Submission to the Inquiry into Business Commitment to Research and Development in Australia by the House of Representatives Standing Committee on Science and Innovation

Pfizer Pty Limited

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1) Introduction

Pfizer welcomes this opportunity to provide a submission to the Committee on the issue of "Business commitment to Research and Development in Australia".

The recent rise in private R&D investment gives reason for optimism, however, we share the concern of many stakeholders that private sector investment in R&D remains significantly below that of many comparable nations.

This submission will be from the perspective of a global pharmaceutical company. A relatively modest shift of pharmaceutical R&D by global companies from other nations to Australia would raise the R&D levels of Australian industry quite significantly. This submission may also provide insight into some of the broader questions posed by the Committee, particularly in relation to *the considerations by which major international corporations site R&D investment.*

Many of these factors pertaining to pharmaceutical industry R&D have been discussed in the *Pharmaceutical Industry Action Agenda Discussion Paper* by the then Department of Industry, Science and Resources. Pfizer encourages members of the Committee to read this discussion paper.[1]

Pfizer invests the greatest amount of funding in pharmaceutical R&D of any of its competitors, in the most research intensive industry in the world. The company's global investment in R&D during 2002 will be around A$8.7 billion, significantly higher than any competitor.

In Australia, Pfizer is investing more than $90 million into R&D between 1999-2004. This investment includes $25 million into early-stage discovery research and basic science collaborations with Australian universities, research institutes and biotechnology- or research-based companies. A further $53 million is being spent on clinical trials with partner investigators (usually hospital based medical specialists). A new Pfizer Biometrics[*] Centre will involve an investment of $14 million from 2002-2004.

As a global and local investor in R&D, we believe Pfizer is well positioned to make a contribution to this Inquiry.

[1] Available via the Medicines Australia website www.medicinesaustralia.com.au
[*] Biometrics is the statistical design and analysis of clinical trials

2) R&D in the Context of the Pharmaceutical Industry

a) Global Pharmaceutical R&D

Annual investment in research and development by the pharmaceutical industry globally is around US$40 billion[2]. The US pharmaceutical industry reinvests around 17% of sales into R&D[3]. Based on corporate tax data compiled by S&P's Compustat, pharmaceutical manufacturers invest a higher percentage of sales revenue in R&D than virtually any other U.S. industry, including high-tech industries such as electronics, aerospace, computers, and automobiles.[4]

Investment in developing a new chemical entity (NCE) is costly, high risk and long term. The latest estimates are that on average an NCE costs US$800 million to research and develop and takes 12-15 years to bring to market.[5] Once approved only one in every three new drugs provides a financial return on the investment necessary to develop and register the drug.

Although the major proportion of pharmaceutical and biotechnology R&D on diseases of humans occurs in the US, Europe and Japan, the R&D value chain is increasingly global. Australia is well positioned to participate more fully in this increasingly global industry, but business must be encouraged and rewarded for taking the risk and committing the resources needed to realise this opportunity.

b) Pharmaceutical R&D in Australia

In Australia, the pharmaceutical industry (including human use biotechnology companies) generates most revenue through the Pharmaceutical Benefits Scheme (PBS), which provides subsidised medicines to eligible consumers. Prices paid to manufacturers for products listed on the PBS are artificially lowered by the Federal Government's monopsony purchasing power.

In effect this restriction on drug prices does not reward innovation and has directly resulted in relatively low rates of R&D investment by the global pharmaceutical industry in Australia.

In recognition of this fact, the previous Labor Government established the Factor (f) scheme which rewarded companies according to their R&D and value added manufacturing commitment. Under the current Government, this was replaced by the Pharmaceutical Industry Investment Program (PIIP) which has a similar focus. These schemes have been successful in encouraging R&D investment by the global industry in Australia. In 1996, the latest date for which concrete figures are available, the pharmaceutical industry invested $250 million into R&D, around 6 percent of sales.[6]

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[2] Scrip Yearbook 2000, Vol 1, p 159
[3] PhRMA Pharmaceutical Industry Profile 2002, Figure 2.2
[4] Price Waterhouse Coopers The Critical Roles of R&D in the Development of New Drugs 2001 cited in PhRMA ibid.
[5] Tufts Centre for the Study of Drug Development, 2001. This includes the opportunity cost of capital.
[6] Pharmaceutical Industry Action Agenda Discussion Paper p 18

In the first year of PIIP, R&D activity by the eligible companies increased by 29 percent.[7]

Pfizer's R&D investments in Australia are in large part the result of the incentives provided by Factor (f) and PIIP. However, these programs should be seen as part compensation for low domestic prices of pharmaceutical products.

