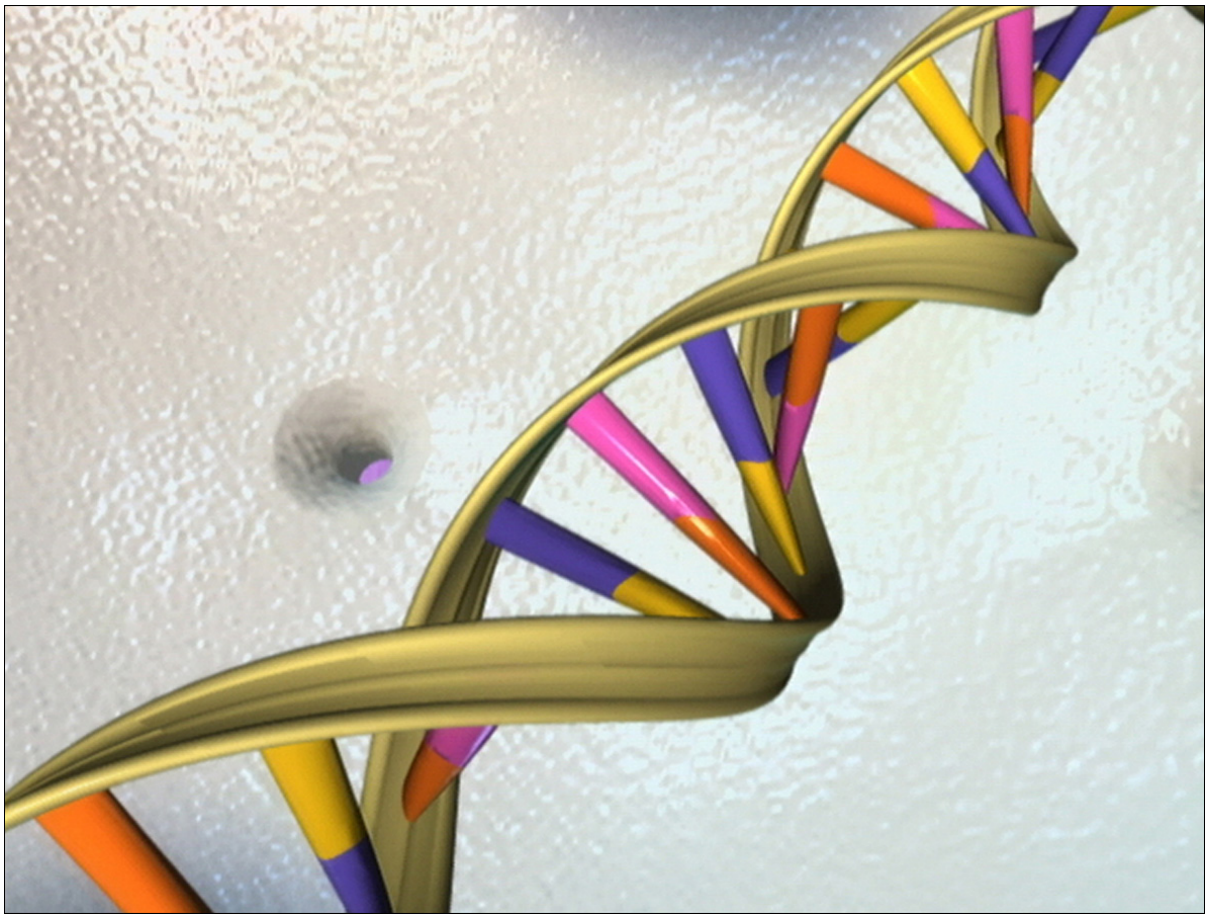
Pharmaceutical Research and Development in New Zealand- On the Brink of the Abyss



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1 Introduction

Research is four things; brains with which to think, eyes with which to see, machines with which to measure and, fourth, money.

Albert Szant-Gyorgyi –Nobel Prize winner 1937 for the discovery of Vitamin C

The development of pharmaceuticals is a business that involves high risk. It encompasses the studied compound entering rigorously controlled clinical trials that often take many years to complete. At any stage in this development the product could be terminated with no prospect of the sponsoring company realising any of the millions of dollars spent on the development so far.

Indeed the pharmaceutical industry, as it moves through its unique corporate life-cycle is devising ways that enable the clinical development time and hence the risk to be as low as possible, yet at the same time clear all the necessary regulatory hurdles. One of the benefactors of a change in the pharmaceutical R&D model are clinical research organisations (CROs)- independent organisations that purely perform clinical research; they do not sell the end product.

Most of the large pharma are based in the USA. However due to the high cost medical environment in America there is a fashion to decentralise research and utilise the affiliates of the company in other countries. Hence the second benefactors of the changing model of pharmaceutical research are those countries who have a first world medical system, high quality and respected researchers and produce cost effective clinical research.

While New Zealand fits the description of a country where theoretically it is ideal to conduct medical research, the paucity of and rapidly diminishing amount of research performed here suggests otherwise.

Since 1993 with the attempted compartmentalisation of healthcare costs in New Zealand, PHARMAC- the government pharmaceutical purchasing agency has had a dramatic effect on the amount spent on pharmaceuticals. While only now are the negative effects of such a restrictive policy on the health and well being of New Zealanders being realised, the effects PHARMAC and government policy on biomedical research and partnerships with local biotechnology companies in New Zealand are even less well acknowledged.

On any bench marking measure New Zealand underperforms when it comes to the quantity of biomedical research performed here. The entrenched hostility towards the pharmaceutical industry, the lack of understanding about how long term, effective partnerships in clinical research occur and an unwillingness to attempt to correct past mistakes means New Zealand's biomedical environment is sliding down the slope to irrelevance

In spite of government rhetoric and attempts to be part of the biotechnology renovation, New Zealand biotechnology is failing to ignite. One of the principle reasons is that the very essence of biomedical innovation that is the corner stone of biotechnology is being destroyed.

Many countries, like New Zealand, have a focus on biomedical research and the opportunities of biotechnology. No country has created as hostile an environment for pharmaceutical companies, the major partner in biotechnological evolution, as has New Zealand. As a result countries like Ireland and Singapore are significantly much closer to the goal of creating a local sustainable biotechnology industry with the associated economic benefits both in terms of the production and sale of new technology but also its manufacture.

As the large pharma affiliates pull out of New Zealand, pharmaceutical biomedical research in is rapidly disappearing and with it are going the associated infrastructure capacity, the world class researchers, the ability to conduct world class research and any chance New Zealand has of being part of the biotechnology revolution in human health.

2 Pharmaceutical Development

If you think research is expensive, try disease
Mary Lasker (1901-1994)

Over 97% of new medicines are created by the pharmaceutical industry (1). However, before any given pharmaceutical company can *sell* a registered medicine they need to develop it. These critical phases involve huge financial risks and vast resources. It is estimated that the pharmaceutical industry spends US $60 billion a year on medical research and development (1).

As can be seen from Figure 1 there are three distinct phases of the development of a medicine:

1. discovery of compounds, animal or pre-clinical phases,
2. clinical or human trials, and finally,
3. registration with government regulatory bodies.

This is where the research and development comes in. Pharmaceutical companies need to conduct clinical trials under strict regulations in centres and with researchers who can guarantee excellent quality research.

Table 1 The Phases of Clinical research

Term	Population studied	Description
Phase I	Small numbers (6-24) Usually healthy volunteers but occasionally in special populations, such as people with kidney failure.	First time in human subjects. This phase looks at the safety of the medicine in man. The way the medicine is handled by the body (pharmacokinetics) is studied.
Phase II	Larger numbers of patients (24-100) with the target disease	These trials look at how effective the medicine is (efficacy) against the target disease.
Phase III	Usually very large trials (250-20000) in people with the target disease	These trials focus on safety but also have measures of effectiveness and ensure that side effects that are only shown in a population rather than an individual are determined.
Phase IV	Any number of patients with the target disease	These are termed “post registration trials” as they occur when the medicine is available. Often they look at local population issues (e.g. obesity)

Table 2 Table of Terms

Term	Description
Sponsored Trial	The trial is designed by a pharma company; the resulting data is the property of the company. All associated trial costs are the responsibility of the company
Supported Trial	These trials are designed by investigators (clinical doctors) with the data usually being the property of the designer. However agreed costs are often met by the pharmaceuticals companies
"Blinded" trial	The majority of trials conducted with pharmaceuticals are randomised (i.e. the patient is randomly assigned to a specific study treatment "arm". What treatment (in terms of dose or active state- vs. non-active or "placebo") is determined in such a way that the patient has no idea as to what treatment they are receiving (blinded). If both the patient and the doctor have no idea the trial is considered "double blinded".

The average cost to produce one single new medicine is estimated to be around US $800 million dollars or higher depending on the therapeutic area (2). The time it takes to list a new medicine, from discovery to registration, also varies but is thought to be, on average, around 15 years. As patent life for a new product is 20 years this leaves five years for the producer to recoup the costs plus make a profit on the previous 15 years investment. While this is an over simplification of the process and does not take into account patent life extension policies and techniques it illustrates the point that new medicine discovery is a very costly and time consuming business.

