Bio-Pharmaceuticals – A Pathway to Economic Growth?

Part II and III: The New Zealand Environment

Report to the Researched Medicines Industry

June 2002

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Preface

The New Zealand Institute of Economic Research (NZIER), based in Wellington, was founded in 1958 as a non-profit making trust to provide economic research and consultancy services. Best known for its long-established *Quarterly Survey of Business Opinion* and forecasting publications, *Quarterly Predictions* and the annual *Industry Outlook* with five-yearly projections for 25 sectors, the Institute also undertakes a wide range of consultancy activities for government and private organisations. It obtains most of its income from research contracts obtained in a competitive market and trades on its reputation for delivering quality analysis in the right form, and at the right time, for its clients. Quality assurance is provided on the Institute's work :

- by the interaction of team members on individual projects;
- by exposure of the team's work to the critical review of a broader range of Institute staff members at internal seminars;
- by providing for peer review at various stages through a project by a senior staff member otherwise disinterested in the project;
- and sometimes by external peer reviewers at the request of a client, although this usually entails additional cost.

Authorship

This report has been prepared at NZIER by Chris Nixon and reviewed by Stephen Gale**.** The research assistance of Frances Gamble is gratefully acknowledged.

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1. INTRODUCTION

This report is the second and third parts of a three part project investigating the linkages between pharmaceutical companies, Government, and the bio-pharmaceutical industry.

To do this, we need to understand what drives the various actions of industry players. This means examining the marketing of pharmaceuticals, the determinants of R&D location, government budgetary pressures, and the relationship between pharmaceutical companies, researchers, and government funders.

The project is in three parts. Part one details the background conditions of the pharmaceutical industry world wide and examines the potential for the pharmaceutical R&D industry in New Zealand. Part two looks at the requirements for more investment by pharmaceutical companies in R&D in New Zealand and the components of those requirements. Part three briefly examines the clinical trials and fundamental research capabilities in New Zealand, the Factor f scheme in Australia (see Appendix A of this report), and the Canadian Patents Act.

1.1 A definitional problem

The bio-pharmaceutical industry involves the discovery of therapeutic agents for development and use in healthcare. Biotechnology processes and approaches are duplicated to treat human and animal diseases as well as drug design, drug delivery, and vaccine manufacture.

However, an economic definition of the bio-pharmaceutical industry is difficult to fully identify. It is not clear on what basis the sector should be statistically measured or whether it is in economic terms a "sector" or a "production process".[1] There are also varying opinions about who is actually conducting bio-pharmaceutical research. Furthermore, the difficulty in defining the industry and secrecy surrounding the financial information means that assessing the size of the industry requires a considerable amount of guess work. While we have described the New Zealand industry in Appendix A we have not attempted to quantify the size of that industry.

This report looks at the diverse groups of researchers, funders (private and government), regulators, and pharmaceutical companies that have an interest in medicines consumed by humans.

The pharmaceutical companies are central to this industry because they are the main researchers, funders, and interface with the New Zealand Government.

1.2 Why the pharmaceutical industry?

The attractions of knowledge based industries are:

- the potential to make more productive use of our generally well-educated workforce (with accordingly higher rates of pay); and
- their strong export potential (knowledge based goods typically facing low barriers in the consuming countries).

[1] A production process could be applied across a number of sectors where firms carry out a wide variety of different economic activities, while a sector implies a group of entities competing in similar markets.

The potential to create spillovers is also an important component of why we are interested in the pharmaceutical industry. In the popular media, the focus is usually fixed on the amount initially invested in any particular industry. However, spillover activity examines the amount of economic activity generated over and above the initial investment (see part 1, section 5 for a discussion of OECD attempts to measure the emergence of knowledge based industries).

1.3 Research methodology

The objective of gathering data and information has been to obtain reliable representative profile data. The process chosen has been to interview 20 participants in what we have loosely termed the bio-pharmaceutical industry and establish prevailing perceptions about the state of the bio-pharmaceutical industry and its future in New Zealand. The project scope has not allowed for normal statistical sampling. This has not been its purpose. The task has been to look for the recurring themes and determine whether opinion is sufficiently consistent across the people and groups spoken with.

We have approached a range of researchers in both the private sector and government organisations, biotechnology companies, and pharmaceutical companies. Feedback has been obtained using a combination of interviews and discussion groups.

The inevitable result of being involved in this project is that we have become now a potential channel of communication with the people and agencies that some groups are trying to influence.

While this is not unexpected, the possibility that the general method we used may have affected the information we received, remains. We note it as a possibility, but suggest its consideration fits alongside all the other theoretical problems with gathering real data. To us, a consciousness of these weaknesses should carry into the way the information is presented and used, rather than force rejection of the information, or any conclusions drawn from it.

Our job has been to test the economic logic of the arguments put forward by the various interested parties and comment on the strength of each argument.

One form of industry examination is cluster analysis (see Porter 1990 for example). While this approach has been criticised for being analytically flawed (Yetton et al, 1992), it has been a popular form of business analysis. According to the Growing an Innovative New Zealand report (2002) p18: "*There is ... insufficient evidence of clustering in the New Zealand economy*...". Therefore, while considered as a possible approach, cluster analysis was not used in this report.

2. ECONOMIC UNDERPINNINGS OF THE PHARMACEUTICAL INDUSTRY

A recurring characteristic of the bio-pharmaceutical industry is that most successful research and marketing arrangements are based on long term partnerships.

The importance of relationships allows us to build a picture of how the industry is organised through the lens of institutional economics. We are able to examine the business of bio-pharmaceuticals through a simple behavioural framework.

To illustrate how each actor in the market behaves, we have adapted a diagram used by Williamson (1985) p73 and introduced some of Kay's (1993) concepts to make it more relevant to the bio-pharmaceutical market.

Figure 1 is the result of this process. Williamson characterises buyer-seller relationships as dependent on:

- the frequency of purchase – some products are purchased repeatedly and some are occasional purchases, and
- the characteristics of the product: standard (e.g. can of cola), specialised (e.g. precision engineering equipment), or customised (e.g. constructing a plant or one-off specific piece of machinery).

In Figure 1 PHARMAC's focus has been on cost containment with strict budgetary constraints. By classifying pharmaceuticals into therapeutic groupings PHARMAC has attempted to describe pharmaceuticals as standard products. The clustering of pharmaceuticals around therapeutic groupings allows PHARMAC to compare pharmaceuticals on price and invariably PHARMAC subsidise the least cost option involved for each therapeutic grouping.[2]

Furthermore, PHARMAC can intervene in the market , at anytime, asking pharmaceutical companies to resubmit prices. Unpredictability of purchase of pharmaceuticals by PHARMAC means that the market can be characterised as a spot contract market.

On the other hand, pharmaceutical companies develop relationships with research teams over the long term. This is characterised in Figure 1 as a relationship contract. Typically, these relationships are built up over a five to twenty year timeframe with each party stating explicitly what it will do in return for research results and funding. This includes clearly defined milestones (e.g. delivery of outputs by researchers) and funding (in exchange for the research outputs). A large amount of time and resources are devoted by the pharmaceutical company to helping the research team produce a highly specific product.

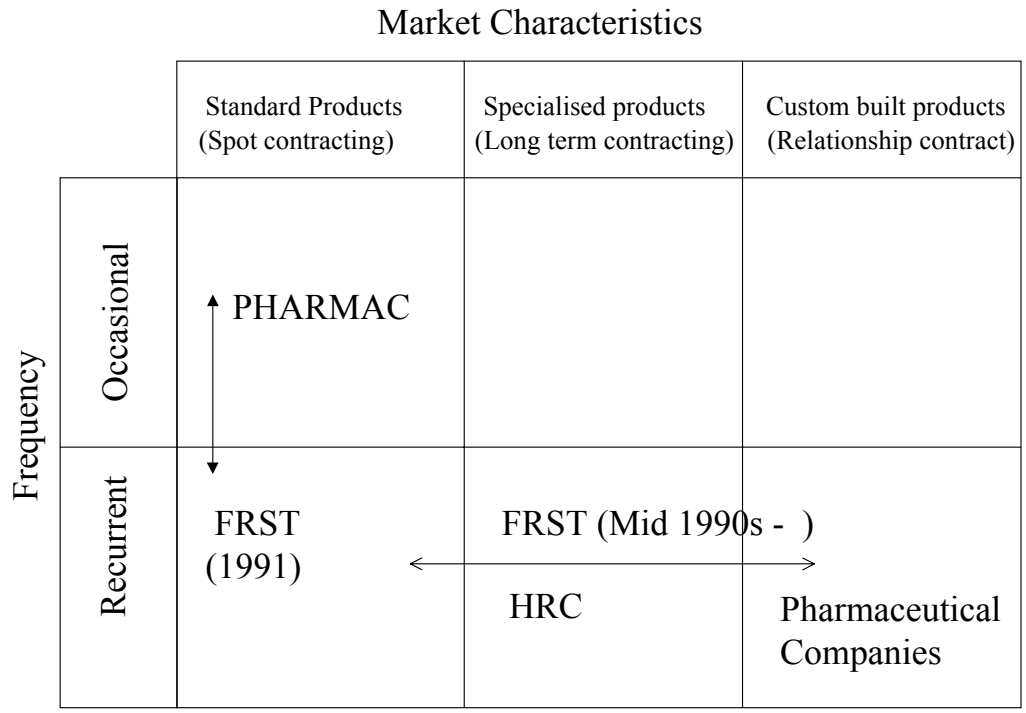
The Foundation for Research Science and Technology (FRST) replaced the DSIR funding model in 1991. In the beginning FRST staged an annual funding round, although it did signal to major funding beneficiaries the intent to fund further into the future. Other smaller providers were funded on an ad hoc basis.

