSL Limited);
- Bristol-Myers Squibb Australia Pty Ltd;
- CSL Limited;
- Eli Lilly Australia Pty Ltd;

[105] Industry Commission, loc. cit.

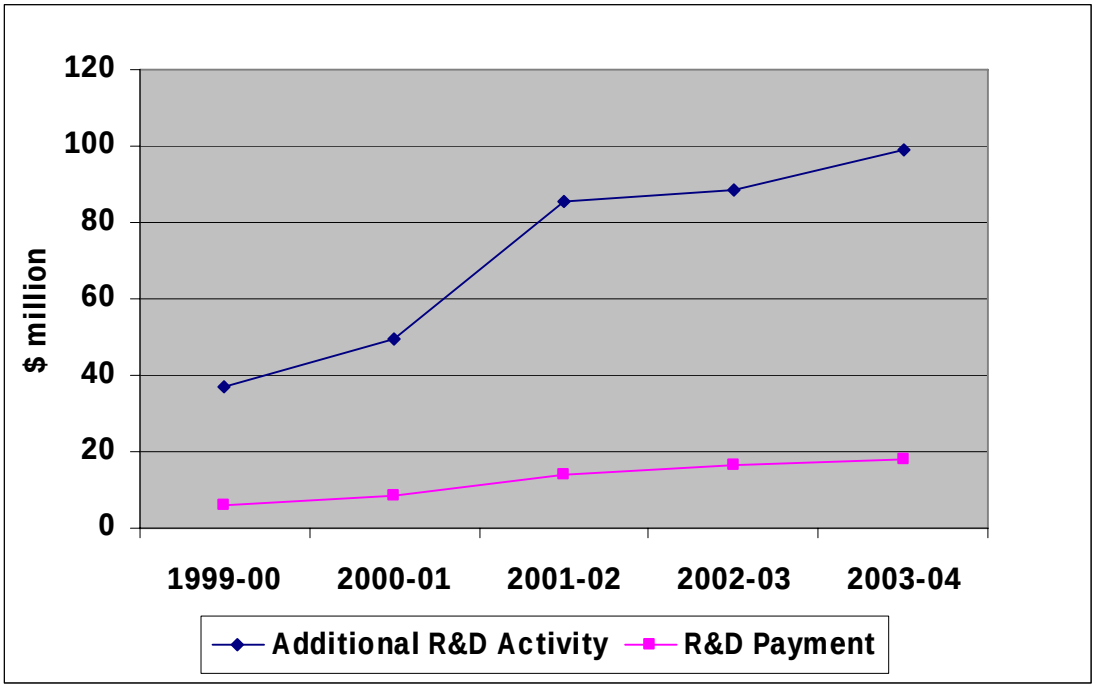
- Mayne Pharma Pty Ltd (now Hospira Australia Pty Ltd);
- GlaxoSmithKline Australia Pty Ltd;
- Janssen-Cilag Pty Ltd;
- Pfizer Australia Pty Ltd; and
- Pharmacia Australia Pty Ltd (now Pfizer Australia Pty Ltd).

### *Outcomes of PIIP*

PIIP companies did not perform the level of additional activity they had forecast when they committed to join the program. Consequently only $246 million (including $63 million for R&D activities and $183 million for production value added activities out of the program's $300 million allocation was spent.[106]