Even with this increased investment, the overall proportion of Australian pharmaceutical sales invested in R&D continues to lag behind the 15-20 percent level, which is the average for the worldwide pharmaceutical industry.[8]

[7] ibid p 63
[8] ibid p 18

3) The Economic Benefit of Greater R&D investment

a) Direct Investment Benefit

The economic benefit of a direct investment by a pharmaceutical company into R&D can be substantial. Northern Hemisphere economies benefit enormously as the leading recipients of the US$40 billion annual investment in R&D by the pharmaceutical industry. California, North-East United States (especially Connecticut and Massachusetts), South-East England, France, Denmark, Switzerland, Sweden, Germany and Japan all have large R&D centres which generate substantial economic inflows.

Whilst the investment level of an estimated $A300 million per annum is lower in Australia, it does create significant economic activity and employment. Employment opportunities in the pharmaceutical and biotechnology industries created through this investment are primarily for highly qualified staff who command relatively high salaries and benefits.

For this reason, individual States in the United States compete fiercely for pharmaceutical and biopharmaceutical companies to locate new R&D facilities in their region. Internationally, countries such as Singapore, Israel and Ireland are very actively courting and fostering the growth of new high tech industries, including biopharmaceuticals.

b) Patent Rights Issue

Before considering the indirect economic benefits of R&D, Pfizer would like to address the issue of whether R&D provides sustainable value if the ownership of the patent or knowledge does not remain in Australia. Much of the research undertaken by global pharmaceutical companies in Australia takes the form of collaborations. In many cases, for example when the outcome of a collaboration is research tools rather than potential pharmaceutical products, the pharmaceutical companies may not take the IP arising from the collaboration overseas, but instead seek a non-exclusive license to enabling IP or allow the IP to be the property of the Australian collaborators, provided they have a research license and/or option to commercialize should the results warrant. In these cases, the Australian collaborator retains enhanced IP, which can generate further economic value.

In the cases where it does retain ownership of the IP, the global pharmaceutical company will pay appropriate market rates to the collaborator. However, not all IP is of the same value. Some may be so tenuous (high-risk) or encumbered by other IP that a modest license fee may be all that can be justifiable. Other IP may point the direction (validated drug target) to a new therapeutic or prophylactics agent, but not describe the active compound itself. In this instance a collaborative agreement to use the IP to discover a new drug may include up front license fees, funded research collaboration, milestone payments and in some instances a modest ongoing royalty. If, however, the IP relates to proof of concept for a potential drug substance, a joint development program (eg the development of Relenza by Glaxo SmithKline and Australian biotechnology company Biota) may be more appropriate where both the parties contribute their respective expertise and development costs, risk and profits are

shared equitably. In none of these cases could it be argued that ownership of the IP needed to remain local in order for Australia to benefit financially. In the case of Relenza, Biota profited substantially from the transaction.

In cases where the Australian branch of a global pharmaceutical company is directly engaged in developing IP for the parent company (without involving an Australian collaborator) the economic benefit consists in the sum of payment for those services by the parent company, as well as the wider benefits of housing such research in Australia (addressed in point d) below). Researchers have suggested that these benefits are greater in the case of R&D centres of excellence, because of their focus on technological development and the voice they give to the Australian subsidiary in global product development.[9]

c) Payments to Institutes, SMEs and Medical Specialists

As stated earlier, many of the funds invested by Pfizer in Australian medical science supports collaborative research with universities, institutes or small-medium enterprises (SMEs) undertaking research in areas of priority interest to Pfizer Global Research & Development. This funding has an economic flow on effect, in that it allows the academic group to pursue their research interests, to support graduate and post-graduate training of young Australian scientists, to gain insights on commercially focused research plans, to acquire major items of equipment, where appropriate to access company reagents or know-how (bioinformatics, assay reagents, drug substances, etc) and to off-set university and institutional infrastructure costs. Income from such licenses and options (discussed under Patent Rights) will allow the researchers to undertake additional or unrelated research activities, which may result in new IP.

