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Chairman's Report 2005

In my report for last year I made reference to administrative changes in the Foundation. I am pleased to be able to report that these have been completed and have greatly enhanced the work of the Foundation and reduced the workload of several of the Trustees who undertook secretarial, administrative and record-keeping duties on a voluntary basis.

The Foundation's professional administrator and secretary to the Board of Trustees has most effectively transformed our records and databases as well as our fundraising systems. These developments have made possible continuous fundraising and tracking of grants made to researchers, and regular oversight of their progress reports.

Fundraising this year has had limited success: prior to Christmas 2004, many charitable organisations had nation-wide appeals supported by intensive television and door-to-door campaigns; furthermore, over the Christmas and New Year periods, the tragic consequences of the Indonesian tsunami deservedly attracted much public attention and financial support which might otherwise have been available for local charities. In spite of this, our Foundation has had some support from private donors to whom we are deeply grateful.

One half of the total funds, which are provided by the Foundation to researchers, continue to be made available to us by Trust Waikato. This Trust's support has made it possible for us to provide seed funding for many research projects which have established the credibility they need to obtain larger grants from national and international sources. The largest grants we have made are for $30,000 for one-year projects, a few of which have been so successful that they have merited further funds from us which have allowed them to continue work to full implementation as treatments for medical conditions.

The Research Grants Committee of our Foundation continues with its work with the efficiency and goodwill to which we have become accustomed. All applicants for grants are required to provide referees' reports and ethical approvals to the standards of the national Health Research Council. We continue to receive more applications of high standard than we can support. To members of the Grants Committee I extend my thanks for their excellent work.

The Finance and Investment Committee has a much lighter workload than it had formerly. The decision to invest in highly rated bonds, rather than in the share market, has guaranteed a steady income without the fluctuations in returns which characterise share market investments. None-the-less, oversight of our policy is still required and I thank members of the committee for their diligence in this. Management of our finances is in the hands of the Treasurer, and I am most grateful for the smooth transition of the role to Rosanna Baird who has carried on the exemplary work of her predecessor in this role.

It is the policy of the Foundation to appoint new trustees as long-serving members retire. This year, we are pleased that Dr Michael Jameson has joined the Board.

For some years Dr Cathy Coleborne, our historian and archivist, has undertaken the major role of preparing for publication the Annual Report, and I thank her for her work in this regard.

To all Trustees I record my gratitude for their continuing contributions to the work of the Foundation.

Michael Selby
Chairman

Year 2005 **Report of the Grants Committee**

I was proud to convene this years funding round with excellent help from each member. Once again there was a wide range of content in the applications which covered health in its broadest sense and also medical research. We were able offer funding to the best eight of 14 requests to a value of $132,000. We were particularly pleased to offer help to two young investigators. Grants involve research into dental health, cancer protecting dietary factors and discovering anti-cancer active compounds in marine plant life. Another project investigates psychological precipitating factors in medical illness.

Medical projects investigate pituitary tumours, severe sepsis, treatment of poisoning and stages of sleep. Yet again projects were supported from a range of institutions namely Agresearch Ruakura, Waikato University, Health Waikato and the Psychology Centre. The committee wishes the investigators all success in their projects.

Noel Karalus

Chair, Grants Committee

Outcome Reports for Recent Grants

Intralipid vs sodium bicarbonate as rescue therapy in rabbit model clomipramine toxicity

Martyn Harvey
Emergency Medicine
Waikato Hospital

Tricyclic antidepressants are drugs commonly prescribed in the treatment of depression and chronic pain syndromes. In overdose they are associated with significant cardiovascular toxicity. Fatalities occur despite aggressive supportive care and administration of sodium bicarbonate, the current standard antidote.

Intravenous lipid emulsions have shown experimental promise in the treatment of a number of lipid soluble drug toxicities in animal models. Our research group has demonstrated the benefits of Intralipid (a lipid emulsion) in rat models of thiopentone (an anaesthetic) and verapamil (a cardioselective calcium channel blocker) overdose. The proposed mechanism for the beneficial effect of lipid emulsions is the formation of a new lipid compartment within the vascular system in which drugs are sequested.

