EXCELLENCE INNOVATION COMPASSION

10 August 2006

The Secretary,
Senate Community Affairs References Committee
Parliament House
Canberra ACT 2600

Dear Sir/Madam,

Re: Inquiry into Gynecological Cancer in Australia

I refer to your letter of May 12th 2006, requesting a written submission addressing the above Inquiry. Our comments relate to the Australian Ovarian Cancer Study and hence are restricted to research-related approaches to ovarian cancer.

BACKGROUND
The Australian Ovarian Cancer Study

The Australian Ovarian Cancer Study (AOCS) is one of the largest cohort studies of ovarian cancer in the world and therefore represents a powerful foundation resource for research on this highly fatal gynaecological malignancy.

AOCS began in 2000 as a collaborative study between researchers at the Peter MacCallum Cancer Centre (PMCC), Queensland Institute for Medical Research (QIMR), Westmead Institute for Cancer Research (Westmead) and University of Melbourne (UoM). In 2001 the US Department of Defense (DoD) awarded the collaborative a Program grant for national molecular epidemiological study of ovarian cancer in Australia, allowing the Australian Ovarian Cancer Study (AOCS) to commence. Funding by DoD occurred through the Ovarian Cancer Research Program (http://cdmrp.army.mil/ocrp/), which has funded major US labs over the last 10 years. AOCS, the only Program funded outside North America by the OCRP, was supported because of our unique ability to conduct a large-scale cohort study of ovarian cancer in Australia. The goal was to ascertain 1000 cases and 1000 controls from the eastern states (VIC, QLD, NSW, SA).

In addition to creating an ongoing resource for ovarian cancer research, AOCS was designed to initially pursue three major research projects. The research projects aimed to identify environmental and genetic risk factors for ovarian cancer, and to discover genetic changes that determine growth of ovarian cancers and their response to chemotherapy.

Since 2003, AOCS has also been supported by a series of 1-3 year grants from Australian State Cancer Councils, enabling collection of detailed clinical information. Cancer Council funding also allowed expansion of collection to TAS and WA so that sample collection is truly national. AOCS was successful in the 2005 NHMRC Project

grant round and secured funding through to 2011 for on-going collection of clinical follow-up data, allowing collection of a minimum of 5-years clinical follow-up data on almost all cases. In addition, we were successful in our 2005 NHMRC Enabling Grant application in obtaining funding to manage and maintain the AOCS Core 10 August 2006

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As of 30 June 2006, AOCS had recruited a total of 1834 women with invasive or borderline ovarian cancer, far exceeding our initial target. We have collected 1080 fresh tumour tissue samples, 1582 blood samples and have received a total of 1815 completed questionnaires. We recruited a total of 1073 control women that did not have ovarian cancer and received 1072 questionnaires and 924 blood samples, again exceeding our initial target. Clinical follow-up had been initiated on all patients via a network of research nurses. Thus far only 26 patients (1%) have been lost to follow-up, despite that fact that 30 - 40% of our patients return to regional areas for on-going treatment.

The systematic collection of comprehensive clinical data on this cohort of patients, including all treatment and clinical outcome information, represents a unique opportunity to examine clinical, genetic, epidemiological and life style factors that impact on clinical outcome in Australian women with ovarian cancer. In addition, the establishment of AOCS has allowed other aspects of gynaecological care to be investigated including pathways to diagnosis, patient quality of life and predictors of bereavement outcomes in the carers of women who have died from ovarian cancer.

To the best of our knowledge AOCS represents the largest prospectively collected linked clinical epidemiological and biospecimen dataset in the world for ovarian cancer. Development of the resource was only possible through the exceptional collaborative spirit of Australian researchers and clinicians, and the willingness of Australian women to improve outcome for future ovarian cancer patients. Although AOCS was by a US DoD grant, it remains completely owned and managed by the Australian consortium members. The consortium members make AOCS available as a resource for national and international research in ovarian cancer, subject to normal ethical and 'good use' guidelines.

COMMENTS IN THE CONTEXT OF THE TERMS OF REFERENCE FOR THE INQUIRY

a) Level of Commonwealth and other funding for research addressing gynecological Cancers

1. *AOCS was only possible because of large-scale US funding.*

AOCS was initially funded through a US$2m competitive, peer-reviewed grant in 2001. No Australian funding was available at that time for a study of this kind. More recently, the NHMRC Enabling grant scheme has provided funding to projects like AOCS. Enabling grants are heavily based on preliminary data and as our initiative involved a newly established collaborative, it is very unlikely that our application would have achieved funding through the NHMRC Enabling or Project grant scheme. (AOCS has subsequently been funded by both schemes on the basis of the substantial progress achieved). The availability of funding targeted at gynaecological cancers would be a huge advantage to realise the full potential of the AOCS resource and for developing studies like AOCS.