Increasingly FRST (during the mid 1990s) and the Health Research Council (HRC) fund on a longer term basis. FRST have changed their funding to a multi-year basis while the HRC has yearly funding rounds but gives funding indications to successful

[2] Cross therapeutic group deals have also been common. This has also forced the price of pharmaceuticals down.

bidders for up to seven years. FRST have made a conscious effort to fund bigger long term projects.

Figure 1: Framework



Source:Adapted from Williamson (1985) and Kay (1993)

In the interviews, researchers also stressed that their successful relationships and networks had been built-up over many years, in some cases stretching back decades.

2.1 Long term relationships[3]

Bio-pharmaceutical companies have based their organisational cultures around long term relationship contracting. Developing effective long term relationships is not a simple exercise. As one researcher put it: "*there are no free lunches in this game*". Long term relationships are:

- expensive to maintain and build upon. Frequent communication is important, which requires constant effort and resources, particularly in the early stages of a partnership.
- characterised by a tendency of research managers to pick winners. This increases the risk (relative to annual competitive tender) of backing your established relationships over others in the market who may have better research techniques or science.
- characterised also by the tendency to exclude new entrants who have new technology or untried technology.

This has particular implications for government developing long term relationships. It highlights the difficulty government science organisations have when faced with the dilemma about what to fund and for how long.

[3] Through out the paper we will refer to Figure 1 to explain the behaviour and attitudes of various groups within the bio-pharmaceutical industry.

Contrast this with pharmaceutical companies who tend to favour long term funding of a particular scientist or team of scientists that is focused on a particular outcome.

2.2 International realities

Undoubtedly R&D and marketing arms of the pharmaceutical business are driven by different economic factors. However, for pharmaceutical companies there are incentives to link R&D activities with marketing. According to the BIE (1995) p11 pharmaceutical companies:

"... appear to trade bundles of local activity for government controlled benefits, including price. Such trades can have a considerable impact on a firm's bottom line, and may involve tens of millions of dollars even in a small country [such as Australia]".

More importantly for whatever reason, most OECD nations not only accept that R&D and pharmaceutical pricing are linked, they compete on this basis for the right to host R&D operations of pharmaceutical companies (see Industries Commission, 1996b pp 47-64).

It is significant that New Zealand has chosen to take a different path from the majority of OECD nations. Senior executives in pharmaceutical companies are well aware of developments in the New Zealand market and will ensure that what they consider a difficult environment does not spread to other countries with much bigger markets.[4] The pharmaceutical companies believe that New Zealand is a difficult market that does not pay its fair share of R&D costs and restricts trading opportunities.

[4] The attention and awareness of the "New Zealand situation" is well out of proportion to the size of the market.

3. NEW ZEALAND CONTEXT

3.1 PHARMAC

3.1.1 Focus on cost containment

There is a general acceptance by pharmaceutical companies that they were able to benefit from the New Zealand market prior to the setting up of PHARMAC in 1993. The steadily rising prices and increasing demand for pharmaceuticals, subsidised by government, through the 1980s alarmed the Treasury to such an extent that by the early 1990s the government decided to control the market more vigorously.

The policy outcome was to set up PHARMAC to regulate the price of pharmaceuticals in New Zealand. If cost containment of pharmaceuticals has been the major driver of the policy then policies adopted by PHARMAC have been an outstanding success. As one interviewee put it "*New Zealand has moved from a relatively high-priced market and low volume, to a low-priced and low volume market"*.

Focusing on price means that "success" can be easily judged by those monitoring pharmaceutical spending. This situation is reinforced by the yearly budgetary cycle and the silo approach to health spending.

The main instrument that PHARMAC uses to control costs is reference pricing. While reference pricing has been used widely in OECD countries, it is the way that it has been introduced into the New Zealand market that has caused comment both domestically and internationally.

Table 1 illustrates this point. Sweden, Denmark, and Norway apply reference pricing only to identical products. The Australian and British Columbian systems group related but different medicines, including patented pharmaceuticals. Germany, New Zealand, and The Netherlands have extended product coverage to all classes used to treat a specific condition. In 1996, Germany excluded patented medicines from reference pricing coverage.

Table 1: Classification of existing pricing schemes according to product coverage

Interchangeability level	Off-patent drugs	Patented and off-patented drugs
Chemical equivalence	Sweden, Denmark, & Norway	-
Chemical and pharmacological equivalence	-	British Columbia & Australia
Chemical, pharmacological, and therapeutic equivalence	Germany	New Zealand & The Netherlands

Notes (1) British Columbia is a small player in the Canadian R&D pharmaceutical market, therefore it does not have the same interest as Ontario & Quebec in developing long term relationships with pharmaceutical companies (see Table 12 in part 1 of the project). (2) the Australian reference pricing regime is limited to six areas.

Source: Guillem Lopez-Casanovas & Jaume Puig-Junoy (2001) p26

PHARMAC's use of therapeutic groups produces two impacts:

- the tension between pharmaceutical companies and PHARMAC when medicines are classified or reclassified to compete with lower priced older products, and
- the possibility that funding older medicines is more costly than funding newer more expensive medicines over the long run (see section 4).

PHARMAC, as the sole buyer of government subsidised pharmaceuticals controls the demand. PHARMAC's power in the market benefits New Zealand if they correctly judge the demand for pharmaceuticals. However, Horn (1998) has produced evidence that regulatory authorities may have misjudged the appropriate mix/use of interventions, specifically the use of pharmaceuticals and appropriate care, to meet demand in the US.[5] If this was happening in New Zealand, then it is possible that PHARMAC have limited the supply of pharmaceuticals to sub-optimal levels.

3.1.2 Standardised products and spot contracting

The economic impact of PHARMAC's pricing policy is to reduce the marketing of pharmaceuticals into the spot market (see Figure 1). How PHARMAC operates in the market will depend on the type of deals struck with pharmaceutical companies. PHARMAC expect pharmaceutical companies to approach them with suggested contract proposals.[6] Depending on the therapeutic group area, competition, and demand, the elements of a PHARMAC contract[7] could include:

- price/volume deals over a 3-5 year timeframe.
- cross therapeutic group deals (bundled deals).
- deals that exclude reference pricing.
- regular tendering rounds.

Outside these contractual arrangements PHARMAC can over a matter of months:

- alter arrangements within a sub-group, and introduce new medicines.
- decide to opt out of funding a particular sub-group.
- not fund new medicines.

PHARMAC's policies introduce a level of unpredictability into the market particularly when companies are asked to, at any time, resubmit pricing proposals to compete with generics.[8]

From time-to-time, companies will re-evaluate their position in the market. This could result in:

- reduced profitability. In the long run, you would expect some of the companies to leave. Fewer companies in the market could increase the market power of the remaining companies and restrict the entrance of new products further.[9]

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[5] Government purchasing agencies by constraining supply to older less expensive medicines has not resulted in either improved patient outcomes or lowered overall total healthcare costs.

[6] Internally at PHARMAC this is called "smart contracting". Communication with Mathew Brougham, PHARMAC.

[7] For more detail see PHARMAC Business Plan 2000-01 and PHARMAC's Annual Review year ending 30 June 2001 available at www.pharmac.co.nz.

[8] In New Zealand patented products compete with generics in the same therapeutic groups. Pharmaceutical companies will maintain a price on a patent product over and above the new reference prices to keep in step with its international marketing plans.

- reduced R&D to even lower levels than currently. As companies pull-out of the market their interest in doing clinical trials wanes. Also the interest in doing fundamental research will depend on the extraordinary efforts of outstanding scientists within New Zealand i.e. only research vital for companies will be done in New Zealand.[10]
- reduce the presence of major pharmaceutical companies in New Zealand with consequent reduced chances of networking between companies and scientists.

