



Submission to the House of Representatives Standing Committee on Industry Science and Innovation into Australia's International Research Collaboration

Clinical Oncological Society of Australia (COSA)

Submission Working Party on Behalf of COSA

Prof Bruce Mann, COSA President
Prof Stephen Ackland, COSA Enabling Group Chair
Prof David Goldstein, COSA Immediate Past President
Prof John Zalcborg, Australasian Gastrointestinal Trials Group

February 12th 2010

Submission to the House of Representatives Standing Committee on Industry, Science and Innovation Inquiry into Australia's International Research Collaboration

Key points

- This submission by Australia's peak multidisciplinary organisation representing health professionals working in cancer focuses on the importance of international academic research collaborations in improving outcomes for cancer patients in Australia and globally.
- Clinical cancer research is crucial to address important unmet needs across the entire spectrum of cancer prevention, diagnosis, treatment and care.
- Participation by Australia in international research collaborations is crucial to ensure the efficiency, sustainability and relevance of its clinical cancer research activity.
- Consolidation of effort at an international level is vital to ensure that patient numbers are adequate to demonstrate the multiple incremental benefits of increasingly targeted and individualised interventions.
- Increased investment in Australia's academic clinical cancer research groups is essential to support a strong and vibrant local clinical cancer research community that contributes actively to and can reap the benefits of the global cancer research agenda.

About the Clinical Oncological Society of Australia

The Clinical Oncological Society of Australia (COSA) welcomes the opportunity to provide feedback to the House of Representatives Standing Committee on Industry, Science and Innovation Inquiry into Australia's International Research Collaboration.

The Clinical Oncological Society of Australia (COSA) is Australia's peak multidisciplinary organisation representing health professionals working in cancer. COSA's mission is to develop and maintain high-quality clinical care for cancer patients in Australia; the promotion and facilitation of cancer research is a critical component of this mission.

COSA provides support for Australia's 13 national Cancer Cooperative Clinical Trial Groups (CCTGs) (see Appendix I for a full list) These groups have a record of world class, international research in oncology. COSA also has a Research Subcommittee and supports cancer professionals in a range of discipline and interest groups including cancer research.

COSA is pleased to see the important issue of international research collaboration being addressed and to have the opportunity to contribute to this Inquiry. This submission represents the views of COSA and the Chairs of all 13 of Australia's Cooperative Cancer Clinical Trial Groups (CCTGs) on issues related to international research collaboration in cancer clinical trials.

Cancer clinical research: international questions, local impact

Cancer survival rates in Australia are among the best in the world. This outcome can reasonably be said to reflect the emphasis on participation in national and international cancer research activity that has been a feature of cancer care in this country.

Clinical, translational and health services research are central to addressing important unmet needs for cancer patients and the broader community. Research questions are relevant across the entire cancer journey, and include issues around prevention, screening, diagnosis treatment, supportive care, follow-up, survivorship, palliative and end-of-life care.

Clinical trials and other forms of cancer research activity have made a significant contribution to improvements in outcomes for cancer patients, including reductions in premature death and disability, improvements in evidence-based cancer care, and cost-effective and efficient health systems. Outcomes of clinical research not only contribute to the development of new approaches to diagnosis and treatment but also inform best practice clinical practice guidelines designed to improve and standardise patient care across the cancer journey. These outcomes provide a rigorous evidence base for improving cancer care in Australia and worldwide.

As treatments and technologies become more sophisticated and care becomes more targeted to individual needs, the population available to test specific research questions is significantly reduced in size. The ongoing benefits of clinical research activity both within Australia and globally will only be realised through international efforts that consolidate effort, expertise and patient populations. It is vital that Australia is a key player in such international collaborations to ensure that the outcomes of potentially ground-breaking research are directly relevant to the Australian population. This argument holds for all aspects of clinical cancer research and all stages of the cancer journey.

This submission should be read in parallel with the COSA and Cancer Council Australia joint submission to the Clinical Trials Action Group on enhancing Australia's position as a preferred destination for clinical trials (see Appendix II).

1. The nature and extent of existing international research collaborations

Australia's clinical cancer researchers have had some degree of success in achieving collaborations with international academic research groups. Such international collaborations have led to important changes in clinical practice guidelines and standards of care that have contributed to improved patient outcomes across a range of areas.

Clinical cancer research in Australia comprises three main areas: clinical trials, translational research and health services research.