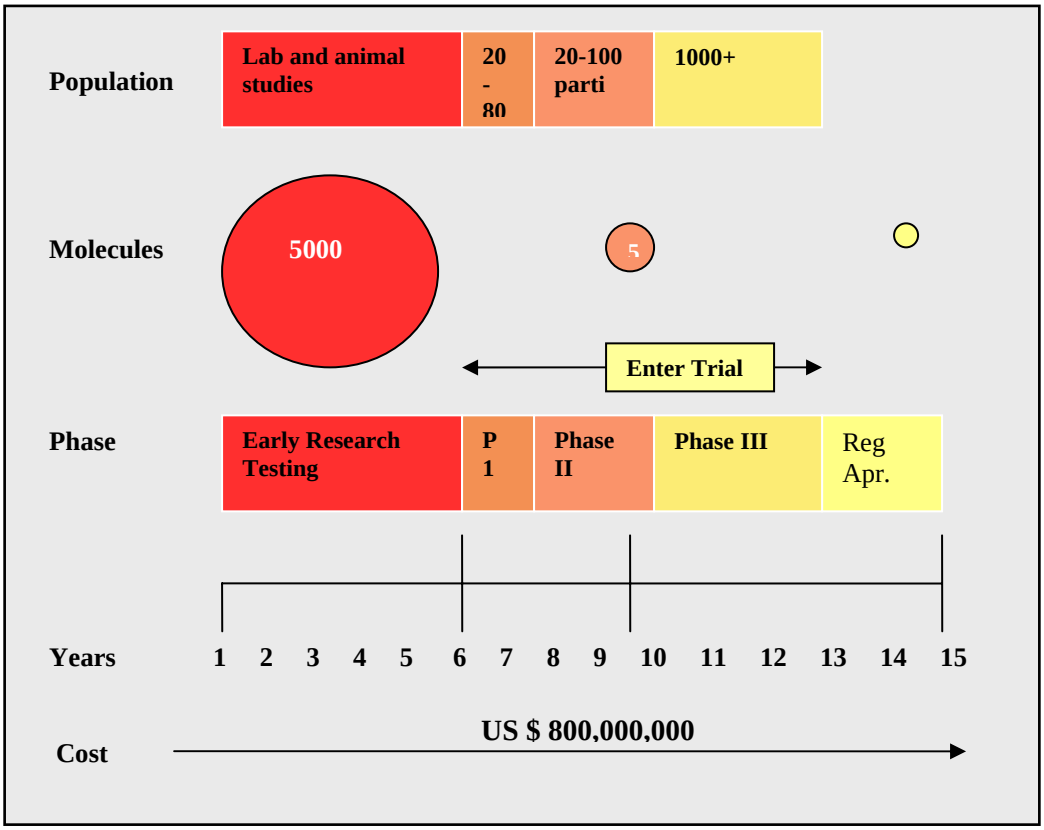
Furthermore the risks for the individual companies are extremely high with the chance of success extremely low: it has been postulated that, on average, of the 5000 molecules that were considered in pre-clinical (animal) trials only one product will become registered by the FDA and sold as a new medicine.

Two additional environmental events add to the risk:

1. Declining periods of exclusivity. This is the time which a pharmaceutical company has sole assess to the market before similar "me too" medicines arrive. While these second-to-market medicines are unique compounds the speed with which they appear after the original is now extremely rapid. For example the first B Blocker to market Inderal, marketed in 1968 had a full 13 years before the next B Blocker appeared. These days the period of exclusivity is measured in months.

2. As the time for development of compounds into medicines increases, in part due to more rigorous regulatory frameworks, the time between registration and patient life expiry (20 years) becomes shorter. Hence the time that a company can recoup the capital cost of development is becoming less. In the USA and Australia, for example, in recognition of this issue there has been patent life extension. However no such extension exists in New Zealand.

Figure 1 The Research and Development Pipeline



As the medicine enters human clinical trials the costs start to escalate:

- **Phase I** US$ 2-12 million
- **Phase II** US$ 10-25 million
- **Phase III** US$ 20-200 million

The costs do not stop there. Once the Phase II and Phase III trials that are carried out in a targeted disorder are completed, the patients who derived a clinical benefit are usually moved to an extension phase trial. These trials tend to be less rigorous in their methodology but have the aim of allowing companies to monitor the safety of their medicine in a longer term context. Importantly they also allow the patients access to the medicine before it is registered and hence a continuation of their new treatment. These extension arms continue until it is mutually agreed to stop, or as in the majority of cases continue until the product gains reimbursement. Often the sponsoring company continues to pick up the associated medical costs and the cost of the medicine.

In addition to these base costs, as each clinical trial only answers one clinical question and more than one medical indication is often sort involving a particular medicine, multiple trials are needed to be performed during each phase. This of course results in an escalation of the development costs associated with the medicine's development.

Why NZ can be a successful R&D centre

New Zealand has an ideal medical environment to conduct medical research. It has a tradition of being involved in the development of and research in many areas of health and clinical advancement. New Zealand also has a reputation of being inventive and a culture of making the most of limited resourcing.

✓ ***The researchers:***

Coupled to this history is that the clinical researchers involved are well trained, often with extensive overseas experience, motivated and efficient. Often they forgo financial advantages of clinical practice to follow a career that because of New Zealand's size means resources are scarce both in financial and human terms. Those resources that are available are often utilised to capacity.

In general there is a collegiality among the various research centres and hospitals, enabling rapid sharing of ideas, dissemination of information and the formation of like minded clinical interest groups.

✓ ***The health system:***

New Zealand's public health system is of a high standard as would be expected from a developed country. New Zealand spends on total healthcare an amount approximately equal to the OECD average, as a percentage of GDP (3). New Zealand enjoys a well trained medical and allied health staff with good access to technical medicine such as radiology. Most clinical research takes place in the broad umbrella of the public institutions although several private research organisations do perform sponsored trials. The private health system provides choice with very little overlap of the public system in terms of sharing facilities.

Accident compensation (ACC) covers medical practice and associated misadventures, ensuring the health care environment has a low rate of litigation.

✓ ***The system of Ethic Reviews. (IEC)***

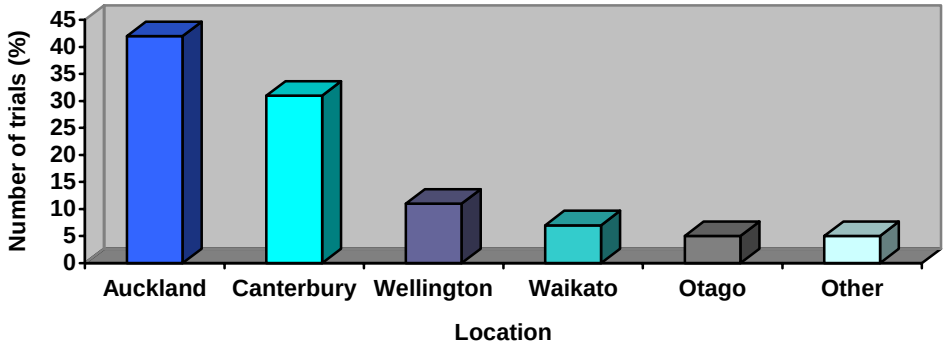
The Ethics committees are independent entities with no ties to health institutions. Their job is to ensure that the patients' health and rights are protected during and after the clinical trial. The committees contain a mix of lay and medical professionals. In New Zealand they have a transparent and open reporting structure, are generally efficient, reliable and effective.

✓ ***Geography***

While geographic position distance New Zealand from the rest of the world, the compactness of its national provincial centres means it is relatively easy to travel about, enabling researchers and people associated with performing research to meet. The majority of

research however is carried out in just two locations, Auckland and Canterbury (Figure 2). While Auckland's share is understandable due to patient population, Canterbury's success seems to reflect a culture in the local healthcare environment of involvement in clinical research that is missing from other provincial areas.

Figure 2 Clinical research location



Adapted from Jull (2005) NZMJ

✓ ***Cost Effectiveness of Performing Clinical research***

Compared to its trading partners New Zealand has relatively high interest rates, low inflation and a moderate standard of living. This means that wages, institutional overheads and medical procedures tend to be less expensive. For example radiological procedures performed in the USA are often three to four times more expensive than the comparative procedure being performed in New Zealand.

As the costs associated with clinical research, broadly cover staff, institutional overhead, procedures and travel, New Zealand tends to have a significant comparative advantage in the provision of health care if the comparison is based on standardised costs.

New Zealand therefore can compete with the emerging research locations of Eastern Europe and Asia but has the advantage of a first world heath system and a strong history of performing high quality research.