3.2 The pharmaceutical companies

Pharmaceutical companies have a long history of involvement in the New Zealand market. It is well known that Glaxo (now Glaxo Smith Kline) started in New Zealand in the late 19th Century. Most of the major pharmaceutical companies have also been in New Zealand for at least twenty years and some trace their origins in the market back to the 1960s.

Naturally, each pharmaceutical company has different attitudes and different strategies at play in the New Zealand market. In general their R&D business fits into the long-term relationships box in Figure 1 (i.e. between pharmaceutical companies and researchers). It has been the successful application of cost containment policies by PHARMAC that have pushed the marketing of pharmaceuticals towards short-term spot contracting, which has caused continuing conflict (see Figure 1).[11]

Below we examine some of the thinking and attitudes that lie behind pharmaceutical company behaviour in the New Zealand market with reference to marketing and R&D, the Government's regulatory stance, and New Zealand based research.

3.2.1 Marketing and R&D

In the minds of pharmaceutical companies, marketing and R&D are linked and will remain so. This position is strengthened by the tacit acceptance by OECD nations that compete amongst themselves for pharmaceutical companies to locate research facilities in their country by reaching agreements on the price of pharmaceuticals.

In the corporate offices of pharmaceutical companies around the world New Zealand is viewed as a difficult market. This attitude/view/perception is reinforced by periodic trips to New Zealand by senior executives of pharmaceutical companies.

Unlike the oil or banking businesses, the importance of long-term relationships in the pharmaceutical business means that sometimes decisions are made for emotional rather than rational reasons.[12] The result of the hostility towards New Zealand has two negative impacts:

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[9] PHARMAC are also worried about this problem when they say: *"the initiatives outlined to manage DHB's expenditure on pharmaceuticals used in hospitals, in conjunction with those policies already in existence in the primary care setting, could impact on the range of pharmaceuticals suppliers in the New Zealand market." (Draft Strategy for Nationwide Purchasing of Hospital Pharmaceuticals 2001 p28).*

[10] PHARMAC also believe that their actions in taking over hospital purchasing could: "*potentially become a factor in the amount of research into pharmaceuticals being conducted in New Zealand*". *(Draft Strategy for Nationwide Purchasing of Hospital Pharmaceuticals 2001 p28)*

[11] Pharmaceutical companies believe that this also drives continued disinvestment in the sector.

[12] Pharmaceutical companies have in the past reduced their presence or withdrawn from the market because of the stance taken by the New Zealand Government on the marketing of pharmaceuticals, even though opportunities for profitable economic activity exist.

- pressure mounts on the local office of the pharmaceutical company to reduce the economic activity already carried out in New Zealand – in this situation, clinical research is the easiest area to cut, and is usually first to be reduced or discontinued.
- unless it is absolutely necessary, no new investments are allocated to New Zealand.

These pressures manifest themselves in different ways in the pharmaceutical companies. The outcomes include:

- limits on the volume of both clinical trials and new fundamental research in New Zealand.
- support for clinical trials in New Zealand only if they support overseas clinical trials.
- supporting clinical trials in New Zealand only if the pharmaceutical company can sell the medicines being researched in New Zealand.
- keeping the same number of clinical trials/new ideas irrespective of PHARMAC and hoping that changes will be made over the long run.
- reviewing their involvement in the New Zealand market ranging from significant retrenchment to total withdrawal.

3.2.2 New Zealand research

The overriding concern of the interviewees is that allowing the existing Government stance towards the marketing of pharmaceuticals negates opportunities for lifting the level of R&D. If the Government stance continued, they said, then the bio-pharmaceutical industry would bump along in an ad hoc fashion with little or no prospect of sustained proactive long-term support from the pharmaceutical companies. While pharmaceutical companies concede that some scientists will attract substantial funding from pharmaceutical companies their funding would be for them only and their operations would be isolated developments that would not lead to the generation of significant clusters of scientific activity within New Zealand that would benefit the economy.

New Zealand is an ideal place to conduct R&D.[13] It has the infrastructure, communications, well-educated researchers, and a well-educated population. These are all features that pharmaceutical companies look for when setting up research facilities.

The pharmaceutical companies we interviewed noted that New Zealand researchers have an abundance of good ideas and novel ways of approaching research questions. However, it is one thing to have a good idea or find a promising molecule; it is totally another to advance those ideas into a marketable product.[14] Specifically the problems are:

- making the right contacts with pharmaceutical companies.
- advancing a promising molecule past the proof of concept phase.
- understanding that forging relationships with potential customers (i.e. the pharmaceutical companies) happens at all stages of the development process. There

[13] Pharmaceutical companies also believe there is no reason why manufacturing should not take place in New Zealand as well. Unlike other products, pharmaceuticals are easily transportable and face relatively few barriers to entry in world markets.

[14] For a more in depth understanding of what pharmaceutical companies require, see Fahey (2002).

was a tendency for researchers to believe that marketing or personal networking was not important or was some vague thing that happened latter.

- there is a perception that New Zealand researchers wanted to do everything themselves rather than look for other institutions that could do parts of the process better than they could do it.[15] A seeming lack of understanding about the role of partnership building. Whole departments in pharmaceutical companies overseas are devoted to seeking out and finding ways of leveraging research and building partnerships.

Pharmaceutical companies are well aware that there are some extremely good researchers in New Zealand that have succeeded in overcoming these problems. One way of raising awareness would be to develop a mentoring scheme where, with funding, these scientists who have succeeded, are able to impart some of their knowledge to other scientists. Also, raising the level of awareness of what is required, whether it be operationalising the research or the details of how to commercialise research, are underestimated and under-funded components of building a knowledge based economy.

3.3 The researchers

In most cases, the businesses have been created independently of the Government stance towards the marketing of pharmaceuticals. They have been built-up with at least twenty years of networking, hard work, outstanding science, and some luck.[16] Successful researchers can not stress enough that building long term relationships are key to the businesses they form. There are no short cuts: "*you have to get out there and do it*".

3.3.1 Sources of funding

Private sector funding is usually on a longer term basis than funding from government sources, although funding from the HRC and FRST is moving towards longer term relationships.

In general there are three sources of funds for researchers:

- pharmaceutical companies are the main source of funds and a new development is the increased funding role of mid-sized biotechnology companies that have formed over the last ten years.
- the agricultural industries in New Zealand have also funded developments particularly where it relates to large animal research (deer, sheep, dairy cows). forage, and forestry. To some extent, this type of research has allowed New Zealand researchers to be involved in areas where New Zealand had some natural advantages over the rest of the world i.e. unique flora and fauna and cheap research material.[17]
- government have also underpinned most research. In fact, most New Zealand researchers have either got there start with state funding or have received on-going

[15] Ironically, those that achieve successful partnerships and leveraging relationships are often criticised for "giving away the intellectual property".

[16] Researchers noted that establishing the relationships was the hardest part of the process. Maintaining the relationships was much easier. The technology such as video conferencing and email had, to some extent, circumvented distance issues.

[17] It costs less, per head, to keep animals such as sheep and goats in New Zealand than it does to keep lab rats in the United States for research purposes.

funding from government through universities, hospitals, FRST, HRC, and other funds.

Commercialisation arrangements come in a variety of shapes and forms. Milestone payments (from pharmaceutical companies), joint venture partnerships, private investors in the stockmarket, individual entrepreneurs, and local investment are the main sources.

3.3.2 The current marketing regulatory regime

Opinions are divided about the need to change the regulatory regime for the marketing of pharmaceuticals in New Zealand. The majority view is that while the research that they manage has been built up independently of the marketing of pharmaceuticals in New Zealand, the attitude of pharmaceutical companies is important in the further development of R&D, particularly if growth of the sector is an objective. For example, if a pharmaceutical company located R&D facilities in New Zealand, students would view it as an ideal career path. As students demanded specific qualifications, the universities would respond by developing courses to fill that need. An increased pool of graduates would allow domestic bio-pharmaceutical companies to buy the necessary labour skills it needed.

The small base of the New Zealand economy means that the proportionate impact of a pharmaceutical company locating in New Zealand would be larger, relative to Australia or Singapore. In the opinion of some researchers, it would not take much for the pharmaceutical industry to become a significant player in the biotechnology sector (see McNabb, 2001).

A minority view of those interviewed suggested that the attitude of pharmaceutical companies towards the purchasing regime in New Zealand made no difference to their research activities. Pharmaceutical companies would respond to good science and fund accordingly.