Clomipramine is a lipid soluble tricyclic antidepressant and as such is likely to respond to treatment with lipid emulsions. In this experiment we plan to determine if, in a rabbit model of clomipramine toxicity, lipid emulsion therapy is useful as an antidote.

Methods: We plan to induce clomipramine toxicity via controlled overdose in anaesthesised rabbits. Features of cardiac toxicity will be specifically monitored. Rabbits will then receive either Intralipid or sodium bicarbonate as an antidote. A group of rabbits will receive both Intralipid and sodium bicarbonate to determine if combined treatment is superior to either treatment alone.

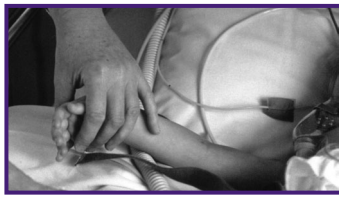
Outcomes: We plan to monitor pulse, blood pressure, and ECG measures of clomipramine toxicity. Following the completion of the experiment a blood sample will be taken to determine blood clomipramine levels.

Expected Benefits: This study aims to demonstrate the effectiveness of Intralipid as an antidote in clomipramine overdose. Comparison will be made with the current standard sodium bicarbonate, and with combined therapy with the two agents. A positive result may lead to the development of new treatment options for human patients with tricyclic antidepressant overdose. Additionally, measurement of drug levels may help to determine the mechanism by which Intralipid acts as an antidote.

Outcome Reports for Recent Grants

An investigation into the health benefits of mindfulness-based stress reduction (MBSR) for a specific range of chronic illnesses

Philippa Thomas
Clinical Psychologist
The Psychology Centre, Hamilton



There is a growing body of evidence suggesting that Mindfulness-based Stress Reduction (MBSR) is effective in alleviating suffering and improving coping related to a broad range of chronic illnesses. For example, Grossman, Niemann, Schmidt, and Walach, in a meta-analysis of studies examining the health benefits of MBSR, published in the Journal of Psychosomatic Research in 2004, identified consistent and relatively strong effect sizes. This analysis noted improvements across psychological health measures (of, for example, quality of life, depression, anxiety, and coping styles) and health outcomes (for example, pain, physical impairment, medical symptoms, and functional quality of life). Further, in a 2003 meta-analysis published in Clinical Psychology: Science & Practice, Baer described MBSR as a cost-effective, group-based approach that can be delivered to clients presenting with a range of difficulties. However, she noted that many studies contained methodological flaws, and concluded that studies addressing key areas (such as the use of control group designs, adequate sample sizes, and evaluation of integrity of treatment and clinical significance of the effects of change) would increase confidence in future findings.

There is limited evidence to date that MBSR is effective with New Zealand populations, and with some kinds of problems. This pilot study will teach people with some specific chronic health problems (such as Graves disease, chronic pain, cardiac problems, and type 2 diabetes) how to practise MBSR techniques. The study will monitor the impact of this training and practice on participants' physical and psychological health over the 8-week period of the MBSR programme. Participants will be followed up one and six months after the end of the programme to see if they are still using MBSR techniques, and to find out how effective they are. If the results of participants in this NZ pilot study suggest that learning MBSR techniques has positive effects on their physical and psychological health, then the study will be continued with the aim of demonstrating conclusively the positive benefits of MBSR for New Zealanders with chronic health problems.

Baer, R.A. (2003). Mindfulness training as a clinical intervention: A conceptual & empirical review. *Clinical Psychology: Science & Practice, (10), 125-143).*

Grossman, P., Niemann, L., Schmidt, S. & Walach, H. (2004). Mindfulness-based stress reduction & health benefits: A meta-analysis. *Journal of Psychosomatic Research, 57, 35-43.*

Outcome Reports for Recent Grants

Identification of biomarkers associated with active phases of periodontal disease

Dr Brendan Haigh and Dr Tom Wheeler (AgResearch)
Dr Kevin Stewart (Wintec)
Dr John Whelan (John R. K. Whelan Periodontics and Dental Implants)

Periodontitis is a common disease resulting from bacteria-induced inflammatory destruction of the tissue supporting the teeth. It can cause a range of symptoms from mild gum bleeding through to severe pain and loss of teeth. Periodontitis is episodic in nature; periods of inflammation and tissue destruction can alternate with periods of minor activity. It is difficult to assess disease activity without detailed ongoing clinical examination.

