OCCASIONAL PAPER SERIES 2

INNOVATION

FOR THE HEALTH OF THE NATION

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MEDICINES AUSTRALIA OCCASIONAL PAPER SERIES
PAPER 02

INNOVATION FOR THE HEALTH OF THE NATION

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INNOVATION FOR THE HEALTH OF THE NATION

Australia is home to some of the world's best researchers and healthcare professionals. It boasts world-class research infrastructure and a stable socio-economic environment. These are all factors that have contributed to the strong growth in investment by the pharmaceuticals industry in Australia; indeed, between 1998 and 2009, the global pharmaceuticals industry invested close to $5 billion in research and development in Australia.

But these factors alone are no longer proving sufficient in attracting investment. Not only has investment growth effectively stagnated, it has in fact declined in several important areas. In clinical research, for example, industry investment has declined by approximately 30 per cent over the last three years. The question now facing policy makers is: will Australia remain at the forefront of medical innovation and reap the multiple benefits that flow? Or should we accept that our time as a nation of innovation has passed? The choice is ours – but the window of opportunity is closing fast.

THE CONTRIBUTION OF AUSTRALIA'S MEDICINES INDUSTRY

By any measure, Australia's medicines industry is one of the nation's most important high-value, high-technology industries.

It employs almost 14,000 people around the country in a range of high-skilled, high-wage jobs. Seventy-two per cent of employees in the industry have some sort of post-secondary education and 19 per cent hold a Masters or PhD degree[1].

Australia's pharmaceutical companies invest more than $1 billion a year in research and development, ranging from basic research right through to clinical trials of new medicines and post-market research of medicines already on the market. The scale of that research and development investment is the third largest by area of business expenditure in Australia, behind the financial services and mining sectors.

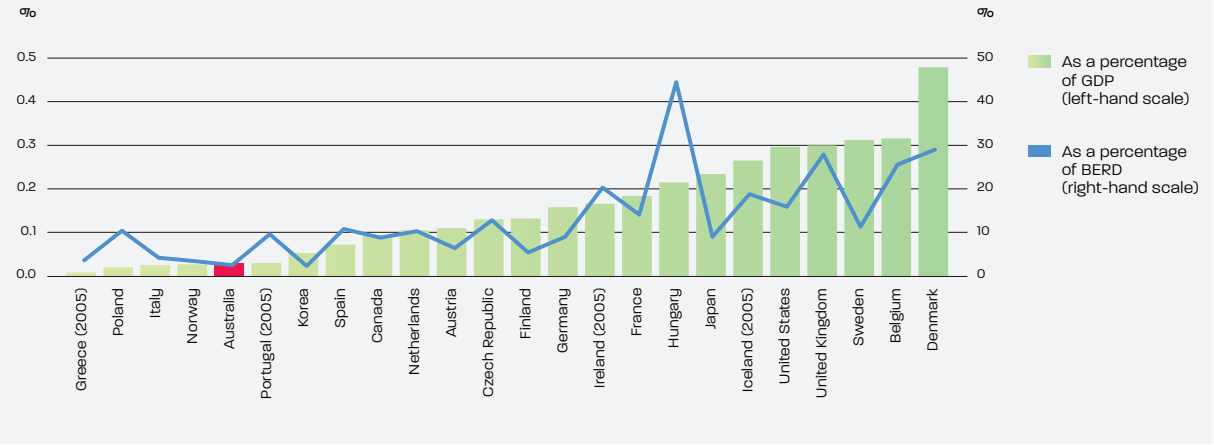
The industry also contributes over $4 billion a year in manufacturing exports, more than any other hi-tech industry. These facts mean that the Australian medicines industry currently exports more and spends more on research and development than the car industry.

The economic contribution of Australia's medicines companies is amplified through substantial linkages with other parts of the medical research sector. For example, 55 per cent of all industry-funded clinical trials in Australia are conducted in partnership with public hospitals and a further 26 per cent are conducted through universities and research institutes[2].

Industry's survival, both here and internationally, depends on its ability to develop new products that treat and prevent illness through new medicines and vaccines. How the industry develops these new treatments is therefore critical to its long-term economic future and its capacity to continue making a considerable contribution to the national economy.