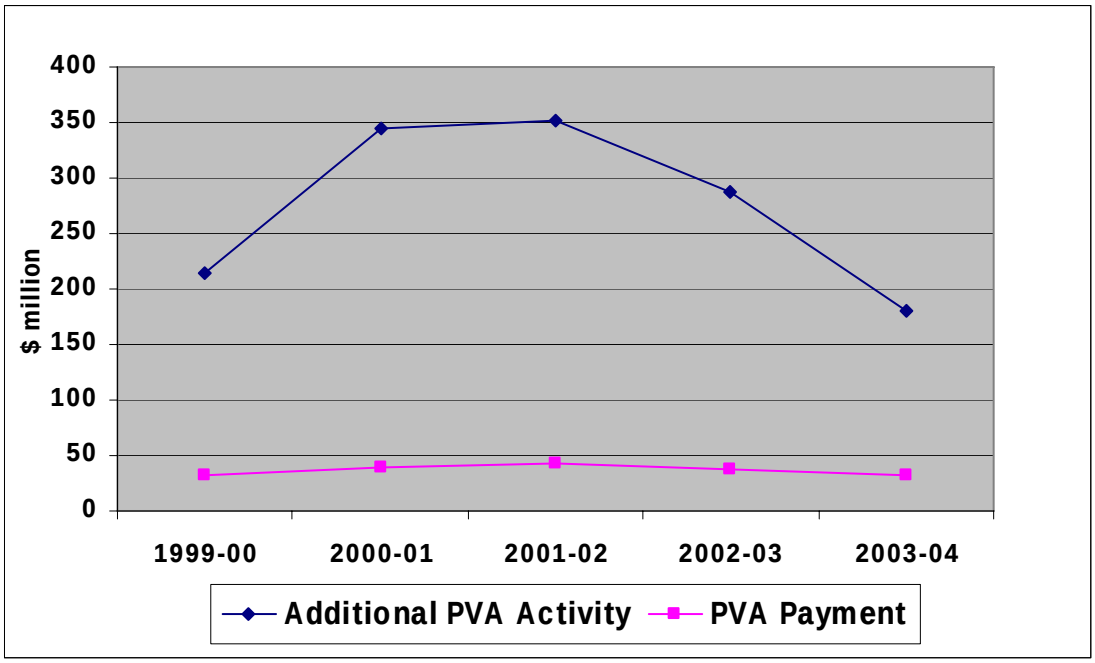
This investment generated an additional $1.74 billion in pharmaceuticals activity, including an additional $359 million of R&D (see Figure C.1) and an additional $1.38 billion in production value added activity (see Figure C.2). PIIP participants undertook over $7 billion of activity, including almost $6.2 billion of PVA and almost $950 million for R&D. While no new facilities were established during the life of PIIP, program participants spent $245.1 million ($289.2 million in today's dollars) on manufacturing infrastructures and capital investments.

**Figure C.1 PIIP Additional R&D Activity**




[106] Pharmaceutical Benefits Pricing Authority, *Supplementary Annual Report 2003-04*, Canberra, 2004.

**Figure C.2 PIIP Additional PVA Activity**




The additional investment encouraged by PIIP was expected to result in over 1,000 new jobs, to add to the approximately 12,000 employees working in the pharmaceuticals manufacturing industry in Australia at the commencement of the program. PIIP aimed to stimulate additional investment in the pharmaceuticals industry so that Australia developed as a regional centre of pharmaceutical R&D and manufacturing excellence.

### *Evaluation of PIIP*

PIIP was evaluated in a 2003 report by the Productivity Commission (PC). The PC found that:

> *"The estimates of additional R&D generated by the program per dollar of subsidy – the 'bang for a buck' – are much higher than have been found for other R&D incentives in Australia and internationally."*
>
> *"The program also appears to have the increased the relative importance of Phase I and II clinical trials and to have increased R&D employment."*
>
> *"PIIP has induced a significant amount of new R&D and, to a lesser extent, value added activity among participants."*

However the PC also found that

> *"The evidence provides mixed signals about the program's effectiveness in stimulating production" and that "it is highly likely that…the costs of the PIIP have exceeded the benefits".*

In assessing the continued relevance of the rationale for the program, the report found that:

> *"The rationale for assistance to the pharmaceutical industry based on price suppression is much less persuasive than conventionally claimed. Nonetheless, some effects on activity are likely. While the magnitude of these effects may not justify a program by themselves they should be taken into account if there are additional grounds for an industry-specific program."*

The report suggested that support of manufacturing was not providing a benefit to the economy and its main recommendation was that any future funding should only subsidise R&D.

> *"The omission of production value added [in future funding proposals] reflects the fact that, while some activity may have been lost as a result of the PBS, the costs of policy intervention overwhelm the benefits of offsetting those losses."*

The Productivity Commission's (PC) evaluation of PIIP found that the costs to the economy of supporting manufacturing exceeded the benefits by $47 million, whereas the benefits to the economy of supporting R&D exceeded the costs by over $17 million. The PC concluded that there was a strong case for supporting R&D, while the case for supporting manufacturing was weak.[107]

The full version of the report can be downloaded from the Productivity Commission's website at http://www.pc.gov.au/study/piip/docs/finalreport.

