

APPENDICES TO REPORT SAFETY AND EFFICACY OF CAM

I. Proposals for Assessment of CAM

Certain proposals and recommendations are made in order to provide a coordinated and scientifically valid approach to the assessment of risk and benefit of complementary and alternative medicine (CAM). These are general in nature, and are designed to help resolve issues regarding research into CAM products generally.

A. Research required to assess risk-benefit

Both risk and benefit need to be scientifically qualified and quantified before assessment of a risk-benefit ratio can be achieved. This involves research into at least the following areas in Australia:

- 1/ The use of Royal Jelly in the Australian population, including a demographic breakdown of use to account for ethnic variations;
- 2/ A double blind, randomised placebo-control trial of selected and unselected patients of sufficient power to determine the type and degree of risks associated with the use of Royal Jelly in Australia
- 3/ The commencement of some pilot studies to assess biological effects and potential benefits of the use of Royal Jelly. The most important would appear to be the use of Royal Jelly to lower lipids and reduce risk factors in cardiovascular disease. Other useful trials would include the use of Royal Jelly in protection against mutagenesis (genetic damage), its effectiveness in the management of human sarcoma, in reducing menopausal symptoms, and in improving the rate of wound healing (especially in diabetics, where this is a significant cause of morbidity).

B. Research required to assess cost-benefit

Benefit must be established before cost-benefit can be assessed. The proposed pilot studies above should be extended into full trials if they show the anticipated benefits, and the trials would need to address the specific question of cost-benefit, comparing the Royal Jelly to the currently accepted products and methods for management of a particular condition.

Outcomes would be compared, and would be related back to the cost of intervention.

While Royal Jelly is a product amenable to prospective double blind placebo control trials, the more general question of the cost-effectiveness of CAM may be better addressed by different research design, such as those currently being discussed and proposed by the US Office of Alternative Medicine (OAM).

C. Problems anticipated for further research

Certain problems may be considered likely in achieving the goals of research outlined above, and include the difficulties in gaining funding for appropriate research.

1. NH&MRC as research vehicle

The National Health and Medical Research Council (NHMRC), as the primary Australian body for government funding of medical and health research, has a responsibility for funding community-relevant research, and research into potential means of improving the cost-effectiveness of medical care in Australia.

The NHMRC paper dealing with the aims of funding to the end of the century does not address the issues of the safety and use of CAM in any way. This document is included in these appendices. The high proportion of the population using these products, as well as the potential for improved and more cost-effective health management, make it a priority that the NHMRC address these research needs and issues, so that true risk-benefit and cost-benefit studies are completed as soon as possible, for Royal Jelly in particular, and for CAM approaches in general.

2. Dept of Family Services and Health

In the projects outlined for the coming year, there is no provision for assessment of the use or effectiveness of CAM products and practices in health care in Australia. 40% of Australians now seek such care, and there is evidence that CAM approaches may be an effective way of maintaining health, reducing medical expenditure, and minimising the risks of unnecessary medical intervention.

The Department has as part of its mission the goal of improving health outcomes for all Australians. This can only be achieved if health care is effective, accessible, and affordable. The medical industry is currently placing health care out of the reach of more Australians each year, and there is an urgent need to assess the potential beneficial impact of the use of CAM in health management. This requires a commitment to research to determine CAM usage patterns, risk and benefit assessment, and assessment of cost-effectiveness.

To this end, the Department may need to introduce specific projects to address these unresolved issues, and may need to direct the NHMRC to support such necessary research.

It is likely that a National Summit would be of benefit in formalising a program to systematically assess the place of CAM products and practices in Australia. The establishment of a section within the NHMRC, based on the OAM within the National Institute of Health in the US, may be a practical means of keeping an ongoing focus on these goals within the Department and the NHMRC.

II. NHMRC Research Program Guidelines

RESEARCHING FOR HEALTH 1996

ADVANCING AUSTRALIAN HEALTH AND MEDICAL RESEARCH INTO THE 21ST CENTURY
*prepared by the Research Strategy and Development Committee of Medical Research Committee
and*

Public Health Research & Development Committee National Health & Medical Research Council

The improvement in life expectancy and quality of life over the past decades reflects the achievements of previous health research. Meeting the health challenges that face Australia as a new century approaches will depend upon a vibrant, broadly based health research effort. Australians recognise this; in a recent survey 89% of Australians said that medical research was "very important" in improving health care.