While the industry is a big R&D performer by Australian standards compared with other industries, we are ranked 20th out of 24 OECD countries in terms of the level of private investment in pharmaceutical R&D. Clearly there is untapped opportunity and the potential to attract a far greater share of global R&D investment.

FIGURE 1 R&D IN THE PHARMACEUTICAL INDUSTRY AS A PERCENTAGE OF BERD AND GDP, 2006



SOURCE OECD 2009 *Science, Technology and Industry Scoreboard 2009*, Paris, p. 59.

1 Medicines Australia, 2010, *The Australian Pharmaceuticals Industry: Winds of Change: Report of the 2009 Medicines Australia Member Economic Survey*, p. 6.

2 Medicines Australia, 2010, *Facts Book 2*, Second Edition, Canberra, p. 14.

INNOVATION IN MEDICINES: COSTLY, RISKY AND HARD TO DO

Developing a new medicine or vaccine is no easy task. To develop a promising chemical or biological compound in the laboratory into a medicine or vaccine that can treat a patient safely and effectively is a long, difficult and expensive process. Pharmaceutical companies operating in Australia and internationally take on the commercial risk of developing these treatments in the hope of making them a commercial success while also developing products to treat a range of humanity's illnesses.

It costs around A$1.4 billion to bring one new biopharmaceutical medicine to market, including the costs of failures[3]. When developing a new medicine, a company needs to earn a commercial return within an effective patent-life of 11 or 12 years to justify the investment of that sort of money. This is one of the key factors governing the pricing of new medicines. If companies are not going to earn a sufficient return over and above the costs of development, it is unlikely they will invest in the development of those medicines.

Factors that contribute to the cost of development include the high failure rate of potential new compounds, the time that it takes to bring a new medicine to market, the complexity of developing new medicines and commercial risk for companies in developing those medicines. For every 10,000 compounds tested for potential medical benefits, only five ever reach clinical trials and only one ever reaches the market[4].

Even for those medicines that make it to the clinical trial phase, the ultimate success rates are low. In the 10 years from 1993 to 2004, the success rate for all medicines in clinical trials was 19 per cent.[5] That is, out of all medicines that made it to the clinical trial phase only 19 per cent achieved approval to be sold on the market. The remaining 81 per cent of compounds fail at different stages of the clinical trial process for various reasons such as the compound proves not to be as clinically effective as originally thought, or due to safety reasons, or the compound proves not to be commercially viable for the company to continue development given anticipated returns and pricing.

In terms of time, it takes on average almost 15 years to have a medicine approved for sale on the market[6]. This includes the five years it takes for the drug discovery process in the laboratory to identify potential compounds that could form the basis for a medicine or vaccine, followed by one and a half years in pre-clinical testing, an average six years to run clinical trials on a medicine, then an average two years for approval by Australia's Therapeutic Goods Administration.

For these reasons, the commercial risks involved for a company in developing a medicine are many and varied. Part of the business of developing new medicines is for companies to decide which molecules to devote time, money and resources to bringing to market. The commercial ramifications for companies when a medicine fails in its development can be significant. It happens quite often that the media will report that a particular company's share price has fallen dramatically after a key compound in that company's portfolio has failed in a particular phase of a clinical trial[7].

3 Kaitlin, K.I. 2010 "Deconstructing the Drug Development Process: the New Face of Innovation", *Clinical Pharmacology and Therapeutics*, 87(3), March, p. 358. Adjusted to current Australian dollars using RBA A$/US$ exchange rate as at 22 December 2010 and ABS Consumer Price Index inflation adjustment cat. 6401.0.

4 Pharmaceutical Research and Manufacturers of America. 2005, *Industry Profile 2005*, Washington.

5 Di Masi, J., Feldman, L., Seckler, A. & Wilson, A. 2010. "Trends in Risks Associated with New Drug Development : Success Rates for Investigational Drugs", *Clinical Pharmacology and Therapeutics*, 87(3), p. 272.

6 Pharmaceutical Research and Manufacturers of America. 2005, *Industry Profile 2005*, Washington, pp. 4-5. Adapted to include the average two-year approval time by Australia's Therapeutic Goods Administration to approve a medicine for sale on the Australian market.