Similarly, payments to SMEs help build company infrastructure (chemical synthesis, bioinformatics, etc), recruit additional staff and enable the staff to gain experience and generate know-how, particularly in project management and quality control of commercially focussed projects. The more successful companies can also use their contract or collaborations with global pharmaceutical companies to raise additional investments from Angel, Seed or Venture Capital funding entities. Such venture capital is often difficult to attract, but is of enormous value to Australian enterprises.

The economic value of R&D undertaken by universities, research institutes and biotechnology SMEs is potentially very significant. By 1996, biotechnology companies developing out of the Massachusetts Institute of Technology in the United States already had a market value of US$22 billion and had generated 10,000 new jobs.[10]

In the case of clinical trials, payments to medical specialists provide revenue to highly skilled professionals and in some cases to Australian hospitals. The collaboration further enables them to increase their patient databases to delineate disease processes and genetic associations for their disease of interest (eg adolescent onset diabetes, chronic venous ulcers, etc). Specialists undertaking clinical trials with new drug

[9] Thorburn, L et al Friend or Foe? Leveraging Multinationals in the Australian Economy, Australian Business Foundation, 2002

[10] MIT News "MIT President Warns Economic Growth is Threatened by Cuts" January 22, 1996

substances have an opportunity to gain early access to more safe and/or effective drugs within their chosen specialty prior to them being generally available. These benefits allow Australian medical professionals to provide continued worldwide leadership in research and patient care.

d) Development of the Knowledge and Skill Base

It has been commented that Australia represents only a small proportion of economic activity and Australians could not maintain their standard of living without access to the global pool of knowledge via multinational companies.[11] This is particularly the case in the biotechnology/pharmaceutical sector.

A critical ingredient for the development of a local biotechnology/pharmaceutical sector is the availability of commercially experienced science-based managers to guide and focus start-up companies during their formative years. Such people frequently gain their commercial experience in global pharmaceutical and biotech companies before taking up leadership roles in SMEs. They have knowledge of the world's best processes used by global companies to manage commercial development. They also understand the needs of large companies when interacting with SMEs and have personal contacts inside global companies that can internally champion interactions with the Australian SME. The importance of business development skills and "championing" to the local biotechnology industry has been emphasised in the *Health and Medical Research Strategic Review.*[12]

At present, Australian SMEs and researchers do not have strong reputations for understanding the perspective of the global pharmaceutical industry, which in part reflects the limited exposure these managers have to global pharmaceutical companies in Australia. The growth of a vibrant R&D sector within international pharmaceutical companies in Australia will increase the likelihood that such skills are available locally to fuel the growth of start up companies.

There is also strong evidence that researchers who have been involved in one successful product commercialisation are likely to be involved in others.[13] This flow on effect can also be expected to hold true for researchers and research managers who gain experience in the private pharmaceutical sector.

Thorburn et al have commented that foreign firms perform more R&D than domestic firms, and this R&D is likely to be performed in high technology sectors than is the case for local companies. [14] As a result, foreign firms are an essential source of knowledge about the processes and value of R&D. This is particularly the case in the pharmaceutical sector.

[11] Thorburn et al p 68
[12] Wills PJ et al 1999 pp 143, 159
[13] Johnston, R et al Enabling the Virtuous Cycle – Identifying and Removing Barriers to Entrepreneurial Activity by Health and Medical Researchers in the Higher Education Sector 2000
[14] p 45

4) Impediments to business investment in R&D

a) Geography

It is unfortunately the case that Australia's distance from major markets and research centres can be a disincentive for international investors. Communications technology has lessened this to some degree, but a relationship to a more proximate research collaborator is still viewed as an advantage by many pharmaceutical researchers. Medical researchers in Australia have many competitors in similar research fields in the United States and elsewhere, and pharmaceutical companies may choose a closer or more familiar research group.