### Pharmaceuticals Partnerships Program ($P^3$)

$P^3$ commenced on 1 July 2004 and will terminate on 30 June 2009. It provides up to $150 million over five years to increase the level of high quality pharmaceuticals R&D in Australia. It also encourages partnerships between pharmaceuticals, biotechnology companies and researchers and the development of medicines for global markets.

$P^3$ had three entry rounds, commencing on 1 July 2004, 1 July 2005, and 1 July 2007. Entry to these rounds was determined by competitive entry. This meant that the program only supported companies that proposed activities of the highest quality and with the greatest potential impact on the competitiveness of the Australian pharmaceuticals industry. Applicants were ranked in order of merit and funded accordingly, if their proposed activity could be accommodated within the program's funding cap. The entry rounds were designed to allow companies flexibility to enter the program at a time best suited to their R&D cycle. Companies did not need to be PBS suppliers to be eligible for the program.

To be eligible, a company had to:

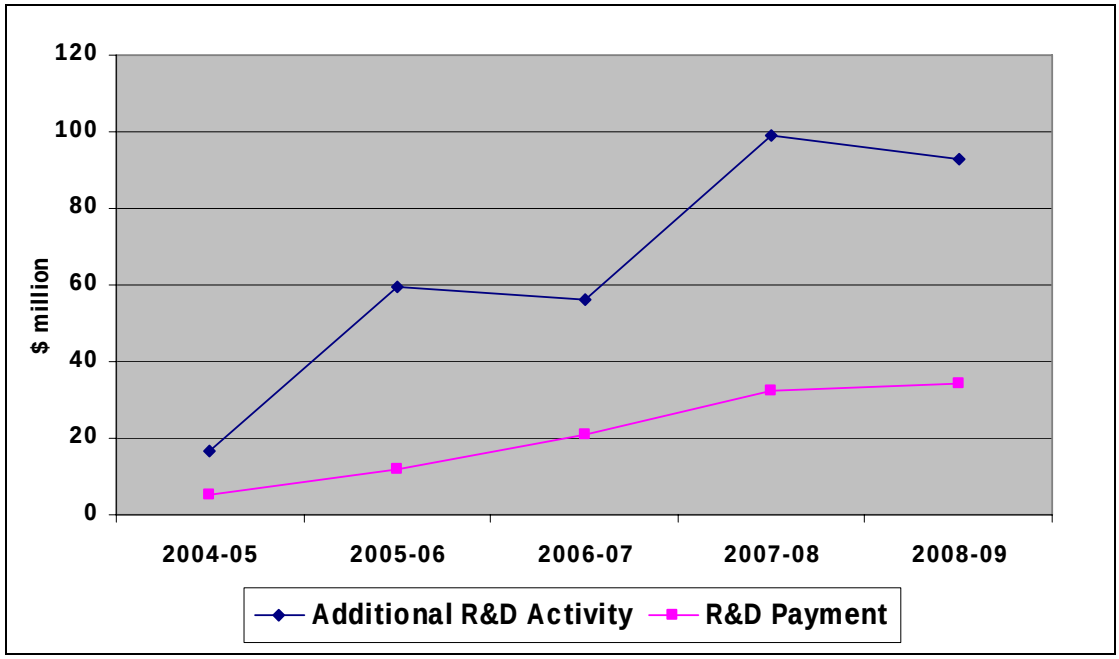
- be incorporated under the corporations Act;
- be part of the pharmaceuticals industry;
- have a three year track record of conducting R&D before entering the program; and

[107] Productivity Commission, loc. cit.

- propose to increase its eligible R&D expenditure above a base level for each year of its participation in the program.

Under Rounds 1 and 2 of the program, $P^3$ paid companies 30 cents for every additional dollar of R&D they performed, up to a cap of $10 million. Round 3 of $P^3$ provided companies with 50 cents for every additional dollar of R&D performed they performed up to a cap of $10 million. Figure C.3 below shows the actual additional activity performed in $P^3$'s first three years and estimates of the final two years. The final years' activity is likely to be less than estimates shown, given recent information gathered, which is yet to be verified.

**Figure C.3 $P^3$ Additional R&D Activity**




Current participants include 14 companies from all stages of the value chain.