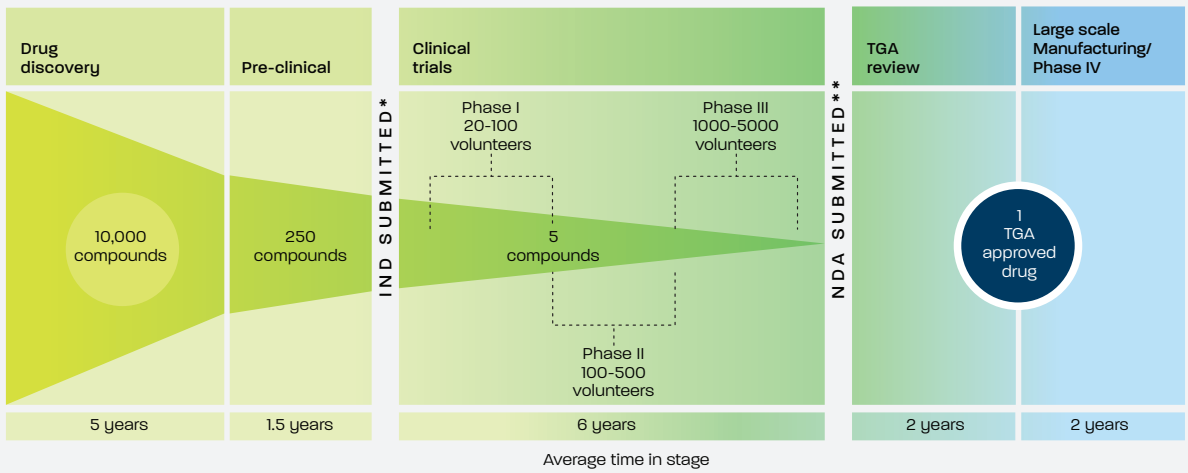
7 For example, on 4 January 2011, shares in Inspire Pharma plummeted nearly 60 per cent after the company announced that its candidate aimed at treating cystic fibrosis failed to meet key goals in a late-stage human study. In January 2007, shares in Telik Inc. plunged over 70 per cent after the company announced that one of its main experimental products to treat ovarian and lung cancers had failed to generate positive outcomes in patients in three separate Phase III clinical trials.

The company also needs to assess whether or not to proceed with a new medicine or vaccine, based on the likely commercial return the company will earn from the suite of potential compounds for development. Prospects depend on factors such as the potential patient group and therefore market size for the compound. Another factor is the likely price the product will earn in the market, which in turn is increasingly being influenced by what price third party payers, be they governments or private health funds, are prepared to pay on behalf of the patients they are subsidising. Companies will also be influenced by the clinical need for the compound, the number of other competing compounds in the market, and which therapeutic areas are likely to have the most growth.

Given the timelines in developing new medicines, the commercial decisions being made today about which therapeutic areas to invest in and what particular new medicines and vaccines to commercialise do not so much influence the availability of new treatments today, but rather influence what new treatments become available in 15 to 20 years' time. For example, if a range of companies decide there is no incentive to invest in the development of new medicines in a particular therapeutic area, it will be in 15 to 20 years' time that those decisions affect the treatment options available to patients.

One current example of this is in the area of antibiotics, where the lack of new antibiotic medicines to treat the growing number of drug-resistant bacteria is the result of decisions made by pharmaceutical companies over the last two decades not to invest in drug development in this area. This has been for a range of reasons including clinical restrictions on the use of antibiotics and the reluctance of third-party payers like governments and private health funds to pay more for new antibiotics over and above the price for old, cheap generic antibiotics.

FIGURE 2 JOURNEY OF MEDICINES – FROM DISCOVERY TO MARKET



Source: Derived from PhRMA, 2005, Pharmaceutical Industry Profile 2005, from Laboratory to Patient: Pathways to Biopharmaceutical Innovation, Washington DC, p4-5

*IND submitted: Investigational new drug application submitted to the US Food and Drug Administration

**NDA submitted: New drug application submitted to the Australian Therapeutic Goods Administration (TGA)

INCREMENTAL INNOVATION IN MEDICINES

Like most innovative industries, innovation in the medicines industry occurs at different stages and paces. Although welcomed, not all invention in medicine is breakthrough or radical innovation. Breakthrough innovation in medicine occurs through major new scientific discoveries, such as the discovery of a vaccine for cervical cancer like Gardasil® or a new molecule to treat leukaemia like Glivec®. However, innovation usually occurs incrementally, where improvements in compounds build incrementally on previous compounds in the same therapeutic area.