If there was a simple, non-invasive marker for periodontal disease activity, a clinician's ability to identify individuals with active periodontal disease and to monitor the effect of periodontal therapy would be greatly improved. This would be of significant benefit to both clinicians and patients. One approach to identifying markers for periodontal disease activity is to examine the protein profile of saliva from individuals with active periodontal disease. Saliva has an important role in controlling how tissues in the mouth respond to bacteria and it is likely that certain proteins will be expressed in saliva during active periods of periodontal disease.

These proteins may serve as 'biomarkers' for the development of simple saliva-based assays for periodontal disease activity. In this project we are going to use a powerful approach called proteomics to search for biomarkers in saliva from periodontal patients. This approach will allow us to compare a large number of the proteins expressed in saliva in a single experiment (over 600 different proteins can be detected in human saliva).

By comparing saliva samples obtained from periodontal patients before they have treatment (when the disease is severe) to a second saliva sample obtained after they finish treatment (when the disease has retreated) we can see which of those 600 proteins has gone up or down in concentration. These proteins will be our candidate biomarkers, as their expression appears to be linked to active periodontal disease. These candidate biomarkers can then be evaluated in further studies to assess their suitability as markers for active phases of periodontal disease.

Detailed Outcome Report

Experimental verification of theoretically modelled sleep-cycle transitions

Logan Voss
Department of Anaesthesiology, Waikato Clinical School, University of Auckland

Although we spend about a third of our lives sleeping, we cannot answer the most basic questions: why do we need to sleep? What happens in the brain as we cycle from quiet slow-wave sleep (SWS) to rapid eye movement (REM) sleep? We may be able to answer some of these questions by comparing natural sleep with a mathematical model that has been developed by Waikato scientists to describe the “enforced” sleep brought on by anaesthetic drugs. The anaesthetic-induced change in brain state from consciousness to coma seems to have deep similarities to general phase changes in physics – such as water freezing to form ice. If we can show that in natural sleep there is a phase transition between slow-wave sleep and REM sleep, this may lead us to better understand why the brain needs to sleep.

As part of a Marsden funded project ("The physics of sleep cycles" Moira Steyn-Ross, lead investigator) a number of predictions have arisen from the theoretical development. The overall aim of this project is to experimentally test these theoretical results as described below.

1) The transition from slow-wave sleep to REM sleep involves a phase transition in the cortex, as evidenced by a non-linear cortical response to linear input from the brainstem (pedunculopontine tegmental nucleus).
2) Activity of inhibitory interneurons and excitatory pyramidal neurons are strongly correlated in slow wave sleep, and uncorrelated in REM sleep.
3) Deep slow-wave sleep is associated with synaptic plasticity; leading to cortical remodelling that is necessary for the continuing function of any finite network.

By testing the above predictions, we hope to verify or falsify the accuracy of the theoretical model.

Detailed Outcome Report

Identification of molecular genetic markers in pituitary adenoma subtypes with high-density cDNA microarrays

Marianne S Elston (Endocrinology Department, Waikato Hospital, Hamilton)
Bruce G Robinson (Cancer Genetics Unit, Kolling Institute of Medical Research Royal North Shore, St Leonards, Australia)
John V Conaglen (Endocrinology Department, Waikato Hospital, Hamilton)

Pituitary tumours are common (approximately 10 - 15% of brain tumours). They can significantly shorten lifespan by interfering with hormone secretion causing either excess- or under-production of hormones. In addition pituitary tumours may affect quality of life, in particular by causing blindness from compression of the optic nerves. Commonly there is a delay in diagnosis with patients suffering from headaches, visual loss and the effects of abnormal hormone levels for months or even years.

Most pituitary tumours are "benign" adenomas and whereas some pituitary tumours demonstrate slow growth with minimal change in size over years to decades, other adenomas show aggressive growth with rapid compression of normal surrounding structures causing significant morbidity. As currently we do not have any way of predicting the behaviour of a pituitary adenoma for an individual patient, frequent clinical and radiological assessments are necessary to establish the pattern of tumour growth.