Pharmaceutical companies also tend to locate their major research centres near large markets, close to sizeable business centres and globally significant pools of research talent, such as Massachusetts and California. The highly significant research capacity of the Massachusetts Institute of Technology has recently attracted a number of pharmaceutical R&D operations including Pfizer, Wyeth, AstraZeneca, Abbott and Novartis. [15]

To overcome these disadvantages, Australia must work harder on other factors affecting investment decisions, including the business environment, cost, and quality of science and skills. It will also require building competitive advantage in certain fields.

b) Business environment

A global company will be influenced in its investment decisions by the perception of the overall business and political environment. A legislative environment which does not reward innovation will create a negative impression of investment conditions. The impact of attitudes by governments, media and the wider community toward a global company is frequently underestimated in terms of its impact on investment decisions. In the pharmaceutical industry in particular, a supportive government and scientific community will generate a favourable impression of Australia as an investment location. In addition, a rewarding local market will place Australia "on the map" and provide local operations with a strong case to advocate for increased investment from the parent company.

As has been stated, the low prices commanded for a product sold through the PBS does have a negative impact on the view of Australia as a business location for global pharmaceutical companies. Perceived inconsistencies and obstacles in listing products on the PBS can add to this impression. PIIP only goes part way to compensate for this situation. In addition, the industry does not always have adequate support from key opinion leaders, including members of the scientific community. Companies look for a supportive environment in which to invest, in which the dynamics of the industry are understood and its value fully acknowledged.

[15] Bio.IT World "Cambridge vs The World" 11 July 2002

c) Research costs and incentives

The cost to establish and maintain investment in Australia is generally low. In addition, clinical trials can still be conducted cost-effectively, although some expenses are rising. However, lower costs in Australia are sometimes not adequate to compensate for the problem of distance from major markets and research centres. In addition, many countries such as Singapore and Ireland offer well-documented incentives to attract investment by the pharmaceutical industry. These incentives generally exceed what Australian State and Federal governments are willing to offer. By way of example, the Government of Connecticut materially assisted Pfizer acquire the prime river-side real estate required to build its global R&D headquarters in that state.

In the case of R&D investment, companies which do not retain the IP in Australia receive no concession for R&D at all, despite the value which the R&D activity generates. Attached is a submission by Pfizer to the Senate Economics Legislation Committee which covers the issues of tax concessions in more detail (Appendix 2).

The PIIP scheme does provide very well targeted incentives to encourage the global pharmaceutical industry to invest in R&D in Australia. In the case of Pfizer, a $7 million investment by the Federal Government (subject to normal taxation) has directly resulted in a $34.9 million additional investment by the company in R&D between 1999-2004. This figure is over and above the investment already in place as a result of the Factor (f) scheme. If the objective of the Federal Government were to build a substantial pharmaceutical R&D presence in Australia, this program could be significantly expanded with exceptional results.

Pfizer notes that the value of the PIIP is currently being investigated by the Productivity Commission for report to the Federal Government.

d) Quality of Local Science

The extent to which global pharmaceutical companies invest in R&D in Australia, will to a large degree depend upon the quality of the medical research available in Australia. This country has a proven record of discovery in the medical sciences, some of which form the basis for currently marketed products.

Very few Australian companies are of a size that they can independently carry the cost and risk of developing and registering new pharmaceuticals or biopharmaceuticals. As a result, publicly funded research institutions play an even more important role here than they do in other countries. It is imperative therefore that the public continues to support the funding of R&D in academic and government institutions in order to create the knowledge that will underpin Australia's role in the creation of the next generation of therapeutics.

The increased funding to biomedical research under the Federal Government's *Backing Australia's Ability* plan is welcome and valuable. However many other countries have likewise increased their commitment to biomedical research. The United States has recently doubled its commitment to the National Institutes of Health (NIH) since 1998, taking the total to US$27.4 billion in 2003, a large proportion of

which is spend on basic biomedical research. The level of investment which the Federal Government can make into public biomedical research is ultimately limited and therefore should be carefully targeted.

e) Quality of the Scientific Workforce

Graduate and post-graduate study at university is essential for the development of skilled employees who can support the growth of a medical sciences industry in Australia. Many gifted students are deciding that the employment security and financial rewards available at the end of many years of studying the "hard sciences" does not warrant their commitment. Many of those who do complete the minimum 7 years of tertiary study to gain a PhD in science go overseas for their post-doctoral experience. There they have excellent employment opportunities with high rewards, particularly in the USA. While the skills, knowledge and experience gained by these ex-patriots is invaluable, the academic and commercial environment must be further developed in Australia to attract them to return to fertilize our local science based industries. The ARC's Federation Fellowships awards are an excellent start to this process, but as yet support relatively few.

