AUSTRALIA NEW ZEALAND
GYNAECOLOGICAL ONCOLOGY GROUP

Senate Submission submitted by Professor Michael Friedlander, Chair, ANZGOG

The following submission will specifically address Point (a) of the Senate Enquiry Terms of Reference "Level of Commonwealth and other funding for research addressing gynaecological cancers".

Gynaecological Cancer Research Trials in Australia

What is ANZGOG and what we do?

A coordinated and integrated approach to Gynaecological Cancer research is essential for clinical advances to be made. ANZGOG was formed for this reason in December 2000. Prior to this there was no national gynaecological trials group in this country. ANZGOG is a multidisciplinary group that comprises gynaecological oncologists, medical and radiation oncologists as well as nurses, data managers and statisticians. All disciplines have a shared interest in, and commitment to, improving the treatment and outcomes of women with gynaecological cancers in Australia and New Zealand. ANZGOG has 130 members, including representatives from more than 30 Gynaecological Cancer Units in Australia and New Zealand. Units are based in metropolitan teaching hospitals, as well as rural and regional centres. It should be stressed that all members voluntarily give their time and make considerable efforts to treat patients in the context of a clinical trial. This significantly increases the workload involved but do so out of their commitment to improving outcomes of women with gynaecological cancers. The members in ANZGOG affiliated institutions treat about 4000 women with gynaecological cancers annually (see Appendix 1). Until the formation of ANZGOG relatively few women with gynaecological cancers had the opportunity to participate in large randomised gynaecological cancer trials and certainly did not have access to international studies.

Clinical trials are the most critical and final stage of the clinical development process for a new treatment or therapy. Participation in randomised trials allows us to define a new standard of care and investigate new and promising approaches to treatment. We are able to fast track new concepts and strategies, the only proven way to increase the chances of cure as well as improve quality of life of patients The overarching aim of ANZGOG is to conduct trials that have the potential to contribute evidence based clinical knowledge that will improve our current understanding of the optimal treatment for gynaecological cancers. The focus is on patient-centred outcomes, which include survival, improved prognosis and a better quality of life. Importantly, investigator-initiated trials address questions of clinical

importance that would otherwise remain unanswered and in so doing have the real potential to contribute to the improved care of Australian women with gynaecological cancer. In the long term these studies are also potentially cost saving through the elimination of ineffective therapies.

Adequate resources are urgently required to develop and rapidly progress clinical trial protocols for all forms of gynaecological cancers. Although the Federal Government has recently recognised the importance of clinical trials and awarded ANZGOG $437,000 in 2006, as part of the Strengthening Cancer Care Initiative, these funds are insufficient for expansion and sustainability, with future funding to be yet determined.

Phase III clinical trials in gynaecological cancer are run almost exclusively within a co-operative group setting. The Australian Clinical Trials Register lists only one trial being conducted outside of this environment. Support for cooperative groups therefore represents the best option for increasing recruitment to clinical trials in Australia. By the end of 2006, ANZGOG will be recruiting patients to five open clinical trials in first line and advanced ovarian cancer and to one cervical cancer study, while continuing follow up of patients on a number of closed trials. Recruitment to current trials open in 2006 is estimated to total 160 patients (of a combined target of 500 patients over 3 years), including 40 well women participating in a screening study. This is from a total of 4000 women diagnosed with or relapsing with gynaecological malignancies (Appendix 1). These figures mean that only 3% of the total patient pool is currently participating in clinical trials in this region. In the US and Europe this figure is substantially higher (6-14%) and ANZGOG would like to see this figure increased to 10% in this region. The main impediment to this occurring is the availability of an ongoing source of funding to cover infrastructure costs.

Clinical trials research requires infrastructure support to carry out the following activities:

(i) Protocol development
(ii) Project management
(iii) Site feasibility assessment
(iv) Ethics committee submissions
(v) Regulatory approval
(vi) Legal and administrative costs associated with contract negotiations
(vii) Provision of clinical trials insurance
(viii) Site activation
(ix) Audit, monitoring and ongoing site management
(x) Database development and maintenance
(xi) Data management
(xii) Statistical monitoring and analysis
(xiii) Report writing and publication.

Estimates of infrastructure costs of running a clinical trial are substantial and depend upon a number of factors, including size, complexity and stage (in start-up, enrolling, or in follow up). Some of these costs must be carried over many years of treatment and follow up.

For ANZGOG to accrue an additional 240 women per year to clinical trials to meet a target of 10% recruitment per year, significant additional funds would therefore be required.