Despite advances in medicine, many patients with pituitary tumours still need invasive surgery and/or radiotherapy directed towards the pituitary gland despite the fact that these tumours are almost always benign. Understanding the gene expression pathways (and possible genetic mutations) in pituitary tumours offers the opportunity for earlier diagnosis, improved prognostic information for individual patients and the potential for intervening by using drugs to modify cell function, such as the use of Glivec in chronic myelogenous leukaemia. Medical treatment rather than the need for invasive surgery, would offer a significant advance for patients suffering from pituitary tumours.

The 4 most common pituitary tumour subtypes (non-functioning, prolactin-, GH-, and ACTH-secreting) will be investigated using a 20 000 gene cDNA microarray to look for expression changes within tumour subtypes and compared to normal pituitary tissue. Statistical tools will then be applied to isolate genes consistently changed within a single tumour subtype. These genes will be further isolated and studied using established techniques with a view to detecting molecular markers to enable earlier diagnosis. This data will potentially provide the foundation for the development of reliable prognostic indicators and even more importantly, the basis for more rational therapy options.

Detailed Outcome Report

Induction of cancer-protective enzymes by vegetable components

Rex Munday
AgResearch, Ruakura Research Centre, Hamilton.

There is increasing evidence that fruit and vegetables are beneficial to our health. In particular, a high intake of these foodstuffs is associated with a decreased risk of contracting cancer. Such evidence has led public health authorities to promote fruit and vegetable consumption, as in the "Five-a-Day" campaigns. There is, however, a lack of knowledge as to the mechanisms whereby these foodstuffs exert their beneficial effects.

We are all continually exposed to chemicals that cause cancer. They are present in our food and in the atmosphere, and they are produced in our bodies by the natural processes of metabolism. We are protected against these chemicals by a family of enzymes, which break them down into harmless substances that are rapidly eliminated from the body. If, however, our enzymatic defences are weak, they will be overwhelmed by the carcinogenic chemicals and cancer will ensue. If we could increase the tissue levels of these enzymes, the body's defence against carcinogens would be strengthened, and our risk of developing cancer decreased.

In work previously supported by the Foundation, we found that tissue activities of these protective enzymes were increased in rats fed compounds derived from plants of the onion family and of the cabbage (Brassica) family. We have recently shown that compounds derived from cabbage-related vegetables are particularly effective in increasing enzyme activity in the urinary bladder. This is very interesting, because epidemiological studies have shown that people who eat a lot of Brassica vegetables have a lower incidence of bladder cancer than those who eat only a little. There is also evidence that Asians, who have a particularly high dietary intake of cabbage-related vegetables, are much less likely to contract bladder cancer than Westerners. Bladder cancer is a common problem in the West, being the fourth commonest cancer in men and the eighth commonest in women. Approaches toward diminishing its occurrence would be very valuable.

We have looked at the effect of feeding a number of vegetables, including broccoli, cabbage, radish, daikon, mustard, watercress, rocket and garden cress, on bladder enzyme levels in rats. All the vegetables increased the activities of the beneficial enzymes, but there was a big difference among the various vegetables in their inductive activity, with garden cress being the best of those studied. We now plan to look at other Brassica vegetables, particularly those related to garden cress and those eaten in Asian countries. We will also investigate the minimum amounts of the vegetables required to produce an effect in rats, so that we can relate this to the amounts that are normally consumed by humans.

Our experiments will shed light on the mechanism of the beneficial effects of vegetables, and lend support to the campaigns to encourage consumption of such foodstuffs. Furthermore, our work on different vegetables may lead to the identification of particular foodstuffs that are especially beneficial in protecting against cancer, particularly cancer of the bladder.

Detailed Outcome Report

Natural Products from Pacific Flora and Fauna

Michèle Prinsep
Chemistry, University of Waikato

At the Chemistry Department of the University of Waikato, Dr. Michèle Prinsep and her students are undertaking research towards finding bioactive and/or novel metabolites from natural sources. The work primarily focuses on two different types of organisms, both of which have proven to be excellent sources of novel, bioactive compounds: marine bryozoans (moss animals) and terrestrial cyanobacteria (blue-green algae). Whilst most emphasis is still on these, the project is being expanded to include investigations of other marine organisms.