3.3.3 Other factors

Despite government assertions that knowledge based economic activity is important to New Zealand's economic future, researchers do feel obstacles have been put in their way.

a) Role of government

While scarcity of money is always a problem for researchers, some felt that there was a need for government to re-examine its spending priorities. They noted that this meant making hard decisions about budget allocations. The Irish example was quoted a number of times, where money was taken away from other spending areas (e.g. pensions) and redirected towards science-based activities (interviews and The Boston Consulting Group, 2002).

In the current funding regime researchers concentrated on the efficiency of the spending being made. Researchers believe that more effort needs to be made on:

- developing long term relationships between the researchers and those funding research. Rather than developing strategies for funding independently from researchers, they believe that better outcomes will eventuate if they are able to have more of an input into the design of the research questions.
- developing long term objectives of research and research priorities. Rather than examining topical research issues, the research should be concentrated on fundamental science (so long as the research objective is clear).

- understanding the amount of resources required to produce a product, patent, or promising molecule.

We have not studied Government-funded research in detail, however, it seems logical to follow the lead of pharmaceutical companies and the way they fund research. The pharmaceutical companies fund research teams rather than promising science. This will require:

- more long term funding (FRST and HRC are moving in this direction).
- more understanding of the science being funded by government agencies responsible (The HRC funding is focused on areas of international research excellence).
- timeframes for partnering outside funders such as pharmaceutical companies i.e. actively encourage joint ventures and partnerships by making research funds contingent on them (FRST and the HRC have initiated some partnership funding).
- more funding directed at developing the commericalisation of research. (FRST are starting to encourage a more commercially orientated funding regime).

One controversial suggestion made by one researcher was to follow the road of the US administration and develop the equivalent of the Bayh-Dole Act of 1984. This legislation allowed academic researchers to take publicly funded research and commercialise it more easily. In a major report for the European Union Gambardella et al (2000) p71 suggested that the US experience offers a:

"*… more flexible environment whereby academic researchers can more easily move into …development … companies [this approach] is more conducive to the raising of new research-based firms and to the corresponding technology-based industry*".

The Bayh-Dole Act:

- incentivitised researchers in universities to improve their networking and marketing of R&D, and
- linked basic research conducted in publicly funded institutions with commercial outcomes.

This approach has its critics, as Gambardella et al (2000) p72 point out:

"*this system can seriously undermine the norms and rules of open science. … the scientific community – unlike profit seeking technologists that operate in firms – diffuse their discoveries through publications and the like. The system of open science has for many years been an important determinant of the diffusion of knowledge in industry, and therefore ultimately industrial growth*".

b) Attitudes towards science

The increased mistrust of science and scientists has followed overseas trends. On the one hand, government are involved in promoting knowledge intensive industries through events like the Knowledge Wave Conference. On the other, biotechnology is poorly understood and politically very sensitive.

Although firmly in the knowledge economy business, some companies will go to great lengths to keep a low profile e.g. one company was asked if they wanted the Minister of the Crown to open a new facility, they responded negatively because they did not want protesters to picket the site. This was despite the fact that no controversial science was being carried out at the facility.

New ways will have to be found to explain complex issues to the general public. It was with some relief that researchers noted that the success of the Royal Commission on Genetic Modification in explaining what was actually happening in biotechnology research.

c) HSNO Act

All researchers were concerned about the ramifications of the HSNO Act and how it will impact on their activities in the long run. The cost of compliance has risen dramatically and it remains to be seen whether the costs of the HSNO process will outweigh the benefits of having these regulations.

3.4 Adequate patent legislation

Strengthening patent laws and addressing other IP issues send a strong message to the industry that they are welcome and are an integral part of developing the sector. Patents are critical in providing companies with incentives to invest in R&D (see part 1 section 2.2.1).

The rationale for introducing patent extensions is to compensate for the time lost in the approval process as the pharmaceutical was tested (see part 1 section 3.2.4). Patents are important because they allow companies to recoup substantial R&D costs associated with bringing pharmaceuticals to market.

There is a debate in the economics literature about whether or not patent extension actually increases economic activity (see for example Sakakibara & Branstetter, 2001). It is not our intention here to prove or disprove the effectiveness of a patent extension. Again, most of the countries that New Zealand seeks to emulate in R&D performance have already approved patent extension legislation (e.g. US, Canada, European Union, and Australia).

By extending patents New Zealand is put on the same footing as other countries. It says to pharmaceutical companies that we want to be part of the global R&D pharmaceutical market, New Zealand welcomes pharmaceutical research, and we have the prerequisites to be taken seriously. Furthermore, it gives R&D investors, both domestic and foreign, more confidence to invest in an inherently risky business (see part 1, section 2) that has the potential for large rewards.

4. CONCLUSIONS

We have abstracted from the real world to capture the essential elements of the choices that face Government. It has not been our intention to deal with the full detailed reality of the bio-pharmaceutical industry, and the report deals with the salient issues only.

Below we have listed the main issues that Government need to consider. The components are:

- building up the knowledge based economy.
- the matching of pharmaceuticals to people to minimise the long term costs of managed care, and
- the introduction of legislation to extend patent life.

4.1 The knowledge economy

In most OECD nations, in situations similar to New Zealand, an agreement between pharmaceutical companies and government over R&D investment and pharmaceutical pricing has occurred. The Australian Factor f scheme and the Canadian Patent Act (see Appendix AA.3 and AA.4) are examples of such programmes.

The evidence suggests that schemes such as Factor f do increase the amount of R&D activity. The Factor f scheme gave direct payments of up to 25% of an aggregate increase in value added for participating companies (see Appendix A A.3 for further detail). The Bureau of Industry Economics (BIE) (1995) estimated that 85% of new activity was generated by the scheme. The BIE are less sure whether the original investments have generated other economic activity (i.e. cluster development), although they do say that to breakeven, the level of "spillover" activity would not need to be very high.

The Centre for Strategic Economic Studies (CSES) (1999) also point to a number of studies that suggest high spillovers of phamaceutical research into the economy (see Appendix A A.3.). On spillover activity the CSES (1999) p40 believe that:

- *"the economy wide social rates of return to R&D are very high … implying very substantial spillovers from other activity.*
- *there is evidence of substantial spillovers from international studies in the case of pharmaceutical R&D, implying social rates of return well above private rates of return, and*
- *it is likely that the spillovers from R&D, and hence the social rates of return to R&D, in the pharmaceutical industry are at least as high as, those to R&D in the economy as a whole."*

It is inevitable that governments will endeavour to encourage industrial development. The bio-pharmaceutical industry has substantial export potential. The agreements reached by the government and pharmaceutical companies, particularly in Australia and Canada, have delivered measurable results. Furthermore, the schemes in modified forms have continued for over 10 years.

4.2 Matching

There is growing evidence overseas that matching the right pharmaceuticals to the appropriate patients as part of programme to manage patients care may both improve patient outcomes and save the overall health budget over the long run (Horn et al, 1998). Horn (2002) suggests that these cost savings could be as much as 30% to 50%. This may be the main motivation for subsidising pharmaceuticals to a greater degree. Recognising the importance of evidence in this process, and as an exploratory pilot project, the RMI has engaged PricewaterhouseCoopers to gather the available statistics and attempt to understand dynamics of the managed care process around selected disease areas.

4.3 Modifying the regulatory framework

By ensuring that the regulatory framework fosters the development of the bio-pharmaceutical industry, the pharmaceutical companies believe that the will be given every chance to grow. Two issues are important:

- protection of IP, for example, not allowing patented products to compete with generics in the same therapeutic group (see section 3.1.1), and
- patent extension (see section 3.4).

As part of an overall package, further modification of the current regulatory framework has the potential to foster growth in R&D industries. It also sends a signal to pharmaceutical companies to say that New Zealand is serious about attracting their business.

4.4 Government funding

Government-funded researchers would like to see a continuation of the trend in long term contracting by government funding agencies and a significant boost in funding. Furthermore a closer relationship between those who fund and those doing the research could improve the efficiency of the research effort. One way to improve the incentives of researchers may also be to investigate further the impact of the Bayh-Dole Act in the US.

5. BIBLIOGRAPHY

The Australian National Audit Office (ANAO) (1993), *Pharmaceutical Industry Development Program – the Factor f Scheme*, Project Audit: Department of Industry, Technology and Regional Development, Audit Report No. 26. 1992-93, AGPS, Canberra.

Bureau of Industry Economics (BIE) (1991), The Pharmaceutical Industry: Impediments and Opportunities. Program Evaluation Report 11 AGPS Canberra.

----------(1995) The Factor f scheme, Canberra

Brain P (1993), The Factor f Scheme. *National Economic Review, No 27* December pp1-11.

Centre for Strategic Economic Studies (CSES) (1999), Pharmaceuticals in Australia: Equity, Cost Containment and industry development. Victoria University Melbourne.