The achievements of Australian health researchers and the need for further support have been presented recently in "Researching for Health" (1994), the strategy for this triennium for the two research funding committees of the NHMRC and in "Research for a Healthy Society" presented to the Prime Minister's Science and Engineering Council in December 1994.

Our vision is for:

a health system that embraces research for the benefits that it can bring a research community responsive to health needs, to which the best and brightest young minds are drawn a country that values its health, understands its dependence on quality research and protects its health by funding research through public and private contributions effective communication, delivering the findings of research to where it is needed to make this a healthier country a commitment to finding cost-effective preventive solutions to health problems in Australia leadership in our region because of the quality of our research and the way we translate it into practice.

Research in the health and medical sciences is essential to provide the knowledge which allows Australia to preserve health, improve quality of life and provide cost-effective health care. We must have a strong, research community working at the highest international standards, across the full range of fields, from "bench-top" through "bedside" to public health and health care delivery. Australia expects its health research workers to:

investigate the causes of ill health which are unique to or especially important in our country, eg Aboriginal health, diseases of the tropical north, asthma, melanoma, Ross River fever, equine morbillivirus contribute Australia's share of the world-wide health research effort critically evaluate overseas research findings and determine their applicability to Australia and take a leadership role in technology transfer determine the best ways of improving the efficiency and effectiveness of our health services and health practices provide a stimulating milieu which retains the most talented Australian researchers and attracts international researchers identify new health challenges, and form effective strategies to meet them build our leadership in health promotion, illness prevention and disease management in our region of the world.

Great scientific research shapes and enriches our culture as much as great art, music or literature. The high quality of Australian research brings our country international recognition and many Australians have received the highest international awards in their fields. The process of research is exciting and creative. It needs people with talent and commitment. It needs governmental and private sector encouragement and support.

STRATEGIES FOR THE FUTURE of the Medical Research Committee and the Public Health Research and Development Committee

To fund research across all areas relevant to the health of Australians, on the basis of excellence, rigorous review and fairness

Our research strategy is guided by six basic principles.

- leadership; shaping Australia's health and medical research future
- vigilance; supporting research which allows early identification and responses to national health problems
- relevance; fostering strategic research and facilitating communication of research findings
- high standards; funding only high quality and original research
- comprehensiveness; maintaining a broad research base in this country
- accountability; for ethical standards, quality, relevance and economic value of its research activities.

RESEARCH GOALS FOR THE TRIENNIUM.

In "Researching for Health", we identified 20 specific goals and targets for this triennium. We have made considerable progress towards meeting these goals in the last 12 months. A summary of the goals and our progress towards meeting them are set out in the Table at the back of this document (Appendix 1).

Some important recent actions of MRC and PHRDC:

A Strategic Reserve Fund has been established, to fund urgently needed "seeding" research in the national interest. The fund currently supports specific research in Aboriginal health and hepatitis G. Proposals regarding food-borne disease and equine morbillivirus are currently being sought. A Research Gap Initiatives scheme is being developed; to identify needs in health for which there are research opportunities not being met currently. New training awards have been provided in breast cancer, nursing and allied health, dementia and Aboriginal health. Establishing a partnership on diabetes with the Juvenile Diabetes Foundation (Australia and international). Procedures to further enhance competitiveness and accountability have been adopted in several areas of funding, including the procedures for the assessment of research plans and performance of block funded institutes and program grants. A combined Assigners Panel for MRC and PHRDC has been established, to provide more comprehensive coverage of expertise and a broader cross-disciplinary pool. PHRDC has undertaken a review of its achievements, strengths and shortfalls. Better

communication methods have been initiated through a newsletter and a "home page" on the Internet. A Gene Therapy committee has been established, to advise on approval of proposals to modify human genetic material experimentally. Our international outlook has been broadened through Memoranda of Understanding established or under discussion with seven countries. The acute shortfall in scientific equipment has been partially addressed, by an additional allocation of \$2.5 million for 1996.

MAKING BEST USE OF CURRENT RESOURCES

Each year MRC and PHRDC redirect resources between competing areas (Training Scholarships, Research Fellowships, Project grants, Programs, block grants to Institutes, Strategic Reserve Fund) in accord with specific recommendations from rigorous peer review and with overall objectives of each committee. In recent years, there has been an increased commitment to support for high quality Research Fellows and 5 year Program grants (Fig. 1), with a relative decline in support for block-funded institutes and 3 year project grants.