### *$P^3$ Participants*

Round 1 participants:

- Acrux DDS Pty Ltd;
- CSL Ltd;
- Hospira Pty Limited (formerly Mayne Pharma Pty Ltd);
- Merck Sharp & Dohme (Australia) Pty Ltd; and
- Novogen Ltd.

Round 2 participants:

- CBio Ltd;
- Peplin Limited;
- Pfizer Australia Pty Ltd; and
- Starpharma Pty Ltd.

Round 3 participants:

- Peptech Limited;
- Janssen-Cilag Pty Ltd (was also in Round 1);
- Progen Industries Ltd;
- Vital Health Sciences Pty Ltd; and
- GlaxoSmithKline Australia Pty Ltd.

The seven withdrawn companies and their withdrawal dates are:

- Amrad Corporation Limited (now part of CSL) – 3 April 2006;
- Alchemia Limited – 27 November 2006;
- Alphapharm Pty Ltd – 18 December 2006;
- Servier Laboratories (Australia) Pty Ltd – 21 May 2007;
- ChemGenex Pharmaceuticals Ltd– 28 November 2007;
- Eli Lilly Australia Pty Ltd – 30 June 2007; and
- Tissue Therapies Pty Ltd – 30 April 2008

Note: Prana Biotechnology Ltd declined a Round 2 offer to participate in $P^3$. Pharmaxis' $P^3$ funding agreement concluded at the end of 2007-08.

### *Evaluation of $P^3$*

$P^3$ was evaluated by Deloitte Insight Economics (Deloitte) in May 2008. Deloitte found that $P^3$ has:

- increased both the quantity and quality of pharmaceuticals R&D in Australia;
- had only a low to moderate impact on half of its key performance indicators; and will likely spend only $96 million of its initial $150 million allocation; and
- generated an overall public/economic impact in the range of -$23.8 million to +$9.8 million, but is very likely to be close to neutral.

Deloitte projected that the program would support over $265 million of additional R&D in return for its $96 million investment and that $P^3$ participating companies would spend over $810 million on R&D over the life of the program.

Deloitte found that $P^3$ should not be renewed in its current form. Deloitte also concluded that the development of a pharmaceuticals sector specific program should not commence unless compelling evidence can be presented why such a program should be developed in preference to a generally available program. Deloitte also commented that:

> *"The program can be assessed as having made some positive contribution in relation to its objectives, with the strongest contribution being made to the attraction of new high quality R&D expenditure."*
>
> *"While the balance of probability is towards a small negative impact, the actual overall public and economic impact of $P^3$ is likely very close to neutral."*

*"Since the introduction of $P^3$ an important change to the 175 per cent Premium R&D Tax Concession partly addresses the issue of access to general R&D support for multinational corporations…this change weakens (but does not completely remove) the case for the appropriateness of $P^3$ into the future, insofar as the most sector specific market failure has now been largely addressed."*

*"The case for the appropriateness of a sector specific intervention now must largely rest on whether the strategic significance of the pharmaceuticals and biotechnology industry in seen to justify such special treatment."*

*"There does not appear to be compelling evidence available to suggest that spillovers for pharmaceuticals/biotechnology R&D are, on the whole, systematically higher than those that would be expected from R&D in other high technology and high innovation intensity industries."*

Deloitte have put forward a range of possible successor programs including:

- not replacing $P^3$ with any new industry specific program, but rather relying upon general measures to provide incentives for industry R&D activity;
- continuing with $P^3$ in its current form;
- refining the design of $P^3$ to increase the inducement rate of the program and drive step change additional R&D investment by large pharmaceuticals companies;
- refining the design of $P^3$ to implement a smaller scheme focused only on Australian emerging pharmaceuticals/biotechnology companies; and
- introducing a new scheme whose purpose is to facilitate only 'partnership' investments in pharmaceuticals related multi-party access infrastructure where the partnerships involve pharmaceuticals companies and the public research sector.[108]

The full version of the report is available on the Department of Innovation's website at http://www.innovation.gov.au/General/Innov-PS/Documents/P3_Evaluation_Final_Report_220508.pdf.