Cancer clinical trials are coordinated under the auspices of two main sectors.

- a) the pharmaceutical industry either directly or through the services of a Contract Research Organisation (CRO)
- b) national multidisciplinary academic networks of volunteer clinicians with an interest in a particular therapeutic area – the Cancer Cooperative Clinical Trial Groups (CCTGs).

Some trials are undertaken by individual hospitals, departments or units. Usually these are smaller trials often an earlier phase, designed to inform design of larger more advanced studies.

This submission focuses on research activity undertaken by Australia's national academic trials networks. Such studies are designed to address clinically important questions that are directly related to improving patient outcomes. They may involve collaborations with the pharmaceutical industry but also include trials of non-drug interventions.

Both clinical trial sectors contribute to the **translational research agenda**, which involves the investigation of blood, tumour or tissue samples to assess the benefits, risks or lack of impact of a given intervention on particular sub-populations of patients.

Australia also has an active **health services research** sector, with a number of organisations, health services, universities and individuals undertaking research projects designed to improve the delivery of health services for cancer patients and their carers.

In each of these three research areas, Australian researchers seek and have had success in achieving collaborations with international academic research groups. Multicentre clinical trials conducted through these international collaborations, have resulted in changes in standards and clinical practice guidelines, and have improved patient outcomes across a range of areas both in Australia and overseas. Some key examples are provided below.

- The **Australian New Zealand Breast Cancer Trials Group (ANZBCTG)** has contributed to multi-national trials for the past 30 years. ANZBCTG has consistently recruited higher than average numbers per head of population. As a result, a number of subsequent multi-national trials have been led by Australian investigators.
- The **Australasian Gastrointestinal Trials Group (AGITG)** has a number of international collaborations including: the Eastern Cooperative Oncology Group (ECOG) (USA); European Organisation for Research and Treatment of Cancer (EORTC); Medical Research Council (MRC) (UK); National Surgical Adjuvant Breast and Bowel Project (NSABP) (USA); and National Cancer Institute of Canada Clinical Trials Group (NCIC CTG). These collaborations have led to trial outcomes that have changed clinical practice, including the use of imatinib for the treatment of gastrointestinal stromal tumours (GIST),¹ adjuvant therapy for the treatment of colon cancer, use of cetuximab for the treatment of metastatic colon cancer,² and use of erlotinib for the treatment of pancreatic cancer.³ International research collaborations have resulted in additional translational studies led by Australian investigators that have altered clinical practice.
- The **Trans-Tasman Radiation Oncology Group (TROG)** is involved in collaborations with international trials groups such as the EORTC and the National Cancer Institute of Canada (NCIC CTG). A growing list of independent international centres are involved in clinical studies initiated by TROG.

While there are excellent examples of international collaboration within the clinical cancer research community, these collaborations have often been achieved in spite of rather than with the support of appropriate investment and are commonly the result of individual relationships and voluntary investment of time and resources.

¹ Clarke SJ et al. Australasian Gastro-Intestinal Trials Group. AGITG DaVINCI Trial: Randomised phase II trial of De Gramont schedule 5-fluorouracil and leucovorin plus irinotecan versus single agent irinotecan in patients with previously treated metastatic colorectal cancer. *Gastrointestinal Cancers Symposium*; 15–17 Jan 2009; San Francisco.

² Karapetis C et al. *K-ras* Mutations and Benefit from Cetuximab in Advanced Colorectal Cancer. *NEJM* 2008;359(17):1757-65.

³ Price M et al. A phase I trial of capecitabine + gemcitabine with radical radiation for locally advanced pancreatic cancer. *British Journal of Cancer* 2009; 100 (1): 37–43.

2. The benefits to Australia from engaging in international research collaborations

International collaboration is central to achieving the patient numbers and infrastructure required to demonstrate incremental benefits of increasingly complex and individualised approaches to cancer care.

Australia's participation in clinical trials is high by international standards, relative to its population size. While local research activity is important and highly relevant, international research collaborations are vital to ensure the impact, efficiency and sustainability of Australia's research activity. The benefits of such international research collaborations can only be demonstrated through an understanding of the limitations of local research activity.