One significant disadvantage of having a relatively small industry research base in pharmaceuticals and biotechnology is that Australian scientists generally have little experience in interacting with industry. The fluidity of relationships between the scientific community and industry has underpinned the dramatic growth of the biotechnology industry in the United States, as scientists have better understood the requirements of commercially viable research projects.

The growing Australian pharmaceutical and biotech industries need more staff skilled in preclinical studies, process development, scale up, manufacturing, clinical development and quality control, as well as global registration, marketing and sales. Collaborations with global pharmaceutical companies, irrespective of the exact nature of those collaborations, will assist Australian staff gain new insights and knowledge of commercial process and practices, which they can in turn utilize and modify to meet local needs.

5) Steps to demonstrate the value of greater R&D

The pharmaceutical and biotechnology industries rely very heavily on R&D to sustain their growth. In this sense, the value of greater R&D does not need to be promoted to companies within these industries.

The business value of greater R&D investments in Australia can best be demonstrated to the global pharmaceutical industry by offering targeted incentives and creating a climate in which pharmaceutical R&D by these companies is recognised, understood and rewarded.

6) Conclusion

If current trends continue, the world pharmaceutical market will reach US$680 billion by 2010, more than twice as large as the 1997 figure of $297 billion.[16] This means the pharmaceutical industry will in all likelihood be one of the fastest growing industries in the world. This growth will be fuelled by intensive R&D investment. One estimate is that between 1982 and 1998, R&D in the pharmaceutical industry as a percentage of sales grew from 10.9% to almost 17%.[17] This upward trend is likely to continue.

Australia will either be a participator in this R&D process or else it will become a passive recipient of pharmaceutical and biopharmaceutical technology. Considering the size of the industry and the extent of local and overseas demand for pharmaceutical products, it is difficult to see how the latter alternative will not damage Australia economically in the medium to long term. Whilst the pharmaceutical industry may undergo some rationalisation, there are still opportunities to participate in the global research chain. Australia can also take advantage of the growing number of collaborations by the global industry with smaller companies.

Attracting significant investment to Australia by R&D intensive industries such as pharmaceuticals requires a particularly strong commitment by the Federal and State Governments to building the economic, business and scientific environment required to overcome Australia's relative isolation from large markets and global talent pools. Further investment by governments must aim to build a critical mass of interaction between the global industry, scientific institutes and small-medium enterprises. Pfizer looks forward to policy outcomes in this direction from the Pharmaceutical Industry Action Agenda process.

[16] Burstall, ML and Reuben, BG Outlook for the World Pharmaceutical Industry to 2010, Decision Resources, December 1999 p.36
[17] ibid p.77

Appendix 1: Comments on the development and growth of Start-Up and SME biotechnology companies

Pfizer's experience in collaborating with research institutes and small biotech enterprises places it in a unique position to comment on the factors affecting the success of such organisations in generating or profiting from research. The following comments are intended to add value to this discussion.

The in-licensing of IP and the out-sourcing of many of the knowledge based processes by global pharmaceutical and biotechnology companies provide a significant opportunity for Australian companies to create wealth and contribute to the GDP. Relatively, the least expensive stage of the drug development cycle is during discovery, albeit that many leads need to be investigated to identify the few with commercial potential. Because of previous commitments to higher education in the sciences, this early phase of product development can be staffed and financially supported within Australia, provided appropriate incentives are provided to recognise the high attrition during this early phase of R&D.

It is generally in the interest of all parties that the inventor/s remain associated with the early stages of commercialization of IP, be they from academia or government institutions. To reward their continued commitment and to encourage entrepreneurship, the inventors and key staff are frequently offered or seek substantial equity in the start-up company, often in the form of share options. It is imperative that such equity be treated for tax purposes as notional and not subject to the tax laws until realised. As many start-up companies fail for a whole variety of reasons, options to purchase shares most often have a very notional value. Currently CSIRO employees are prohibited from taking equity in companies started up to exploit IP generated by them within CSIRO. There is a pressing need to change the employment terms and conditions to encourage and reward entrepreneurship within the organisation.

Appendix 2 - Attached