The Amount of Research performed in New Zealand

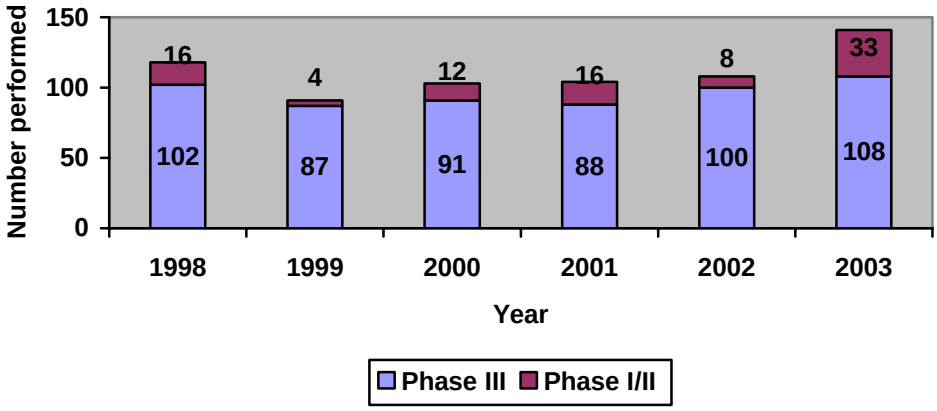
With the advantages outlined above it is therefore surprising to see how relatively little health research is performed in New Zealand. Until very recently the New Zealand government health research expenditure was less than 40% of the OECD average. Similarly the per capita funding for research was about half what it was in Australia (5).

While the directive by WHO in 2005 to register all clinical trials on a publicly accessible website is quickly being implemented worldwide the exact amount of research performed in

New Zealand is difficult to determine. A recent study looking at Phase 1 to Phase III research found that the number of trials performed has remained static since 1998 at just over a 100 per calendar year with the vast majority being Phase III trials (4). This is shown in Figure 3.

It is pertinent to note that nearly 80% of the trials performed in New Zealand in the last 5 years involved clinical research on medicines.

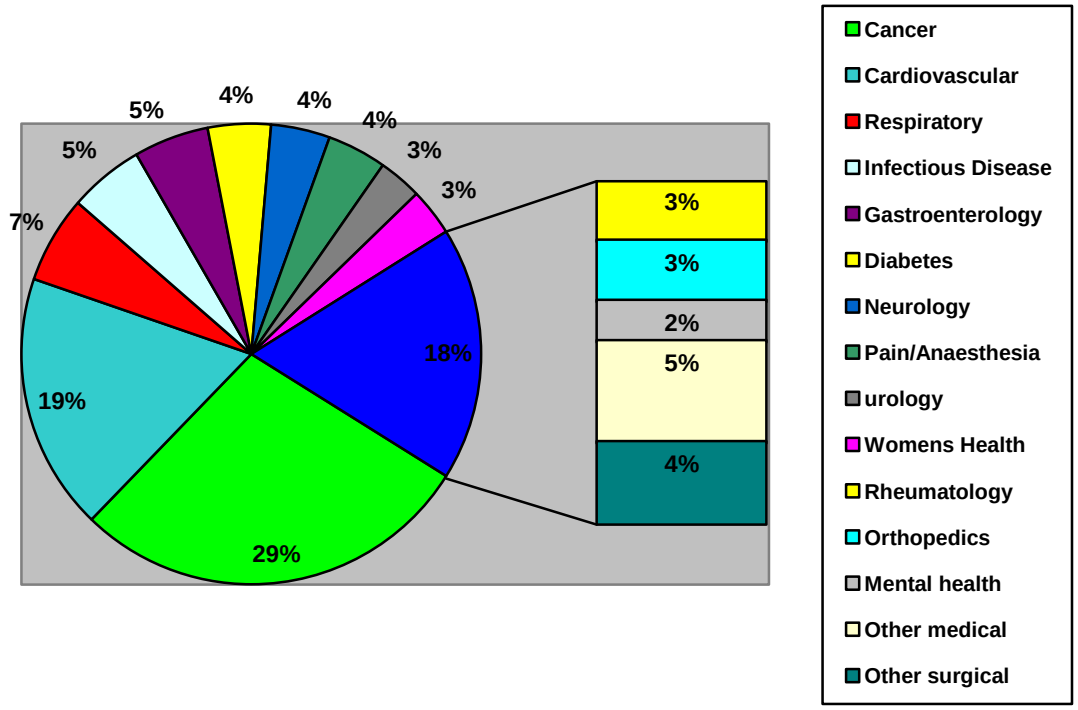
Figure 3 Number of Clinical trial protocols performed: New Zealand 1998-2003



Adapted from Jull (2005) NZ Medical Journal

In terms of therapeutic focus it would seem New Zealand as a country specialises more in the areas of oncology and cardiovascular medicine- nearly 50% of all clinical trials performed in those two areas (Figure 4).

Figure 4 Percentage of Clinical Trials per Therapeutic Area: 1998-2003



The Amount of Pharmaceutical Research Performed Compared to Other Countries

In the period of time covering 1998 to 2003 most of the clinical trials performed in New Zealand involved a medicine as the trial intervention. From 1991 to1999 New Zealand overall spend of pharmaceutical companies in clinical R&D did not change.

The amount of money generated from performing pharmaceutical clinical trials is therefore small- around NZ$20 million dollars (RMI survey 2003). This compares to the A$450 million spend per year in Australia and is but a drop in the ocean of the US$40 to $60 billion spent globally each year by the pharmaceutical industry.

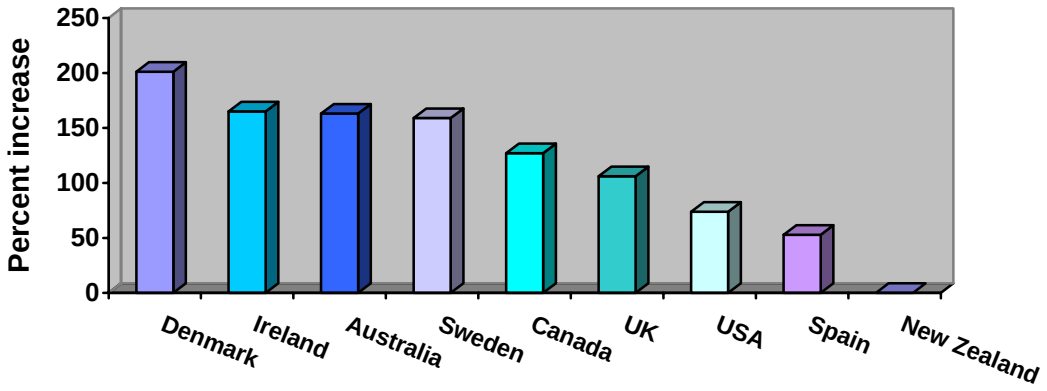
Table 3 The Potential R&D Investment

Conservative estimate of global pharmaceutical R&D spend per year is NZ$80 billion dollars	**If New Zealand attracted 0.25% of this international pool which with local management and a robust local industry should be obtainable it would equate to around $200 million dollars or nearly ten times what is spent now by pharmaceutical companies and nearly triple what the government spends on biomedical research**
	If New Zealand was able to attract 0.9% of this international pool of pharmaceutical research this would be more than the government currently spends on pharmaceutical purchasing

In the eight year period to 1999 New Zealand growth in pharmaceutical research was around zero. This is in stark contrast to other countries in the OECD which registered phenomenal growth as shown in Figure 5. Of the countries measured only one, Italy, had a decrease in the amount of pharmaceutical research performed (6).

Hence to date very little pharmaceutical research or for that matter biomedical research occurs in New Zealand, especially compared to similar sized countries such as Ireland and Denmark or a country often compared with New Zealand, Australia. While public funded biomedical research as managed through the Health Research Council (HRC) has increased in recent years, it is still low as a percent of total health spending when compared to Australia or the UK (5). The issue of lack of private investment in biomedical R&D is further highlighted in that public funding makes up over 72% of the available health funding in NZ. This compares to 30% in the USA and approximately 40% in Australia.

Figure 5 Percentage increase in pharmaceutical R&D spend 1991:1999



Currently worldwide there are over one thousand pharmaceutical trials underway (7), many in areas of interest that the New Zealand government has targeted as priority diseases. For example in the area deemed the highest priority for government attention- oncology - there are nearly 300 products that target various cancers currently in clinical development (Appendix 1). Unfortunately hardly any of the companies involved with the products perform research in New Zealand (Table 4). There is also an increasing trend that if the company can not envisage obtaining reimbursement for a product in a country then they are reluctant to perform research in that country.

It could be argued that in areas like oncology companies that produce medicines that have the potential to save or extend life, should feel a moral obligation to make such products available as earlier as possible through the conducting of local clinical trials. However the government of that country also shares an obligation to ensure the environment is attractive enough for that company to perform clinical research there. Currently that is not the case in New Zealand.