Limitations of local research activity

With the advent of newer and targeted cancer technologies and treatments, the benefits of new or improved approaches are becoming greater but are relevant for smaller sub-populations of patients. While important from a patient perspective, these incremental benefits can be difficult to measure with a small patient population. A similar issue applies to translational research activity which requires adequate numbers of patients with particular characteristics to assess the impact of a specific intervention on a sub-population of patients. In each case, the patient numbers required to demonstrate clear benefits (or otherwise) are larger than a country such as Australia can achieve in isolation.

Australia also often misses out on new and innovative technologies and treatments because of its geographic location and relatively small market. This is particularly relevant as innovative approaches are often developed by biotechnology companies that arise from or are related to, academic centres without the global reach of multinational pharmaceutical companies.

Benefits of international research collaborations

Participation in international research activity offers the opportunity to expand the impact, efficiency and relevance of Australia's clinical cancer research activity through:

- access to a pool of patients of the size required to demonstrate the incremental benefits of new or improved approaches to cancer prevention, diagnosis, treatment and care
- access to treatments and technologies that might otherwise not be available for some years
- reduced duplication of effort with international efforts consolidated to address one agenda
- increased relevance of outcomes from multicentre, international clinical trial activity to the Australian setting.

Importantly, such international collaboration offers direct benefits to patients, including:

- early access to new and innovative cancer technologies and treatments
- improved outcomes due to faster uptake of proven new therapies
- individualised care with therapies tailored to specific patient characteristics.

Participation in international research activity will also ensure Australia's recognition as a centre of excellence for clinical cancer research, which will have a number of benefits including:

- attraction of research funding to Australia
- maintenance and development of world-standard local expertise in scientific, clinical and health services research and clinical care
- spin-off developments in complementary sectors such as biotechnology.

3. The key drivers of international research collaboration at the government, institutional and researcher levels

Drivers of international research collaboration include logistical, financial, and sustainability issues. Ultimately, the key driver for international collaboration is the need to improve the quality of care for people with cancer by supporting high-quality research activity that is undertaken as efficiently and cost-effectively as possible.

At a **government** level, international collaborations provide the opportunity to:

- maximise the return on investment for research dollars invested in Australia by ensuring that research studies are of a size required to ensure that outcomes can be demonstrated and that research is conducted as efficiently as possible
- maintain within Australia a pool of world-class clinical cancer research expertise that leads directly to improved quality of care for the community at large, whilst fostering education and training of the next generation of clinicians
- encourage long-term investment within Australia by the international research community.

At an **institutional level**, international collaborations provide the opportunity to:

- address and participate in research activity that would not be possible within a single centre
- learn from the experience of international clinical trial groups and experts with similar research interests
- meet targets for international peer-reviewed publications arising from local research activity
- fast-track research studies through combined effort, shared protocols and streamlined processes.

At a **researcher level**, benefits of international collaboration include:

- recognition as part of an international community of clinical cancer research expertise
- access to increased research funding and infrastructure to support local interests.

Currently, other countries within the Asia-Pacific region are developing their research infrastructure with funding from governments and industry. In the absence of appropriate investment to support international collaboration, there is a real and significant risk that Australia will lose its standing within the international community and will lose much needed international research investment to other countries within and outside the region.

4. The impediments faced by Australian researchers when initiating and participating in international research collaborations and practical measures for addressing these

The primary impediments to international research collaborations relate to the availability of research funding and infrastructure within Australia. Additional funding for academic research groups is vital to support a strong and vibrant Australian clinical cancer research community that represents an attractive partnership prospect for international research groups.

Impediments faced by Australian researchers in relation to initiating or participating in international cancer research collaborations include:

- inadequate sustained investment to support the conduct of multicentre clinical research activity by academic research groups
- delays in trial start-up processes caused by factors including lack of streamlined and standardised approaches to ethics approval, insurance and other governance issues as well as a lack of common research and regulatory standards at an international level
- lack of appropriate infrastructure to support multicentre research activity including jurisdictional differences in data collection and clinical research funding arrangements.

Other broader barriers to the conduct of clinical trials are outlined in COSA's submission on clinical trial activity to the Clinical Trials Action Group (Appendix II).