Most of NHMRC research support is for either 3 or 5 years. This of course means that there are relatively limited opportunities for major changes in direction within a one year time frame.

PREPARING A VIBRANT, RESPONSIVE, RELEVANT AND STRATEGIC HEALTH RESEARCH SCHEME FOR NEXT CENTURY.

The following issues are under consideration by MRC and/or PHRDC. We are seeking your comments and suggestions.

Expanding Australia's research into the improvement of Aboriginal and Torres Strait Islander health

MRC and PHRDC consider that research into issues which affect the health of indigenous Australians is of special importance. In recent years, both committees have had special initiatives in this area and the joint Strategic Research Fund has been used to support further research in 1995 and 1996. This research considers important ethical and cultural issues and closely involves Aboriginal and Torres Strait Island communities.

We have pioneered new procedures in this area and we now wish to build on these achievements, refining and advancing our procedures and always working in partnership with the people who are the beneficiary of the research.

Priorities and plans for 1997 are currently being finalised by the Aboriginal Health Research Working Party, and research proposals will undergo peer review before being funded from the Strategic Reserve Fund.

Long term cohort studies - how our life-styles affect our health

Long term cohort studies are essential in establishing those lifestyle factors which are modifiable, such as diet, smoking, physical activity, and which impact on the major causes of death (eg cancer and heart disease), on chronic diseases (eg osteoporosis) and on other important public health problems. For example, the most definitive evidence that smoking causes lung cancer, and is implicated in other cancers, heart disease and other major diseases, has come from the British Doctors Study established in the 1950s by Sir Richard Doll. Four decades of commitment from researchers through sustained funding, has seen the fruition of this landmark study in public health. More recently, the US Nurses Health Study run from Harvard University (investigators include expatriate Australians Graham Colditz and David Hunter) is providing vital and accurate information about women's health, in relation to issues such as use of oral contraceptives and hormone replacement therapy, that cannot be obtained in other ways.

Australia is well placed to conduct long term cohort studies; as a politically stable, coherent society with its population in a relatively small number of large cities.. This has already been demonstrated by the ground-breaking Busselton study which has been successfully conducting follow-up studies for over 20 years on the population of Busselton, now spurred on by a new generation of Western Australian epidemiology researchers. The recently established Melbourne Health 2000 study of 42,000 Australian-, Greek- and Italian-born residents makes use of the ethnic diversity of this country. While cohort studies such as these must be large, and considerable resources are needed to establish them in the first place, it is essential that long term follow-up for up to 20 years or more is guaranteed. We are considering how best to support established and new cohort studies which can play a crucial role in identifying better health strategies and the causes of ill health, especially studies relating to the problems related to the changing Australian age profile, as we move into the 21st century.

Stable commitment of resources is needed to allow these studies to. NHMRC can contribute to this by guaranteeing core support, ideally in collaboration with other Commonwealth, State and non-Government organisations. NHMRC can also contribute by facilitating the establishment of stable scientific collaborations essential for their success, but difficult to set up under the current 3 or 5 year funding cycles.

Gaining best value from Health Services Research

Our Strategy is to fund research across all areas of health. Funding for research into the delivery of health services is provided currently through a variety of mechanisms including clinical studies supported by MRC, PHRDC, RADGAC and various programs within the Department of Health and Family Services and in the States and Territories. The fragmentation and lack of coordination inherent in the current situation carries the risk that quality, coverage and efficiency may suffer.

MRC and PHRDC are keen to participate in activities aimed at delineating the most appropriate mechanisms for funding various types of health services research.

NHMRC processes and experience in peer review coupled with the responsive developmental approach adopted by RADGAC could be brought to bear on integrated programs of research dealing with specific health services problems. The PHRDC and MRC, in collaboration with other peak groups, will sponsor a meeting in 1996 aimed at defining options for multidisciplinary research.

A partnership between NHMRC and Commonwealth and State/ Territory Departments of Health may provide a more cost effective high quality program of health services research for Australia, with little additional investment of funds.

Practitioner Research Fellowships - part of the strategy to improve translation of research findings into health care.

The need to better translate research findings into health care practices remains a continuing concern. Improved ways of speeding this translation is a key part of our vision for the future. Similarly the need to ensure that research problems and questions are informed by close interaction with health care and public health practice is a priority for the NHMRC. The development is consistent with and supportive of the furtherance of evidence-based practice and research into health outcomes.