2. Large-scale cohort studies are critically important.
Modern genomic and genetic techniques allow researchers test thousands of genes for their association with risk and response to treatment. Robust statistical associations between an individual's genotype and/or environmental exposures and risk, and between genomic changes in tumours and response to treatment, can only be formed if very large numbers of cases are tested (>100-1000's). Hence large-scale collaborative cohorts, such as AOCS, are critical. The heterogenous nature of ovarian cancer reinforces the need for such cohorts.

Funding for large-scale studies tends to be relatively short term 1-3 years and even Enabling grant funding is limited to 5 years. Such resources become more valuable with the passage of time as clinical outcomes accumulate and the maintenance of these resources is time consuming and expensive in the longer term. Consideration should be given to longer term funding of these resources, with appropriate productivity requirements, given the difficulties in getting them started and their value over time.

b) Extent, adequacy and funding for screening programs, treatment services, and for wider health support programs for women with gynecological cancer;

(c) Extent to which the medical community needs to be educated on the risk factors, symptoms and treatment of gynecological cancers;

(d) Extent to which women and the broader community require education of the risk factors, symptoms and treatment of gynecological cancers; and

1. Genetics is likely to be key to developing an early detection-screening program for ovarian cancer.
The incidence of ovarian cancer in western countries is ~1:3000, at least an order of magnitude less than breast cancer. Hence any screening test that simply stratifies women to be tested based on age alone (say, >50yo) has to be enormously specific if large numbers of false positives are to be avoided. For example, if an early detection test with 99% specificity was applied to 10,000 women, the 100 positive results would

include only ~3 true positives. If a large number of unnecessary interventions are to be avoided (and the associated patient morbidity and cost), it is essential that women be triaged for testing more effectively.

Several very large European and North American studies have demonstrated that ~10-15% of women with apparently sporadic ovarian cancer carry mutations in one of two high-risk genes (BRCA1 or BCRA2). Increasing awareness amongst ovarian cancer patients and GP's of the possibility of a high-risk mutation, improving testing techniques (especially reducing cost) and increasing access to mutation testing could have immediate benefits for female relatives by identifying others at genetic risk and thereby implementing risk-reduction strategies. AOCS is part of an international consortium to map other genes associated with ovarian cancer risk and if successful, these new genes could also be of great value in identifying women who require special surveillance. In addition, serum and urine samples have been collected as part of AOCS, providing a resource that may be useful in the development and/or validation of screening strategies.

2. Experience gained with breast and other cancers highlights the importance of personalized treatment.

Several of the genes that drive the growth of breast cancer cells have been identified and specific inhibitors of their encoded proteins developed. For instance, Herceptin is a new, potent antibody-based drug given to women whose cancer has a specific gene amplification in the Her2 receptor. Herceptin is an excellent example of rational drug design based on understanding the biological properties of the cancer. Currently, ovarian cancer lags well behind breast cancer in the use of molecularly targeted treatments that improve survival.

Recent PBAC experience with Herceptin indicates how new molecularly targeted treatments can lead to emotionally charged community concerns about access. In this context, clinical trials such as the Finnish short-course Herceptin trial (FinHer, *New England Journal of Medicine* Feb 2006), which indicated that a shorter Herceptin treatment regimen was effective and reduced cardiac toxicity, demonstrate the importance of researcher-lead evaluation of new agents to ensure maximum patient benefit, minimum toxicity, and cost-effectiveness of treatment. The Australian New Zealand Gynecological Oncology Group (ANZGOG) is a critical to development of more sophisticated ovarian cancer clinical trials.

Summary:

1. Dedicated gynaecological research funding will enable an increased level of ovarian cancer research in Australia, particularly research that fosters large-scale research collaboration.

2. There are unique opportunities for large-scale cohort studies in Australia that can allow discovery of environmental factors and genes associated with risk, and molecular changes in tumours that dictate response to treatment.

3. Given the low incidence of ovarian cancer, identification of genes associated with risk is likely to be critical to the development of effective screening programs.

4. Much could be gained now by increasing awareness of genetic risk and the development of cheaper and more effective screening strategies for genes such as BRCA1, BRCA2, HNPCC, and p53.

Yours sincerely,

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COMMENTS IN THE CONTEXT OF THE TERMS OF REFERENCE FOR THE INQUIRY

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4. Large-scale cohort studies are critically important.
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Summary:

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7. Given the low incidence of ovarian cancer, identification of genes associated with risk is likely to be critical to the development of effective screening programs.

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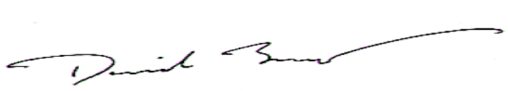

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