Table 4 North American Companies that have three or more Oncology Products in Clinical Development

Company[1]	No of medicines in development	Target Cancer	Development Phase	Does Company perform R&D in NZ[2]
National Cancer Institute	61	All	I-III	Yes[3]
Pfizer	11	K, L, Me, Pa, Thy, L, H, Pr, Br, G	I-III	No
Bristol Myers Squibb	8	G, CR, L, Pr, NSC, O, Pa, Br, R, Br	I-III	No
Wyeth	8	Br, K, Pr, sa, L, NSC, CR, Pa, CML	I-III	No
GSK	7	Me, R, NSC, Pr, Br, Bl, G, K, L	I-III	Yes[4]
Cell Genesys	6	Pr, MM, NSC, Pa	I-III	No
Medarex	5	Me, Pr, CR, NSC	I-II	No
Celgene	4	MM, Pr, GBM, Me, MDS	II-III	No
Cell Therapeutics	4	CR, O, MM, MDS, Nb, CML, Br, O, L, NSC	I-III	No
Introgen Therapeutics	4	Br, Eo, NSC, Pr, Me, L	I/II	No
Novartis	4	Br, H, CR	II-III	Yes
Allos Therapeutics	3	Bn, Ce, GBM	1-IIINDA	No
Antigenics	3	CR, R, L, Me, Mes	I-III	No
AstraZeneca	3	Br, CR	I-III	No
Bayer	3	Br, R, Lv, NSC, CML Bn	I-III	No
Dendreon	3	CR, Br,, O, Pr	I-III	No
Genentech	3	CR, R, Pa, Br, En	I-III	Yes[5]
Genta	3	Br, CR, MM, NSC, R, AML, CLL, Ly, G	I-III	No
INTRACEL	3	Bl, CR	III-NDA	No
IVAX	3	GBM, Br, G , L	I-II	No
Johnson &Johnson	3	Br, Ov, Sa	II-III	No
Mellennium	3	Pr, NSC, Ly	I/II	No
Neopharm	3	GBM, CR, L	I/II	No
OSI Pharmaceuticals	3	L, Pr, G	II	No
Sanofi-Aventis	3	G, Br,	II-III	Yes[6]
SuperGen	3	CR, Pa, NSC, Thy,	I-III	No
Titan	3	Br, CR, NSC, CLL	II-III	No
Viventia Biotech	3	Me, Br, Bl	I/II	No

[1] Companies as listed in the website www.innovation.com. Note: while MSD does perform clinical trials in NZ it does not appear in the website.
[2] Not necessarily in oncology
[3] Almost exclusively in paediatric oncology
[4] Early Phase trials (Phase I) only
[5] Represented by Roche in NZ.
[6] Phase IV only

Key

Cancer Type	Code	Cancer Type	Code	Cancer Type	Code
Gastric	G	Glioblastoma Multiforme	GBM	Small cell	SC
Colorectal	CR			Endometrial	En
Lung	L	Brain	Br	Thyroid	Thy
Prostate	Pr	Gastrointestinal	GI	Adenocarcinoma	AC
Non- small cell	NSC	Gastric	G	Small Cell	SC
Ovarian	O	Cervical	Ce	Mesothelioma	Mes
Pancreatic	Pa	Lymphoma	Ly	Leukaemia	Le
Breast	Br	Eosophageal	Eo	Hodgins disease	HD
Renal	R	Haematological	H	CML	CML
Bladder	Bl	Liver	Lv	Multiple Myeloma	MM
Melanoma	Me	Neuroblastoma	Nb	Neuroendocrine Tumour	NET

The Myth of New Zealand Clinical Trials

Despite the evidence there is however a persistent myth that because New Zealand is an excellent place to do health research, the biomedical industry will continue to allocate research trials to New Zealand regardless of the business environment. The reality is however quite different.

Research does not *have* to be performed in New Zealand. There are many other places around the world that make it far more attractive to undertake research in their countries. Furthermore successful business depends not only on technical expertise but also on forging partnerships. Indeed some believe New Zealand can continue to be an overall importer of scientific knowledge and thus not pay the associated costs. Such an isolatory viewpoint implies therefore that any thoughts New Zealand has of creating a sustainable biomedical industry are fanciful.

Increasingly pharmaceuticals companies that operate in New Zealand are linking the product development of pharmaceuticals (R&D) with the projected possibility of the medicine being reimbursed. This is especially true in chronic diseases, where once the patient has completed the clinical trial and still require the medicine used in the clinical trial, the companies allow the patient to continue on the medicine free of charge, until reimbursement. As the possibility of reimbursement for a particular medicine is so low in New Zealand, companies face the very real liability that once a clinical trial has ended, they are morally obligated to provide the medicine free of charge for an indefinite period of time at their own cost. Such a liability is yet another disincentive for companies to perform clinical trials in New Zealand.

Due to the hostile business environment Dr David Woolner Medical Director of MSD-NZ comments that in his opinion "... New Zealand as a great place to do clinical trials is a myth" (8).

A case study on New Zealand by the Boston Consulting Group also reached the same conclusion that while New Zealand possesses significance research strengthens, government policy through PHARMAC has reduced the country's attractiveness for pharmaceutical R&D

investment. In the report the authors comment that New Zealand has failed to gain its "fair share" of international biomedical investment by a substantial margin (9).

The PHARMAC Factor:

Nearly all pharmaceutical companies that disinvest in New Zealand label the government's pharmaceutical reimbursement policy as the single biggest reason for their withdrawal or downsizing.

Established in 1993, PHARMAC's overall objective is to "...secure for eligible people in need of pharmaceuticals, the best health outcomes that are reasonably achievable from pharmaceutical treatment and from within the funding provided."[7] The core of this objective hinges on curbing the amount of money the New Zealand government spends on pharmaceuticals.

Since its formation, it has become the general opinion of pharmaceutical companies operating in New Zealand that PHARMAC's primary focus is on short-term fiscal savings at the expense of restricting New Zealanders' access to new, better medicines. This view is supported by the fact that compared to Australia, New Zealanders access to new medicines and a wide range of medicines is extremely poor, that is the chance of a company getting their medicine reimbursed at all is very low (10).

With such an unusual and anti-pharmaceutical industry policy, the government is alienating the pharmaceutical industry, making any partnerships with large pharmaceutical companies almost impossible.

This behaviour differs markedly to other countries government policy. Most OECD countries have amended their health research strategies in order to respond to the evolving research environment including an increased emphasis on public-private partnerships (5).

As a direct result of such policies New Zealand has been crossed off the list of countries that can access external funding, including not only those organisations performing pharmaceutical research. A good example of this is the *Wellcome* funding.

For a significant period of time, the Wellcome trust has provided funding for medical equipment and research throughout New Zealand. However since 2003, as cited by Goran Ando, Pharmacia's president of Global Research & Development, this funding was no longer be available in New Zealand "due to the government's policy's embodied in PHARMAC. The funding will continue to be available to every other nation in Asia Pacific region including Australia".

[7] Pharmac website (www.pharmac.govt.nz), "About Pharmac"

Dr Ando comments reflect a very real possibility that New Zealand as well as being geographical isolated, will be isolated from the international medical research community.

"PHARMAC's extreme policies of minimising costs are short sighted and represent an anti innovation policy which will deprive New Zealand patients of better medicines. Major research based pharmaceutical companies see no encouraging signs in New Zealand - rather the opposite - and of course we draw the conclusion that New Zealand does not encourage pharmaceutical R&D.

Thus, the industry will over time move remaining R&D investments to more innovation friendly countries where we are encouraged to work with universities both in early basic research and in clinical research.

One example - Pharmacia recently initiated a prestigious fellowship program in Australia building on the previous Wellcome Foundation program, which has existed for many years. We did however limit the fellowships to Australia rather than keep it open also to New Zealand - a small action but it should be seen together with similar actions of the rest of the industry.

New Zealand has many good scientists. However, without the symbiotic collaboration with the international pharmaceutical industry, it will be at a competitive disadvantage with countries like US, UK, Sweden and Australia and over time risk being marginalized.

It is not reasonable that patients in the US and other countries should subsidise the massive R&D investments to produce better medicines for New Zealand - all developed countries need to share that cost." Dr Goran Ando, President Global R &D (2003)

In mid 2003 Pharmacia was taken over by another multi-national Pfizer. Since the acquisition Pfizer has publicly stated that while they will honour the completion of clinical trials currently underway, they have no intention in the future of placing any research what so ever in New Zealand.

Companies Disinvesting: Reasons why.

Since 2002 they has been a noticeable disinvestment of pharmaceuticals companies in New Zealand. This downsizing has affected both marketing and sales. However it has had most effect on the affiliate's medical and clinical functions (Table 5).

Table 5 The history of Pharmaceutical Company Retrenchment in New Zealand

	Year	Company	
1	1994	**Pfizer**	Pfizer cease research in New Zealand
2	1999	**Eli Lilly**	Eli Lilly cease research in New Zealand
3	2000	**Lundbeck**	Lundbeck exit the New Zealand market and cease all research
4	Mar 2000	**Bristol Myers Squibb**	Bristol Myers Squibb announce it is restructuring – ie. pulling out of New Zealand and discontinuing research
5	Sep 2002	**Servier**	French company, Servier, pull out of planned medical Trials in New Zealand
6	Oct 2002	**Aventis**	Aventis downsize the company; continue to perform some local research activity.
	Jan 2005	**Sanofi Aventis**	Formed –continue to do minimal research managed from Australia.
7	Nov 2002	**AstraZeneca**	AstraZeneca announce it is downsizing its operations in New Zealand and the complete withdrawal of all R&D to Australia. AZ comment that no new research will take place in NZ.
8	2003	**Novartis**	Restructure with decrease in clinical and marketing. All clinical managed from Australia.
9	2004	**GlaxoSmithKline**	GlaxoSmithKline announce restructuring plans, withdrawing 85% of its staff. Any R&D performed here will be managed from Australia.
10	2004	**Pfizer**	After the acquition of Pharmacia, Pfizer cancel a $40 million contract with Auckland University and announce no new research to be performed in NZ.