Bryozoans are collected from New Zealand waters, while cyanobacteria will be collected from so-called "algal blooms" in lakes and other water bodies in the greater Waikato region. All samples are extracted in a suitable solvent and the crude extracts are tested for a wide variety of biological activities, including antitumour, antiviral, antibacterial and antifungal activity. The range of assay systems employed is being expanded to encompass those with an emphasis on different therapeutic areas, including assays which focus on the modulation of mitochondrial stress and inflammatory processes, especially central nervous system (CNS) processes relating to hyperglycemia and oxidative stress.

Once a promising extract has been identified, it is investigated further to isolate the compound/s responsible for the observed biological activity. This involves large-scale extraction, then separation and isolation of the active component/s. The biological activity must be monitored at every step of the isolation process to ensure that it is being concentrated and that no loss of activity occurs.

When a pure biologically active compound is isolated, its structure is determined using a variety of instrumental techniques, especially high field nuclear magnetic resonance (NMR) spectroscopy. If possible, analogues of the isolated compound are prepared to see if the activity can be improved. This research will identify potential pharmaceutical compounds or useful chemicals for biomedical research into the mechanisms that cause and promote cancer and other diseases.

Collection and screening of samples are essential and expensive aspects of this research which are made possible by funding from the WMRF.

Waikato Medical Research Foundation (Inc)

Financial Statements

For the year ended 31 May 2005

Contents	Page

Statement of Financial Position

As at 31 May 2005

	2005	2004
	$	$
Accumulated Funds	$1,220,661	$1,186,350
Represented by:		
Current Assets		
Westpac	37,686	23,240
Investments		
Cash and Equivalents	46,851	96,818
Fixed Income	974,468	939,452
NZ Shares	163,456	128,020
	1,184,775	1,164,290
Total Assets	1,222,461	1,187,530
Current Liabilities		
Accounts Payable	1,800	1,180
Net assets	$1,220,661	$1,186,350

M J Selby
Chairman

29 June 2005

R Baird
Treasurer

27 June 2005

Statement of Movements in Equity

For the year ended 31 May 2005

	note	2005 $	2004 $
Accumulated Funds:			
Opening balance, 1st June 2004		1,186,350	1,210,137
Plus: Net surplus/ (deficit)		34,311	3,178
Revaluation of Investments		-	(26,965)
Closing balance, 31st May 2005		$1,220,661	$1,186,350

Statement of Financial Performance

For the year ended 31 May 2005

	note	2005 $	2004 $
Income			
Dividends		10,296	3,372
Donations	3	17,150	21,572
Grant - Trust Waikato		65,000	65,000
Grants refunded		6,074	-
Interest		72,051	60,891
Income on realisation of Investments		337	-
Unrealised gain on Investments		19,022	-
		189,930	150,835
Expenditure			
Administration expenses including website		12,255	2,299
Advertising and promotion expenses		2,508	6,691
Audit fee		1,654	1,575
Fees paid to auditor for other services		5,490	5,555
Grants	2	132,124	129,810
Portfolio Management fees		-	1,727
Loss on realisation of Investments		1,588	-
		155,619	147,657
Net surplus/(deficit)		$34,311	$3,178

Statement of Cash Flows

For the year ended 31 May 2005

	2005	2004
	$	$
Cash Flows from Fund Raising Activities		
Receipts from donations and grants	82,150	86,572
Less Fundraising expenses	(2,508)	(6,691)
Net cash flow from fund raising activities	79,642	79,881
Cash Flows from Investing Activities		
Receipts from dividends and interest	82,347	64,263
Plus Sale of investments	191,978	288,309
Less Investments made	(194,692)	(306,719)
Less Portfolio management fees paid	-	(1,727)
Net cash flow from investing activities	79,633	44,126
Cash Flows from Research Activities		
Grants made	(132,124)	(129,810)
Administration and audit fees	(18,779)	(9,429)
Grants refunded	6,074	
Net cash flow from research activities	(144,829)	(139,239)
Net increase/(decrease) in cash held	14,446	(15,232)
Add Opening cash brought forward	23,240	38,472
Ending cash carried forward	37,686	3,240
Cash balances in statement of financial position	$37,686	$23,240

Notes to the Financial Statements

For the year ended 31 May 2005

1. Statement of Accounting Policies

Reporting Entity

Waikato Medical Research Foundation (Inc) is a non profit organisation registered under the Incorporated Societies Act 1908.