The OECD has acknowledged: "The value of incremental innovation depends on the extent to which it is evolutionary rather than duplicative. New products can offer significant advances in terms of improved efficacy, fewer adverse side effects, greater patient satisfaction (as tailoring to the individual as possible), better compliance and sometimes even increased cost-effectiveness"[8].

An example is in treating cancer, where individually many new cancer medicines have incrementally added benefit by extending a cancer patient's life by a matter of weeks or months. But as each individual cancer medicine has been an incremental step forward in treatment, collectively the development in technology has extended the life expectancy for cancer patients. For example, between 1988 and 2000, the average life expectancy for cancer patients increased by around four years, largely due to the availability of new treatments, with substantial social and productivity benefits[9].

Incremental innovation also occurs as new uses are found for existing compounds through additional research, an example being Remicade®, which is a chimeric monoclonal antibody that targets specific proteins in the body to help treat a number of inflammatory disorders involving the immune system. Remicade®, which was originally approved for the treatment of Crohn's Disease in 1998, has since received approval for many other indications. Today, it is approved for the treatment of conditions such as plaque psoriasis, rheumatoid arthritis, psoriatic arthritis, ulcerative colitis and ankylosing spondylitis. Research on new uses continues. This sort of innovation is quite normal and is a key part of how the medicines industry identifies and develops new treatments for patients.

8 Organisation for Economic Cooperation and Development. 2008. *Pharmaceutical Pricing Policies in a Global Market*. Paris, p. 56.

9 Lakdawalla, D., Sun, E., Jena, A., Reyes, C., Goldman, D. & Philipson, T. 2010. "An economic evaluation of the war on cancer", *Journal of Health Economics*, 29, p. 333.

LONG LEAD TIMES AND THE IMPORTANCE OF CERTAINTY

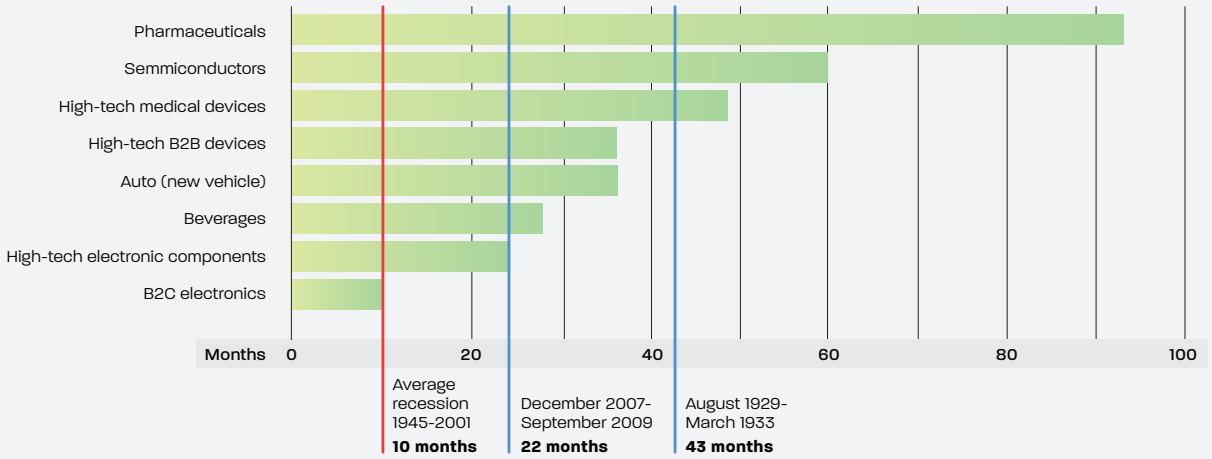
While the medicines industry has a long product development cycle, other industries such as semiconductors, high-tech medical devices, high-tech business to business equipment and the auto industry have much shorter product development cycles.