Coase RH (1937) The nature of the firm. *Economica*, 4 386-405.

Cockburn I & Henderson R (1997), Public-Private Interaction and Productivity of Pharmaceutical Research, *NBER Working Paper No. 6018*, National Bureau of Economic Research, Cambridge Mass.

Fahey K (2002) Collaborating with Multinational Pharmaceutical Companies. *Biomedical Show Case 19th & 20th March*, Auckland.

Gambardella A, Orsenigo L, & Pammolli F (2000), Global competitiveness in pharmaceuticals: A European perspective. *Report prepared for the Enterprise Directorate-General of the European Commission*. November 2000.

Horn S, Phoebe, Sharkey, Phillips-Harris (1998), Formulary Limitations and the Elderly: Results from the Managed Care Outcomes Project. *Am J Mgd Care Vol 4 No 8.*

Horn S (2002), *Ministry of Health Seminar*. Ministry of Health 2002.

Hosseini M, Nagels K, Furth J & Muller M (2001) Driving bio deals. *Scrip Magazine* pp 22-23, December 2001.

Industry Commission (1995), Research and Development AGPS Canberra

---------- *(1996a)*, The pharmaceutical industry: Volume 1. Report No.1, 3rd May 1996.

---------- *(1996b)*, The pharmaceutical industry: Volume 2. Report No.1, 3rd May 1996.

Kay J (1993), *Foundations of Corporate Success*. Oxford University Press.

McNabb D (2001), Sowing the seeds for a new industry. *NZ Business*, September 2001.

Odagiri H and Murakami N (1992), Private and Quasi-Social Rates of Return on Pharmaceutical R&D in Japan. *Research Policy*. Vol 21 p335-45.

PHARMAC (2001) Draft Strategy for Nationwide Purchasing of Hospital Pharmaceuticals. November 2001.

Porter ME (1990), *The Competitive Advantage of Nations*. MacMillan Press.

Sakakibara M & Branstetter L (2001), Do stronger patents induce more innovation? Evidence from the 1988 Japanese law reforms. *Rand Journal of Economics*. Vol 32, No 1 Spring 2001 pp 77-100.

Simon H (1959) Theories of Decision Making in Economics and Behavioural Sciences. *American Economic Review*, 49 pp253-83.

The Boston Consulting Group (2002), Building the Future: Using Foreign Direct Investment to Help Fuel New Zealand's Economic Prosperity. Report to Government.

Williamson OE (1985), *The Economics Institutions of Capitalism.* The Free Press, London.

Vandergrift M & Kanavos P (1997) Health Policy Versus Industrial Policy in the Pharmaceutical Sector: the Case of Canada. *Health Policy*, 41 Suppl.: pp241-260.

Yetton P, Craig J, Davis J and Hilmer F (1992), "Are diamonds a country's best friend?: A critique of Porter's theory of national competition as applied to Canada, New Zealand and Australia". *Australian Journal of Management*, Vol 17, No 1. The University of New South Wales.

APPENDIX A: PART THREE: CASE STUDIES

Part three examines the types of bio-pharmaceutical activity going on in New Zealand, and where possible, quantifies the impact of the research. It also briefly examines the Factor f scheme in Australia and the Canadian Patents Act.

A.1 Clinical trials[18]

A.1.1 What are they?

Pharmaceutical company expenditure on R&D is focused on clinical trials. The main functions of clinical trials are:

- testing the efficacy, scientific validity, and optimal dose relative to a placebo-controlled population on small groups of healthy volunteers in phase I and II (between 20 and 80 people). In phase III studies are expanded to accommodate controlled and uncontrolled trials. These trials are monitored by the authorities and are conducted by independent outside experts. The groups in these trials number between 200 and 3,000.
- gearing the product up for launch, ensuring that there are no harmful side effects in all sections of society (e.g. pregnant women, children, and the elderly).
- conducting post approval trials to highlight the efficacy of the product and support the marketing of the product.

As government regulatory agencies have demanded tighter and tighter standards, the costs of getting approval for pharmaceutical products has increased dramatically (see part 1).

A.1.2 Clinical trials in New Zealand

Pharmaceutical companies attached to the Researched Medicines Industry (RMI) spend approximately $NZ18 million in New Zealand on clinical trials. There are roughly 130 studies being conducted all over the country employing nearly 800 people on a full or part time basis.

Trials are usually conducted by investigators who are able to provide the necessary independence, reputation, integrity, and confidence (of both the pharmaceutical company and international regulatory bodies, including the New Zealand Government) that the results of the research will accurately reflect the impact of the new product on the studied population.[19]

A.1.3 Advantages of locating trials in New Zealand

Pharmaceutical companies note that New Zealand is a natural place for them to want to do clinical trials. The advantages include:

- the calibre of investigators conducting clinical trials is of the highest order and this is recognised internationally by pharmaceutical companies.

[18] See Appendix C, part one, for more detail on clinical trials.

[19] This is another example where the pharmaceutical companies back the researcher rather than the process.

- the results of research and the integrity of researchers and data are rated highly. There is a high degree of trust built up over many years of networking and published results.
- New Zealand researchers deliver on time and on budget.
- researchers are proficient in the language of international pharmaceutical companies i.e. English.
- the research facilities, although in some cases ageing, are of a good standard.
- communications are relatively cheap and effective particularly in the main centres.
- New Zealand is a cost effective place to do trials. Pharmaceutical companies point out the researchers here are well aware of what their counterparts in Australia are charging and try to price themselves accordingly. Nevertheless, there is also a suspicion that researchers are using money from trials to cross subsidise other projects.

A.1.4 Disadvantages of locating in New Zealand

Each company has different strategies at work in the New Zealand market and different attitudes to carrying on research. According to all companies, the role of the New Zealand Government dominates their attitude to the New Zealand market. This means that the amount of clinical trial work is much less than it could be.[20] Their approach to clinical trials falls into three groups:

- Those companies that will continue to do trials in New Zealand regardless of the New Zealand Government stance on the purchasing of pharmaceuticals.
- pharmaceutical companies will not trial medicines in New Zealand that can not be marketed in New Zealand, unless it supports its international operations. This leads to a lower level of clinical trial work and support for R&D than otherwise would have been the case.
- reviewing their involvement in the New Zealand market ranging from significant retrenchment to total withdrawal.

A.1.5 Summary

According to the pharmaceutical companies New Zealand is potentially a very good place to do clinical research. The Government's regulatory environment, they believe, restricts the amount of clinical research.

[20] A number of companies estimate that the capacity exists in the short term to increase clinical trials by four fold.

A.2 Bio-pharmaceutical companies

There are a wide range of bio-pharmaceutical companies operating in New Zealand doing a variety of different activities. According to Hosseini M et al (2001) these companies can be divided into three groups:

- companies that concentrate on providing technology platforms (Tecpros). Tecpros specialise in sub-segments, such as databases and database analysis, technologies that identify gene sequencing, application and production of biochips, and the development of automated systems to improve laboratory efficiency. These companies support the compound development but do not develop the compounds themselves.
- companies that are involved with the development of compounds (Devcos). These Devcos specialise in the downstream pharmaceutical R&D pathway. Typically they take potential pharmaceuticals to the stage I or II level. Devcos specialise in potentially any of the processes along the gene-to-pharmaceutical pathway. Partnerships with pharmaceutical companies are common with these companies.
- the various hybrids in between, which to varying degrees are both technology platform and development companies.

A.2.1 Bio-pharmaceutical activity in New Zealand

The development of the bio-pharmaceutical industry in New Zealand has been based around universities (and their spinoff companies), Crown Research Institutes, and researchers who have worked overseas developing networks and come back to New Zealand.

Typically the biotechnology developments have been greenfield operations and have succeeded through a combination of hard work, luck, personal networks, entrepreneurial ability, and latent leadership skills – or a combination of all or some of those skills. The most important identified attribute was the development of networks overseas. Also the original development of the technology was almost always funded by the New Zealand government.

To date money to fund operations has come from pharmaceutical companies, the mid sized biotechnology companies, agricultural and forestry sector funding within New Zealand, and government.

Secrecy agreements attached to partnership arrangements, the diversity of the technologies being used (which span across different sectors), and companies being unwillingly to reveal sensitive information about their businesses makes it difficult to value the industry and its contribution to the economy. What we do know is that it has grown quickly from very small beginnings.

All research and company development has grown up independently of the pharmaceutical marketing in New Zealand. Furthermore, their current money does not depend upon the New Zealand Government's stance towards the marketing of pharmaceuticals.

However, researchers point to the ad hoc nature of the development of the biotechnology industry, pointing out that there are no "clusters" associated with biotechnology in New Zealand. Their networks are orientated towards overseas suppliers/customers/partners.