Pfizer Inc. In January of 2004 Pfizer signed an agreement with the Auckland University and the Cancer Society of New Zealand to spend $40 million in the next five years in New Zealand on the development of novel oncological targets and antibiotics. Potentially this amount of funding was to be doubled in the ensuing years. This meant Auckland University could spend much needed funding on capital infrastructure to build new laboratories and employ up to 20 fulltime medicinal chemists. In discussion with the Pfizer project managers in the USA, it was indicated that to them, the Auckland collaboration was one of the most effective they had anywhere in the world.

Unfortunately due to an impasse on the funding of atorvastatin (Lipitor) between PHARMAC and Pfizer, Pfizer decided to cancel the contract outright, pay the cancellation penalty and remove all subsequent R&D funding from New Zealand. This was the end of a 16 year partnership.

While it is noted that Roche stepped in and began funding some of the projects at the University of Auckland, the amount of financial support was approximately a quarter of what was available under the agreement with Pfizer.

Astra Zeneca: In 2003 following AstraZeneca pulling out of research in New Zealand , general manager Lance Gravatt was quoted as saying a lack of funding for pharmaceuticals, difficulties with patent protection and intellectual property and the "whole machinery of how research is funded" are the reasons for the company's move[8].

Mr Gravatt added: "We have recently seen a worrying trend towards downsizing and retrenchment of international pharmaceutical company operations in New Zealand. This trend will, unfortunately, have a negative impact on bio-medical research in New Zealand and runs counter to a Knowledge Economy strategy" [9].

Servier: In close succession of AstraZenca's decision, Servier Laboratories announced that they too were reviewing further investment in New Zealand. Servier has contributed more than $30 million to research projects in New Zealand throughout the past five years and is a leader in stroke and diabetes medicines. Servier's Australasian managing director, Barry Young, said the privately owned company had watched its once healthy business in New Zealand slowly erode through the "Government's punitive PHARMAC pricing" [10].

In the same report, Professor Gary Nicholls, professor of medicine at Christchurch School Medicine, stated: "They [the Government] are not prepared to work with the pharmaceutical companies. Pharmac has a very narrow perspective"[6].

In the words of another researcher urologist Dr Stephen Mark. "there is no question that companies look at New Zealand as a relatively hostile place with no commercial benefit" (8).

Dr David Woolner MSD New Zealand's medical director adds a note of warning on behalf of those pharmaceutical companies here in New Zealand still performing clinical research. He comments" If we (MSD) don't exist as a commercial reality here in New Zealand, we will not do trials here" (8).

PHARMAC itself indicated that its own policies over hospital purchasing of pharmaceuticals could "potentially become a factor in the amount of research into pharmaceuticals being conducted in New Zealand" (11). This statement has been borne out in fact in that in real terms there has been a noticeable decline in pharmaceutical research in New Zealand.

As Dr Ralph Richardson- director of ESR (the government organisation of Environment Science and Research) comments that unless the business climate in New Zealand for pharmaceuticals improves, New Zealand is missing the opportunity of being part of one of the main growth areas of the 21st century (12).

However some companies such as Roche, who operate in the same commercial environment as those companies that have withdrawn, have continued to perform research in New Zealand. The reasons for doing so can be broadly categorized into personal relationships and the presence of a clinical department.

[8] NEW ZEALAND Herald, 28 November 2003 "Clinical trials moving"
[9] Ibid
[10] NEW ZEALAND Herald, 2 December 2003 "Drug researcher blames Pharmac"

The Pharmaceutical clinical department.

The pharmaceutical industry in New Zealand is extremely small employing 596 in 2004 down from over 1000 in 1990. Both figures are dwarfed in size by Ireland which employs 12,000 in its pharmaceutical sector. Ireland has an extremely large manufacturing base of pharmaceuticals, whereas New Zealand has none.

In most subsidiaries of pharmaceutical companies there is a department that, while linked to the business operation of the company, concentrates on clinical research. Often such departments have a medical director or director of clinical research and a various number of clinical research associates (CRAs) and managers. The clinical department maintains close contact to a widespread group of local research departments, investigators and nurse co-ordinators.

However when, due to business conditions the pharma company down sizes in a country, the clinical team is one of the first groups to be pulled out, presumably because in the short run they are not going to contribute to the local affiliates increase in sales but their overhead will contribute to a deteriorating profit.

The clinical department is however, one of the fundamental reasons why New Zealand gets any pharmaceutical research. Clinical trials run by large pharmaceutical companies are managed by geographical segment (for example Asia Pacific). In each of these segments, when a trial protocol has been developed, individual countries "bid" for the right to perform the trial in their country. Their success or otherwise is dependent on all those factors that New Zealand has in its favour: good access to high quality investigators, the ability to recruit patients and the cost of performing the trial in that country.

It follows therefore that if New Zealand has no one to bid for those trials, that is no clinical trial medical director or even department, then the trials will not come to New Zealand. As the majority of pharmaceutical research is now managed from Australia- the local link and support has been severed. Australian clinical trial managers will focus on their own country first. If they are allowed to consider New Zealand, they will allocate trials often only if they can not meet the recruitment numbers in their own country.

Thus unfavourable business conditions in terms of pharmaceutical reimbursement resulting in a down sizing of local subsidiaries translate into less pharmaceutical clinical trials being performed in New Zealand. With such an unfavourable business environment continuing the prospect of companies reversing the trend becomes less and less.

Personal relationships

Several prominent New Zealand investigators have excellent relationships with the preclinical and early phase departments of large pharmaceuticals companies. Such relationships are borne out of years of producing high quality data for the companies but also because of personal relationships between the investigator and the company management.

Hence despite the business conditions prevailing that such companies do not have a clinical department or if they do a very small one, clinical research continues to flow to these investigators.

However inevitably the evolvement within pharma companies will mean individual contacts and personal relationships with outside investigators will be lost and so will the flow of clinical research.

With minimal clinical research taking place there is little chance for new relationships to take hold and replace old ones and eventually New Zealand as a place to conduct high quality research will be forgotten.

Singapore

Like New Zealand, Singapore's government believes that biotechnology is a major driver of its future. *Unlike* New Zealand's PHARMAC-centric policy, the Singaporean government has made efforts to attract large high tech firms to conduct medical R&D in the relatively small country. The result is it gains an influx of major skills and even more importantly, local contacts with the headquarters of these firms in the USA, allowing business relationships to mature more rapidly (13).

This culminated in the Singaporean Economic Development Board (EDB) having as one of its key strategic focuses- a fully self sustaining biomedical industry. Similar to Ireland most of the major pharmaceutical companies have made Singapore their global manufacturing hub, due to feedback loops (R&D programs, tax incentives and patent protection) being established that encourage investment. One of the major tasks in attracting talent and resources to Singapore was the sustained development of infrastructure to support biomedical research.

As a result biotechnology as a major pillar of economic development is beginning to flourish with about the same number of start up biotech companies as Australia (14).

Australia

The Australian government has actively worked with the pharmaceutical industry to strengthen research ties that enhance the relationship and enhance investment. New Zealand's government's policy strongly contrasts with this.

Since the 1980s the federal government has had incentive schemes to foster closer ties with and encourage pharmaceutical R&D in Australia. As a result from 1997 to 2003 pharmaceutical R&D in Australia has nearly doubled to A$450 million. Pharmaceutical research funding contributes nearly 15% to the institutional research organisations nationally. Around ninety percent of the companies that have subsidiary offices in Australia perform or support research and development. Between them they contribute to over 260 alliances with research institutions and biotech companies within Australia (15).

The latest government support scheme, the Pharmaceuticals Partnership Program (P3) has taken over from previous government sponsored partnership schemes such as PIIP and Factor (f) scheme. P3 which commenced in July 2004 aims to increase high quality pharmaceutical R&D activity through out the health research value chain including biotechnology. Participating companies receive thirty cents for each additional dollar they spend on eligible research in Australia to a maximum grant of A$10 million.

As more and more research based pharmaceutical companies retrench their staff to Australia, the local contact between New Zealand and corporate headquarters is lost. Having local management of global research business is key to having that company's research capability expand locally. Indeed the first segment of a large pharmaceutical company's team to be retrenched offshore is their R&D staff.

Ireland

Ireland seems a logical place to compare and contrast with New Zealand. It is often influenced by a larger cousin, has a similar sized population and, like New Zealand, sees biotechnology as an important focus for government attention.

Startling different to New Zealand however is the eagerness of the Irish government to partner with large pharma. Nine of the world top ten pharmaceutical companies have manufacturing plants in Ireland.

While the local pharmaceutical industry employs over 12,000 people, there was, until recently, little or no pharmaceutical discovery performed there but things are set to change (16).