Other industries can bring their products to market quicker than the medicines industry. This is why the medicines industry seeks a predictable policy environment, strong intellectual property laws and stable pricing structures. The longer product development cycle exposes the medicines industry to more commercial risk from changes in the policy or business environment while a product is still in development more than in other high technology industries.

FIGURE 3 TYPICAL PRODUCT DEVELOPMENT CYCLES vs HISTORICAL RECESSIONS

Product development cycles are long, while recessions are usually short

One reason companies can't afford to cut innovation when times are tough is that product development cycles tend to be much longer than the average of recent recessions – and for most industries, longer than the current recession date.



SOURCE Jaruzelski, B., and Dehoff, K. 2009. "Profits Down, Spending Steady: The Global Innovation 1000", *Strategy+Business* (57), p. 10, available online at: http://www.booz.com/media/uploads/Innovation_1000-2009.pdf (accessed 8/02/2011).

The discovery-driven medicines industry is a central player in the development of new medicines. According to a US study, overall pharmaceutical companies discover 58 per cent of all medicines approved for sale on the market, while biotechnology companies account for 18 per cent, and universities 24 per cent[10]. Even when only looking at scientifically novel medicines – those whose mechanism of action was novel and/or were the first medicines in a new class of medicines – 44 per cent of those were discovered by pharmaceutical companies, while 25 per cent were discovered by biotechnology companies and 31 per cent by universities[11]. Many of these medicines that were originally discovered by biotechnology companies and universities ultimately are commercialised by the pharmaceutical industry. It is one thing to discover a new medicine, but bringing that medicine to market is another major investment of resources in clinical trials, marketing, distribution, monitoring and the like.

10 Kneller, R. 2010. "The importance of new companies for drug discovery: origins of a decade of new drugs", *Nature Reviews: Drug Discovery*, 9, November, p. 869.

11 Ibid, p. 869.

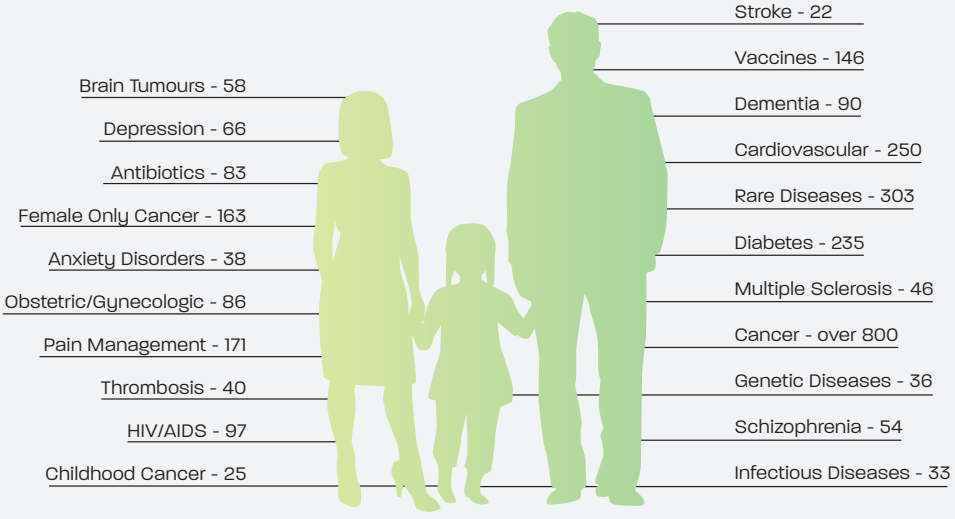
TRENDS IN MEDICINES DEVELOPMENT

Innovation in medicines provides new treatment options for society. People with various illnesses and conditions enjoy the benefits of this innovation in the form of new medicines and vaccines to treat or prevent illnesses, in many cases for conditions for which there had been no effective treatment available.

As an example, a look at the top 20 medicines available on Australia's Pharmaceutical Benefits Scheme today compared with 20 years ago shows the progress that medical technology has made even in the last two decades. The typical product life cycle in medicine, where a new medicine enters the market at a higher price to recoup the huge up-front investment costs of developing the medicine, followed by price reductions after patent expiry with the onset of generic competition, is reflected in the cost of different medicines on the PBS.