Most, but not all, researchers and particularly those in the private sector believe that this is where pharmaceutical companies are crucial to the development of the biotechnology industry. The bio-pharmaceutical industry in New Zealand requires critical mass if it is going to contribute significantly to the knowledge economy. Pharmaceutical companies are the only real source of funds that are capable of significantly contributing to, and achieving critical mass in the bio-pharmaceutical sector.

A.2.2 Advantages of locating in New Zealand

Why locate in New Zealand? The majority of bio-pharmaceutical companies are located in New Zealand for reasons other than economic, with lifestyle being the main factor. Although, researchers note that for the industry to grow strongly, reasons other than lifestyle factors will have to become important.

Biotechnology companies point to a number of advantages:

- the strong agricultural base of New Zealand and the scientific knowledge that researchers have already developed, gives researchers in New Zealand advantages that competing researchers do not have.
- New Zealand's isolation from the rest of the world has produced some unique flora and fauna.
- low cost, good infrastructure, highly trained people etc. (all the things mentioned under clinical trials).

A.2.3 Disadvantages of locating in New Zealand

The attitude of the pharmaceutical companies towards the New Zealand market makes it more difficult for researchers, particular if they can access the research in other countries where long term agreements are put in place, trading off pharmaceutical price increases for increased R&D investment.

Furthermore, most of the developments that have occurred in the bio-pharmaceutical industry have been isolated operations with little or no commercial contact with other New Zealand based bio-pharmaceutical groups. Unless a pharmaceutical company has a major R&D presence in New Zealand then cluster formation will not occur.

The isolated nature of the operations means that there are no ancillary services that feed off the growth of a vibrant bio-pharmaceutical industry e.g. patent attorneys, suppliers of specialised equipment and workers etc.

Establishing contacts with new clients/customers/partners is also difficult. New Zealand based companies have to spend large amounts of time on the road travelling in the US and Europe. However, once contacts are established communications systems have advanced to such an extent that maintaining contacts has become much easier.

A.2.4 Summary

The bio-pharmaceutical industry is very difficult to define, let alone quantify. In New Zealand we have some major projects going on with pharmaceutical companies, however they are isolated activities, happening independently of any other bio-pharmaceutical activity in New Zealand.

The stance taken by pharmaceutical companies means that bio-pharmaceutical research will continue to occur, however it will never be a significant industry in New Zealand.

A.3 Australian situation: Factor f

A.3.1 Motivation for Factor f.

In the 1980's the Australian pharmaceutical industry was perceived to be under threat. The Bureau of Industry Economics (BIE) and the Department of Industry, Science, and Tourism (DIST) noted that Eli Lilly closed its manufacturing facilities, Ciba-Geigy and Upjohn ceased local production, Roche and Riker closed their R&D facilities, and Merck, Sharp, & Dohme and Parke Davis had shifted to varying degrees from domestic manufacturing to imports, Industry Commission (1996a) p95.

According to the industry the reasons for the disinvestment included:

- low prices under Pharmaceutical Benefits Scheme (PBS).
- idiosyncratic and a slow regulatory system.
- the patent system used at the time.

A.3.2 Factor f plan [21]

While the various participants differ in their understanding of why the Factor f scheme was introduced the Industry Commission (1996a) p101 believed that the rationale was to:

> *"promote the development of the sector by partially compensating for low PBS prices in order to regain competitive activity argued to have been lost to Australia as a result of the structural impediment represented by these prices".*

The Factor f plan provided payments by way of agreed prices for pharmaceutical companies that joined the plan. The payments were performance related linking increases in value added on exports, domestic sales, and R&D expenditure by participating companies. Given established participation requirements[22], companies received payments of:

- up to 25% on of the aggregate increase in value added on the company's exports out of Australia. The Pharmaceutical Benefits Pricing Authority (PBPA) had discretion to alter payment rates.
- up to 25% on domestic sales of the aggregate increase in value added on either new products or existing products where existing products were creating additional value added.
- up to 25% on of the aggregate increase in value added on the company's increased R&D. This depended on whether they were already claiming the 150% per cent tax concession for R&D. If companies were claiming the tax concession the rate was kept at 25%, if they were not then they were entitled to claim 50% of the increase relative to the base year.

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[21] The scheme is known as Factor f because it is the sixth in the list of recommendations that the PBPA is required to take into consideration when suggesting prices.

[22] For the first phase of the Factor f programme companies had to meet the following criteria: (1) achieve a ratio of exports to imports of one half within 3 years of the PBPA's offer of price increases, (2) increase exports by 33% in real terms within 3 years of the PBPA's offer of price increases, (3) spend a minimum of 3% of turnover on R&D, and (4) increase spending on R&D by 33% in real terms within 3 years of accepting the PBPA's price increases. The R&D criterion could be waived if a company established a significant plant for the export of active ingredients.

The scheme has been running since 1988 and has gone through a number of changes. In 1992, the Australian Government announced an expansion of the Factor f scheme into Phase II. The main difference between Phase I and Phase II was the increased focus on stricter pricing rules. Specifically these changes were:

- the price increases were capped by the average price of the product in the EU, rather than world prices in Phase I, and
- in Phase I a 10% limit on price increases was imposed. This price cap was removed in Phase II.

In 1999 the Pharmaceutical Industry Investment Programme (PIIP) followed on from the Factor f programme. Table 2 shows some of the main characteristics of the Factor f programmes and the PIIP. The total cost to the government over the period between 1991-92 and 1997-98 was $A550.9 million (or an average of $A88 million per annum).

The PIIP is smaller than Phases II of the Factor f programme and the funding allocated between companies is being done on a competitive basis.

Table 2: The Factor f programme

	Years	No. of companies participating	Main features of the payment system	Total dollars allocated $M over the life of the programme
Phase I	1988-1992	20	Up to 25% of value added	198
Phase II	1992-1999	10	Geared at average EU price and price cap was removed	820
PIIP	1999-2004	10	Similar to Factor f Phase II	300

Source:Industry Commission (1996), CSES (1999)

A.3.3 Results

According to the Industry Commission (1996) p106 the introduction of Phase I saw "*a significant increase in investment, production and R&D. In addition, numerous linkages were formed between companies and Australian medical research bodies* ". Pharmaceutical companies also believed that large benefits had come out of the scheme. Significantly, the single most important change had been the views of their foreign head office about the attractiveness of Australia as an investment market.

A number of studies have been done to analyse the effectiveness of Phase I Factor f programme. These have included:

- The 1991 Bureau of Industry Economics (BIE) review required by law. It found that payments were consistently lower than the 25%, spending some 157.5 million.[23] The BIE concluded that 85% of the increased activity was due to the Factor f scheme. It could not determine whether the funding was welfare enhancing.

[23] This was due to the lower effective payment rates for exports and R&D reflecting: *"the PBPA's discretion to decrease the payment below the 25%"*.

- The Australian National Audit Office (ANAO) tabled its review in 1993. While ANAO considered the administration had been satisfactorily completed it suggested a number of changes, most of which were incorporated in Phase II.
- Brain (1993) on behalf of the Australian Pharmaceutical Manufacturers Association (APMA) estimated the economy-wide impacts of the Factor f scheme. Using multiplier analysis they estimate that for every $1 invested by government the Factor f scheme added $10 to GDP.[24]
- The Industry Commission (1996) assessing a 1995 BIE report was unable to quantify the social benefits of the Factor f programme but found that the flow on effects would only needed to be at a low level for the scheme to break even.[25]

A.3.4 Spillovers

Crucial to any assessment are what is termed "spillover" effects. These are gains that arise from the spending on any particular project. As the BIE (1995) p62 comment:

"In most popular discussion, the benefits of Factor f are considered to be the increases in eligible activity on which Factor f entitlements accrue – the additional value added on exports, value added on domestic sales, and R&D expenditure carried out – as well as any increases in investment expenditure and employment. But in a social welfare framework, benefits are measured not as the additional activity itself but rather as the benefits ***that arise from that activity****."*

As stated above, it has been difficult to quantify the benefits "that arise from that activity" (spillover effects). The cautious approach taken by the BIE is predictable since this is a highly controversial area of economics. The studies quoted above, to varying degrees, imply that by subsidising an industry a country can gain in economic welfare terms.