The ANZGOG Coordinating Centre is part of the NHMRC Clinical Trials Centre at Sydney University where a small but dedicated team of talented staff are responsible for running ANZGOG clinical trial activities. An Executive meets regularly as well as a Research Advisory Committee who are responsible for determining the scientific validity of concepts and new trials and making recommendation to the Executive regarding which trials should be supported. The whole group meets twice a year and there is regular communication with all our members through email and newsletters. A website is also under development which will act as a vital resource tool for members and patients.

Why do we need Co-operative Trials Groups?

The primary reason for the existence of Co-operative Trials Groups is to conduct clinical trials in cancer patients in order to improve patient outcomes (i.e. prolong survival or improve quality of life). As a result, most of these studies tend to be large-scale, multi-centre, randomised phase III studies in which new or experimental therapies and approaches to treatment are compared to standard therapy. These trials are conducted nationally or involve collaborations with international groups. (Co-operative Groups will sometimes conduct exploratory phase II trials to pilot novel therapies and inform the decision-making for larger phase III studies.) The new therapy may be, for example, a new surgical approach, an innovative radiation technique/dosage or schedule, a new drug or a new way of combining one or more of these modalities.

Why are Clinical Trials Important?

Evidence-based medicine requires the judicious use of current best evidence in making decisions about the care of patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available clinical evidence from clinical research. Evidence-based medicine:

- provides a basis for enabling patients to make informed choices about clinical decisions;
- identifies the most effective treatments/procedures and incorporates these as policy and guidelines for clinical practice.

Why fund a Clinical Trials Research Group?

The potential benefits of providing appropriate financial support include:

- Significant improvements in treatment outcomes as a result of increased ability to address fundamental clinical questions based on a sound scientific foundation. These would include important value-added studies (eg quality of life, economic sub studies, radiotherapy and surgical studies, translational research projects and patient preferences studies to better inform medical decision-making). These have all lagged behind

chemotherapy studies due to lack of resources yet they have the capacity to make major improvements in treatment and increase survival.

- Increased nationwide clinical trial activity, which has the potential to improve standards of care as well as ensure awareness of high-quality research results and subsequent incorporation into routine clinical practice.
- Increased national capacity for gynaecological cancer research resulting from increased skills of researchers and development of an environment encouraging critical thinking and rigorous appraisal of new approaches to treatment. This would accrue in part from an increased ability to collaborate with international gynaecological cancer research groups..
- Savings in health care costs from elimination of cancer therapies that may be shown to be ineffective
- It has long been recognised that women who participate in clinical trials have improved outcomes.

What Happens in Other Countries?

Support for the research capacity (infrastructure) of cooperative clinical cancer research groups is provided in the USA, Canada and Europe. This support is lacking in Australia. The National Cancer Institute (NCI) in the USA are committed to adequately supporting gynaecological cancer research and in 2005 provided $80 million for cervical cancer research, $99.2 million for ovarian cancer and $27 million for uterine cancer research. Support for GOG - the US gynecologic cancer trials group - runs at $10 million per annum. The GOG have arguably been the most effective and important collaborative gynecological cancer research group around the world and have had a major impact on the management of women with gynecologic cancers.

Funding has increased dramatically in the UK in recent years. Around five percent of women with gynaecological cancer in the UK are entered into clinical therapeutic trials - many more go into screening trials. Public sector funding is spent in a number of ways: (i) core support to the MRC Cancer Trials Unit; (ii) Department of Health contribution to funding for the actual trials and (iii) funding research nurses in cancer networks around the country; The Medical Research Council and Department of Health, through the Health Technology Assessment Programme are currently funding almost £25m worth of research in ovarian and cervical screening. Sixteen percent of women in Germany participate in ovarian cancer trials with similar percentages in Scandinavia where they have very well established and well resourced clinical trial groups.

Current Clinical Cancer Trial Funding in Australia

Inadequate funding is without a doubt the major reason for the disparity in gynaecological cancer clinical trial activity in Australia compared with other developed countries. Funding for clinical trials in the management and prevention of cancer is limited in Australia. At present, funding falls into two broad categories, (a) trials that are supported by industry and (b) trials that are co-ordinated by the Co-operative Groups.

(a) Industry Funded Trials

Industry funded trials comprise those trials instigated and supported by pharmaceutical companies. These trials are conducted in order to demonstrate the efficacy and safety of the products concerned.

