Joint submission from COSA and the Cancer Cooperative Trials Groups

to the

IHPA Discussion Paper for Development of a table of standard costs for conducting Clinical Trials in Australia

Clinical Oncological Society of Australia

Thank you for the opportunity to comment on the IHPA Discussion Paper for the development of a table of standard costs for conducting clinical trials in Australia. This is a joint submission between the Clinical Oncological Society of Australia and Australia's 14 national Cancer Cooperative Trial Groups.

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; promotion and facilitation of cancer research is a critical component of this mission.

Australia's 14 national Cancer Cooperative Trial Groups have a record of world-class international research in oncology. Please see Appendix One for a list and description of these groups.

Cancer Cooperative Trials Groups (CCTG's) run academic investigator initiated trials that focus on bringing together medical and scientific professionals to identify key clinical questions in the treatment of cancers. CCTG research determines how existing treatments can be used more effectively as well as exploring new therapies. CCTG research is independent of commercial sponsors and driven by the need to answer scientific clinically relevant questions to improve clinical practice. Such trials comprise investigator initiated multi-Centre Phase II/III trials. CCTG's are provided with some infrastructure funding from *Cancer Australia* as well as relying on competitive grants and community fundraising for the conduct of trials. If the clinical trial is using a pharmaceutical company sponsored trial drug the study drug may be provided and there may be some support for central trial processes, but this is most often at an international level, rather than a local level.

There is a clear distinction between research performed by pharmaceutical companies and CCTG's. This difference lies not only between the types of research questions that are being addressed but between the resources and funding models available for clinical trials sponsored by pharmaceutical companies and CCTG's. The CCTG's largely run by volunteer clinicians in Australia struggle financially to carry out their effort and rely on the good will of their members and the voluntary time and support of academic institutions to ensure their important research questions are answered through high quality trials.

The development of a table of standard costs for conducting clinical trials in Australia will enhance the development and delivery of clinical trials in Australia only if the difference in the underlying rationale as well as funding models and available resources between investigator/cooperative trial group research and pharmaceutical company research is fully comprehended and addressed in future recommendations. It is only then that removing uncertainty around the cost of conducting clinical trials for institutions, sponsors,

cooperative groups and researchers at all levels will encourage sustainable growth and activity.

KEY RECOMMENDATIONS

The task of creating a table of standard costs for the entire range of clinical trials conducted in a variety of different settings for different populations and administered and delivered by a diverse group of professionals needs to account for the fact that:

1. Standard care i.e. the same types of interventions and testing that would occur if the patient were not on a clinical trial and treated with standard care in investigator and CCTG initiated multi-centre phase II/III trials in which the institution or the CCTG is the trial sponsor should **not** be costed to clinical trials.
2. Notwithstanding the fact that the cost of standard care should not be costed to clinical trials, with any given trial, there may be interventions or costs over and above the standard of care and these will need to be costed to the trial. In calculating such costs, the type of trial, the phase of the trial and the target population will influence costs and adjustment for these variables needs to be considered.
3. This discussion paper focuses on the public hospital sector, however CCTG's also run trials in private institutions or mixed public/private settings with good outcomes and significant cooperation. Development of a table of standard costs would need to have relevance to the private sector as well as the public.
4. To increase the clarity of the proposed scope of services for costing purposes we recommend that the items in the list are categorised according to sponsors (trial coordination groups and institutions or commercial sponsors) and standard of care. The list as it currently stands is confusing without these categories.
5. The cost of conducting clinical trials across different settings where these need to be captured whether regional or urban or even within the same city will vary greatly as these depend on a range of factors e.g. teaching hospital status, institutional support, Government subsidies etc. and hence, pricing recommendations need to account for these variables.
6. Using the relevant Award to determine hourly rate will be difficult. People employed in the management and conduct of clinical trials are employed under a large variety of Awards. Which Award is referenced and the seniority of the person undergoing the activity will influence cost. We recommend that a review of research professionals and the Awards they are employed under is conducted to inform this process.
7. Funding models and resources available to CCTG's are very different from those of pharmaceutical companies and it is vital that this is considered in any discussion of costing of clinical trials in Australia.

2.2 The Clinical – Tests and Procedures Items

Are the initial definitions for the scope of clinical services included under each item in the "Clinical – Tests and Procedures" sub-list appropriate?