To support this conclusion the CSES (1999) claim in a report prepared for the Australian Department of Industry, Science and Resources quote a number of studies that suggest high spillovers. For example:

- the Industry Commission (1995) in a survey of developed nations conclude that estimated returns from R&D are generally high – much higher than the cost of capital. Of 23 studies examined the unweighted average return from R&D investments in the US was 26% while in Japan it was 54%. The study also found that one off investments in R&D contributed to a continuing annual flow of social benefit in excess of the original investment.
- Odagiri and Murakami (1992) have estimated that between 1967 –1986 that the private rate of return for pharmaceutical R&D was 19% while the social rate of return (to all firms in the industry) was 33%. The higher social rate of return suggests that spillover effects are substantial.
- Cockburn and Henderson (1996) have examined the US pharmaceutical industry between 1960-1988. They found evidence of significant spillovers internally within firms and between firms giving rise to economies of scope. They also found that spillover activity increased after 1978 as the pharmaceutical companies invested more money in R&D.

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[24] The Industry Commission commented that this approach may overstate the gains from the Factor f scheme because it does not take into account any resource constraints i.e. by giving money to one industry the government may preclude other industries from growing – since it takes money away from that industry.

[25] Roughly 5 cents in every dollar for local companies and 23 cents for foreign companies.

The CSES claim that the view of the pharmaceutical industry, the qualified approval from the BIE and the IC, and the international literature on R&D spillovers suggests that the Factor f and PIIP schemes have contributed to the development of the pharmaceutical industry in Australia and led to significant spillover effects.

A.3.5 Implications for New Zealand

The debate over whether or not spillovers occur or at what level may not be crucial to the set of choices facing New Zealand. Most developed countries, whether it is economically right or wrong, support their bio-pharmaceutical industries in some way and link the marketing of pharmaceuticals with the R&D sector. The reality is that countries actually compete with each other and provide incentives to companies, as the BIE (1995) p10 quotes from a submission:

> *"... the big issue here, is to get the business environment right... the critical issue here [that] the Australian government has to realise is [that] its not we, company to company, that are in competition here; the Australian government is in competition with Singapore, with Ireland and everywhere else"*

The BIE (1995) p10 also report that when faced with an unfavourable environment pharmaceutical companies respond in the following way:

> *"...my company can cut off exports from Australia just like that. We can stop doing R&D just like that. We can take it to Singapore. We can take it to Ireland. We can take it anywhere we like and get it done and they are the realities of a global market and a global business."*

The favourable business environment for pharmaceutical companies in most developed nations allows them to pick and choose where they do their research. If New Zealand wishes to develop a bio-pharmaceutical industry to any significant degree then it must be aware of the realities of the pharmaceutical market.

A.4 Canadian Patents Act

A.4.1 Introduction

While developed countries face substantially similar challenges in fostering innovation, policy responses will be, to some degree, country specific and dependent on historical factors. There are also important differences among countries in the capacities and traditions of their science and technology policy institutions. Despite this, by understanding the mechanisms of innovation and technology diffusion in a knowledge based economy, there is room to learn from successes and failures in addressing common objectives.

The unique feature of the Canadian experience is the attempted balancing of industry policy with health policy and the building of an innovation culture. In the pharmaceutical industry, an independent quasi-judicial Patent Medicines Price Review Board (PMPRB)was set up in 1987 to administer an agreed process between industry and government to achieve these two aims.

In Canada, patents and marketing approvals for medicines are a federal responsibility. Provision of health services and, where Governments do this, the purchase of medicines is a provincial responsibility. Thus, the federal policy relating to patents may not be totally "in sinc" with a provincial policy for the purchase of medicines.

For the pharmaceuticals industry, this means that each state has a different programme to reimburse drug costs. While private insurance programmes, in one form or another, meet the majority of costs, the Federal Government purchases approximately 32% of all drugs in Canada.[26]

The history associated with patents is also relevant. In 1969 the Canadian Patents Act was amended so that compulsory licences could be granted to any generic manufacturer who applied for a compulsory licence. The royalty rate payable under such a compulsory licence was 4%. This effectively neutralised any patent advantage for pharmaceutical companies in Canada.

A.4.2 The deal

The PMPRB was set up as part of a deal between the government and the pharmaceutical industry in Canada. Under the Patent Act amendments (1987 and 1993) the federal government abolished compulsory licences.[27]

In return, patent owners agreed to price scrutiny (through the PMPRB) and Canada's Research Based Pharmaceutical Companies made a public commitment that the brand name pharmaceutical industry would increase its R&D expenditure as a percentage of sales to 10% by 1996.

The PMPRB is mandated to:

- ensure that the prices charged by manufacturers of patented medicines in Canada are not excessive;
- report annually to Parliament on the price trends of all medicines in Canada; and
- report annually to Parliament on the ratio of research and development expenditures to sales by patentees.

[26] Vandergrift and Kanavos (1997)

[27] The negotiations associated with the Uruguay Round were crucial in the abolition of compulsory licences. Under the TRIPs agreement Canada would have been required to abolish compulsory licences by 1995.

Also, as part of the deal generic companies were permitted to "spring board" their applications for approval to market generic equivalents to the patented medicines, so that they could launch their product as soon as the patents expired.

As regards the research, Table 3 shows the strong rises in the amount of R&D conducted by the companies.

To determine if the price of a patented drug sold in Canada is excessive, the PMPRB applies factors set out in the Patent Act as its price guidelines:

- existing patented drug prices cannot increase by more than the Consumer Price Index.
- most new patented drug prices are limited so that the cost of therapy is in the range of the cost of therapy for existing drugs used to treat the same disease.
- breakthrough drug prices are limited to the median of the prices for the same drugs charged in other specified industrialised countries that are set out in the Regulations under the Patent Act.

Table 3 : Canadian pharmaceutical company expenditures

Year	Companies reporting	Total R&D expenditure[1] (C$M)	Change from previous year (%)	Total sales revenue (C$M)	Change from previous year (%)	R&D-to-Sales Ratio	
						All Patentees (%)	participating Patentees (%)
1988	66	165.7		2,718.0		6.1	6.5
1989	66	244.8	47.4	2,973.0	9.4	8.2	8.1
1990	65	305.5	24.8	3,298.8	11.0	9.3	9.2
1991	65	376.4	23.2	3,894.8	18.1	9.7	9.6
1992	71	412.4	9.6	4,164.4	6.9	9.9	9.8
1993	70	503.5	22.1	4,747.6	14.0	10.6	10.7
1994	73	561.1	11.4	4,957.4	4.4	11.3	11.6
1995	71	625.5	11.5	5,330.2	7.5	11.7	12.5
1996	72	665.3	6.4	5,857.4	9.9	11.4	12.3
1997	75	725.1	9.0	6,288.4	7.4	11.5	12.9
1998	74	798.9	10.2	6,975.2	10.9	11.5	12.7
1999	78	894.6	12.0	8,315.5	19.2	10.8	11.3

Notes: (1) Total expenditures include current expenditures, and allowable depreciation expenses. If the expenditure funded by government grants are excluded, the ratios for all patentees and for the Research Based Pharmaceutical Company group are 10.7% and 11.3% respectively for 1999.
Source:PMPRB Annual report

A.4.3 On going tensions

The adoption of the agreement has created tension between various sectors in the Canadian pharmaceutical market. For example:

- provincial governments carry the fiscal cost of extended patents. With newer, more expensive pharmaceuticals maintaining longer periods of market exclusivity, the

relationship between the federal and provincial governments has been put under strain. The provincial governments have suggested that the Federal Government has pushed industrial policy at the expense of health programmes.

- the generic pharmaceutical industry, which is substantial in Canada, complained that the Patent Amendment Act delayed market access unduly. A generic drug could not be sold until all relevant patents had expired. If a patent holder started proceedings to protect a single patent, the regulations allowed for the delay of the clearance for up to 30 months, effectively extending the patent. The Research Based Pharmaceutical Companies brought numerous such cases to the Federal Court of Appeal, with the effect of delaying the entry of generic products.

A review in the House of Commons by the Standing Committee on Industry concluded that the patent terms must remain. While the Canadian Government supports this stance, the issue remains controversial.

Public policy theorists would argue that linking pharmaceutical patent legislation and price control with industrial development initiatives is unlikely to be the best way to proceed. The two policy areas are logically distinct and the best settings in each area may vary independently over time.

Patent policy and pricing agreements will affect both R&D incentives and the level of pharmaceutical supply to New Zealand. Industrial development policy focuses on the sectors with the best potential for mutual reinforcement and the best way to apply government help and funds to trigger growth. The incentives to maintain marketing offices in New Zealand – and hence to supervise some kinds of R&D – will depend on the profitability of local operations.

A.4.4 Development of the biotechnology industry

Since the agreement between the Federal Government and the pharmaceutical companies, the growth of R&D expenditure has been impressive (see Table 3). It is generally thought that the R&D growth, particularly in Quebec and Ontario, over the last 10 to 15 years was partly the result of these changes and partly the result of provincial Government inducements for setting up or expanding research facilities.