The good news today is that over 2,950 medicines and vaccines are in development by the global medicines industry to help people live a better, healthier and more productive life. There are more than 800 medicines in development to treat cancer, 303 to treat rare diseases, 250 to treat cardiovascular disease and 235 to treat diabetes. Australia is playing its part in this global effort and in 2010 over 18,000 Australians took part in a clinical trial.

FIGURE 4 MEDICINES UNDER DEVELOPMENT



SOURCE Pharmaceutical Research and Manufacturers of America, New Medicines, available at www.phrma.org/research/new-medicines

PROTECTING AND GROWING AUSTRALIAN INNOVATION

Australia can point to a long record of medical innovation. We currently boast some of the best research capability and infrastructure in the world. This is an advantage on which we must capitalise.

Investing in innovation means investing in Australia's future. It means creating high-wage jobs for thousands of Australians. And it means giving Australians early access to new technologies.

However, after more than two decades in which Australia's reputation as a global hub of R&D excellence has grown, our competitiveness as a destination for global clinical trials is under threat from emerging trial locations in Asia, Eastern Europe and South America. The number of clinical trials in Australia has fallen for two successive years (2008, 2009) for the first time since 1998, and is likely to have fallen for a third successive year (2010) when the Therapeutic Goods Administration releases the latest data in March.

The right policy levers will be essential to ensure Australia is well placed to protect and grow its innovation base.

- The R&D tax credit, for example, which Medicines Australia has supported since the policy was first proposed, will effectively reduce the cost of undertaking eligible R&D in Australia by up to 10 per cent, making Australia more globally competitive as an investment destination for pharmaceutical and biotechnology R&D.
- A more efficient regulatory system for the 800 clinical trials undertaken in Australia each year will further improve our international competitiveness. This means harmonising the complex and cumbersome ethical review process for clinical trials that are conducted at multiple sites in different states and territories, so companies are not discouraged by excessive red tape from investing in Australia. Clinical trials make a substantial contribution to the national economy by creating high-value jobs and injecting much-needed funding into research institutions. A simplified, streamlined system would mean keeping more of our top research scientists engaged in Australian R&D and attracting greater investment to our universities and other research institutions.
- The Federal Government's appointment of a Clinical Trials Action Group, charged with the task of raising Australia's profile as a preferred destination for conducting clinical trials, was a positive move. The group reported to the Government in June 2010 and its recommendations present an opportunity to turn around the decline in clinical research.
- A strong intellectual property framework is another key driver of innovation because it provides R&D investors confidence that they will be able to recoup their investment without the threat of unauthorised use by competitors of intellectual property derived from the research. Indeed, intellectual property protection is the cornerstone of innovation.
- And business certainty is paramount. Companies investing billions of dollars into any technology will not do so unless there is policy stability.

These are the policy levers that present an opportunity for Australian innovation. Without them, global investment in pharmaceutical R&D in this country is likely to decline dramatically over the coming years. We have a small window of opportunity. Australia must decide whether it will remain at the forefront of innovation and reap the health and economic rewards, or whether it is ready to relinquish its global reputation as a nation that innovates for health.

MEDICINES AUSTRALIA MEMBER COMPANIES

Abbott Australasia
Actelion Pharmaceuticals Australasia
Alcon Laboratories (Australia)
Allergan Australia
AMGEN Australia
Andrew's Refrigerated Transport
AstraZeneca
Baxter Healthcare
Bayer Healthcare Pharmaceuticals
Biogen Idec Australia
Boehringer Ingelheim
Bristol-Myers Squibb Australia
Celgene
Commercial Eyes
Covance
CSL
Eli Lilly Australia
FIT BioCeuticals
Fresenius Kabi Australia
Genzyme Australasia
Gilead Sciences
GlaxoSmithKline Australia
IDT Australia
IMS Health Australia
iNova Pharmaceuticals
Invida Australia
Ipsen
Iris Interactive
Janssen
Kendle
KMC Health Care
Lundbeck Australia
Merck Serono Australia
MSD
Mundipharma
Norgine
Novartis Pharmaceuticals Australia
Novo Nordisk Pharmaceuticals
Nycomed
Pfizer Australia
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