Yes.

Do the initial definitions cover all relevant services? What services are missing?

- Study drug administration
- Magnetic Resonance Imaging is not included under medical imaging
- Patient education is not included

Please suggest changes to tighten definitions as appropriate.

Other clinical tests or procedures 1.5.1

- Including diagnostic and treatment related procedures including study drug administration

Medical Imaging 1.3.1

- Magnetic Resonance Imaging
- Including measurement and reporting of medical imaging for clinical trial purposes

Radiation Therapy 1.4.1

- Including ongoing quality assurance as per clinical trial protocols

Screening Visit and Health Assessment 1.1.1

- Patient education

2.3 The Clinical – Trial Support Services

Are the initial definitions for the scope of services included under each item in the "Clinical – Trial Support Services" sub-list appropriate?

Departmental Ongoing Administration Fees

- Procedures associated with the long term follow up of clinical trial patients should be included here.

Pharmacy/Investigational Drug related – Staff training (drug specific) 2.4.1

- Training of pharmacy personnel in trial procedures specific to study drug should be included here

Bio specimen – related – Bio specimen collection and processing (central and local) 2.5.1

- Include shipping for central analysis or storage

Do the initial definitions cover all relevant services? What services are missing?

Departmental Ongoing Administration Fees 2.3.1 initial definition does not cover all services

Please suggest changes to tighten definitions as appropriate.

The definition of Departmental Ongoing Administration Fees 2.3.1 could be further expanded to include:

- Management of clinical trial resources including human and infrastructure
- Training of all staff involved in conduct of clinical trial including pharmacy, nursing, pathology and radiology
- All procedures associated with ongoing ethical review including submission and review of amendments, revision of patient information and consent forms and annual reports.
- All procedures associated with the long term follow up of clinical trial patients (as above)

2.4 The Non-Clinical Services

Are the initial definitions for the scope of services included under each item in the "Non-clinical services" sub-list appropriate?

Preparation of research proposal item 3.1.1 requires more detail. The activity 'preparation of protocol' involves many different activities and services

Do the initial definitions cover all relevant services? What services are missing?

Item 3.1.1 preparation of protocol includes the following activities which are not listed:

- New proposal reviews and external peer review plus administration associated with this
- Review by Scientific Committee for endorsement of development and final approval
- Review of protocol by research team, quality assurance team, quality of life committee and health economics representative.
- Trial Development Teleconferences

The activities of a Trial Management Committee or a Data and Safety Monitoring Committee are not listed. These activities come under both Project Development and Implementation.

Are any services/activities duplicated on the non-clinical services sub-list?

Investigator meetings are mentioned in 3.1.2 and 3.1.8. Reference to investigator meeting could be removed from 3.1.2

There is duplication between Ongoing administration, monitoring and reporting 3.2.6 and Trial centre data management, data analysis and ongoing administration monitoring and reporting 3.2.8

Are any services/activities duplicated between the clinical trial support services sub-list and the non-clinical services sub-list?

There are a number of duplications between Departmental Protocol Review, Departmental Establishment/Set up Fees and Departmental Ongoing Administration Fees in the Clinical – Trial Support Services sub-list and Project Development and Project Implementation in the Non-Clinical Services sub- list. While they refer to clinical and non-clinical services there is still a potential for duplication and confusion.

An example of this is:

- Reference to "local feasibility of the study" in item 2.1.1 and "study feasibility at the site" in item 3.1.2

Please suggest changes to tighten definitions as appropriate.

Departmental Protocol Review 2.1.1

Definition of local feasibility could be tightened to "The process usually involves a review by a panel drawn from the above mentioned Departments of the scientific merit and local feasibility of the study in terms of resources, patient population and logistical considerations".

Duplication between items 3.2.6 and 3.2.8 could be addressed by removing reference to CRF completion and data management from item 3.2.6.

Definitions could be tightened generally by defining at what levels the activity is occurring i.e. whether costs are institutional (site) related, sponsor or cooperative group based. Some standard costs will be common to all levels however distinguishing the level would increase clarity around what the activities represent.

3.1 Principles to be used in costing the NHMRC List of standard items for clinical trials

Are the principles for developing the table of standard costs reasonable?