The primary practical measure that is needed to overcome these impediments is increased investment in Australia's academic clinical cancer research groups. Such investment would ensure that Australia can develop and sustain a vibrant and effective clinical cancer research community that can participate as an active partner on the international cancer research stage. A component of this requirement is that funding from granting agencies for Australian research activity should be able to be distributed to other international sites where leadership for such trials arises in Australia. In contrast to funding from European and American agencies, there is currently no flexibility in Australia to provide per-patient funding from Australian-led research to collaborating Asian centres

The return on investment will be improved by a range of other practical strategies to increase the efficiency of Australia's research activity, such as:

- streamlining of trial approval and management processes across jurisdictions, such as under the HoMER initiative
- collaboration at an international level to develop common standards and regulatory policies
- linkage of all types of health record data, including demographics, pathology, radiology, cancer registries, and clinical trial registries
- government funding for insurance, which would provide valuable support for CCTGs and free up funding that could be reallocated directly to research
- acceleration of the roll-out of e-Health, including incorporating features that will assist in managing clinical trials
- a move away from individual state-based funding models for hospitals involved in clinical research, to ensure uniform arrangements across the nation
- enhancement of the ANZCTR, including an investigator portal, patient portal and ability to undertake extensive searches

- strategies to improve patient recruitment, including community and health professional educational initiatives, promotion of information about available trials and increased infrastructure funding to support positions such as clinical trial coordinators
- enhanced CCTG funding (given the substantial increase in CCTGs that has occurred in recent years with no increase in CCTG infrastructure funds).

5. Principles and strategies for supporting international research engagement

Maintaining a world-class local research community

Australia's engagement in international research activity will include measures to support the development of a strong independent clinical trials capacity that has international standing as well as enhancement of international pharmaceutical investment.

Maintenance and enhancement of Australia's contribution to international cancer research activity will be dependent on its capacity to participate in multicentre clinical trials and to demonstrate efficient and effective research skills.

Key success factors in maintaining a world-class local research community include:

- a vibrant series of national academic co-operative CCTGs with skills and expertise in each of the key disease groupings
- the availability of a skilled clinical trials workforce, including world-class medical and scientific researchers, trial co-coordinators, data managers and biostatisticians
- investment and collaborative development of the infrastructure and resources required to support and enhance research in Australia, such data collection and biobanking
- the development of a strong institutional culture within hospitals in support of research and innovation.

Australia's efforts also need to be considered in terms of other activity within the region. In particular, the intensive approach of Asian countries, such as Taiwan and Korea, to upscale investment in clinical trials infrastructure in their hospital system risk a dramatic downturn in Australia's current success in being a leading contributor to multinational trials and all of the positive health benefits to the Australian community cited above

Encouraging pharmaceutical and independent trial investment

In considering initiatives to encourage Australia's involvement in international research activity, COSA recognises the central importance of encouraging pharmaceutical industry investment in clinical trials in Australia. Benefits for investigators of participating in industry-funded clinical research include:

- giving patients early access to new therapies
- improving the standard of care leading to better health outcomes
- providing Australian health researchers with global recognition for their expertise
- providing practical experience for Australian staff in conducting clinical trials
- providing funds for academic research

- retaining researchers in the Australian health and hospital system.⁴

Direct measures to facilitate pharmaceutical industry engagement may include both investment incentives and measures to improve Australia's competitiveness in streamlining ethics and governance. However, the single most important factor in retaining and enhancing industry commitment is a viable, thriving local research community. It is through increased support for the CCTG system for conduct of independent investigator-initiated clinical trial activity that the clinical trials environment in Australia becomes strong. This not only supports Australia's overall public interest but also creates an environment of activity and experience that encourages pharmaceutical trial engagement.

Publication and dissemination of research findings

Promotion of Australia as a world-class centre for cancer research activity requires routine and regular publication and promotion of cancer research data and findings. Publications in peer reviewed publications and presentations at international forums should highlight the strengths of clinical research in Australia including:

- the availability of functional clinical research networks and expertise
- the potential to value-add through the availability of infrastructure such as well-annotated tumour and blood banking
- translational research capacity (pharmacokinetics, pharmacogenetics, pharmacogenomics)
- bioinformatics
- expertise in quality of life research
- expertise in cost-effectiveness and health economics analyses.

Increased promotion of participation in both local and international trials to clinicians through co-operation between Australian and international trials groups, presentations at local and international meetings and workshops and support for international principal investigators to visit Australia and present trial data at local meetings.

A national research agenda

Australia's position as a centre for international cancer research activity would be strengthened by consolidation of a national cancer research agenda that identifies priority areas for research activity and encourages uniform approaches to funding, governance and infrastructure. Within this agenda, clinical trial and research data should be used to set targets for, drive and monitor improvements in performance as part of a clinical trials enhancement strategy. Governments should develop, monitor and report against performance indicators related to the financial and in kind investment provided to enhance clinical research activity.