To increase this interaction and to strengthen the research capability in health service agencies, we will establish a new Fellowship scheme for health practitioners who wish to make a career of combining research and health care delivery. Practitioners from the full range of medical, dental, allied health and public health practice would compete for Fellowships, working in their professional field and acting as effective conduits of research findings and research skills into improved health practice.

An additional innovative feature of this proposal is that joint sponsorship with other bodies may be possible. It may be possible to enter into agreements with Commonwealth and State Departments of Health and other relevant agencies, so that the Fellowship could be held jointly (part-time) with positions in health care delivery. This would extend the number of Fellowships which could be offered and also ensure commitment by the service agencies to the outcome.

Understanding the human genome - challenges for society and health care

Information about our genetic make-up is expanding rapidly as a result of many medical research efforts around the world. Isolating and characterising genes involved in human diseases is already possible, with the number expanding rapidly. Australian medical research has contributed to these developments and continues to participate in research which is leading to a greater understanding of the human genome at the basic level.

International and local research is now having a direct impact on the Australian community. Individuals can obtain information on their susceptibility to an increasingly wide group of diseases including some cancers which have a defined

genetic component. Just as the risk of heart disease can be partly predicted by cholesterol and blood pressure tests, so will DNA genetic tests be used to identify specific risk factors. For some diseases caused by a single gene malfunction ("defect"), there will be the prospect of "gene therapy", to fix the "defect" or introduce a "healthy" gene instead. The first attempts to treat human disease by gene therapy have already begun in Australia. There are likely to be increasing calls for gene therapy across an expanding range of diseases. The prospects for health raised by research into human genes raises new ethical and social issues, which need to be assessed and addressed. The implications of genome research and the indigenous people are particularly relevant in this respect.

We propose to strengthen our research in understanding the human genome and the health impact of this knowledge, via our project and Program schemes. We plan new NHMRC Fellowships and scholarships to provide molecular biology and genetics training for bright young researchers across the spectrum. It is also anticipated that our block funded institutes will work increasingly in this area.

There are opportunities too for "Research Gap Initiatives", to seed new research in areas where understanding the gene regulation may offer the hope of new treatment options. These may include cystic fibrosis, mental health areas such as schizophrenia, Alzheimer's disease and others, birth defects, thalassemia and other diseases of the blood, and many more. The genetic information emerging about highly prevalent diseases in our society, such as diabetes and breast, colon and prostate cancer, hold much promise for the future.

New Viral Diseases

The unexpected appearance of new viral infectious diseases is a major issue facing Australia and the world as we move towards the new century. It has already been necessary to use our Strategic Reserve Fund to fund urgent research into Hepatitis G and into equine morbillivirus. Internationally, the spread of Ebola and other diseases is causing alarm. We therefore expect that we will need to mount a growing research effort in this area.

We will establish new training awards in this area and investigate the value of establishing a network in research into new viral diseases. We will participate actively in any discussions regarding the desirability of establishing a Communicable Diseases Control Centre in Australia.

Ensuring an international health research effort by developing research partnerships with other countries.

We wish to build bridges with other countries in our research effort, to gain from each other's efforts and different approaches, and to ensure that Australia's research effort continues to be at the highest international standards.

We already have Memoranda of Understanding with Germany, INSERM (France),

Switzerland and the European Union, and discussions are under way with New Zealand, Indonesia and South Africa. With Japan, workshops have been held on cancer and another on hypertension is scheduled.

It is time to offer leadership and support for the health research program of other countries in our region, especially the other countries of APEC, and we are discussing with AusAID ways of facilitating such programs.

Maintaining a comprehensive health research effort - support for the competitive research grants scheme

To meet the challenges of next century, we must maintain and strengthen high quality research in all the areas of health relevant to Australians. We need a critical mass of intellectual activity and there must be constant renewal, provided by the stimulus of training new bright minds, competition for available resources and the opportunity to build teams. We need a balance between directed research and research of immediate applicability on the one hand, and competitively funded research which may have longer term goals on the other. Our country's ability to respond quickly to new health care challenges depends too on sufficient high quality researchers in appropriate fields. For instance, our response to HIV/AIDS was greatly assisted by Australia's leading virologists, epidemiologists and immunologists. The current response to hepatitis G will rely on Australia being able to call on the training and knowledge of researchers in infectious disease, hepatology and public health. For example, our ability to benefit from new links with Japan in cardiovascular disease has depended on Australia's leading international reputation in hypertension. Meeting the challenges brought by a better understanding of the human genome will depend on a strong group of molecular biologists, able to translate this research into many clinical and public health areas, informed by public and professional ethical debate.