Yes, however there is often 'timing' differences between application submission and actual receipt of funds. Ideally the pricing model for all costs (activity based, unit and standard) should allow for an annual inflation figure once the funding becomes active. The funding should also allow for annual increments for each year that the trial is active under grant funding.

Are there any principles that should be modified or deleted? Should additional principles be adopted?

Additional costs associated with the additional labour involved in clinical trials should be covered by a multiple of the MBS not the MBS without amendment.

Please suggest wording changes and /or additional principles where necessary

Nothing further to add.

3.2 Costing the clinical tests and procedure sub-list

Is the proposed method for deriving the standard costs for each item on the NHMRC sub-list for clinical tests and procedures (including clinical consultation services) reasonable?

Yes

Are there any items for which the costing approach should be modified?

1.1.1 Clinical services provided specifically for the purpose of screening and health assessment

This item refers to several activities some of which will be undertaken by medical practitioners and some of which may be carried out by research staff including screening assessment, medical record review and vital signs. Use of the MBS fee as a surrogate would not cover this.

1.5.1 Other clinical test or procedures

If study drug administration is to be included here costing using the MBS item may be problematic. Currently there are MBS item numbers for intravenous chemotherapy but not for oral anticancer drugs, so a distinction needs to be made to ensure all drugs administered on a clinical trial are costed adequately. Pharmaceutical Benefits Scheme cover of drugs as standard will also vary from state to state in public hospitals. Some public hospitals admit patients for chemotherapy and others do not. For example NSW patients are typically not admitted to public hospitals for chemotherapy and the MBS item numbers are forgone in order to have the Pharmaceutical Benefits Scheme cover the drugs; in other states the reverse is true.

Please suggest alternative costing approaches where appropriate

Item 1.1.1 could be costed by choosing the best available method of unit cost for each identified nursing or medical service item.

No further comments.

3.3 Costing the clinical trials support services sub-list

Is the proposed method for deriving the standard costs for each item on the NHMRC sub-list for clinical trial support services reasonable?

Yes, however using the relevant Award to determine hourly rate will result in large fluctuations in cost. People employed in the management and conduct of clinical trials are employed under a large variety of Awards. Which Award is referenced and the seniority of the person undergoing the activity will influence cost.

Are there any items for which the costing approach should be modified?

Item 2.4.1 Staff training (drug specific)

Costing should be per trial per site

Please suggest alternative costing approaches where appropriate

See above.

3.4 Costing the non-clinical services sub-list

Is the proposed method for deriving the standard costs for each item on the NHMRC sub-list for clinical trial support services reasonable?

Generally the proposed method is reasonable as long as annual increases in costs are allowed for.

Items 3.2.6, 3.2.7, and 3.2.8 which are costed per trial site per quarter will be influenced by numbers of participants recruited. Trials with large numbers of participants will require more minutes of labour. This needs to be accounted for.

Are there any items for which the costing approach should be modified?

3.2.4 Medical records set-up, access and storage

Will be required for both screening and recruiting patients regardless of actual recruitment. This cost would be better addressed by a per trial site costing.

Please suggest alternative costing approaches where appropriate.

As above

3.5 Potential need for adjustment to standard costs

Is there a need to provide for adjustments to the standard costs based on any of the identified factors?

Yes all of the possible factors for consideration listed are relevant. Please see additional comments below:

Phase of trial. Some activities will be more or less intensive according to the phase of the trial. Phase one trials for example require increased ethical oversight and more stringent reporting and tracking of adverse events compared to later phase trials. The phase of the trial will impact costs.

Target Population of trial. Higher needs groups also include participant populations with need for complex care such as in palliative care and oncology trials.

A table of standard costs would need to consider the additional costs associated with paediatric clinical trials. It is standard practice in paediatric oncology to enrol all patient on clinical trials as treatment for both frontline and relapsed disease. However there is an additional cost above the standard cost for conducting a clinical trial in paediatrics because the cost for some procedures is greater due to the age of the child. An example of this is procedures such as radiation therapy planning, PET, MRI and surgical procedures including a bone marrow aspirate, require a general anaesthetic in children. In this particular instance provision for a paediatric general anaesthetic loading would need to be included in trial costing, where these interventions are over and above the standard of care.