In July 2005 the Irish government announced three large R&D investments in Ireland by pharmaceuticals companies[11]. These included:

a. Bristol Myers Squibb Co. will establish a collaborative biopharmaceutical research program with Dublin University and the National university of Ireland. The project will involve 32 new research positions and funding of over US $10 million.
b. Pfizer Inc. is to invest over US$ 22 million in a high containment development facility which will enable it to have the technical capability and interaction with R&D at an early stage in the life cycle of new products.
c. Genzyme Corp will spend US$8 million to expand its process research and development capability.

It is salient to note that two of the companies above have no presence in New Zealand and the third Pfizer has recently withdrawn all research and development from New Zealand.

[11] Pfizer, BMS and Genzyme launch R&D projects in Ireland. Web release wwww.pharmamanufacturing.com

What therefore are the benefits to New Zealand as a country and its citizens for encouraging pharmaceuticals companies to return and start performing clinical research?

For the patients

✓ Access to new medicines

A patient enrolled in a clinical trial may gain access to a novel medicine often years in advance of when the medicine will be registered and otherwise commercially available

New Zealand has considerably poorer access to medicines than Australia due to restrictions on reimbursement controlled by PHARMAC (10). Due to the unavailability of many new treatments in New Zealand, many patients' only chance of access to the treatment that they require is to either purchase it themselves or be part of a clinical trial.

This is particularly true of diseases that have relatively small number of patients for example Parkinson's disease. In a clinical trial performed in New Zealand not only did patients get access to the new investigational product but also the comparator product. The latter is the "gold standard" treatment currently reimbursed throughout the world for the treatment of Parkinson's disease and only available in New Zealand via this clinical trial.

✓ An extensive medical review process

Evidence suggests that patients have better clinical outcomes when they are enrolled in trials as compared to standard care

Some clinicians believe the best patient care occurs through clinical trials as the focus is not on cost of additional investigations or time spent in hospital but on a rigorously documented outcome.

Furthermore it appears that patients have better clinical outcomes when they are enrolled in trials as compared to standard care. This is due to a number of factors including: closer monitoring and follow-up, the mandatory use of the best treatment in the control arm and lastly, better patient compliance[12].

For clinicians

✓ Access to new medicines

In being part of a clinical trial the specialist gains access to and experience with potential new treatments. Experience and access is gained also for the bench mark medicine that are routinely available elsewhere but otherwise not available in New Zealand. Often the clinician

[12] Professor Harvey White- personal communication

has practiced overseas where such treatments are considered the "standard of care" and wish to incorporate them into their practice here.

✓ Scientific value

One of the many interests a specialist clinician has is being part of the development of cutting edge technology. Their interest in research coupled with the desire for new and improved methods of treatment for their patients means that the potential attractiveness of a job (for example a professorship) could depend on access and resources to conduct clinical research. This is also true of nurses involved part-time or fulltime in clinical research.

Investigator initiated trials are a prime example as to how local pharmaceutical management is extremely important in gaining access to resources that the specialist clinician requires in order to perform a clinical trial with a particular medicine. On occasions, the company will not only supply the medicine free of charge but also contribute to the overall cost of performing the trial. Without local management support, and unless the relationships with key departments corporately are established, the chances of resource support are slim.

Often instead of having to set up specific local trials it is possible to "piggy back" local research questions to that of large multinational pharmaceutical trials, enabling the local researcher to perform unique research that leads to the development of international expertise. An example is cardiovascular researchers in Christchurch becoming world leading in the development of the use of BNP (brain natriuretic peptide) as a biomarker in cardiovascular disease.

✓ Economic value

All clinical research has an infrastructure cost. Economies of scale indicate that the more trials one is able to perform the relatively cheaper it is to maintain a good quality staff and facilities. Multiple research grants also allow a researcher to allocate more funds to non-subsidized research of their own choosing. Hence a paucity of pharmaceutical clinical trials to perform means the fixed costs of maintaining a high class clinical trial research unit begin to become untenable meaning highly trained staff are let go or move overseas and New Zealand's capacity to perform research declines.

✓ Education Value

A healthcare environment which consistently introduces junior doctors to clinical research produces many leaders in their field in medicine (19).

Being involved in clinical research enhances communication with colleagues throughout the world, via investigators meetings (which are usually held as international meetings abroad) and on issues of mutual interest which fosters benchmarking by New Zealand clinicians about what is standard practice in the medical world. This active involvement enables the assimilation of new knowledge and techniques from overseas more rapidly that otherwise would have to be gleaned passively from journals or overseas conferences.

Practicing clinicians alter their medical practice on the results of clinical trials. There is increasing evidence to suggest that those clinicians involved in research alter their clinical practice significantly before the results of the clinical trials are published (18). Therefore such clinicians practice medicine theoretically in advance of those not involved in clinical trials. Thus taking part in biomedical research aids the up-skilling of doctors and nurses not only in the latest treatments available but also in the scientific rationale behind the treatments.

A spin off of the relationship with local pharmaceutical companies is the potential support of a range of medical education programs in New Zealand that otherwise would not happen. This includes the resource and support clinician and study staff training in key areas of clinical trial management (GCP/ICH) and other regulatory guidelines essential for maintenance of standards in health research in New Zealand.

For Hospitals

✓ Treatment costs

The cost savings to a public hospital generated by enrolling patients in clinical trials should be a significant driver of increased demand *by the hospital managers* for clinical trials- something that seems to have not been registered on the financial radar of nearly all New Zealand hospitals.

In the USA due to the complexity and involvement of private insurance there is a sustained debate about the cost benefit of performing clinical research (17). However outside of the USA especially in publicly funded health care systems like New Zealand there is a strong economic argument for a robust clinical trial environment.

Outside of America when a patient is enrolled in a pharmaceutical clinical trial all the associated treatment costs and in the majority of cases, the pharmaceutical costs become the responsibility of the sponsoring pharmaceutical company. Often trials of new medicines involve comparison against current "standard of care" In these trials the cost of the standard of care medicine (that is the medicine the patient would have received and paid for by the government if they were not in a trial) is also paid for even if it is rival company's product. This results in potential significant cost savings to hospitals at a time when pressure on hospital budgets to control spiralling healthcare costs seems to be greater than ever.

Several international studies have indicated that for a range of medical conditions such as community acquired pneumonia or even essential hypertension, enrolment in pharmaceutical clinical trials actually saves the hospital and the health system money (20,21).

This is often a significant amount of money especially in areas like oncology where new medicines tend to be very expensive. Oncology clinical trial patients will not only have access to the latest development in pharmaceutical care but at no cost to the hospital (or patient) in terms of treatment costs (radiology, clinical input, overhead expense) and significantly reduced, and in many instances no pharmaceutical cost. This means that scarce financial resources which normally would be used to treat these patients can be utilised elsewhere to treat other patients.

In America approximately 5% of patients with cancer are treated in a clinical trial (17); this figure reaches nearly 14% in the UK. In New Zealand the figure is probably less than 1%. If however a robust clinical trial environment was encouraged and New Zealand oncology patients reached the same levels of involvement as America this would equate to a saving for District Health Boards approaching tens of millions of dollars- money that can then be spent else where.

Furthermore a robust clinical research environment engenders the development of private clinical research centres (CRC). These should be especially interesting to budget conscious public hospital managers for two reasons. Firstly the CRCs bear the financial risk of all clinical trial management and tasks. Secondly by the very nature of performing clinical research the CRCs take clinical trial participants and hence associated costs out of the public hospital 'circulation" for the specific disease for the duration of the trial which is often a significant period of time.

For New Zealand

Biomedical research is good for the economy. Evidence from America indicates that for every dollar spent on health R&D returns at least $5 in national economic benefit (22).

Outside of the economic benefits in order to restore and hopefully enhance New Zealand's reputation in the health research world, clinical research and partnering with pharmaceutical companies is absolutely vital.

There is inadequate funding to retain and attract leading professors and researchers who otherwise struggle on government health funding. Indeed, a significant amount of researchers' time in this country is spent trying to write grant applications for the relatively small pool of research funding.

Sustainable relationships with pharmaceutical companies allows New Zealand to be part of worldwide initiatives such as the Wellcome Foundation. These types of programmes are becoming increasingly difficult to attract to New Zealand due to the government's policies of medicine reimbursement and the subsequent impact on the business environment.

Access to more resources will enable up-skilling of New Zealand health researchers via both training and financial programmes. As illustrated in the Singapore example, it also attracts highly skilled immigrants to work in New Zealand in the health research sector. These issues are key platforms of the government initiative termed the Knowledge Economy drive.

6 The flow-on effects of the disinvestment by pharma in New Zealand.

In the current environment, it is inevitable that the amount of money currently available to health researchers will not create a sustainable biomedical R&D environment in New Zealand. There will be more reliance on government funding and less attraction of private industry investment.

Added to this there will be a:

✘ *Continued "brain drain"*

The attraction for science graduates and local researchers to take their skills abroad (where funding and resources are more accessible) is growing. While there has always been the potential for such a situation to occur, by actively shutting out the pharmaceutical industry (the biggest spender on health R&D in the world) the government is effectively increasing the exodus of health science from New Zealand.