Employment in the Canadian pharmaceutical industry (1997)

Brand name pharmaceutical industry	20,000
Generic pharmaceutical industry	5,600
Medical biotechnology companies	6,700

Source: Statistics Canada

As well as the big multinational pharmaceutical companies, Canada has generic drug manufacturers, small and medium size biotechnology companies and a well-established contract research network of universities, hospitals, and private research organisations.

As well as being a significant employer (see adjoining table), the Canadian pharmaceutical industry has 15 of the top 50 spenders of R&D in Canada.

Table 4 shows the number of employees, the R&D expenditure per annum and wages paid to employees in 1999.

Table 4 : Estimated, employment numbers, R&D expenditure, and employment value added
1999

Province	No's employed	R&D expenditure (C$M)	wages and salaries (C$M)
Alberta	770	47.6	121.8
British Columbia	1,025	26.4	162.1
Manitoba	316	19.5	50.0
New Brunswick	143	2.6	22.6
Newfoundland	72	3.8	11.4
Nova Scotia	267	78.0	42.2
Ontario	9,396	381.4	1500.0
Prince Edward Island	3	0.4	1.5
Quebec	8,846	340.4	1400.0
Saskatchewan	152	6.8	24

Source:Rx&D & Statistics Canada

The two most important provinces in Canada for bio-pharmaceutical research are Ontario and Quebec where the brand name pharmaceutical companies spend nearly C$3 billion on employee wages and over $700 million in other R&D expenditure. In addition the bio-pharmaceutical industry employs over 18,000 people in those two provinces alone.

A growing feature of the Canadian biotechnology sector, which follows international trends, is the large number of start up firms that have contractual arrangements with multinational pharmaceutical companies. The number of biotechnology firms involved in bio-pharmaceutical research in Canada is second only to the United States.

There are also numerous examples of multinational pharmaceutical companies making significant research investments for individual research efforts conducted by public and private sector organisations. In Ontario, for example, C$2.6 billion has been invested in R&D since 1988 of which approximately 22% has been awarded to hospitals and universities.

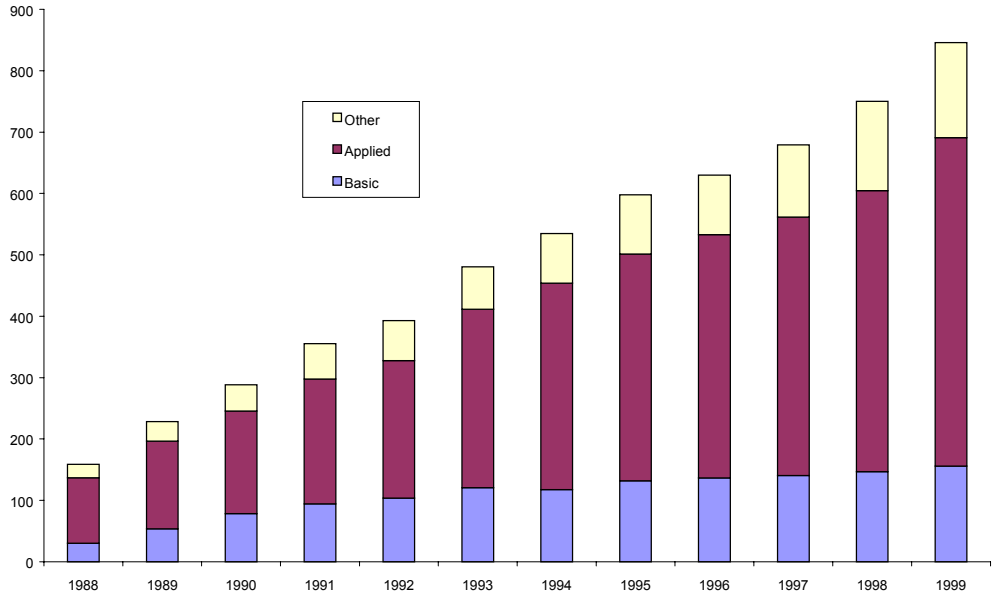
A.4.5 Basic research

Of most interest in the Canadian experience, is the increased basic research in Canada funded by pharmaceutical companies. This rise from C$30.3 million in 1988 to $155.9 million in 1999, to 18.9% of the total research done by the pharmaceutical industry. The increase in basic research is significant because it is the basic research, i.e. the work that advances scientific knowledge without specific application, which is more likely to create spill-overs into other knowledge economy activities. Furthermore, the amount of research carried out by hospitals and other learning institutions is increasing, while the

amount done by pharmaceutical companies internally is decreasing in line with world trends.

Figure 2: Current Canadian R&D expenditure by research type

Canadian $ millions



Note: Research by Rx&D companies only.

Source:PMPRB

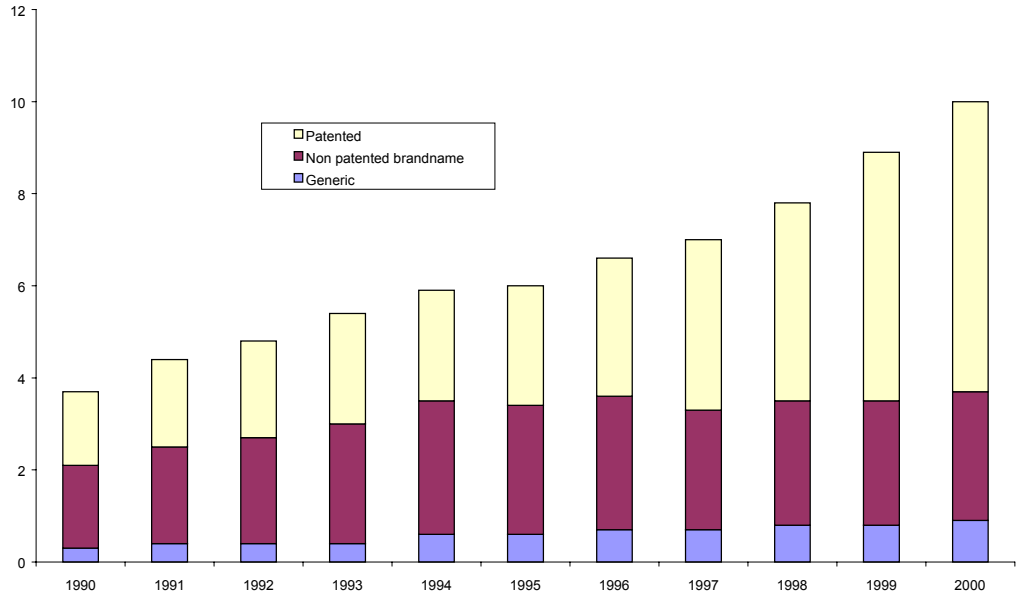
A.4.6 Summary

The pharmaceutical industry in Canada, like New Zealand, is dominated by a number of large multinational enterprises. Most have Canadian subsidiaries, which along with a few domestic companies dominate the sale and distribution of drugs in Canada.

The annual sales of patented and the non patented drugs are shown in Figure 3. Brand name pharmaceuticals outsell generics and patented pharmaceuticals are an increasing proportion of total sales (63% in 2000).

Figure 3: Sales of patented and non patented pharmaceuticals

1990 – 2000, Canadian $ Billions



Source:PMPRB and IMS Health in the PMPRB Annual Report

The pharmaceutical industry believe that the introduction of the patent strengthening legislation has:[28]

- dramatically increased investment in the Canadian pharmaceutical R&D industry and given confidence to that industry to invest substantially more in the future;
- led to an increase employment in the industry by over 30%;
- increased the number of biotechnology firms from around 25 to over 200 in less than a decade – with the majority being in healthcare (59%); and has
- still allowed the generic drug sector to become 3 times bigger than it was in 1990, even though its market share is smaller.

The government has also been an important contributing source of financial support for the biotechnology industry. These policy supports include: funding basic research, directing educational funds towards developing a supply of highly trained people, and financial assistance for research infrastructure, start-ups, and innovation.

While the industry development has been impressive, there is still controversy between Federal and Provincial governments and between generic and the Research Based Pharmaceutical Companies.[29] These controversies relate to the trade-off between industry policy and health policy. Pharmaceutical companies argue that deals such as that struck with the Canadian Government are necessary for a country to secure research activity. From an economic point of view, it seems plausible that countries are effectively competing in offering favourable investment environments but the OECD framework seems to provide a better guide as to how to proceed than the specific Canadian example.

[28] Comment by Merck Frosst Canada Inc

[29] Other reasons for the growth in R&D of the Canadian market include proximity to market, lower labour costs relative to the US, a high level of skill, and strong ties with the European market.

The 20 year patent term introduced by the Canadian Government was directly in response to its obligations under GATT TRIPS. In making this change they moved from a system that provided 17 years from date of grant.