Trial sponsor. There is significant variation between types of sponsors and funding and resources available to different sponsors. It would be essential to consider adjustment to the standard costs for trials based on the characteristics of the trial sponsor.

Location of trial sites. Adjustment to the standard costs for trials where sites are located in remote regional and rural areas would be important to support ongoing development of clinical trials and increase patient participation in these areas. The cost of conducting clinical trials across different settings whether regional or urban or even within the same city will vary and requires further consideration.

There are only 8 children's cancer centres in Australia. Regional and rural patients often have to travel long distances or relocate to participate in paediatric clinical trials. Additional funding for paediatric participant related costs should be considered.

CCTG's also conduct clinical trials within private institutions and mixed public/private settings. Therefore a table of standard costs would need to have relevance for the private sector.

Standard care versus trial specific care. Standard costs associated with clinical trials run by CCTG's should only be derived from those activities over and above standard care. It is important to consider that while a patient may be on a clinical trial many of the costs incurred will be part of the standard of care for that patient. Medical consultations, tests and procedures on clinical trials are often the same as standard care.

The more difficult issue is whether commercial sponsors should be expected to fund standard of care treatments and investigations for example, when commercial studies compare a new treatment to a standard of care (e.g. is a new patented drug better than the standard treatment of X for a given disease). This requires an in-principle decision by the IHPA. However, although this could be viewed as the health system is subsidising the commercial sponsor, the fact remains that these costs would be incurred in any case and in the spirit of encouraging ongoing investment in novel health care and understanding that clinical trials in general whether investigator initiated or commercial trials to varying degrees improve health care overall and provide earlier access for Australians to innovative treatment, the same principles should apply to commercial studies i.e. the sponsor should not have to pay for standard of care costs.

Are there other factors that should be considered for potential adjustments to the standard costs?

Nothing to add

Please suggest methods for adjusting standard cost to account for the factors where considered necessary.

No further comment

CONTACT
Marie Malica
Executive Officer
Clinical Oncological Society of Australia (COSA)
GPO Box 4708, Sydney NSW 2001
Ph: (02) 8063 4100
Email: cosa@cancer.org.au

Appendix One – Cancer Cooperative Trial Groups in Australia

Australasian Sarcoma Study Group (ASSG) aims to improve outcomes for sarcoma and related tumours in the Australian community by undertaking outstanding research.

Australasian Gastro Intestinal Trials Group (AGITG) is Australia's largest independent non-profit organisation conducting clinical trials into gastrointestinal cancers.

Australasian Leukaemia & Lymphoma Group (ALLG) is the only not for profit organisation designing and delivering investigator initiated clinical trial research into blood cancers.

Australasian Lung Trials Group (ALTG) is a multi-disciplinary organisation dedicated to reducing the incidence, morbidity and mortality of lung and thoracic cancer in Australia and New Zealand.

Australian New Zealand Breast Cancer Trials Group (ANZBCTG) conducts an independent, collaborative breast cancer clinical trials research program to save lives from breast cancer.

Australian and New Zealand Children's Haematology and Oncology Group (ANZCHOG) are the leading body representing the interests of children and adolescents with blood diseases and cancer.

Australia New Zealand Gynaecology Oncology Group (ANZGOG) supports collaborative research to improve outcomes of women with gynaecological malignancies through randomised clinical trials.

Australia New Zealand Melanoma Trials Group (ANZMTG) coordinates and conducts quality research for melanoma control.

Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) develops and conducts cancer research in urogenital and prostate cancers.

Cooperative Trials Group for Neuro-Oncology (COGNO) aims to conduct investigator initiated and collaborative group trials addressing important clinical questions in patients with brain tumours.

Palliative Care Clinical Studies Collaborative (PaCCSC) is a national multicentre research network to support clinical studies in palliative care.

Primary Care Collaborative Cancer Clinical Trials Group (PC4) develops and conducts cancer research in primary care.

Psycho-oncology Cooperative Research Group (PoCoG) aims to develop capacity and collaboration to conduct large-scale, multi-centre psycho-oncology and supportive care research.

Trans-Tasman Radiation Oncology Group (TROG) is a cooperative multidisciplinary organisation dedicated to the control of cancer through quality multicentre research into radiotherapy.