Hence for those clinicians who see clinical research as an essential aspect of their professional lives the negative environment of lack of biomedical support becomes a strong driver to push them off shore. An example is world-renowned cardiovascular researcher, Professor Stephen MacMahon, who in 2000 left New Zealand for Sydney due to the difficulty in securing long term funding (23).

✘ Lack of educational support

Another spin-off of locally managed pharmaceutical companies leaving New Zealand is the support of educational activities they have previously funded. A major pharmaceutical company has recently withdrawn its funding of professorial chair in one of New Zealand's leading universities.

As the government maintains its inflexibility through PHARMAC, pharmaceutical company relationships with universities (such as support of graduate programs and scholarships) are slowly dying out and there is nothing to replace the vacuum.

As companies disinvest there is also less likelihood for sponsorship to help doctors and researchers to attend international meetings or to hold medical meetings of an international standard in New Zealand.

✘ Lack of non-government organisation (NGOs) support

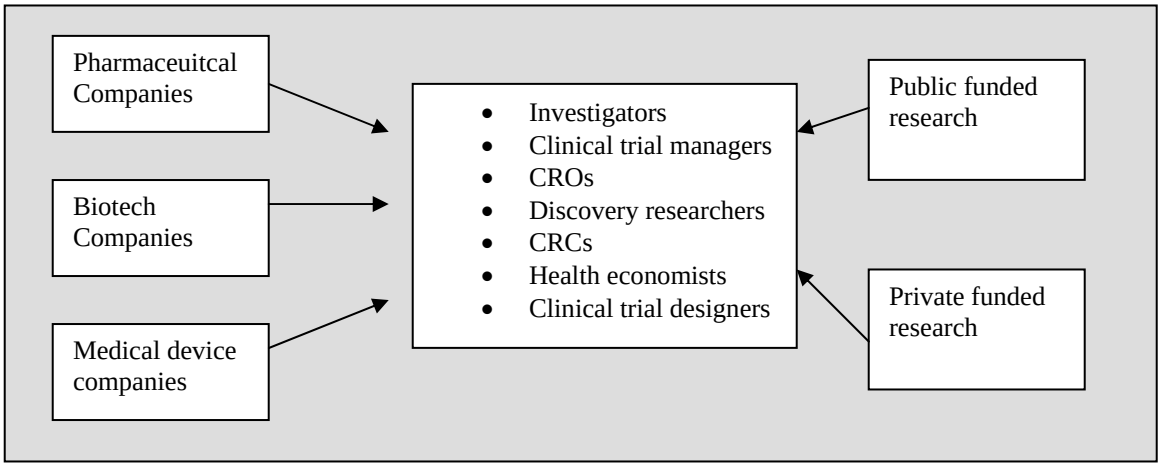
Traditional pharmaceutical companies have supported a variety and range of NGOs but research related public health related. Examples are GSK and Youthline, Pharmacia and The Arthritis Foundation. Again such funding is put in jeopardy as the number of pharmaceutical

companies in New Zealand dwindles. This will result in patient support organisations vying for an increasingly smaller pool of funding.

✘ Lack of clinical trial management infrastructure support

Publicly funded and privately funded research utilise the same research infrastructure- (Figure 6). It follows therefore that the less privately funded research that is performed, more publicly funded research need to be available in order for the viability of the research model to continue.

Figure 6 Interrelationship of Clinical research staff



Unfortunately the international pharmaceutical industry today looks on New Zealand as somewhat of a pariah. Due to the perceived New Zealand government's hostility, as embodied in PHARMAC, most internationally based pharma companies would rather invest their R&D spend in almost any other country but New Zealand. In such an environment, without bidding for research by local management, R&D activities in New Zealand and importantly New Zealand's ability to perform them will fade.

As Professor Mark Richards commented (23)

"As a consequence [of government policy] and in contrast to other OECD nations where the pharmaceutical companies plays a major role in collaborative support of biomedical research, there is currently a major 'disinvestment ' by the industry in New Zealand"

As the infrastructure to perform health research is dismantled in New Zealand the obvious down stream effect is that New Zealand will no longer be perceived to be a good place to perform any health research due to a paucity of suitably trained people. This will have flow on effects for the biotech sector, the medical device industry and health research in general.

Biotech companies, especially in early in the company life cycle, do not have the internal resources to sustain internal clinical trial management – hence the need to often outsource the clinical trial production and implementation to a clinical research organisation (CRO).

The main source of clinical trials for CROs on a global basis, still however is large pharma. Indeed the model of pharmaceutical development seems to indicate that pharma are increasingly viewing the "bottleneck" of clinical trial development as being better handled by external (CRO) resources rather than an internal research and development unit (24). This fashion to outsource clinical research may further be encouraged as large pharma consolidate and the new merged companies try to control fixed costs.

While this trend is noted globally there is little to suggest that the CRO industry in New Zealand is following suit, One of the major reasons is that pharma companies with some presence in New Zealand, are choosing not only to not provide internal resources for clinical trial research, they are not prepared to do perform much research at all here.

Thus biotech companies basing themselves in New Zealand suffer a double blow. Firstly partnerships with big pharma are coloured by New Zealand's policy for reimbursement of pharmaceuticals. Secondly there is a lack of local clinical trial management resource and skills that allows the biotech companies to use the one competitive advantage being located in New Zealand affords them: cost competitive clinical trial production.

✘ Lack of international support for biotechnology growth

Biotechnology is the current focus of an intense government effort. However, it is very possible that without the support of pharmaceutical companies a sustainable environment will not be created for biotech in this country. This is mainly due to two factors: one is money, and the second is the lack of scientific commercialisation expertise.

The biotech industry is a high technology industry, developing as an outgrowth of the international biomedical R&D industry. A strong local R&D system modelled and integrated with international best practice and involvement will result in the high technology industry growing faster and to become more embedded in New Zealand. One of the reasons that the US has become the world leader in high technology industry is because of the strong feedback loops (R&D programs, tax incentives, patent protection) between government, universities and the existing high technology industry. This model is now being implemented in Denmark and Germany, with the latter, producing over 300 new biotech companies in the last ten years.

Another example of the success of feedback loops is The Massachusetts Institute of Technology. MIT has created over 4,000 companies in the past four decades. These companies have an annual turnover of $240 billion and employ 1.1 million people (25). In comparison these feedback loops are extremely weak in New Zealand, or non-existent in relation to the government and the international pharma industry. This means that as the indigenous R&D framework declines the chance of biotechnology as a high technology industry becoming embedded in New Zealand becomes less and less.

As outlined earlier, the costs involved in pharmaceutical development are huge, and these same costs apply to the biotech companies. Many are at the early stage of pre-clinical activities that (in comparison) are relatively inexpensive. However once the biotech company has a viable pharmaceutical candidate, it then needs to perform extensive human studies. This means the biotech company needs an investment vehicle that is either prepared to

partner the medicine through its development *or* assign the biotech company enough money to complete the development itself. In both cases there is only one industry that would currently provide such a partnership - the pharmaceutical industry.

It is a salient feature of the New Zealand biotech market place that when compared to Australia, the number of New Zealand based companies is notable by their absence. Over 100 Australian based biotech companies are listed on the ASX; New Zealand does not possess a tenth of that. In other words while New Zealand may possess all the building blocks for successful biotechnology ventures, the political environment has created a significant barrier that very few companies can overcome.

It is certainly possible that the government may be able to create start up funding in terms of facilities or seeding grants, but in reality, without the downstream partners who have the experience in and the capital to support the commercialisation of novel products, the biotech industry will be consigned to an expensive experiment that never quite got there.

New Zealand is not alone in trying to build a biotech industry. There is significant competition in trying to attract suitable partners. New Zealand is alone in the world in its policy to discourage partnerships with the largest resource funder of biotechnology: the pharmaceutical industry.

On the scientific commercialisation front it is probably prudent to note that nearly all successful biotech companies anywhere in the world have ex-biotech or more commonly ex-pharmaceutical staff as their senior management.

7 Is the Wrong Ministry in Charge of Health Research?

The significant negative effects of PHARMACs policies raise the question as to why the New Zealand government has not attempted to rectify the situation in any meaningful way. Perhaps the answer lies in the organisational structure of health funding in New Zealand

The effects of PHARMACs policies have been targeted solely to reduce the spend on pharmaceuticals: the area of responsibility of the Ministry of Health (MoH). The flow on effect of marked restriction of market access to pharmaceuticals companies is a restriction to clinical trial access to New Zealand researchers and patients. This latter aspect as discussed above impacts adversely also on other biomedical enterprises including biotech companies.

The responsibility for research and scientific endeavours however (both agriculture and health) however falls under the auspices of the Ministry of Science and Technology (MoRST). Various studies undertaken by the New Zealand Treasury indicate the difficult of achieving re-allocation of resources in the New Zealand public finances. even when the same department is in charge of multiple (yet siloed) budgets. Hence a real issue in New Zealand's biomedical research environment in that MoRST, responsible for research endeavour, has no direct role or influence over one of the biggest dampeners on private biomedical research investment- pharmaceutical reimbursement policies and PHARMAC.