⁴ The Inaugural survey of investigator perceptions on the value of industry funded clinical research Commissioned by the PIC RDTF: conducted March 2009 and compiled by NSW Clinical Trials Business Development Centre: www.clinicaltrials.org.au

Appendix I: Australian Cooperative Cancer Clinical Trials Groups

- The [Australasian Sarcoma Study Group](#) (ASSG) provides the infrastructure for collaboration between multi-disciplinary teams (MDT), which comprise specialist health professionals working together to discuss your case and how best to manage your treatment and care (for example, specialist cancer doctors and nurses and supportive care clinicians such as social workers, psychologists and physiotherapists).
- The [Australasian Gastro Intestinal Trials Group](#) (AGITG) mission is to improve outcomes for patients affected by GI cancer. Involving the community at all levels of the institute to raise awareness and funds for the prevention and treatment of GI cancer in Australia and New Zealand.
- The [Australasian Leukaemia & Lymphoma Group](#) (ALLG) is an independent non-profit organisation established by clinicians who care for patients with leukaemia, lymphoma and related blood diseases. It aims to improve the treatment of these patients and to foster collaboration with other relevant groups both national and international. It also aims to fund appropriate research and specific programs to reduce the burden of such diseases for present and future generations, and to increase the understanding of such diseases by appropriate research including clinical trials.
- The [Australasian Lung Trials Group](#) (ALTG) is Australia and New Zealand's lung and thoracic cancer clinical research group. The ALTG is a multi-disciplinary organisation dedicated to reducing the incidence, morbidity and mortality of lung and thoracic cancer and improving the quality of life of lung and thoracic cancer patients in Australia and New Zealand through the coordination and facilitation of high quality clinical research.
- The [Australian New Zealand Breast Cancer Trials Group](#) (ANZBCTG) is dedicated to the control of breast cancer through quality research.
- The [Australian and New Zealand Children's Haematology and Oncology Group](#) (ANZ CHOG) aim is to encourage and support education and the advancement of knowledge in all aspects of treatment and childhood cancers. Emphasis is on advances in molecular biology, and the opportunities afforded by those advances for the improvement in diagnosis, treatment and prediction of outcomes of therapy.
- [Australia New Zealand Gynaecology Oncology Group](#) (ANZGOG) was established to foster and support collaborative research throughout Australia and New Zealand and improve outcomes of women with gynaecological malignancies through randomised clinical trials.
- The [Australia New Zealand Melanoma Trials Group](#) (ANZ MTG) was established in 1999. Its first project was to design and support randomised phase III trial in melanoma comparing adjuvant radiotherapy to observation in patients with resected nodal disease. Since then the ANZ MTG has successfully met the target patient recruitment for this trial and is in the process of developing 4 new clinical trial protocols. The ANZ MTG has recognised the need to centrally promote and support melanoma trials for investigators and consumers.
- The [Australian and New Zealand Urogenital and Prostate Cancer Trials Group](#) Ltd (ANZUP) Limited is a public company limited by guarantee and incorporates APUG (Australian Prostate & Urogenital cancers Group) and ANZGCTG (Australian & New Zealand Germ Cells Trial Group). The group is multidisciplinary in composition and is dedicated to best practice and innovation in urogenital and prostate cancer clinical trials.

- [Co-operative Trial Group for Neuro-Oncology](#) (COGNO) is a newly formed national neuro-oncology trial based group based at the NHMRC Clinical Trials Centre, located at the University of Sydney. COGNO's mission is: "The achievement of better health outcomes for patients and those affected by brain tumours through clinical trials research."
- [Primary Care Collaborative Cancer Clinical Trials Group](#) (PC4TG)
- The [Psycho-oncology Cooperative Research Group](#) (PoCoG) was established in 2005, in response to a recognised need to develop the capacity and co-ordinated collaboration to conduct large-scale, multi-centre psycho-oncology and supportive care research.
- The [TransTasman Radiation Oncology Group](#) (TROG) is Australia and New Zealand's specialist clinical research group for radiotherapy. TROG is a cooperative multidisciplinary organisation dedicated to the control of a wide range of cancers through quality multicentre research.

Appendix II Joint Submission to the Clinical Trials Action Group on enhancing Australia's position as a preferred destination for clinical trials

Separate attachment to emailed submission