General Accounting Principles

The general accounting principles recognised as appropriate for the measurement and reporting of income and financial position on an historical cost basis, except for valuation of investments, have been consistently followed by the Foundation. Accrual accounting has been used to match revenue and expenses.

Particular Accounting Policies

The following particular accounting policies which materially affect the measurement of income and the financial position have been applied.

Investments

Investments are valued at market value in NZ dollars.

Income Tax

The Waikato Medical Research Foundation (Inc) has been approved for legal charitable status and has obtained from the Inland Revenue Department an exemption for income tax.

Differential reporting

The Society qualifies for differential reporting because of it's size and nature. The Society has taken advantage of all available differential reporting exemptions, except in that it has produced a Statement of Cashflow.

Changes in Accounting Policies

The Waikato Medical Research Foundation (Inc) has changed it's policy in relation to the treatment of the gains/losses arising from the revaluation of investments. Previously investments were revalued and the resulting gain/loss recorded as a movement in Accumulated Funds. The gain/loss is now recorded in the Statement of Financial Performance. This change has resulted in a gain of $17,771 recorded as income in the current year.

Notes to the Financial Statements

For the year ended 31 May 2005

2. Grants Made

	2005	2004
	$	$
A Braakhuis	-	12,810
M Cree	-	20,000
R Cursons	20,000	-
G Devlin	-	27,000
M Elston & Associates	20,000	-
B Haigh & Associates	15,228	-
M Harvey	9,750	-
R Munday	25,146	20,000
M Prinsep	15,000	-
R Subramaniam	-	22,000
P Thomas & Associates	15,000	-
L Voss	-	28,000
L Voss & J Sleigh	12,000	-
	$132,124	$129,810

3. Donations

General	7,150	1,572
Bryant Trust	-	15,000
Souter Trust	-	5,000
A Meade	2,000	-
A Oakley	5,000	-
V E Worth Estate	3,000	-
	$17,150	$21,572

4. Commitments & Contingencies

At balance date there are no known contingent liabilities. (2004: Nil)

At balance date there are no known capital commitments. (2004: Nil)

Auditor's Report

STAPLES RODWAY
dynamic financial answers

To the Members of Waikato Medical Research Foundation (Inc)

We have audited the financial report on pages 12 to 16. The financial report provides information about the past financial performance of the Foundation and its financial position as at 31 May 2005. This information is stated in accordance with the accounting policies set out on page 15.

Trustees' Responsibilities

The Trustees are responsible for the preparation of a financial report which fairly reflects the financial position of the Foundation as at 31 May 2005 and the results of operations and cash flows for the year ended on that date.

Auditor's Responsibilities

It is our responsibility to express an independent opinion on the financial report presented by the Trustees.

Basis of Opinion

An audit includes examining, on a test basis, evidence relevant to the amounts and disclosures in the financial report. It also includes assessing:

- the significant estimates and judgements made by the Trustees in the preparation of the financial report; and
- whether the accounting policies are appropriate to the Foundation's circumstances, consistently applied and adequately disclosed.

We conducted our audit in accordance with New Zealand Auditing Standards. We planned and performed our audit so as to obtain all the information and explanations which we considered necessary in order to provide us with sufficient evidence to obtain reasonable assurance that the financial report is free from material misstatements, whether caused by fraud or error. In forming our opinion we also evaluated the overall adequacy of the presentation of information in the financial report.

Other than in our capacity as auditor we have provided accounting services to the Foundation.

Unqualified Opinion

STAPLES RODWAY
dynamic financial answers

We have obtained all the information and explanations we have required.

In our opinion the financial report on pages 12 to 16 fairly reflects the financial position of the Foundation as at 31 May 2005 and the results of its operations and cash flows for the year ended on that date.

Our audit was completed on 29th June 2005 and our unqualified opinion is expressed as at that date.

Staples Rodway

Chartered Accountants
Hamilton

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- ○ or become an Annual Subscriber
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Address _____

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Cheque enclosed $ _____

○ Please send me a receipt

Post to:

Waikato Medical Research Foundation
Peter Rothwell Academic Centre
Private Bag 3200
Waikato Hospital, Hamilton

We have a new website: www.wmrf.org.nz
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Fax (07) 839 8712