Identification of priority areas and direction of resources to those areas is of course essential but this cannot occur exclusively at the expense of the broad health research effort. We need to maintain a strong competitive research program if we are to have a flexible and responsive research community. In fact, much of the research funded under the open, competitive grants scheme of MRC and PHRDC is indeed in priority areas. For example, over half of the present NHMRC supported research is relevant to the Goals and Targets of the Better Health Committee (cardiovascular disease, cancer, mental health and injury).

This competitive system is under stress, as shown in Figure 2. The number of project grants funded has been essentially "no growth" for the last six years (see Figure 3). Over the last four years, the success rate for applications has been well below the average of about 35% of the late 1980's, as indicated in Figure 4. The cost of research is also increasing. The average cost of new grants has grown strongly in recent years, by approximately 50% this decade, as shown in Figure 5. This reflects the rapid increase in the cost of projects, especially clinical trials, epidemiological research and molecular genetics. The overall situation is summarised in Figure 6.

It will be essential that the total number of project grants supported (MRC and PHRDC) be increased from the current 1241 to at least 1500 by the end of the decade, to ensure that there are adequate numbers of health professionals active across the spectrum of research who are able to translate new research-gained knowledge into health care delivery practice.

Current industrial initiatives with the use of enterprise bargaining are also now having an adverse effect, affecting the salary components of grants for which productivity gains have already been made prior to award. Our ability to support team and multi-disciplinary research is constrained; with no expansion of the number of Institute block grants since 1985 beyond the original five institutes and Program Grants now held at 20. A successful attack on future health problems will include building more multi disciplinary approaches, via modest increase in special Units, networks, Programs and Institutes.

[Figures not included]

Research "gaps".

The establishment of special Units has been one way in which the NHMRC has responded to gaps in our research effort in the past (eg Social Psychiatry, Road Traffic Accidents, Environmental Toxicology). Issues which are currently under discussion as requiring special attention and new initiatives include the prevention and better management of injury, several areas of mental health including schizophrenia, Alzheimer's, dementia and factors leading to suicide in the young, and breast and prostate cancer.

Backing innovation - special "innovation" grants.

In a very tight funding environment, it can be hard for truly innovative, "out-of-left-field" research to gain funding. With funding being available for only one in four applications, creative but high risk plans can sometimes miss out on funding against highly rating applications in established fields by investigators with well-established track records. We therefore wish to establish a limited number of grants in a special "Innovation Initiative" scheme. These projects will be identified using the competitive yearly RGIC system. An example of the research that might be supported by "Innovation Initiative" grants could have been Marshall's work on *Helicobacter pylori*. With NHMRC and other support, Marshall showed that this bacterium was an important cause of gastric ulcers, amenable to relatively simple curative therapy. This finding will relieve much human suffering and save money over more expensive alternative therapy. However, it was supported in the days when MRC success rates were about 35%, not 25%, and thus such work may not be supported in the current financial climate.

New initiatives in clinical research

Australia needs a research program across all facets of health. Recently, concern has been expressed that, in times of tight funding, clinical research may be at risk. The Medical Research Committee is currently examining this issue, using a broad definition of clinical research as any health or medical research which involve the investigator interacting directly with other individual human beings. There are particular challenges facing such research. It can be expensive, there are special ethical considerations and it is often very time consuming.

However, clinical research is of key importance to the future health of Australians since it applies findings from in vitro and animal studies to human beings. It is crucial in ensuring the translation of basic findings into better health care. Since most health research is performed elsewhere in the world, Australia must have clinicians trained in critical evaluation of this research so that we adopt the best and most cost-effective new therapies and preventative measures. It is essential that there are adequate numbers of clinicians trained in research in this country so that our health care uses the best methods and treatments. Finally, clinical research is also an engine driving the development of the good questions for basic research.

Currently, clinical research comprises about one fifth of all MRC funded Projects Grants, with additional clinical research in Programs and Institutes. There are many structural and financial impediments to the development of a research career by health care practitioners and the new Practitioner Research Fellowships (proposed above) is one response to this need. However, further action is needed to ensure that we can best translate research findings into health care.

We seek to establish special multidisciplinary Centres for Clinical and Hospital-based research, on a merit basis and taking into account geographical factors. These Centres will have a charter to foster training in research for health professionals who seek to undertake research with patients and human subjects. We will consult with other health organisations on how this might be best achieved.

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