### Pharmaceuticals Industry Action Agenda

The Pharmaceuticals Industry Action Agenda (PIAA) was a ten-year industry growth strategy. It was developed by industry stakeholders during 2001 and 2002, and had as its vision a doubling of Australia's share of the global pharmaceuticals industry by 2012. The PIAA recognised that further growth of this industry was unlikely to eventuate by chance. The consequences of failing to grasp the opportunities were seen to be that the Australian industry would become a smaller player in the global market, reducing its capacity to generate significant wealth and health outcomes.

[108] Deloitte Insight Economics, loc. cit.

The PIAA developed a ten year, 16 point plan to double the size of the Australian pharmaceuticals industry.[109] A three year implementation phase followed the launch of the Action Agenda in November 2002.

The PIAA also set out goals and actions that it would aim to achieve. The goals, actions and their progress by 2005 are set out in the Third Year Implementation Report. The full version can be viewed at: http://www.pharmacouncil.com.au/news_pdfs/PIAA%203rd%20yr%20Imp%20Report.pdf.

The PIAA was independently evaluated in 2005. The evaluation found that:

> *"The vision, goals and actions represented an appropriate framework in which a range of issues of concern to the industry might be addressed."*

And that:

> *"In three years, good progress has been made on implementing the sixteen actions of the Action Agenda."*

The PIAA was found to have achieved three outcomes:

> *"1. Bringing the industry together in away which has not occurred in the past;*
> *2. Formulation of a long term industry growth strategy; and*
> *3. Support for the introduction of an industry development program – Pharmaceuticals Partnerships Program ($P^3$)."*

The PIAA was also found to have had sufficient funding provided by both Government and industry, have been run efficiently, and that it was a useful instrument in promoting the development of the Australian pharmaceuticals industry.[110]

Further outcomes of the PIAA include the formation of the Pharmaceuticals Industry Council (PIC), which was established in June 2006. PIC brings together three peak industry bodies, Medicines Australia, Generic Medicines industry of Australia, and AusBiotech. PIC is responsible for three associated working groups, the Pharmaceuticals Industry Development Taskforce (PIDT), the Research and Development Taskforce (RDTF), and the Pharmaceuticals Education Council (PEC). These groups carry out work, under the PIC banner, relevant to their specific area and comprise members with expertise in the fields of health and industry policy, R&D and biopharmaceutical/science education.

[109] Department of Industry, Tourism and Resources, *Pharmaceuticals Industry Action Agenda – Local Priority: Global Partner*, Canberra, 2002.
[110] Department of Industry, Tourism and Resources, *Evaluation of the Pharmaceuticals Industry Action Agenda*, Canberra, 2005.

## References


Australian Bureau of Statistics, *Manufacturing Industry, Australia, 2006-07,* (cat. no. 8221.0), 2008.

Australian Bureau of Statistics, *Research and Experimental Development Businesses, Australia,* (cat. no. 8104.0).

Carr K, *Government Announces Review of the National Innovation System,* media release, Parliament House, Canberra, 22 January 2008.

Carr K, *Government Releases Innovation Review Paper,* media release, Parliament House, Canberra, 9 September 2008.

Carr K and N Roxon, *Govt Revitalises the Pharmaceutical Industry Working Group,* media release, Parliament House, Canberra, 8 April 2008.

Centre for International Economics, *Pharmaceuticals Partnerships Program – First Year Evaluation*, Canberra, 2006.

Crean S, *Government Review of Export Policies and Programs*, media release, Parliament House, Canberra, 21 February 2008.

Department of Health and Ageing, *National Medicines Policy 2000*, Canberra, 1999.

Department of Industry, Tourism and Resources, *Australian Services Sector Trends*, Canberra, 2007.

Department of Industry, Tourism and Resources, *Evaluation of the Pharmaceuticals Industry Action Agenda*, Canberra, 2005.

Department of Industry, Tourism and Resources, *Pharmaceuticals Industry Action Agenda: Local Priority-Global Partner*, Canberra, 2002.

Department of Industry, Tourism and Resources, *Report on a Survey of Australia's Phase I Clinical Trials Units*, Canberra, 2007.

Deloitte Insight Economics, *Evaluation of the Pharmaceuticals Partnerships Program,* 2008.