8 Summary

The New Zealand Government policy on the pharmaceutical industry that is so heavily imbedded in PHARMAC is reaching a “watershed”. Increasingly pharmaceutical companies are linking the placement of clinical research with the prospect of the product in clinical development being reimbursed in the country.

While rhetoric from the government has been forth coming there has been no evidence of a change in the government stance that offers any encouragement to pharmaceutical companies to reverse these trends and restart their investment in biomedical programs and partnerships.

Clinical research is vitally important to the health system in New Zealand. It could be a major contributor to hospital cost control, it could help retain and develop some of our brightest and most able clinical researchers and it could help sustain the biomedical infrastructure. Importantly it could enable New Zealanders access to novel medicines years in advance of those medicines being routinely available.

In the last few years it has been increasingly clear that it is impossible to have PHARMAC in its present form and also have a robust biomedical environment from which to develop a sustainable local biotechnology industry.

Increasingly New Zealand based biotechnology companies needing to partner with large pharma to move their product through its cycle of development are finding that while their science may be attractive, being based in New Zealand is a hindrance to such a relationship.

Hence New Zealand has a choice:

- Back PHARMAC and its extremely restrictive policies of pharmaceutical access as is currently the case. In doing so New Zealand will continue down the road of alienation, intransigence and ultimately marginalisation in the race for an economy built on scientific success and the knowledge economy, trumpeting about occasional successful biomedical ventures which, by their infrequency, illustrates the point or.

- Draw back from the brink, work out the relationships with pharmaceutical companies, help retain its top researchers and develop the health research landscape that could not only evolve into an embedded local biotechnology sector but is also so important to the future success and health of New Zealanders.

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Appendix 1 Pharmaceutical Oncology Trials currently underway: North America based Companies

Company	No of medicines in development	Target Cancer	Development Phase
3 m Pharmaceuticals	1	Me	I
Abbott Laboratories	2	Pr, Bn, R, L, O	II
Advanced Life Sciences	1	Me	I
AEterna Labs	1	NSC	III/NCI trial
Agouron Pharmaceuticals	2	NSC, L, Pr,	III
Alfacell	1	Mes, NSC,	I-III
Allos Therapeutics	3	Bn, Ce, GBM	1-IIINDA
American Bioscience	1	NSC	I/II
Amgen	**2**	**GI, CR, NSC**	**I-III**
Angiotech	1	Eo	I
ANorMED	2	MM, Ly, CR, NSC	II-III
Antigenics	3	CR, R, L, Me, Mes	I-III
Aphton	2	Eo, G, Pa, Pr	I-III
ARIAD pharmaceuticals	3	MM, Ly, En, GBM, Sa	I II
Arqule	1	Ce, CR, L, G	I
AstraZeneca	3	Br, CR	I-III
Aton	1	H	II
Aventis Pasteur	1	Me	I/II
Bayer	3	Br, R, Lv, NSC, CML Bn	I-III
Berlex	2	L, Br	NDA
Bioenvision	1	Pr	II
Biogen	**1**	**Bn**	**III**
Biomedica	1	Br, CR, R,	II
Biostratum	1	CR, Me	I
Bone Care International	2	Pr, Br, CR,	I-II
Bristol Myers Squibb	8	G, CR, L, Pr, NSC, O, Pa, Br, R, Br	I-III
Cancer Therapeutics	1	R, Me	II
CancerVax	2	Me, NSC	I-III
Celgene	4	MM, Pr, GBM, Me, MDS	II-III
Cell Genesys	6	Pr, MM, NSC, Pa	I-III
Cell Pathways	1	Pr, R, CLL	II
Cell Therapeutics	4	CR, O, MM, MDS, Nb, CML, Br, O, L, NSC	I-III
CEL_SCI	1	Pr, Head and neck	II
Cephalon	1	Pr, AML	II
Chiron	2	Me, Ly, CR	II
Chugal Pharma USA	2	MM	I-II

Coley Pharmaceuticals	1	MM, NSC, Me	II
Corixa	1	Br	III
CuraGen	1	MM	II
Cytogen	1	Br, MM, Pr	I
DEKK-TEC	1	Br	I
Dendreon	3	CR, Br,, O, Pr	I-III
Direct Therapeutics	I	GBM	III
Eisai	2	Br, CR, NSC	II
Elan	1	Br	III
Entremed	1	Me, NET	I-II
Enzon	1	Me	III
Epimmune	1	CR, L	I-II
Galencia pharmaceuticals	1	Br, Pr	I
Genaera	1	Pr	II
Genelabs	I	L, SC	II
Genentech	3	CR, R, Pa, Br, En	I-III
Genta	3	Br, CR, MM, NSC, R, AML, CLL, Ly, G	I-III
Genvec	1	Pa	II
Genzyme general	2	R, Me, NSC	II
Geron	1	Pr	I/II
GSK	7	Me, R, NSC, Pr, Br, Bl, G, K, L	I-III
GlycoGenesys	2	L, MM, CR, Pr, Pa	I/II
Human Genome Science	2	CR, NSC, L, Ly, MM	I-II
Hybridon	1	Br, Ce, En	I/II
ICN Pharmaceuticals	1	CR	I
Ilex Oncology	1	L, Me	II
ImClone System	1	Me	I
Immune Response	1	Br	I
Immunex	1	L, SC	II
ImmunoGen	2	CR, G, Pa, MM, SC	I/II
Immunomedics	1	Pa	I
Intarcia	1	Br	III
INTRACEL	3	Bl, CR	III-NDA
Introgen Therapeutics	4	Br, Eo, NSC, Pr, Me, L	I/II
ISIS	2	NSC, L, Pr	I, III
IVAX	3	GBM, Br, G , L	I-II
Johnson &Johnson	3	Br, Ov, Sa	II-III
Lescarden	1	K	II/III
Ligand Pharma	2	Br	II
Lorus Pharmaceuticals	2	Pr, Pa	I/II
Lutpold Pharma	1	Me	III
Medarex	5	Me, Pr, CR, NSC	I-II
MedImmune	2	NSC, Pr, Me	II
MGI	1	L	II
Mellennium	3	Pr, NSC, Ly	I/II
National Cancer Institute	61	All	I-III

Neopharm	3	GBM, CR, L	I/II
NeoRx	1	MM	III
Neurocrine Bioscience	1	GBM, K, L	II
Northwest Biotherapeutics	2	GBM, Pr	II-III
Novacea	1	NSC, Pr	II
Novartis	4	Br, H, CR	II-III
Novelos Therapeutics	1	NSC	I/II
OSI Pharmaceuticals	3	L, Pr, G	II
OXIGENE	1	Br, Ce, CR, L,O, Pr Thy	I/II
Peregrine	1	Br, CR	I
Pfizer	11	K, L, Me, Pa, Thy, L, H, Pr, Br, G	I-III
Pharmacyclics	2	Ce, Pr, Br, GBM, MM, NSC, K, CLL, Ly	I, III
Progenics	2	Me, Pr	I, III
Raven	1	AC	I
Salmedix	1	Mes, Br, NSC, Pa	II
Sanofi Pasteur	2	Cr,	I-II
Sanofi-Aventis	3	G, Br,	II-III
Schering Plough	2	Me, NSC, Le	II-III
Seattle genetics	2	HD, Ly, MM	I-II
Serono	1	Br, Pr	II
Shire Pharmaceuticals	1	Pr	III
Southwest Oncology	1	Me	III
Spectrum	2	Bl, Pr	II
SuperGen	3	CR, Pa, NSC, Thy, Le	I-III
Telik	1	Br,CR, NSC,O	II/III
Therion	2	Br, CR, L, Pa, NSC	III
Titan	3	Br, CR, NSC, CLL	II-III
Transgene	1	Pr	II
TransMolecular	1	GBM	II
Triangle Pharmaceuitcals	I	Br, L, NSC	II
Tularik	2	Eo, Lv, O, Ly	II
United Biomedical	1	Pr	I
United Therapeutics	2	BR, Me	I
Vertex Pharmaceutical	1	H	I
Vical	1	Me	II
Vion	1	Pa	II
Viventia Biotech	3	Me, Br, Bl	I/II
Wyeth	8	Br, K, Pr, sa, L, NSC, CR, Pa, CML	I-III
Zivena	1	NSC	I/II

Compiled from data available at www.innovation.org. Accessed September 3rd 2005

Key

Cancer Type	Code	Cancer Type	Code
Gastric	G	Glioblastoma Multiforme	GBM
Colorectal	CR		
Lung	L	Brain	Br
Prostate	Pr	Gastrointestinal	GI
Non- small cell	NSC	Gastric	G
Ovarian	O	Cervical	Ce
Pancreatic	Pa	Lymphoma	Ly
Breast	Br	Eosophageal	Eo
Renal	R	Haematological	H
Bladder	Bl	Liver	Lv
Melanoma	Me	Neuroblastoma	Nb
CML	CML	Neuroendocrine Tumour	NET
Muliple Myeloma	MM		
Small cell	SC	Small Cell	SC
Endometrial	En	Mesothelioma	Mes
Thyroid	Thy	Leukaemia	Le
Adenocarcinoma	AC	Hodgins disease	HD