The evidence derived from industry trials significantly contributes to the treatment of cancer. However, the primary motivation of organisations involved in the design and instigation of these trials are inevitably driven primarily by the companies' interests. Furthermore, industry trials are usually very specific in the treatments studied, usually involving new pharmaceuticals rather than addressing broader issues relating to treatment options such as surgery and radiotherapy.

In general collaborative groups do not carry out Industry Sponsored studies unless the group can collect and analyse the data and publish the findings independently.

(b) Co-operative Group Trials.

Clinical trials that address issues that question optimisation of current practice are generally not supported by industry. Considerable clinical expertise is needed to analyse current best evidence and to determine the important questions that need to be addressed. Hence, only a co-operative group could have determined that addition of cisplatin to radiotherapy significantly improved the chances of curing locally advanced cervical cancer; that intraperitoneal cisplatin chemotherapy significantly improves the outcome of women with surgically debulked stage 3 ovarian cancer; that second look laparotomy following chemotherapy did not improve outcomes in women with advanced ovarian cancer; that women with well staged early ovarian cancer do not require further chemotherapy and the list goes on and on. These studies without exception, have all been undertaken by collaborative groups and changed practice around the world.

How is ANZGOG currently supported?

Initial seed funding to establish ANZGOG was provided by the NCI through the Clinical Trials Evaluation Program (CTEP) and also via the US GOG. In addition, we obtained a number of unrestricted grants from pharmaceutical companies as well as donations from patients and their families and a few generous philanthropists. Our first study was GOG 182, a large multi-centre international trial that recruited over 4000 patients internationally in just over 2 years. ANZGOG recruited 184 patients to this trial which was a considerable effort for our first trial and should be compared with 360 from the UK and 67 from Italy which both have well established gynaecological clinical trials groups.

In addition to the grant provided by the Federal Government "Strengthening Cancer Care" initiative, we have also received an infrastructure grant from the Cancer Institute NSW for 2 years. We share this grant with the Australian Gastrointestinal Cancer Trials Group (AGITG), which is also housed in the NHMRC Clinical Trials Centre. The State Cancer Councils recently awarded a grant to fund an individual trial. This funding is provided to support local data

management and associated local institutional costs for specific trials. In the case of State Cancer Councils, these funds are generally only available on a state-by-state basis although they make an invaluable contribution to clinical research around Australia. However, they do **not** fund the infrastructure needs **and are only temporary**. State Cancer Councils fund a vital component of the clinical research network, but this component is distinct from the infrastructure required to support the activities of a national co-operative research group.

Gynaecologic cancer research requires an ongoing commitment for **recurrent** funding from the Federal Government for infrastructure support and to increase capacity to carry out studies of national and international importance. Traditionally it has been very difficult to obtain NHMRC funding for clinical trials and this remains an important barrier to increasing clinical trial activity. With increased infrastructure funding, there will be an ensuing increase in the Groups' trial activities, which will increase our capacity to fund the research components of specific trials through the NHMRC and other granting agencies.

Conclusions

Adequate funding would greatly enhance the ability of ANZGOG to play a vital role in improving Gynaecological cancer control through trials of prevention and screening as well as testing new therapies and improving on results achieved with current well established modalities of surgery and radiotherapy. We would also have the opportunity to explore research partnerships in our region as well as internationally.

The benefits of funding a comprehensive national gynaecological cancer trials based research program will include:

- Demonstrable gains in patient outcomes;
- Improved links with the international clinical research community via increased opportunities for international collaborations;
- Increased acceptance of trial results by practising clinicians given their involvement in the research process;
- Greater awareness and compliance with best-practice protocols including the benefits accrued through audit and oversight of all units involved in clinical trials;
- Improved access to clinical trials for women in regional and rural Australia;
- Opportunity to address specific issues faced by Aboriginal and Torres Strait Islanders with gynaecological cancers.

APPENDIX 1

Number of Patients seen each year at Units that are members of ANZGOG (from survey of ANZGOG institutions conducted in 2000).

PRIMARY INVASIVE CASES

Primary Site	
Cervix	863
Endometrial Adenocarcinoma	988
Ovary	923
Trophoblastic	137
Fallopian Tube	41
Uterine Sarcoma	65
Vagina	62
Vulva	204
Sub-Total	**3283**

RECURRENT

Primary Site	
Cervix	114
Endometrial Adenocarcinoma	125
Ovary	367
Trophoblastic	2
Fallopian Tube	10
Uterine Sarcoma	25
Vagina	14
Vulva	43
Sub-Total	**700**

Total	**3983**