DiMasi J A and H. G. Grabowski, "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Economics 28,* 2007, quoted in Pharmaceutical Research and Manufacturers of America, *Pharmaceutical Industry Profile*, 2008.

Economist Intelligence Unit, *Benchmarking Study of the Characteristics of the Australian and International Pharmaceuticals Industries,* 2005.

Epsicom Business Intelligence, *The World Pharmaceutical Markets Fact Book 2008,*

German Association of Research Based Pharmaceutical Companies, *Statistics*, 2007, <http://www.vfa.de>.

Gillard J, *A Higher Education Revolution*, media release, Parliament House, Canberra, 13 March 2008.

"Global pharma market grew to $712 billion last year", *Scrip*, no. 3357, 30 April 2008.

Hopper K and L Thorburn, *2008 BioIndustry Review Australia and New Zealand*, 2008.

Hajos A and S Kamble, "The road to site selection in India", *Good Clinical Practice Journal*, vol. 15, no. 6, 2008.

IBISWorld, *Medicinal and Pharmaceutical Product Manufacturing in Australia: C2543*, 2008.

IBISWorld, *Pharmaceuticals Wholesaling in Australia: F4797*, 2008.

IMS Health quoted in European Federation of Pharmaceutical Industries and Associations (EFPIA), *The Pharmaceutical Industry in Figures 2008*, 2008.

Institute for Management Development, *IMD World Competitiveness Yearbook 2007*, 2008.

Intellectual Property Research Institute of Australia, *Review of Pharmaceutical Patent Extension and Springboarding Provisions in Various Jurisdictions*, 2002.

Kauffman - The Foundation of Entrepreneurship, *The Globalization of Innovation: Pharmaceuticals*, 2008.

Lewcock A, "Pharmas to lose $100bn to generics", *DrugResearcher.com*, news article, 22 February 2007, <http:www.drugresearcher.com>.

Medicines Australia, *Australian Pharmaceutical Industry at a Crossroads: Report of the 2007 Medicines Australia Member Economic Survey*, 2008.

Organisation for Economic Co-operation and Development, *OECD Science, Technology and Industry Scoreboard 2007*, 2007.

Pharmaceutical Benefits Pricing Authority, *Supplementary Annual Report 2003-04*, Canberra, 2004.

Pharmaceuticals Industry Council, *Clinical R&D in Australia: Innovation and Global Competitiveness*, report on the 3rd Pharmaceuticals Industry Council R&D Taskforce Forum, Sydney, 2-3 April 2008.

Pharmaceutical Research and Manufacturers of America (PhRMA), *Drug Discovery and Development: Understanding the R&D Process*, 2007.

Pharmaceutical Researchers and Manufacturers of America (PhRMA), *Pharmaceutical Industry Profile 2008*, 2008.

Plag S, "Pharmageddon: Is Big Pharma Broken?", presentation of Credit Suisse research to European Healthcare Group, December 2007.

PriceWaterhouseCoopers, *Pharma 2020: The vision. Which path will you take?*, 2007.

Productivity Commission, *Evaluation of the Pharmaceutical Industry Investment Program*, 2003.

Productivity Commission, *Public Support for Science and Innovation*, Canberra, 2007.

Rankin J, J Mason, N Kottege and N Y Andersson, "Clinical trials of unapproved medicines in Australia", *The Medical Journal of Australia*, vol. 18, 2006.

"Report finds poor management scuppers almost half of all licensing deals", *Scrip*, no. 3330, 25 January 2008.

Swan W, *Australia's Future Tax System*, media release, Parliament House, Canberra, 13 May 2008.

The Allen Consulting Group, *Drivers of Pharmaceutical Investment: Understanding Australia's Competitive Position*, report to Medicines Australia and Research Australia, 2006.

The Industry Commission, *The Pharmaceuticals Industry*, 1996.

The Review of the National Innovation System, *Venturous Australia*, Canberra, 2008.

Therapeutic Goods Administration, *Clinical Trials at a Glance*, <http://www.tga.gov.au/ct/ctglance.htm> viewed 24 September 2008.

United States Government Accountability Office, *New Drug Development: Science, Business, Regulatory and Intellectual Property Issues Cited as Hampering Drug Development Efforts*, 2006.

Warburton R and P Hendy, *International Comparison of Australia's Taxes*, 2006.